Shock, Cardiac Arrest, and Resuscitation
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The required knowledge regarding basic life support (BLS), advanced cardiovascular life support (ACLS), and postresuscitative care in the United States and Europe was updated by the American Heart Association (AHA) and European Resuscitation Council (ERC), respectively, in 2015 [1–3]. These new updates have guided the global treatment strategies of critical and emergency care [1–3]. However, in spite of these new guidelines, some studies have reported that the survival rates and neurological outcomes of patients experiencing out-of-hospital cardiac arrest (OHCA) were still not obviously improved in recent years [4–6]. Resuscitating a patient with OHCA is still a challenge for primary physicians; therefore, better treatment strategies are necessary. Novel categories that focus on postresuscitative care, resuscitation, or shock management are still of interest to scientific researchers. To improve patient outcomes, current guidelines, and knowledge can be clinically applied or even challenged. In this special issue, we would like to provide an opportunity to widely introduce related works discussing shock, cardiac arrest, and resuscitation.

First, topics related to cardiopulmonary resuscitation (CPR) training and quality control were described in detail. S. R. Gauna et al. introduced and discussed a system that provided accurate feedback on the chest compression depth and rate on soft surfaces. Their solution compensated for mattress displacement and avoided overestimation of the compression depth. In addition, C. Ahn et al. evaluated smartphone applications for CPR training in South Korea. Their study suggested that smartphone-based CPR training apps should include accurate CPR information and be easy to use for any layperson who could be a potential rescuer in real-world incidents. J. H. Lee et al. discussed the effect of the duration of BLS training on the students’ subsequent cardiopulmonary and automated external defibrillator skills. They concluded that the retention of high-quality CPR skills required longer and more hands-on training, particularly with automated external defibrillators (AEDs). S. Calicchia et al. reported a training experience on a BLSD (Basic Life Support and Defibrillation) module designed for a group of pupils in an Italian primary school. They found that life-saving maneuvers can be effectively taught to primary school students. M. Sadrawi et al. focused on analyzing the quality of CPR using a filtered raw ECG signal. The results showed that patients younger than 60 years of age with a higher complexity of CPR-intrinsic mode functions and increased amplitude differences have a higher survival rate. W. W. D. Yong et al. also analyzed the quality of CPR training. In their study, the pedagogy recommendations for
trainers of dispatcher-assisted CPR programs were developed using the Delphi method. A. Khoury et al. evaluated the factors that might influence the performance of bag-valve-mask ventilation. Y.-J. Syue et al. considered the prognosis of patients who experienced in-hospital cardiac arrests of cardiac and noncardiac origin during night shifts. They found that in-hospital cardiac arrests (IHCA) that occur at night correspond to an increased mortality, which was more apparent for IHCA of cardiac origin than for those of noncardiac origin.

Second, this issue includes an animal model of ventricular fibrillation induced cardiac arrest reported by G. K. Venkata et al. Their study concluded that postarrest myocardial dysfunction resulted in segmental wall motion defects primarily in the left anterior descending coronary artery region. Furthermore, there were no perfusion defects in the involved segments. In addition, there are two articles discussing cardiovascular disease and biomarkers for predicting sepsis. C.-M. Lin et al. found that a “resistance index” from a carotid ultrasound could detect flow changes before and after the stenting procedure, thus having a great capacity to replace the role of the computed tomography perfusion exam. M.-Y. Huang et al. noted that dynamic changes in the procalcitonin and procalcitonin clearance could serve as a predictor of survival in critically ill patients with severe sepsis. Finally, in this special issue, we have an excellent review article focused on hypotensive resuscitation among trauma patients. The authors (M. M. C. et al.) mentioned that lowering target blood pressures in trauma patients might be more beneficial than highly aggressive fluid resuscitation in prehospital and hospital settings. However, this new concept still requires more trials or evidence to clarify this result. Finally, this special issue highlights several articles that report improvements in CPR training, quality control, resuscitation strategies, and sepsis prediction. We believe that readers could obtain useful information from this issue.

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References
A Feasibility Study for Measuring Accurate Chest Compression Depth and Rate on Soft Surfaces Using Two Accelerometers and Spectral Analysis

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Background. Cardiopulmonary resuscitation (CPR) feedback devices are being increasingly used. However, current accelerometer-based devices overestimate chest displacement when CPR is performed on soft surfaces, which may lead to insufficient compression depth. Aim. To assess the performance of a new algorithm for measuring compression depth and rate based on two accelerometers in a simulated resuscitation scenario. Materials and Methods. Compressions were provided to a manikin on two mattresses, foam and sprung, with and without a backboard. One accelerometer was placed on the chest and the second at the manikin’s back. Chest displacement and mattress displacement were calculated from the spectral analysis of the corresponding acceleration every 2 seconds and subtracted to compute the actual sternal-spinal displacement. Compression rate was obtained from the chest acceleration. Results. Median unsigned error in depth was 2.1 mm (4.4%). Error was 2.4 mm in the foam and 1.7 mm in the sprung mattress ($p < 0.001$). Error was 3.1/2.0 mm and 1.8/1.6 mm with/without backboard for foam and sprung, respectively ($p < 0.001$). Median error in rate was 0.9 cpm (1.0%), with no significant differences between test conditions. Conclusion. The system provided accurate feedback on chest compression depth and rate on soft surfaces. Our solution compensated mattress displacement, avoiding overestimation of compression depth when CPR is performed on soft surfaces.

1. Introduction

Quality of cardiopulmonary resuscitation (CPR) is key to increase survival from cardiac arrest. Providing chest compressions with adequate rate and depth is difficult even for well-trained rescuers [1]. When cardiac arrest occurs in hospital, the patient is usually lying on a bed. Mattresses tend to deform and move downwards during CPR, thus reducing the efficiency of chest compressions [2]. The work required to perform chest compressions increases in proportion with the distance traveled by the rescuer’s hands, so the compression of the mattress increases workload and consequently also rescuer fatigue [3].

Resuscitation guidelines recommend providing CPR on firm surfaces when possible [4, 5]. Transferring the patient to the floor would ensure a firm surface, but it cannot always be done safely and promptly. Another alternative would be the use of backboards, which can be placed beneath the patient during CPR to increase the area over which the compression force is spread and reduce the amount of mattress compression. However, it is not clear whether the use of backboards alone improves compression depth [6–9].

The deformation of the mattress during CPR is variable, dependent on factors such as target depth, patient weight, type of mattress, and the use of a backboard [3]. This makes it difficult for rescuers to assess whether they are providing
chest compressions with an adequate depth. The use of monitoring and feedback devices during CPR can help rescuers to improve quality of chest compressions [10, 11]. However, devices that do not take into account the underlying mattress will overestimate compression depth [12]. Single accelerometer-based devices measure chest displacement. When chest compressions are provided on a mattress, they sense the sum of the chest compression (sternal-spinal displacement) plus the mattress deflection [12, 13]. Assuming that chest displacement corresponds to chest compression depth, these devices will incorrectly coach the rescuers, potentially causing too shallow chest compression. So far, accelerometer-based CPR feedback devices cannot perform accurately on soft surfaces.

In this study, we present a solution to provide feedback on compression depth and rate when compressions are delivered on soft surfaces. The system used two accelerometers: one was placed on the chest of the patient to measure chest displacement (sternal-spinal displacement plus mattress deflection) while the other was placed at the back of the patient to measure mattress deflection. To estimate compression depth and rate from acceleration, we applied an algorithm based on the spectral analysis of consecutive 2-second segments of the involved acceleration signals [14]. The system was evaluated in a simulated resuscitation scenario with different surfaces. CPR providers, and CPR conditions.

2. Materials and Methods

2.1. Study Design. The aim of the study was to quantify the error in the estimation of chest compression depth and rate during CPR performed on soft surfaces. For this assessment, we collected recordings using a sensorized manikin to provide the gold standard. Our secondary results were comparisons of the measured error as a function of several influencing factors: type of mattress, backboard use, and compression rates. To study the influence of the mattress, we used two models with different compositions, foam and sprung. We also wanted to study the influence of providing compressions with slower (80 cpm), recommended (100 cpm), and faster (120 cpm) rates, as this influences depth.

We designed our study as a randomized crossover study. Before starting the data collection, each participant practiced continuous chest compressions with the manikin placed on the mattress and their hands on the chest accelerometer. Then, we randomly grouped participants in couples and each couple performed 12 experiments: with each mattress with and without the backboard and for the three different compression rates. Each experiment consisted of 3-minute sessions with a first minute of continuous chest compressions, followed by a rescuer change, and a 2-minute series of 30 compression instances with 5-second pauses in between. Compressions were provided with the mattress placed on the floor and with rescuers kneeling beside the manikin. Target depth was always 50–60 mm and compression rate was guided using a metronome. The order of the experiments was randomized for each couple. Between consecutive experiments, rescuers had a 10-minute break. The ethical committee for research involving human subjects of the University of the Basque Country (CEISH UPV/EHU BOPV 32, 17-2-2014) approved the experimental protocol (M10-2015-208-RUIZ-OJEDA).

We calculated the sample size taking into account the standard deviation per record of the method reported in a previous study [15] and fixing a 95% confidence level and a margin of error lower than 3%. This yielded a sample size of 3 records (couples) per testing condition, but we fixed it to four for safety. The eight participants were selected randomly from a main group recruited for different ongoing studies on measuring CPR quality with accelerometers. They had no previous experience in CPR training. All of them attended a 2-hour CPR basics course including a period of training with the manikin placed on the floor. They were trained for a compression depth of 50–60 mm and a compression rate of 100 cpm (metronome guided). All of them signed the informed consent for the different experiments proposed, including this study on soft surfaces. The written informed consent was the only inclusion criterion.

2.2. Equipment and Data Collection. We used a CPR manikin torso (Resusci Anne CPR, Laerdal Medical AS, Stavanger, Norway) and placed a resistive sensor (SPI-4, Celeste Transducer Products Inc., Chatsworth, CA, USA) inside its chest to measure the reference chest displacement signal. We placed distributed weight plates inside the manikin increasing its weight up to 20 kg to provide a more realistic simulation of a human torso. For CPR experiments, we used two types of mattresses: foam (800 × 2000 × 90 mm, Pardo, Zaragoza, Spain) and sprung (900 × 1800 × 100 mm, Pardo, Zaragoza, Spain). Some experiments were conducted with a backboard (CPR Board, Ferno, Wilmington, OH, USA) placed between the mattress and the manikin (Figure 2).

We used two triaxial accelerometers (ADXL330, Analog Devices, Norwood, MA, USA) each one encased in a metal box. One accelerometer was placed on the center of the manikin’s chest and the other one beneath its back (Figure 1). During the experiments, we recorded the chest displacement and the two acceleration signals using an acquisition card (NI USB-6211, National Instruments, Austin, TX, USA) connected to a laptop computer, with a sampling rate of 250 Hz and 16-bit resolution.

For this study, we collected a database consisting of forty-eight 3-minute episodes, twelve per couple according to the protocol described in Section 2.1.

2.3. Spectral Method for Feedback on Rate and Depth. To estimate the chest and back displacement from the corresponding recorded acceleration values, we applied an algorithm based on the spectral analysis of the acceleration during chest compressions [14]. We designed this algorithm as an alternative to the classical approach of discrete double integration to calculate displacement from acceleration, which presents several drawbacks already discussed in the literature [15, 16]. The algorithm is based on the quasi-periodicity of acceleration during short intervals of chest compressions. Thus, both the acceleration and the displacement can be represented by the first N harmonics of their Fourier series.
Figure 1: Experimental setup (I). The Resusci Anne manikin fitted with a resistive sensor (shown in the bottom circle). The two triaxial accelerometers encased in a metallic box: one is on the chest (shown in the top circle) and the other is on the floor. The acquisition card and the laptop computer are on the left.

Figure 2: Experimental setup (II). The manikin was loaded with weights (see right side of the figure) and placed on a mattress, with or without a backboard beneath its back (represented by a dark gray rectangle). One triaxial accelerometer was placed on the chest of the manikin and the other beneath its back.

decomposition. With this mathematical model, the algorithm provides the mean compression depth and rate achieved by the rescuer every 2 seconds.

Figure 3 shows an example of the method. For each interval, we applied the spectral method to the chest acceleration to compute chest displacement, \( d_{\text{chest}} \), and to the back acceleration to obtain mattress displacement, \( d_{\text{mat}} \). Then, the actual chest compression depth (sternal-spinal displacement) was calculated as the difference between both values: \( d_{\text{cc}} = d_{\text{chest}} - d_{\text{mat}} \). Chest compression rate \( r_{\text{cc}} \) corresponded to the fundamental frequency of the chest acceleration.

2.4. Data Analysis and Performance Evaluation. Episodes were divided into 2-second consecutive nonoverlapped analysis intervals. The spectral method was applied to every interval to compute one value of depth and rate per interval. These values were compared to the ones obtained after processing the reference compression depth signal (\( d_{\text{ref}} \) and \( r_{\text{ref}} \), resp.). We defined error1acc as the difference between \( d_{\text{chest}} \) and \( d_{\text{ref}} \), that is, the error resulting from using a single chest accelerometer to estimate compression depth. Similarly, we defined error2acc as the difference between \( d_{\text{cc}} \) and \( d_{\text{ref}} \), that is, the error resulting from using two accelerometers to estimate compression depth.

The distributions of the chest and mattress displacement and of the errors in the measurements with one and two accelerometers did not follow a normal distribution according to the Lilliefors test for normality. Values are described by the median and interquartile range (IQR). Wilcoxon rank sum test was used for comparison between two groups, and Kruskal-Wallis test was used for multigroup comparisons. Bonferroni correction was applied to account for multiple comparisons.

3. Results

Baseline characteristics of the eight participants selected for the study were women 62% and mean (SD) age 22.5 (1.4) years. Table 1 shows the median (IQR) computed chest and mattress displacement, the reference chest compression depth, and the unsigned error using one or two accelerometers for the different mattress/backboard combinations. Mattress compression was significantly higher for the sprung surface \( (p < 0.001) \), and it significantly reduced with the backboard for both surfaces: from 10.4 mm (9.5, 11.4) to 7.0 mm (6.4, 7.4) with \( p < 0.001 \) and from 37.2 mm (35.0, 40.0) to 24.0 mm (21.6, 27.9) with \( p = 0.002 \), for foam and sprung mattress, respectively. Global median mattress compression was 17 mm (8, 32).

When only the chest acceleration was used, the global median of the error in the estimation of compression depth (error1acc) was 18.1 mm (7.2, 32.8), which corresponded to a percent error of 41.1% (15.3, 72.9). With two accelerometers, the error decreased to 2.1 mm (0.9, 3.6), which corresponded to a percent error of 4.4% (2.0, 7.5). For the different surfaces, median error1acc was 7.2 mm (4.4, 9.9) in the foam and 32.8 mm (25.2, 37.9) in the sprung mattress \( (p < 0.001) \). Median error2acc decreased to 2.4 mm (1.2, 3.9) in the foam and to 1.7 mm (0.8, 3.2) in the sprung mattress \( (p < 0.001) \). The use of a backboard significantly affected the results for both surfaces, \( p < 0.001 \) (see Table 1), but compression rate did not have any significant influence. Figure 4 shows the distribution of error2acc, as a function of the different mattress/backboard combinations. Results are provided separately for every target rate and globally.
Figure 3: Example of the computation of chest compression depth and rate. The spectral analysis of the chest and back acceleration every 2 seconds allows computing chest displacement and mattress displacement. Subtraction of both values gives the actual chest compression depth, $d_{cc} = 50$ mm. Estimated average rate $r_{cc}$ was 99.4 cpm.

Table 1: Computed chest and mattress displacement ($d_{chest}$ and $d_{mat}$), reference chest compression depth ($d_{ref}$), and unsigned error in the estimation of the spinal-sternal displacement with one accelerometer (error1acc) and two accelerometers (error2acc), for different mattress/backboard combinations.

<table>
<thead>
<tr>
<th>Mattress Parameter (mm)</th>
<th>$d_{chest}$</th>
<th>$d_{mat}$</th>
<th>$d_{ref}$</th>
<th>error1acc</th>
<th>error2acc</th>
</tr>
</thead>
<tbody>
<tr>
<td>Foam</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Backboard</td>
<td>55.6 (51.7, 58.8)</td>
<td>7.0 (6.4, 7.4)</td>
<td>48.5 (45.4, 51.6)</td>
<td>4.5 (2.8, 6.8)</td>
<td>3.1 (1.5, 4.5)</td>
</tr>
<tr>
<td>No backboard</td>
<td>56.6 (52.1, 60.2)</td>
<td>10.4 (9.5, 11.4)</td>
<td>46.0 (42.0, 48.9)</td>
<td>9.1 (7.4, 11.2)</td>
<td>2.0 (0.9, 3.1)</td>
</tr>
<tr>
<td>Sprung</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Backboard</td>
<td>69.9 (62.3, 79.6)</td>
<td>24.0 (21.6, 279)</td>
<td>45.8 (40.5, 51.8)</td>
<td>25.2 (22.4, 29.0)</td>
<td>1.9 (0.9, 3.3)</td>
</tr>
<tr>
<td>No backboard</td>
<td>83.4 (78.4, 89.1)</td>
<td>37.2 (35.0, 40.0)</td>
<td>46.0 (42.6, 49.7)</td>
<td>37.7 (34.9, 41.4)</td>
<td>1.6 (0.6, 3.1)</td>
</tr>
<tr>
<td>Global</td>
<td>61.9 (55.5, 78.7)</td>
<td>17.0 (8.0, 32.5)</td>
<td>46.7 (42.7, 50.4)</td>
<td>18.1 (7.2, 32.8)</td>
<td>2.1 (0.9, 3.6)</td>
</tr>
</tbody>
</table>

Global error in rate estimation was 0.9 cpm (0.4, 1.6), which corresponded to a percent error of 1.0% (0.4, 1.7). No statistically significant differences were found for the different test conditions. Figure 5 shows the global distribution of the error in rate. In the modified Bland-Altman plot, dashed lines represent the median of the error (0.0 cpm) and the 95 percent limits of agreement (−3.3, 3.4 cpm).

4. Discussion

In this study, we proposed a technical solution to provide accurate feedback on chest compression depth and rate when CPR is provided on soft surfaces. The system uses two accelerometers, one placed on the chest and the other beneath the back of the patient. Our algorithm accurately estimated compression depth and rate by spectral analysis of chest and back acceleration proving that CPR feedback on soft surfaces could be feasible.

Global median error of the method with two accelerometers was 2.1 mm (4.4%) in depth and 0.9 cpm (1%) in rate estimation. This performance is comparable to the one reported by the same method when CPR was provided on the floor, with errors below 2 mm and 1.5 cpm [14]. Accurate estimation of compression rate was expected, as it was directly computed as the fundamental frequency of the chest acceleration. In contrast, depth estimation is usually very challenging in this scenario. The accuracy of our method in the different test conditions, however, proved its stability (median error below 3.2 in all cases).

Our results confirmed the compression depth overestimation of single-accelerometer-based CPR devices when used on soft surfaces. Global median chest displacement, that is, estimated compression depth with a single accelerometer, was 62 mm, whereas the actual compression depth was 47 mm (Table 1). This led to an unacceptable median error of 41%. Other studies reached similar results: Beesems and Koster evaluated the performance of a commercial accelerometer-based CPR device [17], reporting a measured depth of 54 mm (foam) and 56 mm (air mattress), compared to the manikin’s reference of 42 mm and 35 mm, respectively.

Using one accelerometer, results were different depending on the type of mattress. Delivering compressions with the manikin on the sprung mattress was much more difficult than on the foam one. The sprung mattress presented less stiffness, and consequently mattress compression was much higher than with the foam one. In addition, participants had difficulties generating the required downward chest displacement (perpendicular to the chest) with the sprung mattress.
Acceleration was observed in the $x$-axis and $y$-axis of the chest sensor not contributing to the vertical movement. This could explain the very high overestimation of chest compression depth with a single accelerometer (median error $1\text{acc}$ 32.8 mm), even with the backboard. With two accelerometers, however, mattress displacement was very accurately compensated in both surfaces. Error ($\text{error2acc}$) decreased drastically to 2.4 mm in the foam and 1.7 mm in the sprung. Mattress sinking and lateral movements were very well compensated between the two sensors and thus accuracy increased.

Aase and Myklebust suggested in 2002 [16] the use of two accelerometers to estimate chest compression depth in moving environments. One accelerometer measured chest acceleration and the other one floor acceleration. In that study, both recorded acceleration values were subtracted before applying the algorithm for computing chest compression depth. Oh et al. [18] applied integration and detrending to chest and back acceleration for computing chest and mattress displacement waveforms, respectively. In both approaches, the difficulty lies in that when two oscillating signals (acceleration or displacement) are added or subtracted, an error in the synchronization of the signals would introduce a phase error and could significantly modify the waveform of the resulting signal. Small asynchrony between both signals would result in unacceptable errors in the estimation of compression depth. For tight synchronization, these approaches
would require a wired connection between the two accelerometers which could complicate the practical implementation.

In contrast, our algorithm processes independently consecutive intervals of each acceleration. Chest and mattress displacement values are separately computed and then subtracted every 2 seconds. This approach is simpler and eliminates the need for fine synchronization between the two sensors. Even if the analysis time intervals were not perfectly aligned, the error in the subtraction of both computed distances would be small. This could allow wireless communication between both accelerometers.

This study presented some limitations. First, we used a single resuscitation manikin. Even though we increased its weight to provide a more realistic simulation of a human torso, manikin differs in stiffness from a human chest, and there are also wide variations in the morphology of human chest. However, our simulated experimental setup provided a framework to test the method’s accuracy in a wide range of test conditions. Second, the accuracy of the method could vary if CPR were provided by experts, especially if they are familiarized with in-hospital compressions. A well consolidated CPR technique with a more stable acceleration pattern could increase the algorithm’s accuracy. The clinical applicability of our proposal would therefore require prospective validation studies with CPR experts, more surfaces, and different patients.

5. Conclusion

The system described in this study provided accurate feedback on chest compression depth and rate during CPR administered on two types of mattresses, foam and sprung, using two accelerometers and spectral analysis of the acceleration. Error in the estimation of compression depth was significantly reduced with respect to that reported with a single accelerometer. Our solution compensated mattress displacement, avoiding overestimation of compression depth when CPR is performed on soft surfaces. Quality of chest compressions in these scenarios could therefore be enhanced to adhere to resuscitation guidelines recommendation.

Competing Interests

The authors declare that there are no competing interests regarding the publication of this paper.

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References


Research Article

Teaching Life-Saving Manoeuvres in Primary School

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Introduction. In the event of sudden cardiac arrest (SCA) early intervention provided by a layperson can be life-saving. Teaching first aid in primary school may increase the lifelong ability and motivation of young people to take action in an emergency.

Objective. The aim of this article is to report a training experience on BLSD (Basic Life Support and Defibrillation) designed for a group of pupils in an Italian primary school, with assessment of its effectiveness at a distance.

Methods. The assessment was carried out using a multiple choice questionnaire on a sample of 130 pupils aged 11-12, 62 trained in BLSD and 68 as a control group. The trained group also performed an emergency simulation to assess their learning of practical skills.

Results. Using the t test, significant differences emerged in the questionnaire scores between the case-control group. The results of the skill test were positive, even for the most difficult manoeuvres such as opening airways, assessing breathing, or using an AED (Automated External Defibrillator).

Conclusion. Although there are still some open questions regarding the ability to retain these skills in the medium/long term, the study shows that life-saving manoeuvres can be effectively taught to primary school pupils.

1. Introduction

In the event of sudden cardiac arrest (SCA) early intervention (within 3–5 minutes) with CPR (Cardiopulmonary Resuscitation) and defibrillation increases survival rates [1–3]. That is why it is important for all citizens to be able to recognise a cardiac emergency and administer first aid while the advanced life support arrives. Many studies have shown that what actually prevents the ordinary citizen from intervening in the event of an emergency is the fear of doing something wrong, whereas bystanders who are trained in manoeuvres are more likely to take action [4].

The question that arises then is how to spread knowledge of these manoeuvres to a large proportion of the population, in a percentage that would increase the rate of intervention. According to a study provided by the Red Cross on First Aid in Europe, the countries with a higher percentage of citizens that are able to respond to an emergency (Norway, Germany, Austria, and Iceland) have laws that make first aid training compulsory either at school, in the workplace, or when applying for a driving license [5, 6]. That is why, in many countries where teaching is not yet compulsory, the scientific community and resuscitation and rescue associations are working to raise awareness within institutions of the importance of including teaching First Aid manoeuvres in school curricula [7, 8]. In Italy only recently the teaching of first aid at school has been planned [9]. Sensitivity to these issues has grown in recent years, driven by a series of legislative initiatives that have focused attention on the use of AED (Automated External Defibrillator), especially in high-traffic public environments, such as schools, or where there is high risk, and by several projects conducted by associations and individual educational institutes.

When it comes to training very young individuals the greatest doubt is about their ability to learn how to provide assistance like an adult, especially when thinking in terms of the cost/benefit ratio. Providing data on the effectiveness of training, including the purposes of adapting educational programmes for a younger audience, proves to be an essential step in facilitating and guiding educational institutions and the relevant ministries in introducing specific training programmes. The aim of this work is to report a training
2. Materials and Methods

2.1. Training. The experience was conducted by instructors from the IRC training network (Italian Resuscitation Council) for the Community and was included in the PAD (Public Access to Defibrillation) project, called “The heart of Monte Porzio” and run by the Municipality of Monte Porzio Catone (Rome), to underline the concept of the community taking responsibility in the event of sudden cardiac death and to communicate an idea of a “community of hearts,” both in a practical and a symbolic way. In just a few months 14 AEDs have been distributed across the local area and more than 100 people have received training, including members of the Police and Civil Protection, teachers and school staff, coaches, and ordinary citizens. Two AEDs have been deployed within the school, one for each location.

The challenge was to structure a successful educational path, usually structured for an adult target, which was adequate to not only transfer practical skills, but also to involve young people on a motivational level. Fifth grade junior school and third grade middle school pupils, for a total of 141 children from 9 to 12 years old, were chosen as the primary target for training. The course was designed with preference to an active learning method, based on simulations and exercises in groups [10]. With the aim of raising awareness within the children's living environment, to emphasise the importance and the social aspect of knowing what to do in case of emergency, teachers and parents were also involved in the process.

The activities, carried out over a period of 3 months and described below, have been defined on the three areas of expertise (knowledge, know-how, and know how to be) and the respective learning objectives [11] (Table I).

### Table I: Areas of expertise and learning objectives.

<table>
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<tr>
<th>Areas of expertise</th>
<th>Learning objectives</th>
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| Knowledge          | Theoretical knowledge regarding the following:  
                     (i) Cardiovascular system, respiratory system, and nervous system  
                     (ii) Cardiac arrest: causes and therapy  
                     (iii) Importance of activating the chain of survival |
| Know-how           | Practical skills regarding the correct sequence of action:  
                     (i) Assessment of environmental safety  
                     (ii) Assessment of consciousness  
                     (iii) Alerting emergency number  
                     (iv) Assessment of breathing  
                     (v) Cardiac massage (only for third year middle school students)  
                     (vi) Use of AED |
| Know how to be     | Skills related to the proper way to deal with an emergency without being panic-stricken:  
                     (i) Raising awareness of the importance of acting quickly in an emergency and activating PAD projects |

experience on BLSD (Basic Life Support and Defibrillation) with assessment of the effectiveness at a distance, carried out at a primary school in the Province of Rome.

2.1.1. Preliminary Activities in the Classroom. Teachers were involved right from the planning stages, with a series of brainstorming meetings which allowed us to

(i) transfer and verify the feasibility of learning objectives,
(ii) raise awareness and inform teachers on the topic of first aid,
(iii) share teaching materials and worksheets, also used in a similar experience within the same training network [12],
(iv) plan an educational path integrated with the school curriculum.

During this phase, concepts regarding the cardiovascular apparatus, cardiac arrest, and emergency situations were transferred. Furthermore, a series of corresponding activities was organised to give wide range to the youngsters' creativity and to their community spirit:

(i) “Design a logo for the project: The Heart of Monte Porzio,” a contest that allowed primary school children to imagine the graphic line of the PAD project.
(ii) “You don't need to be a superhero to save a life,” a contest sponsored by the Ministry for Education whereby the third grade middle school pupils produced spot advertising and the fifth grade junior school children drew animated cartoons.
(iii) Creation of a teaching video on First Aid: with their cameras at the ready, the instructors played the role of directors and the children actors, to simulate an emergency scene.
2.1.2. **Workshops with BLSD Instructors.** The workshops were held by instructors who are qualified in compliance with ERC (European Resuscitation Council) 2010 Guidelines. A total of four meetings were held, each of which was about two hours:

(a) **First Workshop: What Do We Know?** The children's experiences of first aid were collected via a brainstorming session in the classroom as they began to think about case studies, discussing them in small groups with the support of facilitators and instructors. In this way it was possible to “fix some points” about the state of consciousness/unconsciousness, the call to the emergency number, and the emotional state of the moment.

(b) **Second Workshop: Now Let’s Learn What to Do.** After a brief theoretical introduction, practical training was carried out on a manikin, in small groups. The whole sequence, consisting in assessment of environmental safety, assessment of consciousness, alerting emergency number, assessment of breathing, chest compressions (without rescue breathings), and use of the AED, was taught only to third year middle school students. The main doubts concerned the transfer of skills to fifth grade junior school children in relation to chest compressions and the use of the AED. Since some studies report a reduced ability to exercise effective chest compressions and providing rescue breaths in this age group [13,14], we opted for teaching the use of the AED, but not chest compressions and ventilation.

(c) **Third Workshop: What Have We Learnt?** In collaboration with the municipal administration, the police, and local associations, a sort of public celebration was organised in the school gym, which included

(i) the awarding of the best logo which has also become the official logo of the PAD project,
(ii) the projection of the video on First Aid filmed in the school,
(iii) the delivery by the Mayor of “heart-saving citizen” certificates and t-shirts with the project logo.

In this way, the children were able to incorporate their experience into a social and civic dimension, strengthening the awareness of their own skills.

(d) **Fourth Workshop: Let's Tell Our Parents about Our Experience.** During the final meeting, aimed at raising awareness within the family environment and sharing the path with their parents, the pupils were given the floor to talk about their experience using materials they produced themselves: slides, videos, and so forth.

2.2. **Assessment.** A year later the effectiveness of the training experience was assessed using a multiple choice questionnaire on a sample of 62 pupils aged 11-12 (37 males, 25 females). Only the children from the fifth year juniors were assessed, due to the difficulty in tracing the third year middle school youngsters who had now moved on to upper schools. The questionnaire was subsequently administered to a control group of 68 pupils of the same age (37 males, 31 females), from a different school, who had never taken part in first aid courses. The questions investigated different aspects of knowledge and know-how and also considered willingness to personally take action in the event of an emergency. The case group was also given a skill test to assess the learning of practical skills and reaction times, expertise that is difficult to assess with a questionnaire.

3. **Results**

3.1. **Questionnaires.** Analysis was carried out using the SPSS® 21.0 software (IBM® Corporation, Armonk, NY, USA). For each correct answer a score of 1 was given, up to a total of 15 points. None of the children obtained a full score. The highest score was 13.5 (90% of the answers correct) obtained by 4 children belonging to the “case” group only. Using the t test, significant differences emerged in the scores obtained in the questionnaires between the case-control group (p < 0.005), whereas there were none between genders.

When looking more closely at some of the questions, where there was a greater difference in scores, it emerged that the children who received training showed greater ability in handling and dealing with an emergency situation, even after a year. Faced with concrete cases, for example, they are more likely to assess the environment, ensuring that they are safe from danger too. As far as calling the emergency number is concerned, this can be done by both samples; however, the case group is better prepared to provide information in the right way.

3.2. **Skill Test.** The skill tests were carried out by qualified instructors who had also taken note of the critical issues most frequently encountered during the execution of the manoeuvres. For each manoeuvre performed it was possible to assign three different colours: green, when it was done properly and without suggestion; yellow, in the case of minor errors or in the case of manoeuvres remembered after receiving advice; red, in the case of severely incorrect or forgotten manoeuvres. Figure 1 shows the percentage of manoeuvres correct, prompted, and incorrect.

As seen in other studies [15], the stress factor caused by the presence of the instructors should be taken into consideration, as well as the time elapsed since the course was held. Despite this, the overall results appear to be positive, even for the most difficult manoeuvres from a technical point of view, such as opening the airways and assessing breathing.

The evaluation of environmental safety, though in the questionnaires there was the main difference with the control group, is often overlooked, probably because the children felt they are in a safe environment (the school gym). Data confirm the critical issues noted by the instructors and concern, above all, hyperextension of the head and assessment of breathing, which are often only remembered when prompted by the instructor. Advanced life support providers are alerted spontaneously by most of the students (69.35%) with just a very small percentage needing advice (19.35%). Furthermore,
more than 60% of the children, when left to freely express the content of the call to the emergency number, remembered the key information to be provided (Figure 2).

As far as using the AED is concerned, no particular problems have been reported. The majority of students are able to position the electrode pads correctly, deliver the shock safely, and handle the situation (Figure 3).

4. Discussion

The study shows that life-saving manoeuvres can be effectively taught to primary school pupils. In addition, the use of the AED proved to be easy to learn, even by the smallest children, as they quickly and easily internalised what it was for, where and how to position the electrode pads, and, above all, the need to ensure safety.

In this regard, and in view of the limited data available in literature, there was some uncertainty within the group of instructors on whether to teach the use of this device, which is generally used by an adult audience. The results were surprisingly positive: thanks to the greater familiarity of youngsters with technology, the safe learning of the AED seemed to be “child’s play.”

Although there are still some open questions regarding the ability to retain these skills in the medium/long term, our study confirms other data reported in literature that there is no “ideal” age when First Aid training is more effective [13, 15, 16]. Indeed, researches on memorising psychomotor skills suggest that early training contributes to maintaining a high level of skills over time [17] and children who have received training are more ready to intervene in case of emergency than their peers [15]. Apart from practical skills, which require constant retraining to be maintained over time, BLSD courses can change the attitudes and behaviour of youngsters at a time of life when they easily absorb new information [18].

The conclusions of a study conducted in Norway observing the behaviour of trained children (4-5 years) confirm that beginning education to first aid at an early age leads to include it in the activities and in the habits of everyday life and contributes to keep empathy towards others active [16]. Another study, conducted in a school in Barcelona, concludes that school offers the best setting to study these manoeuvres and such training increases the self-esteem of children and it could potentially contribute to saving lives [19].

Involving students in programmes to teach life-saving manoeuvres can respond, even in the long term, to the need to increase the percentage of the population that is able to respond in case of emergency, as school offers privileged access to a large proportion of the community, including members of families [17]. The school setting, like other places for socialisation, such as the workplace, is able to provide to a wide range of potential rescuers and future adults the opportunity of learning and absorbing the concepts of First Aid over time, because it facilitates frequent retraining [20]. Even in the short term it is important that children at least know how to alert emergency system correctly, since many cardiac arrests occur at home, often in the presence of relatives and friends [18].

In Italy we are still a long way from including these skills in school curricula and even amongst teachers learning emergency manoeuvres is left to the will of the individual and the sensitivity of the local community. The involvement of
teachers could, however, be a key factor to spread the culture of emergency and to facilitate frequent retraining. In fact, many studies have shown that teachers, if properly trained, are perfectly able to teach their students the main manoeuvres [13]. In a study conducted in Ireland, for example, a model of “chain” teaching BLS was successfully tested where the teachers who trained the children were in turn trained by undergraduates in medicine [21, 22]. There is also a whole range of tools (such as self-training kits or animated videos) that can support teachers in their task [23].

5. Conclusions

In Italy, legislation on the use of AEDs and the widespread use of PAD projects, also in schools, are giving a great boost to the spread of the emergency culture. Our experience confirms that teaching kids is possible, effective, and fun. The critical issue is raising awareness and encouraging the participation of institutional partners (school administrators, teachers, local administrators, and parents) who show resistance and mistrust that are difficult to overcome. Including the teaching of key BLSDs manoeuvres in the school curriculum could respond to the aim of improving safety culture in school environments, raising awareness among adults and, at the same time, transferring this culture to younger generations, leading, in the long term, to structural change.

Competing Interests

The authors declare that there is no conflict of interests regarding the publication of this paper.

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References


Research Article

Ventricular Fibrillation-Induced Cardiac Arrest Results in Regional Cardiac Injury Preferentially in Left Anterior Descending Coronary Artery Territory in Piglet Model

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Objective. Decreased cardiac function after resuscitation from cardiac arrest (CA) results from global ischemia of the myocardium. In the evolution of postarrest myocardial dysfunction, preferential involvement of any coronary arterial territory is not known. We hypothesized that there is no preferential involvement of any coronary artery during electrical induced ventricular fibrillation (VF) in piglet model. Design. Prospective, randomized controlled study. Methods. 12 piglets were randomized to baseline and electrical induced VF. After 5 min, the animals were resuscitated according to AHA PALS guidelines. After return of spontaneous circulation (ROSC), animals were observed for an additional 4 hours prior to cardiac MRI. Data (mean ± SD) was analyzed using unpaired t-test; p value ≤ 0.05 was considered statistically significant. Results. Segmental wall motion (mm; baseline versus postarrest group) in segment 7 (left anterior descending (LAD)) was 4.68 ± 0.54 versus 3.31 ± 0.64, p = 0.0026. In segment 13, it was 3.82 ± 0.96 versus 2.58 ± 0.82, p = 0.02. In segment 14, it was 2.42 ± 0.44 versus 1.29 ± 0.99, p = 0.028. Conclusion. Postarrest myocardial dysfunction resulted in segmental wall motion defects in the LAD territory. There were no perfusion defects in the involved segments.

1. Introduction

The incidence of pediatric cardiac arrest in United States is about 16,000 cases per year [1]. Despite efforts to improve the quality of cardiopulmonary resuscitation (CPR), the establishment of AHA CPR guidelines, and recommendations from the International Liaison Committee on Resuscitation (ILCOR) regarding CPR and emergency cardiovascular care,
survival from in-hospital and out-of-hospital cardiac arrest in children remains poor.

In a prospective cohort study involving US and Canadian Resuscitation Outcomes Consortium (ROC) sites, the incidence of pediatric out-of-hospital cardiac arrest (OHCA) was 8.04 per 100,000 per person-years and survival to hospital discharge among this population was 6.4% [2]. In-hospital cardiac arrest has better survival chances because of shorter delay in initiating resuscitation. Of the 2 studies that looked at in-hospital cardiac arrest, one reported incidence of in-hospital cardiac arrests to be 5.5% in children admitted to Pediatric Intensive Care Units (PICUs), out of which 62.7% achieved return of spontaneous circulation (ROSC) and 19.5% survived to hospital discharge [4]. Another study reported 3% incidence in cardiac arrest in all children admitted to Children's Institute in Sao Paulo, Brazil, during one year of the study. 64% attained ROSC and about one-third survived to hospital discharge [4].

Cardiac dysfunction and hypoxic brain injury are responsible for a greater degree of morbidity and mortality in the postarrest recovery period [5–8].

Cardiac dysfunction after ROSC clinically manifests as decreased contractility and as a global decrease in wall motion. This state of heart failure has been referred to as “global stunning,” “postresuscitation syndrome,” and “postarrest myocardial dysfunction.” Postarrest myocardial dysfunction is reversible and its onset, severity, and duration are directly related to the duration of cardiac arrest [9, 10]. Postresuscitation syndrome is a significant contributor of early morbidity and mortality, worsening to cardiogenic shock and, consequently, multiorgan dysfunction syndrome (MODS). In an adult retrospective study looking into the causes of cardiogenic shock, out-of-hospital cardiac arrest was the etiology in 31 of 459 patients. Despite being of small number compared to other groups, they had the highest rate of ECMO support. In addition, this particular group suffered 54.8% 7-day mortality and 74.2% 30-day mortality, which are twice as high compared to other etiologies of cardiogenic shock [11]. With such small number of patients surviving after being resuscitated in both pediatric and adult population, research into understanding the pathogenesis of postarrest myocardial dysfunction, its management, and prediction of mortality assumes utmost importance.

Postarrest myocardial dysfunction is multifactorial and there is no clearly defined pathogenesis. Ischemia, reperfusion injury, inflammation, and related cytokines, catecholamines, microvascular injury, and defibrillation individually or in combination cause postresuscitation myocardial failure [12–14].

Postarrest myocardial dysfunction manifests as uniform decrease in wall motion [14]. This was demonstrated by contrast ventriculography and transthoracic echocardiography in swine model. In all the published studies on swine postarrest myocardial dysfunction, VF was left untreated for 10 min and 15 min [9], 12 min [14], and 7 min [10]. In an early study that looked into functional and metabolic derangements in the myocardium after 4 min of untreated VF, wall motion defects were not studied [15]. In a study that compared the durations of untreated VF (4 min, 7 min, and 10 min) on diastolic dysfunction, there was 100% survival in 4-minute group and progressive worsening of diastolic function from 7 min to 10 min [16].

There are no studies to show if lesser duration of untreated VF would result in segmental wall motion defect in contrast to global and more severe dysfunction with VF of longer duration. Further, there is no evidence on how wall motion defects initially manifest and how they progress as duration of VF progresses. Hence, we chose 5 min of fibrillation-induced cardiac arrest, to be in between the spectrum of 100% survival with minimal dysfunction and worse diastolic function with global wall motion defects. Moreover, all these studies used echocardiography which may not define a regional wall motion defect as good as MRI (Magnet Resonance Imaging) does, used in our current study.

Global decrease in wall motion associated with postarrest myocardial dysfunction has been attributed to transient compromise of coronary perfusion [14]. Since this entails measuring coronary blood flow during cardiac arrest and resuscitation and is not technologically feasible, researchers relied on indirect evidence trying to look for frank myocardial infarction. Myocardial ischemia leading to an infarction and consequently regional wall motion defects requires no further questioning [17]. In addition, wall motion defects were shown to have high correlation with the duration of ischemia. There is a gap between the amount and duration of restriction of myocardial blood flow during cardiac arrest and resuscitation, wall motion abnormalities, and perfusion defects.

Wall motion was studied using contrast ventriculography and transthoracic echocardiograms in previously published literature [9]. Cardiac MRI is the gold standard in structural, functional, and perfusion analysis in humans. Its use in animals has also been validated for cardiovascular studies [18].

The aim of the study was to demonstrate if uniform global wall motion abnormality would manifest after ROSC from 5 min of untreated VF and to detect perfusion defects in areas of myocardial wall motion defects.

2. Materials and Methods

The study was approved by University of Florida Health Science Center Institutional Animal Care and Use Committee (IACUC) and conducted in accordance with its guidelines. Animals were randomized to two groups. The first group underwent baseline cardiac magnetoresonance imaging (MRI) and the second group underwent electrical induced VF leading to cardiac arrest followed by cardiopulmonary resuscitation (CPR) according to American Heart Association (AHA) guidelines. After achieving ROSC, there was a 4-hour observation, after which the animals underwent cardiac MRI.

2.1. Animal Preparation. Six-week-old (weight 15 ± 1.99 kg) farm piglets (University of Florida Swine Unit) of either sex were used in the study. The animals were sedated with intramuscular (IM) injection of Ketamine (15 mg/kg/dose). The level of sedation was maintained with 5% isoflurane.
in 100% oxygen delivered via nose cone. An intravenous access was obtained in the ear lobe. Oral endotracheal intubation was performed and depth of anesthesia was maintained with isoflurane between 1.5% and 3%. Ventilation was provided with rate- and volume-regulated ventilator (Surgivet Vaporstic Anesthesia Machine, Smiths Medical, USA). Continuous end-tidal carbon dioxide (CO₂) was measured with inline end-tidal CO₂ monitor (Nellcor). Rate and tidal volumes were adjusted to maintain end-tidal CO₂ between 35 and 45 mmHg. Electrocardiographic (EKG) leads were placed and heart rate and rhythm were continuously monitored.

After getting vascular access and oral endotracheal intubation, the animals that were randomized to baseline cardiac MRI study underwent no further invasive monitoring. Only heart rate, oxygen saturations, respiratory rate, end-tidal CO₂, and noninvasive blood pressure (NIBP) measurements were recorded.

Cutdowns were performed in the second group using sterile surgical technique to expose left internal jugular (IJ) vein, and femoral artery was accessed for invasive BP monitoring. A vascular introducer sheath (5 F and 15 cm) was placed in the left IJ and advanced to the junction of superior vena cava (SVC) and right atrium (RA). An 8 F catheter was placed in either of the femoral arteries for invasive blood pressure (BP) monitoring (fluid filled catheter transducer). A noncoated guide wire was passed into right ventricle via the sheath in left internal jugular vein. Its location within the right ventricle was confirmed by fluoroscopy. Alternating current was delivered into right ventricle via this guide wire to induce VF. Heparin (50 units/kg/dose) was given as a single bolus dose.

CPR was initiated after 5 min of untreated VF (no chest compression and no ventilation); CPR was performed in strict accordance with AHA Pediatric Advanced Life Support (PALS) guidelines. The same PALS certified provider performed chest compressions in all the experiments with a rate of 100/minute and 30:2 compressions to ventilation ratio. Defibrillation was attempted initially with 70 J biphasic current with subsequent shocks being 150 J. During the CPR, an epinephrine bolus 0.01 mg/kg (1:10,000) was given when necessary according to AHA guidelines. ROSC was defined after sustained palpable pulse and aortic systolic blood pressure greater than 60 mmHg for at least 1 min. After having achieved ROSC, the animals remained intubated and mechanically ventilated. Anesthesia was continued and the animals were monitored in the operating room for an additional 4 hours. All animals had cardiogenic shock secondary to postarrest myocardial dysfunction. Circulation was supported using epinephrine infusion. Function and perfusion studies were performed using 3-Tesla strength MRI. After data acquisition, the animals were humanely euthanized using euthanasia solution (Beuthanasia®).

2.2. MRI Protocol. Cardiac MRI was performed with the 3-Tesla Philips scanner, Achieva Whole Body MRI System (Philips Medical Systems, Best, Netherlands). Cine images were obtained by using turbo field echo sequences. Matrix position was 150 × 192. Other parameters for cine data are as follows: slice thickness 8 mm, contiguous slices, flip angle 15°, TR 5.33, echo 3.21, and minimum of 12 phases for each cardiac cycle were performed. Field of view was 77% (dimensions being (1.21 × 150 = 181.5 mm), (1.21 × 192 = 232.32 mm), and (18 cm × 23 cm)) and the final resolution was 1.21 square mm.

Perfusion studies were done by steady state turbo field echo. Three slices were used one each at base, midwall, and apex. Matrix position was 61 × 104. Flip angle was 20°. Repetition time was 3.2 milliseconds and echo time was 1.6 milliseconds. Field of view was 1.25 × 61 = 76.25, 1.25 × 104 = 130, and 7.6 cm × 13 cm. Inversion time was 105 milliseconds.

2.3. Data Acquisition and Analysis. CAAS MRV (Magnetic Resonance Ventricular Analysis) research software (Pie Medical Imaging) was used to analyze the MRI data. Epicardium, endocardium, and papillary muscles were manually delineated. Heart segmentation was performed according to AHA guidelines [19]. 112 heart parameters were collected including 17-segment wall motion.

2.4. Statistical Analysis. Data are presented as mean ± SD (standard deviation) or absolute number and percentages. The data was analyzed using unpaired t-test. The p value of ≤0.05 was considered statistically significant in all tests. The analyses were performed using SPSS 13.0 software (SPSS, Chicago, IL). Interobserver variability was reduced by having 3 individuals, who are trained in CMR analysis, trace the myocardium during heart cycle, and analyze the data in a blinded fashion.

3. Results

3.1. Animal Characteristics. Twelve animals (6 per group) were randomized to baseline and cardiac arrest. Both groups did not have any statistical difference with respect to age (6 weeks), height, weight, and body surface area (BSA), as shown in Table 1. All animals survived to 4 hours after resuscitation and completion of MRI data acquisition.

3.2. Basic Hemodynamic Parameters. Heart rate (HR, beats/min) in the baseline group was 92.33 ± 8.52 compared to 118.33 ± 33.15 in the postarrest group (p = 0.03) (Table 2). This difference is attributed to epinephrine infusion that was administered at an average 0.12 mcg/kg/min to support the blood pressure in the cardiac arrest group secondary to

<table>
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<tr>
<th>Parameter</th>
<th>Baseline</th>
<th>Cardiac arrest</th>
<th>p value</th>
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<tr>
<td>n</td>
<td></td>
<td></td>
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<tr>
<td>Age, weeks</td>
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<tr>
<td>Weight, Kg</td>
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<tr>
<td>BSA, Kg/m²</td>
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<td>0.51 ± 0.01</td>
<td>0.14</td>
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</table>

BSA, body surface area.
cardiac shock. There was no difference in the rest of other hemodynamic data in the 2 groups. Ejection fraction (EF) in the baseline group was 46.43 ± 9.62 compared to 39.52 ± 13.51 in the postarrest group (p = 0.17). Stroke volume (SV, mL) in the baseline group was 18.34 ± 4.12 compared to 16.20 ± 5.16 in the postarrest group (p = 0.24). A similar trend was observed with respect to Stroke Volume Index (SVI); baseline 33.54 ± 6.64 compared to 31.35 ± 9.93 in the postarrest group (p = 0.11). Left Ventricular End Systolic Volume Index (LVESVI) in the baseline group was 39.48 ± 3.36 compared to 43.02 ± 11.12 in the postarrest group (p = 0.028).

3.3. Function Analysis. Segmental wall motion (mm) in segment 7 (midanterior, left anterior descending (LAD)) was 4.68 ± 0.54 in baseline group versus 3.31 ± 0.64 in postarrest group, p = 0.0026. In segment 13 (apical anterior, LAD), it was 3.82 ± 0.96 in baseline versus 2.58 ± 0.82 in postarrest, p = 0.02 (Table 3). In segment 14 (apical septal, LAD), it was 2.42 ± 0.44 in baseline versus 1.29 ± 0.99 in postarrest group, p = 0.028. The comparison of wall motion is shown in Figures 1(a) and 1(b). The first picture is a bull’s eye representation of segmental wall motion score, which is color-coded according to the legend on the side of the picture. The second picture is a representation of the same animal after resuscitation; note that wall motion scores are much lower than previous bull’s eye picture.

3.4. Perfusion Analysis. There was no difference in the perfusion parameters between baseline and postarrest myocardial dysfunction.

4. Discussion

Immediate mortality after resuscitation from cardiac arrest is primarily caused by myocardial dysfunction and hypoxic brain injury [8]. Postarrest myocardial dysfunction is manifested by decreased contractility and relaxation. On echocardiogram, it manifests as global wall motion defect [9]. There is an unexplored area between the extent and duration of myocardial blood flow restriction during cardiac arrest and resuscitation and the progression of wall motion abnormalities to a global dysfunction and finally cardiogenic shock.

Published studies involving swine on global decrease in wall motion reported resuscitation times after 7 min [10], 10 min, and 15 min of untreated cardiac arrest [9]. Animals with longer untreated cardiac arrest suffered from earlier manifestation of severe cardiogenic shock. In one study, hemodynamic parameters were studied after 4 min of untreated cardiac arrest, but wall motion was not studied [15]. Literature search revealed no studies on progression of wall motion defects from cardiac arrest through resuscitation and progression into postarrest phase. We are the first to report that, after 5 min of untreated cardiac arrest, segmental wall motion defects involved primarily the segments in left anterior descending (LAD) artery.

The animals that were studied in the cited references were of the age that ranged from 12 to 16 weeks [15]. In addition, the animals weighed 25 ± 2 Kg [14], 26 ± 1 Kg [9], 29 ± 1 Kg [20], 37 ± 2 Kg [21], 38 Kg to 45 Kg [16], and 40 ± 4 Kg [10]. We chose swine aged 6 weeks and weighed 15 Kg to replicate pediatric age group. Hence, we were unable to compare our hemodynamic data to previously published ones.

The coronary anatomy of swine is similar to that of humans with minor variations [22]. In majority of humans, right coronary artery is dominant [22]. Similar finding was reported in swine coronary artery distribution [22]. An important difference between the two coronary artery distributions is “Anterior Interventricular Vessel (AIV)” [22], which is LAD counterpart in swine, ends proximal to apex; in humans, it crosses the apex [22]. This is the reason for not observing wall motion defects in segment 17 (apex) in our swine model.

In all CPR experiments, chest compressions, defibrillation, and epinephrine are confounders to functional and perfusion data analysis.

Chest compressions have not been shown to cause localized wall motion abnormality. Although cardiac contusions were noted on necropsy in previously published studies, there
Figure 1: (a) Bull's eye representation of segmental wall motion score of baseline animal. (b) Bull's eye representation of segmental wall motion score of the same animal in Figure 1(a) but after resuscitation.

were no transmural contusions. All of the contusions were localized to anterior portion of right ventricle, which does not happen to be our area of interest [9].

Defibrillation has been shown to be equivocal in causing myocardial dysfunction after resuscitation from cardiac arrest. However, in a study where defibrillation dose as high as 303 ± 38 J was tested without inducing cardiac arrest, there was no myocardial dysfunction [9].

The effect of epinephrine on segmental wall dyskinesis has not been reported.

In this experiment, we have established that wall motion defects are not uniform when resuscitated after 5 min of untreated VF. The defects were primarily present in the left anterior descending coronary distribution. It is our speculation that left ventricle is exposed to higher afterload and energy requirements and may be more susceptible to ischemic injury. In addition, we could not demonstrate any perfusion defects in segments 7, 13, and 14. Transient compromise in blood flow not to an extent to cause frank ischemia may have caused myocardial dysfunction. Our perfusion findings are in congruence with previously published reports of absence of ischemia in tissue sections [9]. The mechanisms underlying this dysfunction have not been conclusively defined. This remains an area of opportunity for further research.

Our study has several limitations. A shortcoming of our study is 5 min of cardiac arrest. Cardiac arrest was 10 min in one study that demonstrated uniform global wall motion defect [9]. Coronary artery anatomy was not studied prior to starting the experiments. Epinephrine was used to support hemodynamics in the animals that were resuscitated. Epinephrine helped to maintain cardiac output in these animals while MRI was being obtained. There was no statistical difference in ejection fraction in both groups due to use of epinephrine in the group which underwent resuscitation. Epinephrine might also have altered the wall motion findings.

Our control group animals did not undergo CPR; an ideal control group would be to include animals that did not undergo cardiac arrest but received chest compressions and resuscitation. Since this experiment was terminal in nature, we could not establish the reversible nature of postarrest myocardial dysfunction.

5. Conclusion

Myocardial dysfunction following ventricular fibrillation-induced cardiac arrest results in nonuniform regional wall motion abnormalities especially in the left anterior descending artery territory. However, the abnormalities may not represent ischemia or infarction since perfusion studies did not reveal any defects.

Global ischemic insult resulted in segmental wall motion abnormality preferentially in left anterior descending artery territory. Higher heart rate and no significant difference in cardiac index were due to epinephrine infusion in cardiac arrest group.

Competing Interests

The authors declare that they have no competing interests.

Acknowledgments

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References


Research Article

The Prognosis of Cardiac Origin and Noncardiac Origin in-Hospital Cardiac Arrest Occurring during Night Shifts

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Background. The survival rates of in-hospital cardiac arrests (IHCA) are reportedly low at night, but the difference between the survival rates of cardiac origin and noncardiac origin IHCA occurring at night remains unclear.

Methods. Outcomes of IHCA during different shifts (night, day, and evening) were compared and stratified according to the etiology (cardiac and noncardiac origin).

Result. The rate of return of spontaneous circulation (ROSC) was 24.7% lower for cardiac origin IHCA and 19.4% lower for noncardiac origin IHCA in the night shift than in the other shifts. The survival rate was 8.4% lower for cardiac origin IHCA occurring during the night shift, but there was no difference for noncardiac origin IHCA. After adjusting the potential confounders, chances of ROSC (aOR: 0.3, CI: 0.15–0.63) and survival to discharge (aOR: 0.1; CI: 0.01–0.90) related to cardiac origin IHCA were lower during night shifts. Regarding noncardiac origin IHCA, chances of ROSC (aOR: 0.5, CI: 0.30–0.78) were lower in the night shift, but chances of survival to discharge (aOR: 1.3, CI: 0.43–3.69) were similar in these two groups.

Conclusion. IHCA occurring at night increases mortality, and this is more apparent for cardiac origin IHCA than for noncardiac origin IHCA.

1. Introduction

According to the Get with the Guidelines- (GWTG-) Resuscitation registry, the outcomes following in-hospital cardiac arrest (IHCA) have recently improved [1, 2]. This has been attributed to the improvement in the management of acute coronary syndrome (ACS), which also results in a decline in the numbers of IHCA of cardiac origin [1–4]. However, several studies show that the survival rates of IHCA remain low during nights [5–10]. The reason for poor prognosis of IHCA during the night shift might be multifactorial, potentially including healthcare staff and hospital staff as well as the differences in the etiologies of cardiac arrest. Matot et al. reported that unwitnessed cardiac arrest is more prevalent during a night shift. They reported that resuscitation during this shift may not be associated with poorer outcomes, independent of the witnessed status [5]. To our knowledge, studies on the association between the etiology of cardiac arrest in different shifts and patient prognosis are relatively scarce. In this study, to understand the distribution of the etiologies of IHCA in different shifts and their influence on clinical outcome, we compared the prognoses in different shifts by stratifying the etiologies of IHCA into cardiac origin and noncardiac origin. We aimed to determine whether the etiologies of IHCA influence the patient’s prognosis during a night shift.

2. Materials and Methods

2.1. Study Design. This retrospective study was approved by the Chang Gung Medical Foundation Institutional Review Board. Based on the understanding that all data in the patient and physician records used in the analyses have been anonymized and deidentified, the ethics committee approved the research protocol with a waiver of informed consent.

2.2. Study Setting. This study was conducted across the Kaohsiung Chang Gung Memorial Hospital, a tertiary teaching
hospital, with 2715 beds, including 1388 beds in the adult general ward and 203 beds in the adult intensive care unit (ICU). The resuscitation team in the study included the physicians and nurses on duty. An emergency response team at the institute provided round-the-clock aid for those in need. All members of the resuscitation team were certified in advanced cardiac life support (ACLS). The primary care nurse was responsible for recording all of the resuscitation efforts, procedures, and medications on a standardized resuscitation data form during the event.

2.3. Participants. Patients aged 18 years or older who experienced a cardiac arrest requiring cardiopulmonary resuscitation (CPR) or defibrillation in general wards were included in the analysis. Only index events were included. An index event is defined as the first arrest for patients having more than 1 arrest during the same hospitalization period. Exclusion criteria included (1) patients receiving only resuscitation drugs or positive pressure ventilation without chest compression or defibrillation, (2) patients receiving palliative treatment or signing “do not resuscitate (DNR)” order, and (3) patients experienced EP would be consulted, and a final decision was made after group discussion. The outcome is the return of spontaneous circulation (ROSC) for more than 20 minutes with no further need for chest compressions and survival to hospital discharge. Neurological outcome was determined using Cerebral Performance Category (CPC) score which allocates a score of 1 for good cerebral performance, 2 for moderate performance, 3 for poor performance, 4 for comatose or vegetative status, and 5 for brain death. In this study, patients with a score of 1 or 2 were defined as those with favorable neurological outcomes.

2.4. Study Protocol. Patient data were drawn from in-hospital cardiac arrest registry of the Kaohsiung Chang Gung Memorial Hospital from January 2008 to December 2011. Event details were recorded by the responding nurses and primary physician of the resuscitation team who had attended the event. The data contains variables derived from Utstein data reporting guidelines for in-hospital cardiac arrest [11–13]. The patient outcome after cardiac arrest occurring during the night shift (00:00–8:00) was compared with that during the day (8:00–16:00) or evening (16:00–24:00) shift.

2.5. Measures. Independent variables comprised time of event, basic patient characteristics, comorbidities of Charlson Comorbidity Index (CCI) [14], main morbidity on admission, admission department, interventions before IHCA, first documented cardiac rhythm, discovery status at the time of event, and possible cause of cardiac arrest. The discovery status at time of event was included if there was a deteriorating disease course, if events were witnessed, and if there was bystander CPR. A deteriorating disease course was defined as a respiratory rate of $\leq 5$ or $\geq 32$ breaths/min, a pulse rate of $\leq 40$ or $\geq 140$ beats/min, systolic blood pressure of $<90$ mmHg, and a sudden fall in the level of consciousness by 2 or more Glasgow Coma Scale (GCS) points within 8 hours before cardiac arrest [15]. The possible cause of cardiac arrest was categorized into cardiac origin and noncardiac origin. To determine the etiology of the cardiac arrest, 2 experienced EPs independently selected one of the following possible causes: cardiac, respiratory, cerebral, or metabolic causes, sepsis, exsanguination, hypothermia, drug overdose, or others [16]. Reviewers also consulted the initial treating physicians, if available, to clarify details and possible etiologies. If opinions were inconsistent, the 3rd experienced EP would be consulted, and a final decision was

2.6. Data Analysis. For continuous variables, the data were summarized as the mean and standard deviation (SD) and analyzed by Student’s t-test. The distributions of categorical variables were summarized as numbers and percentages, and Chi-square test was used to evaluate the associations between outcome groups. In the multivariate analyses, binary logistic regression models were applied to assess the effect of the night shift on documented patient outcomes to adjust for the potential confounding factors including patient’s age, sex, CCI, first documented cardiac rhythm, witnessed cardiac arrest, and bystander CPR. Effects were estimated in terms of adjusted odds ratios (aORs) and the corresponding 95% confidence intervals (CIs). Results were considered statistically significant for two-tailed $p < 0.05$. The statistical analysis was conducted using SPSS version 12.0 (SPSS, Chicago, IL) for Windows.

3. Result

3.1. Patient Demographics. During the study period, 544 adult patients with IHCA occurring in general wards were analyzed. A total of 331 (60.8%) patients developed cardiac arrest during the day or evening shift, and 213 (39.2%) patients developed cardiac arrest during the night shift. Table 1 reveals the patients’ age, sex, predisposing diseases, and primary cause of admission in the two study groups, which shows no significant difference between study groups.

3.2. Event Characteristics. Table 2 reveals the characteristics of cardiac arrest. There was no significant difference between the two study groups in the distribution of the wards in which the arrest occurred and interventions prior to cardiac arrest. The percentages of patients who developed cardiac arrest with the predictable deteriorated disease cause were similar in the two study groups. The distributions of cardiac origin and noncardiac origin of cardiac arrest were also similar in the two study groups. However, the first documented cardiac rhythm was different in the two study groups. Patients who developed cardiac arrest during the night shift were more likely to be found with asystole rhythm. In contrast, fewer patients were witnessed to have collapsed and received bystander CPR during the night shift.

After stratifying the causes of cardiac arrest, in cardiac origin IHCA, the incidence of witness arrest and bystander CPR in the night shift was less by 41.4% and 20.2%, respectively, than in morning and evening shifts combined (Figure 1(a)). In noncardiac origin IHCA, the chance was 23.7%
Table 1: Patient demographics.

<table>
<thead>
<tr>
<th></th>
<th>Day/evening (331)</th>
<th>Night (213)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Age</strong></td>
<td>67.1 ± 15.17</td>
<td>68.1 ± 14.84</td>
<td>0.428</td>
</tr>
<tr>
<td><strong>Male</strong></td>
<td>196 (59.2%)</td>
<td>124 (58.2%)</td>
<td>0.817</td>
</tr>
<tr>
<td><strong>Charlson Comorbidity Score</strong></td>
<td>4.5 ± 2.57</td>
<td>4.8 ± 2.53</td>
<td>0.201</td>
</tr>
<tr>
<td><strong>Predisposing disease</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Coronary artery disease</td>
<td>49 (14.8%)</td>
<td>30 (14.1%)</td>
<td>0.816</td>
</tr>
<tr>
<td>Congestive heart failure</td>
<td>53 (16.0%)</td>
<td>29 (13.6%)</td>
<td>0.446</td>
</tr>
<tr>
<td>Cerebral vascular disease</td>
<td>76 (23.0%)</td>
<td>52 (24.4%)</td>
<td>0.697</td>
</tr>
<tr>
<td>Chronic pulmonary disease</td>
<td>72 (21.8%)</td>
<td>48 (22.5%)</td>
<td>0.830</td>
</tr>
<tr>
<td>Chronic liver disease</td>
<td>72 (21.8%)</td>
<td>62 (29.1%)</td>
<td>0.052</td>
</tr>
<tr>
<td>Chronic kidney disease</td>
<td>127 (38.4%)</td>
<td>76 (35.7%)</td>
<td>0.527</td>
</tr>
<tr>
<td>DM</td>
<td>129 (39.0%)</td>
<td>79 (37.1%)</td>
<td>0.659</td>
</tr>
<tr>
<td>Malignancy</td>
<td>104 (31.4%)</td>
<td>67 (31.5%)</td>
<td>0.993</td>
</tr>
<tr>
<td>Hematologic disease</td>
<td>20 (6.0%)</td>
<td>12 (5.6%)</td>
<td>0.843</td>
</tr>
<tr>
<td>Psychiatric disorder</td>
<td>10 (3.0%)</td>
<td>3 (1.4%)</td>
<td>0.229</td>
</tr>
<tr>
<td><strong>Primary cause of admission</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cardiovascular disease</td>
<td>32 (9.7%)</td>
<td>14 (6.6%)</td>
<td>0.205</td>
</tr>
<tr>
<td>Cerebral vascular disease</td>
<td>13 (3.9%)</td>
<td>13 (6.1%)</td>
<td>0.246</td>
</tr>
<tr>
<td>Infection</td>
<td>106 (32.0%)</td>
<td>81 (38.0%)</td>
<td>0.150</td>
</tr>
<tr>
<td>Complication of liver cirrhosis</td>
<td>21 (6.3%)</td>
<td>23 (10.8%)</td>
<td>0.063</td>
</tr>
<tr>
<td>Complication of renal failure</td>
<td>22 (6.6%)</td>
<td>12 (5.6%)</td>
<td>0.634</td>
</tr>
<tr>
<td>Complication of DM</td>
<td>10 (3.0%)</td>
<td>2 (0.9%)</td>
<td>0.107</td>
</tr>
<tr>
<td>Malignancy</td>
<td>67 (20.2%)</td>
<td>36 (16.9%)</td>
<td>0.332</td>
</tr>
<tr>
<td>Hematologic disease</td>
<td>15 (4.5%)</td>
<td>4 (1.9%)</td>
<td>0.100</td>
</tr>
</tbody>
</table>

Table 2: Event characteristics.

<table>
<thead>
<tr>
<th></th>
<th>Day/evening (331)</th>
<th>Night (213)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Department of events</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Internal medicine</td>
<td>297 (89.7%)</td>
<td>193 (90.6%)</td>
<td>0.469</td>
</tr>
<tr>
<td>Surgical medicine</td>
<td>24 (7.3%)</td>
<td>17 (8.0%)</td>
<td></td>
</tr>
<tr>
<td>Other</td>
<td>10 (3.0%)</td>
<td>3 (1.4%)</td>
<td></td>
</tr>
<tr>
<td><strong>Intervention before events</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Oxygen therapy</td>
<td>163 (49.2%)</td>
<td>115 (54.0%)</td>
<td>0.280</td>
</tr>
<tr>
<td>Inhalation therapy</td>
<td>29 (8.8%)</td>
<td>28 (13.1%)</td>
<td>0.103</td>
</tr>
<tr>
<td>Vascular access</td>
<td>306 (92.4%)</td>
<td>201 (94.4%)</td>
<td>0.386</td>
</tr>
<tr>
<td>Antibiotics therapy</td>
<td>199 (60.1%)</td>
<td>128 (60.1%)</td>
<td>0.995</td>
</tr>
<tr>
<td>Inotropic agent</td>
<td>7 (2.1%)</td>
<td>2 (0.9%)</td>
<td>0.294</td>
</tr>
<tr>
<td><strong>First documented cardiac rhythm</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>VT or pulseless VT</td>
<td>19 (5.70%)</td>
<td>2 (0.90%)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>PEA</td>
<td>222 (67.10%)</td>
<td>114 (53.50%)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Asystole</td>
<td>90 (27.20%)</td>
<td>97 (45.50%)</td>
<td></td>
</tr>
<tr>
<td><strong>Discovery status at time of event</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Deteriorated disease course</td>
<td>189 (57.1%)</td>
<td>108 (50.7%)</td>
<td>0.144</td>
</tr>
<tr>
<td>Witnessed</td>
<td>256 (77.3%)</td>
<td>98 (46.0%)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Bystander CPR</td>
<td>135 (40.8%)</td>
<td>50 (23.5%)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td><strong>Possible cause of cardiac arrest</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cardiac origin</td>
<td>115 (34.7%)</td>
<td>85 (39.9%)</td>
<td>0.223</td>
</tr>
<tr>
<td>Noncardiac origin</td>
<td>216 (65.3%)</td>
<td>128 (60.1%)</td>
<td></td>
</tr>
</tbody>
</table>
and 14.0% less, respectively (Figure 1(b)). The cardiac origin IHCA during night shifts presented 26.1% more asystole rhythm and 12.4% less shockable rhythm (VF and pulseless VT) in the initially documented cardiac rhythm compared to those during morning and evening shifts combined (Figure 2(a)). For noncardiac origin IHCA, they were 12.8% more and 0.9% less, respectively (Figure 2(b)).

3.3. Outcome of Cardiac Arrest. The overall ROSC rate and survival to discharge rate for the whole study group were 40.1% and 5.1%. Figure 3 reveals the outcomes of cardiac arrest stratified by cause of cardiac arrest during each of the shifts. The ROSC rate of cardiac origin IHCA was 24.7% lower during the night shift than during the day or evening shift ($p < 0.001$), while it was 19.4% lower for noncardiac origin IHCA ($p < 0.001$). The survival rate of cardiac origin IHCA was 8.4% lower during the night shift than during the day or evening shift ($p = 0.014$); however, the survival rate of noncardiac origin IHCA showed no difference compared to that in the other shifts ($p = 0.579$).

Controlling for the potential confounders with multivariate logistic regression including patients’ age, sex, CCI, first documented cardiac rhythm, witnessed event, and bystander CPR, the adjusted odds ratio of ROSC and survival to discharge between the night shift and day or evening shift combined in cardiac origin IHCA and noncardiac origin IHCA are demonstrated in Table 3. The chance of ROSC (aOR: 0.3, CI: 0.15–0.63) and survival to discharge (aOR: 0.1, CI: 0.01–0.90) of cardiac origin IHCA was lower during the night shift than during the day or evening shift. For noncardiac origin IHCA, the chance of ROSC (aOR: 0.5, CI: 0.30–0.78) was lower during the night shift than during the

### Table 3: Cardiac arrest outcomes by day/evening versus night.

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Day or evening shift</th>
<th>Night shift</th>
<th>aOR</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Cardiac origin</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>ROSC</td>
<td>Reference [1]</td>
<td></td>
<td>0.3*</td>
<td>0.15–0.63</td>
</tr>
<tr>
<td>Survival to discharge</td>
<td>[1]</td>
<td></td>
<td>0.1*</td>
<td>0.01–0.90</td>
</tr>
<tr>
<td><strong>Noncardiac origin</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>ROSC</td>
<td>Reference [1]</td>
<td></td>
<td>0.5*</td>
<td>0.30–0.78</td>
</tr>
<tr>
<td>Survival to discharge</td>
<td>[1]</td>
<td></td>
<td>1.3</td>
<td>0.43–3.69</td>
</tr>
</tbody>
</table>

*Significant factor.

ROSC: return of spontaneous circulation. aOR: adjusted odds ratio, for patient’s age, sex, CCI, first documented cardiac rhythm, witnessed cardiac arrest, and bystander CPR.
day or evening shift, but the chances of survival to discharge (aOR: 1.3, CI: 0.43–3.69) were similar in the two study groups.

Figure 4 displays the distribution of patients’ survival to discharge in the Cerebral Performance Category score. Among patients with either cardiac or noncardiac origin IHCA, only 1 patient in each group had good cerebral performance during the day or evening shift and the others had poor performance, were comatose, or had vegetative status. Three patients during the day or evening shift and one patient during the night shift had moderate performance. The others had poor performance, were comatose, or had a vegetative status.

4. Discussion

Previous studies reported that survival rates from in-hospital cardiac arrest are lower during nights [5, 6]. In this study, we attempted to compare the prognoses of patients developing IHCA during night, morning, and evening shifts with cardiac origin cause and noncardiac origin cause. We found that, for cardiac origin IHCA, both ROSC and survival to discharge were significantly lower for patients who were resuscitated during the night shift when compared to morning and evening shifts combined. In noncardiac origin IHCA, ROSC was significantly lower for patients developing cardiac arrest in the night shift, but chances of survival to discharge were similar in the two study groups. The demographic characteristics, departments of events, interventions before events, and the distribution of cardiac origin and noncardiac origin IHCA of the study population undergoing resuscitation in the various shifts were similar. However, there were more unwitnessed arrests, higher incidence of asystole, and less shockable rhythm (VF and pulseless VT) during the night shifts. After adjusting these potential confounding factors with multivariate logistic regression, resuscitation during night shifts had lower chances to achieve ROSC in both cardiac origin IHCA and noncardiac origin IHCA, but night shifts had lower chances of survival to discharge in cardiac origin IHCA, which is not evident in noncardiac origin IHCA. It is believed that the most likely reason for the incidence of ROSC and survival to discharge being lower at night is the fact that more arrests were unwitnessed, and it could be proven by the fact that asystole was more frequent at night. However, after adjusting for the cardiac rhythm, the outcome of IHCA at night was still poorer. It might be explained by the delay of activation of resuscitation team and limitation of hospital facilitation such as percutaneous transluminal coronary angioplasty or extracorporeal membrane oxygenation.

According to previous studies, one of the predictors of good prognosis after IHCA is the event being witnessed [3, 4, 17–20]. In this study, the witnessed events were lower during night shifts than during morning and evening shifts combined by 31.3%. The lower rate was more obvious in cardiac origin IHCA (41.4%) than in noncardiac origin IHCA (23.7%). Bystander CPR rate was also lower in the night
shifts by 17.3%. Again, the lower rate was more remarkable in cardiac origin IHCA (20.2%) than in noncardiac origin IHCA (14.0%). These might explain why the lower rate of ROSC and survival to discharge were more marked in cardiac origin IHCA (24.7% and 8.4%, resp.) than in noncardiac origin IHCA (19.4% and no difference, resp.). The underlying cause for lower rate of witnessed events and bystander CPR for cardiac origin IHCA compared to noncardiac origin IHCA may be due to patients making less noise during cardiac origin IHCA as compared to those with noncardiac origin IHCA. Patients that develop noncardiac origin IHCA usually show signs of choking or major bleeding such as gastrointestinal bleeding or upper aerodigestive tract tumor bleeding, noises from which help alert the patient’s caregiver to identify the events. Another evidence for delayed discovery of cardiac origin IHCA was the initial documented cardiac rhythm. The increased rate of asystole rhythm for IHCA at night was higher for cardiac origin IHCA (26.1%) than for noncardiac origin IHCA (12.8%), which may contribute the poorer prognosis.

The overall rate of survival to discharge and favorable neurological outcome (with CPC score of 1 or 2) were conspicuously lower in this study than in others. According to the previous study, the survival to discharge rates increased from 13.7% in 2000 to 22.3% in 2009 and significant neurologic disability among survivors decreased from 32.9% to 28.1% in 2000 and 2009, respectively [1, 2]. One possible explanation was that the previous study included IHCA patients both in general wards and in ICUs. According to previous study, patients being monitored played an important role in good prognosis after IHCA [3, 4, 17–20]. Patient monitoring is more difficult in general wards than in ICUs. Besides, there are also differences in the healthcare economics, patient expectation, and provider practice patterns in Taiwan. Although do not resuscitate orders have started to be accepted by people in Taiwan, there were still some patients receiving CPR, with predictable deteriorating disease course in terminal diseases. The lower possibilities of successful resuscitation for these patients might also result in the poor prognosis.

5. Conclusion

This study offers further insight into the complex relationship between in-hospital resuscitation during the night shift and increased mortality, and this phenomenon is more obvious in cardiac origin IHCAs than in noncardiac origin ones.

6. Limitations

There were several limitations to this study. First, it was a single center study. Second, the retrospective nature of the study made it difficult to assemble data and judge the precise etiology of cardiac arrest by chart review because of the lack of objective information. Third, practice patterns in Taiwan differ in some ways that are quite remarkable compared to the US and other Western countries, particularly related to decisions regarding “do not resuscitate” order. We believe that these differences may influence the interpretation of the result by other medical systems. Fourth, this study could not trace the patients’ outcomes after discharge, so no long-term mortality rate or quality of life was documented.

Competing Interests

The authors declare that there are no competing interests regarding the publication of this paper.

Authors’ Contributions

Yuan-Jhen Syue and Jyun-Bin Huang contributed equally to this work. Chia-Te Kung and Chao-Jui Li contributed equally to this work.

Acknowledgments

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References


Research Article

Evaluation of Smartphone Applications for Cardiopulmonary Resuscitation Training in South Korea

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Objective. There are many smartphone-based applications (apps) for cardiopulmonary resuscitation (CPR) training. We investigated the conformity and the learnability/usability of these apps for CPR training and real-life supports.

Methods. We conducted a mixed-method, sequential explanatory study to assess CPR training apps downloaded on two apps stores in South Korea. Apps were collected with inclusion criteria as follows, Korean-language instruction, training features, and emergency supports for real-life incidents, and analyzed with two tests; 15 medical experts evaluated the apps’ contents according to current Basic Life Support guidelines in conformity test, and 15 nonmedical individuals examined the apps using System Usability Scale (SUS) in the learnability/usability test.

Results. Out of 79 selected apps, five apps were included and analyzed. For conformity (ICC, 0.95, \( p < 0.001 \)), means of all apps were greater than 12 of 20 points, indicating that they were well designed according to current guidelines. Three of the five apps yielded acceptable level (greater than 68 of 100 points) for learnability/usability.

Conclusion. All the included apps followed current BLS guidelines and a majority offered acceptable learnability/usability for layperson. Current and developmental smartphone-based CPR training apps should include accurate CPR information and be easy to use for laypersons that are potential rescuers in real-life incidents. For Clinical Trials. This is a clinical trial, registered at the Clinical Research Information Service (CRIS, cris.nih.go.kr), number KCT0001840.

1. Introduction

Sudden cardiac arrest (SCA) remains a leading cause of death in developed countries, including South Korea, despite efforts devoted to prevention of SCA [1–3]. Although there are many factors that dictate the outcomes of SCA, it is well known that survival rates are up to three times higher when cardiopulmonary resuscitation (CPR) is performed immediately after SCA [4, 5]. Various methods for demonstrating high quality CPR and immediate recognition of cardiac arrest, including face-to-face training and video-based instruction for bystanders, have yielded improvement in participation rates during incidents of SCA [6, 7]. However, only 12–42% of cardiac arrest patients witnessed by the layperson received CPR during out-of-hospital cardiac arrest (OHCA) [8–10]. The low rate of layperson intervention may be due to a failure to recognize cardiac arrest or a lack of confidence due to insufficient CPR training/education [11].

Recently, many medical and healthcare applications (apps) have been developed and registered in online mobile apps stores, because there is no limitation in time and space [12, 13]. In particular, a number of smartphone-based apps have been developed by public institutions and companies in order to enhance CPR education [14–17]. Smartphone-based apps could be an important and epochal medium, as they overcome the limitations of traditional CPR training and remind users, particularly layperson, of CPR. However, one flaw in app-based CPR training and education is that some apps may not adequately reflect current guidelines, potentially resulting in the transmission of incorrect information. Even some apps adhering to current guidelines may not be useful for layperson, as the apps might be difficult to operate...
and users may have low interest in their use. In one study, Kalz et al. [14] reported that very few apps reflect current BLS guidelines and offer an acceptable level of usability for layperson rescue.

As of January 2016, 85.2% of the South Korean population owned smartphones, a number that is steadily on the rise [18]. Additionally, many smartphone-based CPR training apps have been downloaded in South Korea, though no study has systematically investigated the CPR training apps. We assessed the conformity of smartphone-based CPR training apps to current CPR guidelines and evaluated the learnability and usability of the apps in incidents of SCA.

2. Materials and Methods

2.1. Setting and Participants. This mixed-method, sequential explanatory design study was approved by the Institutional Review Board of Hanyang University Hospital (Seoul, South Korea) (IRB HYUH2015-08-012-001) and was conducted in September 2015. The mixed-methods sequential design consisted of identification of smartphone-based CPR training apps, examination of conformity of apps to the 2010 American Heart Association Basic Life Support (AHA BLS) guidelines, and learnability and usability testing. Fifteen AHA BLS-certified healthcare providers and fifteen laypersons with no CPR training were recruited for the first and second phases of the study, respectively. Participants were recruited voluntarily by a notice on a bulletin from September 21, 2015, to September 30, 2015. Each potential participant received written information regarding the purpose of the study, and all participants provided written informed consent.

2.2. Materials and Experimental Methods. A Galaxy S4 smartphone (Samsung Electronics Co., Seoul, South Korea) with android (mobile operating system of Google) and an iPhone 5 (Apple Inc., Cupertino, CA, USA) with iOS (mobile operating system of Apple) were used for our investigation. Both mobile operating systems have a 99.8% market share in Korea (iOS 23.1% and android 76.7%) [19]. Therefore, we searched for and identified mobile apps from the Google Play Store and the Apple App Store, the two largest online stores for mobile apps (as of September 2015). Search terms included “cardiopulmonary resuscitation” OR “CPR” OR “chest compression” OR “basic life support” in both English and Korean languages. In South Korea, the proportion of true-born Korean is 97.8% [20], and almost all use and speak Korean language with low diversity of languages [21]. Therefore, we excluded apps with no Korean language in screening. And selected versions in the Google Play Store that were also present in the Apple App Store. From the selected apps, we excluded apps that did not contain CPR-related content and had error for operation of apps. Finally, we included apps that contained the following features: (1) training features and (2) emergency support for real-life incidents. “Emergency support for real-life incidents” means that layperson could be served guidance or accurate information for CPR within apps in real cardiac arrest situation; we selected this as mandatory feature. The identification and selection of apps included in this study are based on Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) guidelines [22].

First Test: Conformity Test of Smartphone-Based CPR Apps to 2010 AHA BLS Guidelines Checklist. We made the conformity checklist using the AHA BLS checklist for education by authors. The conformity checklist contained 10 items as follows: (1) how to check a patient’s response and abnormal breathing, (2) how to activate the emergency medical system, (3) how to get someone to bring an automatic external defibrillator (AED), (4) correct CPR sequence (chest compression, airway, breathing, C-A-B), (5) existence of hands-only CPR for lay-rescue, (6) how to begin CPR rapidly, (7) proper compression position of the chest (i.e., lower half of the sternum), (8) adequate chest compression depth (i.e., at least 5 cm or 5-6 cm), (9) proper chest compression rate (i.e., at least 100 or 100–120 numbers/min), and (10) mention of complete chest decompression. Each item was scored on a numeric scale (0; nonexistent or incorrect information, 1; insufficient information, 2; sufficient information), with a maximum possible score of 20 points.

Second Test: Learnability and Usability Test of Smartphone-Based CPR Training Apps Using the System Usability Scale (SUS). For learnability and usability evaluations, we used the modified System Usability Scale (SUS), a simple but reliable method for evaluating the usability of a technological product or service [23–25]. The SUS consists of 10 questions: five positively worded questions (odd-numbered domain) and five negatively worded question (even-numbered domain) as follows:

**Modified System Usability Scale (SUS) Questions**

1. I think that I would like to use this product frequently.
2. I found the product unnecessarily complex.
3. I thought the product was easy to use.
4. I think that I would need the support of a technical person to be able to use this product.
5. I found the various functions in this product were well integrated.
6. I thought there was too much inconsistency in this product.
7. I would imagine that most people would learn to use this product very quickly.
8. I found the system very awkward to use.
9. I felt very confident using the product.
10. I needed to learn a lot of things before I could get going with the product.

Questions (4) and (10) represent a value of learnability for laypersons, while the other questions represent a value of usability. The SUS showed the domains as five scales numbered from 1 (strongly disagree) to 5 (strongly agree). To obtain a score, the following formulas are used:

**SUS Score Calculation:**

\[ \text{Score} = \frac{5}{(2)(n-1)} \sum_{i=1}^{10} (5 - Q(i)) \]

where 

\[ Q(i) \] 

is the score to question \( i \).

1. Positively worded domains = (score – 1).

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2.3. Data Collection. We recorded background information pertinent to the apps included in this investigation. Basic information consisted of (1) manufacturer, (2) number of downloads, (3) purchase cost, (4) last update, (5) type of content (video instruction, text instruction, audio instruction, video simulation, animation, and graphics), (6) purpose of the app, (7) underlying guideline, (8) target user (including pediatric), (9) detection of AED location, (10) supply of auditory guidance, (11) feedback system (compression rate and/or depth), and (12) direct connection to activate for Emergency Medical Service (EMS).

In the conformity test, each participant had 10 minutes of evaluation time for each app and five minutes of resting time before each evaluation. In the SUS learnability and usability test, each layperson had 30 minutes of evaluation time for each app and 10 minutes of resting time before each evaluation in the silent room with one observer. If layperson was not familiar with the device or had problems operating or controlling the device, observer helped them providing guidance. The order in which apps were evaluated was randomized for each participant.

2.4. Statistical Analysis. Data were compiled using a standard spreadsheet program (Excel; Microsoft, Redmond, WA, USA) and were analyzed using the Statistical Package for the Social Sciences (SPSS) 18.0 for Windows (SPSS Inc., Chicago, IL, USA). We generated descriptive statistics, and data are presented as the mean ± standard deviation (SD). We calculated an intraclass correlation coefficient (ICC) for all questions in tests of both phases. p values of < 0.05 were considered statistically significant. In the conformity test, we assessed the results by 5 Likert scales: (1) very high; 20 ≥ score ≥ 16 points, (2) high; 16 > score ≥ 12, (3) moderate; 12 > score ≥ 8, (4) low; 8 > score ≥ 4, (5) very low; 4 > score ≥ 0. A mean score of SUS > 68 is an acceptable value of learnability and usability, based on the current literature [14, 26].

3. Results

3.1. Apps Selection. A total of 511 apps and 349 apps were identified through the Google Play Store and the Apple App Store, respectively. After removing duplicates, we selected apps that consisted of CPR training in the Korean language. 79 apps were retrieved after screening, and then we operated and evaluated these apps in detail. 16 apps did not have CPR training feature, 54 apps did not have emergency support for real-life incidents, and 4 apps had errors when they were operated. Finally, five apps met our mandatory criteria (Figure 1). Two apps were registered in the Google Play Store, one was registered in the Apple App Store, and two were registered in both stores. Notable attributes of these apps are presented in Table 1, including basic app information, mandatory features, and feedback systems. Three apps had auditory guidance for the compression rate (by metronome), and only the “UCPR” app had feedback systems for the compression rate and depth (by accelerometer). There were no apps for pediatric BLS.

3.2. Results of Conformity to CPR Guidelines. The intraclass correlation (ICC) for the conformity checklist was 0.95 (p < 0.001, 95% Confidence Interval (CI) 0.93–0.97). The results of conformity to AHA 2010 BLS guideline testing are shown in Table 2. The apps we investigated, whose mean scores in conformity to the AHA 2010 BLS guidelines evaluation (in parentheses) were as follows: “UCPR” (MELab) (17.80±1.01), “cardiopulmonary resuscitation” (Academica) (16.40±1.88), “information for emergency medicine” (Ministry of Health and Welfare) (16.13±1.24), “cardiopulmonary resuscitation” (INOVIEW network) (14.73±1.09), and “management for medical emergencies” (Fantalog) (13.47±2.94). Analyses of the conformity scores for each question are shown in Figure 2. Three questions fulfilled all of the apps (Q4, Q6, and Q9). Three apps did not fulfill “mention of complete chest decompression” (Q10).

3.3. Results of Learnability and Usability Evaluation Using SUS. Three apps earned well over 68 points in learnability and usability testing, and the “information for emergency medicine” app had the highest score (81.17 points) (Table 2). For learnability, the “cardiopulmonary resuscitation” (INOVIEW network) app had 17.00 points, less than one point more than the “information for emergency medicine” app (16.30 points) (Figure 3).

4. Discussion

Although there are various methods for CPR training, most methods are not comprehensive [27]. Effectiveness and accuracy of CPR training are important factors, and retention of skills and knowledge is essential [28]. A reminder CPR video clip on a mobile phone was effective for education retention by trainees at three months after initial training [29]. A CPR animation instruction on a mobile phone was also effective in checklist assessment and time-interval compliance in trainees [30]. Smartphones are easy to access for civilians, and smartphone-based apps could provide both text and video clips for CPR. Alternatively, CPR training apps could be used for both CPR training and education retention after training. In this study, five of 79 smartphone-based CPR training apps met our mandatory criteria. The total download numbers of CPR training apps have been counted to be about several hundred thousands, ranging from about 1,000 to 1,000,000 times for each app. CPR training apps with incorrect or insufficient CPR information could result in layperson unintentionally harming the victim in real incidents. Thus, these apps should be examined by experts prior to public release.

Smartphone-based CPR training apps could provide auditory guidance through speakers, feedback for high quality chest compression using accelerometers, and the nearest AED location using global positioning system (GPS) sensors [15–17, 31]. Three of the five apps we examined incorporated auditory guidance of chest compression rate using a metronome, though just one app had an audiovisual
### Table 1: Characteristics of included apps.

<table>
<thead>
<tr>
<th>Title</th>
<th>Cardiopulmonary resuscitation (CPR)</th>
<th>Cardiopulmonary resuscitation</th>
<th>Information for emergency medicine</th>
<th>Management for medical emergencies</th>
<th>UCPR</th>
</tr>
</thead>
<tbody>
<tr>
<td>App information</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Manufacturer</td>
<td>Academica</td>
<td>INOVIEW network</td>
<td>Ministry of Health and Welfare</td>
<td>Fantalog Interactive Co., Ltd.</td>
<td>MELab</td>
</tr>
<tr>
<td>Icon image</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Number of downloads</td>
<td>Unknown</td>
<td>10,000–50,000 (android)</td>
<td>500,000–1,000,000 (android)</td>
<td>500,000–1,000,000</td>
<td>1,000–5,000</td>
</tr>
<tr>
<td>Purchase cost</td>
<td>Free</td>
<td>Free</td>
<td>Free</td>
<td>Free</td>
<td>Free</td>
</tr>
<tr>
<td>Last update</td>
<td>March 5, 2013</td>
<td>April 24, 2013</td>
<td>July 7, 2015</td>
<td>June 8, 2011</td>
<td>December 3, 2014</td>
</tr>
<tr>
<td>Distributor</td>
<td>iOS</td>
<td>Android, iOS</td>
<td>Android, iOS</td>
<td>Android</td>
<td>Android</td>
</tr>
<tr>
<td>Language</td>
<td>Korean</td>
<td>Korean</td>
<td>Korean</td>
<td>Korean</td>
<td>Korean</td>
</tr>
<tr>
<td>Mandatory features</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Training feature</td>
<td>Educational video or animations</td>
<td>—</td>
<td>O</td>
<td>O</td>
<td>—</td>
</tr>
<tr>
<td>Real-incident animation instructions</td>
<td>—</td>
<td>O</td>
<td>—</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>Real-incident picture instructions</td>
<td>O</td>
<td>O</td>
<td>O</td>
<td>O</td>
<td>O</td>
</tr>
<tr>
<td>Real-incident audio instructions</td>
<td>—</td>
<td>O</td>
<td>O</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>Emergency support for real incidents</td>
<td>O</td>
<td>O</td>
<td>O</td>
<td>O</td>
<td>O</td>
</tr>
<tr>
<td>Special features</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>AED location</td>
<td>—</td>
<td>—</td>
<td>O</td>
<td>—</td>
<td>O</td>
</tr>
<tr>
<td>Auditory guidance</td>
<td>—</td>
<td>O</td>
<td>O</td>
<td>—</td>
<td>O</td>
</tr>
<tr>
<td>Feedback</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>Compression rate</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>Compression depth</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>Pediatric BLS</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>Direct connection to activate for Emergency Medical Service (EMS)</td>
<td>O</td>
<td>O</td>
<td>O</td>
<td>O</td>
<td>O</td>
</tr>
</tbody>
</table>
Table 2: Mean, standard deviation, and rank of conformity checklist score to the AHA 2010 BLS guidelines and modified System Usability Scale (SUS) score.

<table>
<thead>
<tr>
<th>Title (manufacturer)</th>
<th>Conformity Mean ± SD</th>
<th>Rank</th>
<th>Learnability and usability Mean, SD Rank</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cardiopulmonary resuscitation (Academica)</td>
<td>16.40 ± 1.88</td>
<td>2</td>
<td>56.67 ± 23.58</td>
</tr>
<tr>
<td>Cardiopulmonary resuscitation (INOVIEW network)</td>
<td>14.73 ± 1.09</td>
<td>5</td>
<td>78.17 ± 20.49</td>
</tr>
<tr>
<td>Information for emergency medicine (Ministry of Health and Welfare)</td>
<td>16.13 ± 1.24</td>
<td>3</td>
<td>81.17 ± 19.01</td>
</tr>
<tr>
<td>Management for medical emergencies (Fantalog)</td>
<td>13.47 ± 2.94</td>
<td>4</td>
<td>61.50 ± 19.54</td>
</tr>
<tr>
<td>UCPR (MELab)</td>
<td>17.80 ± 1.00</td>
<td>1</td>
<td>70.50 ± 24.33</td>
</tr>
</tbody>
</table>

SD: standard deviation.

---

Feedback system for both the chest compression rate and depth (using an accelerometer). Several simulation studies have demonstrated that both smartphones and smartwatches with an accelerometer could be good alternative devices [32–34]. Two of the five apps were able to locate the nearest AED. The addition of audiovisual feedback is advisable in smartphone-based CPR training apps.

We included support for pediatric BLS as a special feature of this study. However, no app solely supports pediatric BLS. Although there are few pediatric arrest patients compared to adults, CPR training apps should also include an explanation of pediatric BLS.

All five apps analyzed in this study were designed well, yielding more than 12 points in conformity testing. For the tenth question, however, only two apps had sufficient explanation of complete chest decompression, which is a factor as important as chest compression [35, 36]. In October 2015, international CPR guidelines were changed, and CPR training apps should be updated according to new guidelines [36, 37]. High scores on the SUS scale indicate that the
Figure 2: Analysis of information fulfillment for the conformity checklist. Fulfillment of sufficient information (a) in each question and (b) in each app. Q1, how to check the patient’s response and abnormal breathing; Q2, how to activate the emergency medical system; Q3, how to get someone to bring an automatic external defibrillator (AED); Q4, correct cardiopulmonary resuscitation (CPR) sequence [chest compression, airway, breathing, C-A-B]; Q5, existence of hands-only CPR for lay-rescue; Q6, how to begin the CPR rapidly; Q7, proper compression position of chest (i.e., lower half of sternum); Q8, adequate chest compression depth (i.e., at least 5 cm or 5-6 cm); Q9, proper chest compression rate (i.e., at least 100 or 100–120 numbers/minute); Q10, mention of complete chest decompression.

Figure 3: Mean learnability and usability testing scores of five apps using the System Usability Scale (SUS).
product or service is easy for the user to learn and handle. Three of the five apps we examined yielded SUS scores greater than 68 points. Some apps with high scores in conformity testing did not yield high scores in learnability and usability testing. In the future, easy-to-use, accurate CPR training apps should be developed.

There are several limitations to this study. First, user interest in CPR training apps improves educational transmission, and we did not attempt to find the interest factor in this study [14]. Second, the resident population of foreigners in Korea is growing every year, according to the South Korean Census. An investigation of CPR training apps that consist of various languages would be required for further examination. Not all CPR training apps evaluated in this study offered training in other languages. Finally, we conducted this study with two types of smartphones. An individual’s skill or familiarity with a particular type of smartphone might have biased learnability and usability scores.

5. Conclusion

In conclusion, five CPR training apps followed current BLS guidelines, and three offered an acceptable level of learnability and usability for layperson. Current and development smartphone-based CPR training apps should include accurate CPR information (considering new international guidelines) and should be easy to use for laypeople that are potential rescuers in real-life incidents of SCA.

Competing Interests

The authors declare that there is no conflict of interests regarding the publication of this paper.

Authors’ Contributions

Chiwon Ahn and Jaehoon Oh conceived the study, designed the trial, and obtained the research funding. Yeongtak Song, Juncheol Lee, Hyungoo Kang, and Tae Ho Lim supervised the trial conduct and data collection. Yeongtak Song, Juncheol Lee, Hyungoo Kang, and Tae Ho Lim analyzed the data statistically, Chiwon Ahn and Yongtak Cho drafted the manuscript, and all authors contributed substantially to its revision. Jaehoon Oh takes responsibility for the paper as a whole. Chiwon Ahn and Yongtak Cho contributed equally to this work.

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References


Research Article

DARE Train-the-Trainer Pedagogy Development Using 2-Round Delphi Methodology

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1. Introduction

Out-of-hospital cardiac arrest (OHCA) is one of the main causes of death, of which 65.4% occur at home in Asia [1]. Annually, there are 700,000 cardiac arrest cases in Europe and more than 400,000 cases in America [2]. In Singapore, the annual incidence of OHCA is at least 1,400 cases, of which only 3% survived to discharge [3].

International studies have shown that early cardiopulmonary resuscitation (CPR) improves the chances of survival [4]. Furthermore, a review of several large-scale studies emphasised the importance of dispatcher-assisted CPR in improving bystander CPR and OHCA survival rates [5, 6].

Locally, the bystander CPR rate is only around 20% [3]. Clearly, there is a need to improve these rates which can be done via a local dispatcher-assisted CPR programme. To do so, we conceived a simplified programme for the lay public to learn how to perform effective CPR and use an AED while guided by a medical dispatcher over the telephone.

Traditional CPR classes focus heavily on the rescuer working alone. In our programme, we focus on the rescuer cooperating with the dispatcher. The trainers of this community outreach programme are individuals who are both CPR and AED certified. They guide the participants during the hands-on session, providing constructive feedback and correcting their CPR technique. Currently, there is no formal train-the-trainer curriculum for a dispatcher-assisted CPR training programme. This train-the-trainer model is an established tool used by organisations which gather content from experts to educate trainers pooled from the community, in order to enable them to instruct target audiences. The advantage of such a model is that it can be propagated...
in the long term by multiple trainers who can disseminate information back to the community in a timely fashion, making this cost-effective and sustainable [7].

As of now, there is no formal pedagogy to train the trainers how to teach the lay population dispatcher-assisted CPR. We aim to write a structured train-the-trainer curriculum to regulate and homogenize the type of information and the way it is conveyed to the participants during the sessions.

2. Methods

2.1. Setting. The Dispatcher-Assisted first REsponder (DARE) programme is an hour long programme and includes an explanatory video and an instructor-led hands-on session. This is shorter than the usual CPR and AED certification course which spans at least 4 hours and does not include a humorous video. The participants will learn to recognize a cardiac arrest, dial the local emergency number, familiarize themselves with the medical dispatcher’s commands, and perform effective CPR on manikins and how to use an AED.

2.2. Study Design. To come up with the trainers’ curriculum, consensus was gathered using the Delphi approach [8]. This method involves recruiting a panel of experts to answer questions pertaining to the areas of concern.

The study was exempted from institutional review board approval.

2.3. Study Participants. A panel of 20 local experts well-versed in cardiopulmonary resuscitation (CPR), from 9 different institutions, was invited to be a part of the study. These included those who are medically trained, who are personally involved in overseeing the current DARE curriculum, and/or who are first-aid instructors. Their areas of expertise vary and include, but are not limited to, emergency medicine, out-of-hospital cardiac arrest, and education.

2.4. Study Protocol and Data Collection. First, a pilot group, comprising 4 people who were familiar with DARE or were involved in studies that used the Delphi method, was created. The principal investigator worked with the pilot group to draw up a questionnaire based on literature review and the feedback from trainers. After discussing with the pilot group, we edited the questionnaire and chose to focus on questions related to 10 core areas. These areas are as follows:

(1) The focus of general CPR
(2) How the train-the-trainer session should be conducted
(3) Recognition of cardiac arrest
(4) How CPR should be taught
(5) Teaching the usage of AED
(6) Precourse reading materials
(7) Frequently asked questions
(8) Trainers’ qualities and qualifications
(9) Assessment of trainers
(10) Continuity of the programme

The expert panel was created and care was taken not to include the panelists from the pilot group.

2.4.1. Round One of Delphi Method. The first-round Delphi questionnaire was distributed to the experts in December 2015 through an online questionnaire portal (SurveyMonkey™). They could provide any specific comments perceived to be necessary to drive a primary consensus. The first round was completed after about one month in January 2016. This first questionnaire consisted of dichotomous answers (yes/no), ranking questions, multiple choice questions, and some required open-ended responses. Open-ended responses allowed the experts to give their input, to clarify the interpretation of the question, and to expose common fallacies. Primary consensus was achieved when 70% of respondents were in agreement for dichotomous and multiple choice question.

This cut-off point was used based on previous studies suggesting that a minimum of 70% agreement is needed for validity when using the Delphi method [9–11].

2.4.2. Round 2 of Delphi Method. The expert panel was informed of round one’s preliminary results and of their individual comments. Data of which items had obtained consensus and which had not, with the overall agreement percentage obtained by the experts, were presented to the panel. Items that either did not obtain consensus in the first round but had 60–69% agreement or had some ambiguity in phrasing were included in the second questionnaire. Comments and additional options from round one were taken into consideration and included into round two as well. Where possible, the exact phrasing as round one was used. For multiple choice questions with 60–69% agreement and ranking questions, where possible, the questions were converted to yes/no options for clarity.

The second round of Delphi was administered through the previous portal in February 2016 for 3 weeks with the same expert panel. Questions with more than 70% of agreement were regarded as a secondary consensus. We summarized the issue lists from the primary and secondary consensus as the final step by reviewing them via e-mail to establish the recommendations on the curriculum for a dispatcher-assisted train-the-trainer programme. The English language (without translation) was used as the working language in all steps. Figure 1 is a summary of the process undertaken for the 2-Round Delphi Methodology.

2.4.3. Statistical Analyses. For each item, statistical analysis was performed and the agreement rates were calculated with percentages and frequencies.

3. Results

20 experts participated in this study. After opening up the first round of the Delphi surveying for 1 month, 25 issues arrived at a consensus. After opening up the second round of Delphi surveying for the same amount of time, an additional 14 issues arrived at a consensus. A total of 70 consensus statements were agreed by the expert panel. No agreement was reached
Delphi process: round 2

(i) Collation of results from Delphi round 1
(ii) Design second questionnaire based on information collected from Delphi round 1
(iii) Expert panel receives second questionnaire that includes items that did not receive primary consensus. The items' round 1 rating and feedback from the expert panel were made known in the second questionnaire. Administration of second questionnaire

Delphi process: round 1

(i) Administration of questionnaire

Expert panel formation

(i) Recruitment of 20 experts

Pilot group formation

(i) Formation of pilot group
(ii) Brainstorm core topics for the trainers' curriculum
(iii) Convert collected information into structured

Figure 1: Flow of process.

4. Discussion

This study is the first of its kind and aims to gather the viewpoints of experts regarding a suitable curriculum for a dispatcher-assisted CPR, train-the-trainer programme. We found that there was 100% agreement on elements that revolved around these core domains:

1. How the train-the-trainer session should be conducted
2. Recognition of cardiac arrest
3. How CPR should be taught
4. Precourse reading materials
5. Frequently asked questions
6. Assessment of trainers

All of the experts agreed that the trainers should correct the hand-positioning of participants when carrying out CPR. The instructors could instruct them of the changes verbally or physically move the participants' hands into the right position. 25% of the experts disagreed that trainers should physically correct the participants' hand position. One of the experts gave feedback that it could be potentially awkward for a male trainer to touch a female participant's hand.

100% of the experts agreed that the curriculum should include a question-and-answer guide so that the trainers will give standardised answers confidently. Common topics that participants in previous DARE training sessions brought up include the need for a good Samaritan law, the risk of being sued, and the fear of breaking ribs during CPR.

The expert panel agreed unanimously that, in assessing the trainers, their ability to conduct the lessons and classroom management skills are important aspects. This suggests that it is not just the theory of resuscitation that should be taught to the trainers but educational methods employing domains including psychology and communication.

Agonal breathing is abnormal breathing that is reported to be present in about 40% of OHCA [12, 13]. It is often confused by bystanders as a sign of life [12, 14] causing CPR to be delayed or withheld, which is associated with poorer outcomes. It was agreed that bystanders’ descriptions of agonal breathing should be taught to the trainers. Trainers should be familiar with layman's description of agonal breathing, which could include gasping and noisy breathing [12, 13] and emphasise to lay participants the importance of recognising agonal breathing as a sign of cardiac arrest. They should also dispel any misconception of agonal breathing being a sign of life.

The panel experts all agreed that recognising cardiac arrest, calling 995, and cooperating with the dispatcher for telephone-assisted resuscitation, as well as how to find and use an AED, were important areas that should be included in the curriculum.

Traditionally studies have shown that CPR should not be omitted in the context of a traumatic cardiac arrest [15]. 100% of our experts agreed that the curriculum should specify that CPR be carried out in a victim who has had a fall.
### Table 1: List of items that obtained consensus.

<table>
<thead>
<tr>
<th>Consensus statements</th>
<th>Consensus statements showing agreement from Delphi survey rounds 1 and 2</th>
<th>Number of respondents in agreement</th>
<th>%</th>
<th>Established in round</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>(1) The focus of general CPR</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>(a) Early access is the most important aspect to focus on during the trainers’ programme</td>
<td>14</td>
<td>70.0</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>(b) Early CPR is the second most important aspect to focus on during the trainers’ programme</td>
<td>15</td>
<td>75.0</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>(c) Early defibrillation is the least important of the three aspects to focus on during the trainers’ programme</td>
<td>16</td>
<td>80.0</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td><strong>(2) How the train-the-trainer session should be conducted</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>(a) There should be more than one person (instructor) conducting the session for the trainers</td>
<td>14</td>
<td>70.0</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>(b) There should be hands-on component for the trainers during the session</td>
<td>18</td>
<td>90.0</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>(c) The session should not be conducted entirely through a video for standardisation</td>
<td>14</td>
<td>70.0</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>(d) Qualification an instructor should have to carry out the session</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>CPR/AED instructor level</td>
<td>18</td>
<td>94.7</td>
<td>2</td>
<td></td>
</tr>
<tr>
<td>CPR/AED trained</td>
<td>17</td>
<td>89.5</td>
<td>2</td>
<td></td>
</tr>
<tr>
<td>(e) Video for the train-the-trainer programme should be of a professional tone</td>
<td>17</td>
<td>89.5</td>
<td>2</td>
<td></td>
</tr>
<tr>
<td>(f) Video for the train-the-trainer programme should be of a matter-of-fact (factual) tone</td>
<td>16</td>
<td>84.2</td>
<td>2</td>
<td></td>
</tr>
<tr>
<td>(g) Video should not cater to English speaking trainers only</td>
<td>16</td>
<td>84.2</td>
<td>2</td>
<td></td>
</tr>
<tr>
<td>(h) The video should have both subtitles and voice-over in other languages</td>
<td>14</td>
<td>70.0</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>(i) Hands-on component should be conducted after the video screening</td>
<td>16</td>
<td>80.0</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>(j) During the train-the-trainer session, there should be time allocated for each trainer to role-play with fellow trainers to be the main instructor</td>
<td>17</td>
<td>89.5</td>
<td>2</td>
<td></td>
</tr>
<tr>
<td>(k) Topics to be included in the curriculum</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>(i) Calling 995 and dispatcher’s assistance</td>
<td>19</td>
<td>100.0</td>
<td>2</td>
<td></td>
</tr>
<tr>
<td>(ii) The importance of quality CPR/AED</td>
<td>16</td>
<td>84.2</td>
<td>2</td>
<td></td>
</tr>
<tr>
<td>(iii) How to carry out CPR and the concerns faced when performing CPR</td>
<td>16</td>
<td>84.2</td>
<td>2</td>
<td></td>
</tr>
<tr>
<td>(iv) Spotting common CPR mistakes</td>
<td>16</td>
<td>84.2</td>
<td>2</td>
<td></td>
</tr>
<tr>
<td>(v) How to find and use an AED</td>
<td>19</td>
<td>100.0</td>
<td>2</td>
<td></td>
</tr>
<tr>
<td>(vi) Material to motivate bystanders to step up and respond to a cardiac arrest</td>
<td>14</td>
<td>73.7</td>
<td>2</td>
<td></td>
</tr>
<tr>
<td>(vii) DARE’s objectives and effectiveness</td>
<td>17</td>
<td>89.5</td>
<td>2</td>
<td></td>
</tr>
<tr>
<td>(viii) Importance of the trainer in DARE</td>
<td>19</td>
<td>100.0</td>
<td>2</td>
<td></td>
</tr>
<tr>
<td>(ix) Address the introduction of the CPR card (tells you the depth of chest compression) and MyResponder Application (notifying myResponder to nearby cardiac arrest cases who may render first aid before ambulance arrival)</td>
<td>16</td>
<td>84.2</td>
<td>2</td>
<td></td>
</tr>
<tr>
<td>(x) Recognising a cardiac arrest</td>
<td>19</td>
<td>100.0</td>
<td>2</td>
<td></td>
</tr>
<tr>
<td>(xi) Trainers’ ethics</td>
<td>14</td>
<td>73.7</td>
<td>2</td>
<td></td>
</tr>
<tr>
<td><strong>(3) Key points in recognising a cardiac arrest</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>(a) Bystanders' descriptions of agonal breathing should be taught to the trainers</td>
<td>20</td>
<td>100.0</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>(b) Warning signs like that of lack of breathing should be taught</td>
<td>14</td>
<td>73.7</td>
<td>2</td>
<td></td>
</tr>
<tr>
<td>(c) Head-tilt-chin-lift should be covered during the trainers’ training session</td>
<td>15</td>
<td>75.0</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>(d) Tapping on the shoulders of a person in possible cardiac arrest should be taught to the trainers</td>
<td>18</td>
<td>90.0</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>(e) Checking for danger should be included in the curriculum</td>
<td>17</td>
<td>85.0</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Consensus statements showing agreement from Delphi survey rounds 1 and 2</td>
<td>Number of respondents in agreement</td>
<td></td>
<td></td>
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<tr>
<td>---</td>
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<td></td>
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<tr>
<td><strong>(4) How CPR should be taught</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>(a) Locating the landmark for chest compression: trainers should be taught to position hands in between the nipples</td>
<td>15 (78.9)</td>
<td>2</td>
<td></td>
<td></td>
</tr>
<tr>
<td>(b) The latest American Heart Association updated guidelines stated for rescuers to push hard and fast. However, the guidelines state that compressions should be at least 5 cm but not greater than 6 cm and that chest compressions should be performed at a rate of 100 to 120/min. In a basic resuscitation programme like DARE, the new guidelines should not be taken into consideration and implemented in our train-the-trainer curriculum</td>
<td>15 (78.9)</td>
<td>2</td>
<td></td>
<td></td>
</tr>
<tr>
<td>(c) Trainers should correct the positioning of the DARE lay participants</td>
<td>20 (100.0)</td>
<td>1</td>
<td></td>
<td></td>
</tr>
<tr>
<td>(d) Trainers should physically move the participant's hands into position</td>
<td>15 (75.0)</td>
<td>1</td>
<td></td>
<td></td>
</tr>
<tr>
<td>(e) The same resuscitation method can be taught during the session to be applied to a child in possible cardiac arrest</td>
<td>15 (75.0)</td>
<td>1</td>
<td></td>
<td></td>
</tr>
<tr>
<td>(f) Precautions specific to the paediatric age group should be taught to the trainers</td>
<td>15 (75.0)</td>
<td>1</td>
<td></td>
<td></td>
</tr>
<tr>
<td>(g) CPR should still be instituted to a person in cardiac arrest who had a fall</td>
<td>20 (100.0)</td>
<td>1</td>
<td></td>
<td></td>
</tr>
<tr>
<td>(h) CPR should still be carried out although the patient has a chest injury</td>
<td>18 (94.7)</td>
<td>2</td>
<td></td>
<td></td>
</tr>
<tr>
<td>(i) CPR should still be carried out although the patient has a spinal injury</td>
<td>18 (94.7)</td>
<td>2</td>
<td></td>
<td></td>
</tr>
<tr>
<td>(j) CPR should still be carried out although the patient has bony fractures [rib(s)/limb(s) etc.]</td>
<td>18 (94.7)</td>
<td>2</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>(5) Teaching the usage of AED</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>(a) The person conducting the training session should be using a real AED trainer set to demonstrate how to operate it to the trainers</td>
<td>15 (75.0)</td>
<td>1</td>
<td></td>
<td></td>
</tr>
<tr>
<td>(b) All trainers should practice on a real AED set made for trainers during the session</td>
<td>14 (73.7)</td>
<td>2</td>
<td></td>
<td></td>
</tr>
<tr>
<td>(c) At any one point in time, only 1 person should be operating the trainer AED</td>
<td>15 (78.9)</td>
<td>1</td>
<td></td>
<td></td>
</tr>
<tr>
<td>(d) It is necessary for every trainer to be taught how to use a community AED</td>
<td>16 (80.0)</td>
<td>1</td>
<td></td>
<td></td>
</tr>
<tr>
<td>(e) During training, a real community AED set should be available for the trainers to familiarise themselves with</td>
<td>14 (70.0)</td>
<td>1</td>
<td></td>
<td></td>
</tr>
<tr>
<td>(f) Trainers should be taught where AEDs are found in the community</td>
<td>19 (95.0)</td>
<td>1</td>
<td></td>
<td></td>
</tr>
<tr>
<td>(g) When applying the AED chest pads, the modesty of a female patient should be taken into consideration</td>
<td>16 (84.2)</td>
<td>2</td>
<td></td>
<td></td>
</tr>
<tr>
<td>(h) Her top should be lifted up slightly and not completely to paste the chest pads</td>
<td>16 (80.0)</td>
<td>1</td>
<td></td>
<td></td>
</tr>
<tr>
<td>(i) If she is wearing a dress, the entire dress should not be removed and expose her lower extremities to apply the AED pads</td>
<td>15 (75.0)</td>
<td>1</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>(6) Reading materials catered to the trainers’ session</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>(a) Budget should be set aside for the trainers’ precourse materials</td>
<td>18 (90.0)</td>
<td>1</td>
<td></td>
<td></td>
</tr>
<tr>
<td>(b) A trainer’s manual (to be given out on the training day itself) should be provided for the trainers</td>
<td>18 (90.0)</td>
<td>1</td>
<td></td>
<td></td>
</tr>
<tr>
<td>(c) The trainer’s manual should include a DVD of the trainer’s video</td>
<td>15 (75.0)</td>
<td>1</td>
<td></td>
<td></td>
</tr>
<tr>
<td>(d) The trainer’s manual should include basic CPR and AED guidelines</td>
<td>20 (100.0)</td>
<td>1</td>
<td></td>
<td></td>
</tr>
<tr>
<td>(e) The manual should be translated to cater to non-English speaking trainers</td>
<td>14 (70.0)</td>
<td>1</td>
<td></td>
<td></td>
</tr>
<tr>
<td>(f) There should be an online prelearning component for the trainers prior to attending the training session</td>
<td>15 (78.9)</td>
<td>2</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Consensus statements</td>
<td>Number of respondents in agreement</td>
<td>%</td>
<td>Established in round</td>
<td></td>
</tr>
<tr>
<td>----------------------</td>
<td>-----------------------------------</td>
<td>---</td>
<td>---------------------</td>
<td></td>
</tr>
<tr>
<td>(7) Frequently asked questions</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>(a) Trainers should be allowed to answer DARE participants’ questions based on their own knowledge</td>
<td>14</td>
<td>70.0</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>(b) There should be a fixed Q&amp;A guidelines for the trainers to refer to and answer from when posed with questions from DARE participants</td>
<td>20</td>
<td>100.0</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>(c) The trainers should be taught to direct all questions to the person conducting the session for the DARE participants that day</td>
<td>14</td>
<td>70.0</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>(d) If participant trainers have any controversial questions during the train-the-trainer’s training session, the questions should be collated and answered after a consensus from the DARE coordinators is reached</td>
<td>18</td>
<td>94.7</td>
<td>2</td>
<td></td>
</tr>
<tr>
<td>(e) Should participant trainers have any questions during the session, they should approach the DARE coordinators directly during the training</td>
<td>14</td>
<td>73.7</td>
<td>2</td>
<td></td>
</tr>
<tr>
<td>(8) Trainers’ qualities and qualifications</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>(a) The minimum qualification a trainer should have before he/she is allowed to sign up to be a trainer for the DARE programme is BCLS and AED certification</td>
<td>14</td>
<td>70.0</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>(b) In view that the DARE programme hopes to reach out to the elderly as well, trainers who are well-versed in dialects should be taught how to teach lay participants in dialects</td>
<td>19</td>
<td>95.0</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>(c) In view of the high dependency on IT equipment to deliver the session, trainers should be taught how to operate IT equipment (i.e., projectors, computers, and basic IT skills)</td>
<td>16</td>
<td>80.0</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>(d) Adolescents (teenagers/students) who are allowed to become a trainer in the future should receive monetary remuneration</td>
<td>17</td>
<td>85.0</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>(9) Assessment of trainers</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>(a) Trainers should be assessed prior to training to gauge their competency level and suitability</td>
<td>17</td>
<td>85.0</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>(b) Trainers should be required to complete and pass an assessment after the training session before becoming an official DARE trainer</td>
<td>18</td>
<td>90.0</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>(c) Trainers should be assessed on their competency and knowledge in DARE/CPR and AED technique</td>
<td>18</td>
<td>94.7</td>
<td>2</td>
<td></td>
</tr>
<tr>
<td>(d) Trainers should be assessed on their ability to conduct the lessons and manage the classroom</td>
<td>19</td>
<td>100.0</td>
<td>2</td>
<td></td>
</tr>
<tr>
<td>(e) Trainers should be assessed on their attitude, communication skills, and confidence when teaching</td>
<td>18</td>
<td>94.7</td>
<td>2</td>
<td></td>
</tr>
<tr>
<td>(10) Continuity of the programme</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>(a) E-mailing the trainers is the best platform to disseminate updates to the trainers</td>
<td>16</td>
<td>84.2</td>
<td>2</td>
<td></td>
</tr>
<tr>
<td>(b) It is necessary for qualified DARE trainers to attend refresher courses (training session again)</td>
<td>14</td>
<td>70.0</td>
<td>1</td>
<td></td>
</tr>
</tbody>
</table>

Note: total number of responders was 20 for the first round and 19 for the second round.

CPR, cardiopulmonary resuscitation; BCLS, basic cardiac life support; AED, automated external defibrillator; DARE, dispatcher-assisted first responder; Q&A, question and answer; IT, information technology.
Table 2: List of items which did not achieve consensus.

<table>
<thead>
<tr>
<th>Statements</th>
<th>Respondents</th>
</tr>
</thead>
<tbody>
<tr>
<td>The instructor who carries out the train-the-trainer session should be a healthcare professional with a current BCLS certificate</td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>11 57.9</td>
</tr>
<tr>
<td>No</td>
<td>8 42.1</td>
</tr>
<tr>
<td>Duration of training session</td>
<td></td>
</tr>
<tr>
<td>2 hours</td>
<td>7 35.0</td>
</tr>
<tr>
<td>1.5 hours</td>
<td>4 20.0</td>
</tr>
<tr>
<td>1 hour</td>
<td>9 45.0</td>
</tr>
<tr>
<td>What should be the maximum number of trainers per session for the train-the-trainer programme? (This is in view that there is only one instructor conducting the programme)</td>
<td></td>
</tr>
<tr>
<td>4 to 6</td>
<td>8 40.0</td>
</tr>
<tr>
<td>8 to 10</td>
<td>8 40.0</td>
</tr>
<tr>
<td>12 to 20</td>
<td>4 20.0</td>
</tr>
<tr>
<td>In view that agonal breathing is reported to be present in about 40% of OHCA, is agonal breathing the only kind of respiration the trainer should be taught to look out for before doing CPR</td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>10 50.0</td>
</tr>
<tr>
<td>No</td>
<td>10 50.0</td>
</tr>
<tr>
<td>Warning signs like that of impending collapse (chest pain, diaphoresis/perspiration, shortness of breath, and drowsiness) should be taught</td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>13 68.4</td>
</tr>
<tr>
<td>No</td>
<td>6 31.6</td>
</tr>
<tr>
<td>Are dispatchers able to teach head-tilt-chin-lift over the phone</td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>9 45.0</td>
</tr>
<tr>
<td>No</td>
<td>11 55.0</td>
</tr>
<tr>
<td>Trainers should be taught to not teach head-tilt-chin-lift to the lay participants</td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>8 42.1</td>
</tr>
<tr>
<td>No</td>
<td>11 57.9</td>
</tr>
<tr>
<td>Materials to motivate trainers attending the trainer’s course should be covered in the curriculum</td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>12 63.2</td>
</tr>
<tr>
<td>No</td>
<td>7 36.8</td>
</tr>
<tr>
<td>Importance of maintaining airway should be covered in the curriculum</td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>11 57.9</td>
</tr>
<tr>
<td>No</td>
<td>8 42.1</td>
</tr>
<tr>
<td>How trainers can enhance their communication skills should be covered in the curriculum</td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>11 57.9</td>
</tr>
<tr>
<td>No</td>
<td>8 42.1</td>
</tr>
<tr>
<td>What should the maximum ratio of participant trainers: AED trainer set be</td>
<td></td>
</tr>
<tr>
<td>1:1 to 2:1</td>
<td>5 26.3</td>
</tr>
<tr>
<td>3:1 to 4:1</td>
<td>11 57.9</td>
</tr>
<tr>
<td>5:1 to 6:1</td>
<td>3 15.8</td>
</tr>
<tr>
<td>When applying the AED pads, should the entire bra be removed or just the bra straps be removed</td>
<td></td>
</tr>
<tr>
<td>Entire bra</td>
<td>9 45.0</td>
</tr>
<tr>
<td>Bra straps only</td>
<td>11 55.0</td>
</tr>
</tbody>
</table>
Table 2: Continued.

<table>
<thead>
<tr>
<th>Issues on which consensus could not be reached</th>
<th>Statements</th>
<th>N</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Should participant trainers have any questions during the session? They should e-mail the question(s) to an address provided</td>
<td>Yes</td>
<td>10</td>
<td>52.6</td>
</tr>
<tr>
<td></td>
<td>No</td>
<td>9</td>
<td>47.4</td>
</tr>
<tr>
<td>Should participant trainers have any questions during the session? They should write the questions down on a piece of paper given</td>
<td>Yes</td>
<td>12</td>
<td>63.2</td>
</tr>
<tr>
<td></td>
<td>No</td>
<td>7</td>
<td>36.8</td>
</tr>
<tr>
<td>Should adolescents who are in uniform groups be allowed to be a trainer? (i.e., adolescents whose CCA is NCC/scouts/girl guides/St John’s/other uniform groups)</td>
<td>Yes</td>
<td>12</td>
<td>63.2</td>
</tr>
<tr>
<td></td>
<td>No</td>
<td>7</td>
<td>36.8</td>
</tr>
<tr>
<td>How often should trainers be updated with new information</td>
<td>Once a month</td>
<td>0</td>
<td>0.0</td>
</tr>
<tr>
<td></td>
<td>Once every 6 months</td>
<td>2</td>
<td>10.5</td>
</tr>
<tr>
<td></td>
<td>Once a year</td>
<td>5</td>
<td>26.3</td>
</tr>
<tr>
<td></td>
<td>Whenever there are updates</td>
<td>12</td>
<td>63.2</td>
</tr>
<tr>
<td></td>
<td>Never</td>
<td>0</td>
<td>0.0</td>
</tr>
</tbody>
</table>

The experts unanimously agreed that the materials given out to the trainees should include current national CPR and AED guidelines. With this material given out before course, it allows the trainers to refresh their memory on the guidelines, reducing unnecessary questions that might be asked during the programme.

5. Strengths

The Delphi method was employed in preference to other consensus-achieving methodologies because it is convenient to implement. It is the most time-efficient methodology, as the questionnaires are completed individually, at the expert’s own convenience. Consolidation of the results gathered is released for all experts to review, allowing a certain amount of interaction between them [11]. Additionally, this anonymous method [8] eliminates bias resulting from personal status and institutional role in achieving consensus [16].

6. Limitations

In this study, there were a few limitations. Firstly, the expert panel was made up of people chosen by invitation to partake in this study. As such, their opinions may not be representative of universal viewpoints. All of the experts were from Singapore. They have worked in Singapore and are familiar with the local resuscitation field. Hence the results might only be relevant in the local setting and should this pedagogy be extended into other settings, certain changes would have to be made or the questionnaire could be redistributed to experts of that specific country. Additionally, the entire study from the administration of the first questionnaire to the closure of the second questionnaire took place within a 2.5 months’ period. Within that amount of time, it could be possible that new research in the area might have arisen in the meantime and that the results gathered from this study were overridden by the new research.

7. Future Studies

Based on our study, we would like to come up with a train-the-trainer programme that can be launched at a national level. This model appears to be a feasible approach to promote adoption of curricular content on a national scale. Using the results of our study, we can also come up with precourse materials for the trainers to review prior to attending the session. They can even use the materials to revise their knowledge before teaching lay participants.

Future studies can include an audit of both trainers and participants, to see if the execution of the resultant programme is effective. Comparison of the outcomes of the trainers before and after the implementation of the train-the-trainer curriculum should be made. The difference in performance of the trainers after having undergone the current training programme and the new trainer’s curriculum should be evaluated as well. Gaps should be addressed and improvements should be made accordingly based on qualitative and quantitative surveys.

8. Conclusion

Recommendations for pedagogy for trainers of dispatcher-assisted CPR programmes were developed using the Delphi
method. These recommendations should be validated in practical settings.

**Ethical Approval**

The Centralised Institutional Research Board (CIRB iSHaRe Ref 201509-00085) has approved the study and waived the need for consent.

**Competing Interests**

The authors report a grant from Temasek Cares, during the conduct of the study. The authors declare that there are no competing interests regarding the publication of this paper.

**References**


Hypotensive Resuscitation among Trauma Patients

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Hemorrhagic shock is a principal cause of death among trauma patients within the first 24 hours after injury. Optimal fluid resuscitation strategies have been examined for nearly a century, more recently with several randomized controlled trials. Hypotensive resuscitation, also called permissive hypotension, is a resuscitation strategy that uses limited fluids and blood products during the early stages of treatment for hemorrhagic shock. A lower-than-normal blood pressure is maintained until operative control of the bleeding can occur. The randomized controlled trials examining restricted fluid resuscitation have demonstrated that aggressive fluid resuscitation in the prehospital and hospital setting leads to more complications than hypotensive resuscitation, with disparate findings on the survival benefit. Since the populations studied in each randomized controlled trial are slightly different, as is the timing of intervention and targeted vitals, there is still a need for a large, multicenter trial that can examine the benefit of hypotensive resuscitation in both blunt and penetrating trauma patients.

1. Introduction

In the United States, trauma is the leading cause of death for persons between the ages of 1 and 44 years and the fifth leading cause of death overall [1]. Globally, over 5 million people die of injuries each year, accounting for 9% of the world’s deaths [2]. Hemorrhagic shock is a principal cause of death among trauma patients accounting for approximately 30–40% of deaths within the first 24 hours after injury [3]. Vascular disruption, blood pressure, volume resuscitation, and the time between injury and hemostasis are all factors that contribute to the magnitude of hemorrhage [4].

Over the past 30 years, there has been a renewed interest in research focusing on the optimal resuscitation strategies for trauma patients, specifically those with uncontrolled hemorrhage, in hopes of decreasing mortality from hemorrhagic shock. This review focuses on hypotensive resuscitation, also called permissive hypotension. This resuscitation strategy uses limited fluids and blood products during the early stages of treatment for hemorrhagic shock in order to maintain a lower-than-normal blood pressure until operative control of the bleeding can occur. The goal is to limit additional bleeding due to “popping the clot” while still providing oxygen to the tissues [4, 5]. The use of restricted fluids has been shown to improve outcomes in animal models [6]; until recently, few randomized controlled trials on hypotensive resuscitation existed in trauma patients [7–11].

2. History of Fluid Administration and Resuscitation Strategies

The idea of hypotensive resuscitation was introduced as far back as 1918 when Walter Cannon reported observations from
World War I in “The Preventive Treatment of Wound Shock.” Cannon stated that

"Injection of fluid that will increase blood pressure has dangers in itself. Hemorrhage in a case of shock may not have occurred to a marked degree because blood pressure has been too low and the flow too scant to overcome the obstacle offered by a clot. If the pressure is raised before the surgeon is ready to check any bleeding that may take place, blood that is sorely needed may be lost [12]."

After World War II, Beecher reiterated that when blood transfusions or surgery are inaccessible, rapid plasma administration is not desirable; the plasma may elevate the blood pressure to a degree where increased bleeding occurs. Instead, the time for fluid administration is when surgery is available [13].

However, animal research in the 1950s and 1960s found value in supplementing the replacement of lost blood with both whole blood and a balanced salt solution [14, 15]. A suggested treatment algorithm for trauma patients presenting to the emergency room in hemorrhagic shock proposed using a large-gauge needle or catheter to immediately infuse 1000 to 2000 mL of crystalloid (i.e., lactated Ringer’s solution or 5% dextrose in water) over the course of approximately 45 minutes. While the fluids were being infused, the patient’s blood was typed and cross-matched so that whole blood could later be administered [16–18]. The use of crystalloids for initial resuscitation was conveyed as beneficial because it raised the blood pressure to a normal level and reduced the amount of whole blood needed by patients [16–18].

Critics of aggressive fluid resuscitation cite the abovementioned complications, while those skeptic of hypotensive resuscitation are concerned with the potential harmful effects of decreased oxygen delivery to the various tissues of the body, which could result in inadequate perfusion and subsequent organ failure [32]. Since the early 1990s, a handful of randomized controlled trials have been conducted in trauma patients either in the prehospital or in-hospital and intraoperative setting [7–11].

3. Complications Attributable to Aggressive Fluid Administration

A critique of large volume fluid resuscitation is that the administration of excessive fluid contributes to and exacerbates the lethal triad of hypothermia, acidosis, and coagulopathy, thereby increasing bleeding and mortality [21–24].

Hypothermia and acidosis inhibit the generation of thrombin and the availability of fibrinogen leading to increased or continued bleeding [25]. Trauma patients are already at an increased risk of hypothermia due to the potential to lose body heat while at the scene of the injury, through decreased heat production attributable to hemorrhagic shock and diminished oxygen consumption or from open cavities during operative procedures [4, 24]. Infusing 2 liters of 25-degree Celsius saline or lactated Ringer’s solution decreases a 70-kilogram patient’s body temperature by up to one-third of a degree Celsius [26]. Infusing warm rather than room temperature fluids is an important component of fluid resuscitation. While fluid warming prevents additional heat loss, additional measures such as warming blankets and heated trauma bays and operating rooms need to be incorporated as well [4, 25, 27].

Coagulopathy, the inability for the blood to clot, is present on admission to the hospital in approximately 25% of trauma patients [28]. Medical interventions, like giving large quantities of fluid, are thought to aggravate coagulopathy through multiple pathways. When fluids are given, the increased blood pressure may cause the thrombus that was forming to become dislodged, thus contributing to continued bleeding [29]. Large volumes of fluid can also dilute the coagulation products that are within the blood, especially if the fluids used to replace lost blood do not contain platelets or other clotting factors [4, 21, 29].

Lastly, large volume fluid resuscitation has been associated with increased mortality [7, 10, 30] and other comorbid conditions [21, 29]. Among a blunt trauma population, Kasotakis et al. found large volume crystalloid fluid resuscitation was not associated with increased mortality, but it was associated with many complications including acute lung injury/adult respiratory distress syndrome, multiple organ failure, abdominal compartment syndrome, and surgical site infections. Additionally, time on the ventilator, intensive care length of stay, and the overall hospital length of stay were increased in patients with higher volumes of crystalloid resuscitation [31].

4. Aggressive versus Hypotensive Fluid Administration

Critics of aggressive fluid resuscitation cite the abovementioned complications, while those skeptic of hypotensive resuscitation are concerned with the potential harmful effects of decreased oxygen delivery to the various tissues of the body, which could result in inadequate perfusion and subsequent organ failure [32]. Since the early 1990s, a handful of randomized controlled trials have been conducted in trauma patients either in the prehospital or in-hospital and intraoperative setting [7–11].

5. Hypotensive Resuscitation Randomized Controlled Trials

Five randomized controlled trials have been conducted over the past 30 years to explore the differences between restricted and aggressive fluid administration. None of these studies were conducted in pregnant women.

Bickell et al. conducted the landmark prospective, randomized study examining immediate versus delayed fluid resuscitation among penetrating trauma patients, which found greater survival in patients treated with delayed resuscitation compared to immediate resuscitation. Patients ≥16 years old who suffered a penetrating torso injury and had a systolic blood pressure (SBP) of 90 mmHg or lower were included in this trial. The intervention was conducted in the prehospital setting. The immediately resuscitated group received rapid infusion of Ringer’s solution while being transferred to the hospital; fluid administration was continued at the hospital if the SBP was below 100 mmHg.
The delayed resuscitation group did not receive fluids in-route or when initially arriving at the hospital. With the exception of the fluid administration described, both groups were otherwise treated following the same protocol. Both groups could receive fluids once under anesthesia to maintain prespecified vitals in the operating room. Over approximately 3 years, 598 patients completed the study, of which 51.7% were immediately resuscitated and 48.3% received delayed resuscitation. In addition to increased survival in the delayed versus immediate resuscitation group (70% versus 62%, \( p = 0.04 \)), the delayed group had a shorter hospital length of stay. No differences were found between groups in the rates of respiratory distress syndrome, sepsis, acute renal failure, coagulopathy, wound infection, or pneumonia [7].

Turner et al. did not randomize trauma patients but rather paramedics, in order to examine the effect of the intravenous fluid administration policy that was being used to treat trauma patients in the prehospital setting. In this study, paramedics followed one of two protocols and crossed over to the opposite protocol halfway through the study. In Protocol A, intravenous fluids were administered at the scene to all adult trauma patients who would typically receive intravenous fluids. In Protocol B, fluids were withheld from the patients until arrival at the hospital or were given in a delayed manner when the time to the hospital was scheduled to take over one hour. Over 17 months, 1309 patients were randomized into the study; 699 (53.4%) followed Protocol A and 610 (46.6%) were treated by Protocol B. There was no difference in mortality at 6 months after the injury; 73 (10.4%) people in Protocol A died and 60 (9.8%) people following Protocol B died. There was no difference between the two groups in the number of patients with at least one of the following complications: adult respiratory distress syndrome, sepsis, acute renal failure, coagulopathy, wound infection, pneumonia, fat embolism, or pulmonary embolism. While the study included all trauma patients, the population was primarily made up of blunt injuries; only 24 (1.8%) penetrating injuries occurred in the study. Finally, the protocol compliance was poor. Only 31% of patients in Protocol A actually received intravenous fluids [8].

The third randomized controlled trial by Dutton et al. studied blunt and penetrating trauma patients with ongoing hemorrhage and at least one SBP < 90 mmHg. At the hospital, patients were prospectively randomized to a conventional group that received fluid administration to reach SBP > 100 mmHg while those in the low group received fluid to target SBP of 70 mmHg. A combination of crystalloid or blood products was used. For both groups, fluid administration ceased after reaching the target blood pressure. During a 20-month enrollment period, 110 patients were enrolled in the study with half of the patients (\( n = 55 \)) in each group. Interestingly, despite a target SBP of 70 mmHg and greater than 100 mmHg, the average SBP during bleeding was 100 ± 17 and 114 ± 12 (\( p < 0.001 \)), respectively. No difference was found in the in-hospital mortality when trauma patients with hemorrhage were resuscitated at the hospital with conventional (target SBP > 100 mmHg) and low (target SBP: 70 mmHg) strategies. Perhaps the higher-than-intended SBP in the low group contributed to the equal number of deaths in each group (\( n = 4 \) per group). Among the four patients in the conventional group who died, two patients died while actively hemorrhaging and the other two died of multiple organ failure. In the low strategy resuscitation group, 3 patients died while actively hemorrhaging and one died from fulminating hepatic failure after suffering a grade V blunt liver injury that required a near total resection and embolization. This study only examined overall in-hospital mortality and did not look at mortality at different time points or additional complications [9].

An out-of-hospital, prospective, randomized pilot trial conducted by Schrieber et al. assessed the feasibility and safety of hypotensive resuscitation for the early resuscitation of patients with traumatic shock due to blunt or penetrating trauma. Trauma patients who were older than 15 years with an out-of-hospital SBP of ≤ 90 mmHg were studied. Patients randomized to standard resuscitation received an initial 2 L bolus of fluid with additional fluid given to maintain SBP of 110 mmHg. In the controlled resuscitation group, a 250 mL bolus of fluid was only given to maintain SBP of 70 mmHg. The early resuscitation efforts continued until two hours into the hospital stay or until the hemorrhage was under control, whichever came first. One hundred ninety-two patients were randomized; 95 (49.5%) received standard resuscitation and 97 (50.5%) underwent controlled resuscitation. Patients who were randomized to controlled resuscitation received approximately 1 L less of fluid during the early resuscitation period than those with standard resuscitation. While the difference in 24-hour mortality (5.2% versus 14.7%) and in-hospital mortality (8.4% versus 16.5%) was not statistically significant between groups, it did favor controlled resuscitation. Interestingly, when injury type was examined, the blunt trauma subgroup that received controlled resuscitation had decreased mortality (3.2% versus 17.7%; adjusted odds ratio: 0.17; 95% confidence interval: 0.03–0.92). No statistically significant differences were observed in the need for major surgical procedures, renal function, ICU-free days, or ventilator-free days. Schreiber et al. concluded that hypotensive resuscitation is feasible and safe for the initial resuscitation of trauma patients [10].

Most recently, Carrick et al. published the results of their study that included younger patients (14–45 years) with penetrating injury who underwent a laparotomy or thoracotomy to control hemorrhaging; the hypotensive resuscitation strategy was implemented intraoperatively. The experimental group had a targeted minimum mean arterial pressure (MAP) for resuscitation of 50 mmHg (LMAP) and the control group targeted a minimum MAP of 65 mmHg (HMAP). The trial enrolled 168 patients (86 LMAP, 82 HMAP). In the end, this trial was terminated early due to temporal changes in processes of care, lack of equipoise, slow accrual, and futility and therefore was underpowered and unable to demonstrate an improvement in 30-day mortality. While there was a 5% difference in mortality favoring the hypotensive group, this was not statistically significant. Secondary complications were examined; no differences were noted between the two study groups in acute myocardial infarction, stroke, renal failure, hypotension, coagulopathy, thrombocytopenia, anemia, and infection (\( p > 0.05 \) for all). Acute renal injury
was significantly higher in the HMAP group (13% versus 30%, \( p = 0.01 \)). Like in the Dutton et al. study [9], although the LMAP and HMAP study groups had different target intraoperative MAPs, no difference was observed in the mean MAPs recorded intraoperatively (65.5 ± 11.6 mmHg versus 69.1 ± 13.8 mmHg, \( p = 0.07 \)). While the mean MAP for each patient was not statistically different between groups, when analyzing each intraoperative mean arterial pressure recorded approximately every 20 seconds, the amount of time spent below the target MAP was significantly less for the LMAP group compared to the HMAP group (12.6% versus 35.2%, \( p < 0.001 \)). This suggests that it is not as difficult for a patient to independently maintain an intraoperative MAP above 50 mmHg as it is to maintain one above 65 mmHg [11].

In the brief descriptions of the randomized controlled trials above and in Tables 1 and 2, it is evident that each study takes place in a slightly different location, with differing populations and various fluid administration protocols. Three of the studies were conducted in the prehospital setting [7, 8, 10] and two were conducted upon arrival to the hospital [9] or intraoperatively [11]. Two studies were conducted within only penetrating trauma populations [7, 11], whereas three examined blunt or penetrating traumas [8–10]. Three studies excluded patients with a known or suspected head injury [9–11]. The studies by Turner et al. and Schreiber et al. specifically excluded burn patients [8, 10]. To be included in the Bickell et al. and Carrick et al. studies, a patient had to have an operative procedure performed [7, 11]. Finally, the fluid administration process for each study varied; Bickell et al. and Turner et al. gave a specified amount of fluid regardless of vitals [7, 8], Dutton et al. and Schreiber et al. gave fluid to a targeted SBP [9, 10], and Carrick et al. administered fluid to a targeted MAP [11].

Though the outcomes of each study differed, none of the studies found restricted fluid resuscitation to be harmful or worse than large volume fluid resuscitation (Tables 1 and 2). Bickell et al.’s prehospital study was the only study that found significantly increased survival in patients who received delayed fluid resuscitation compared to those in the immediate resuscitation group (70% versus 62%, \( p = 0.04 \)) [7]. The other four studies did not find a significant difference in mortality. However, mortality at 24 hours (5.2% versus 14.7%) [10], in-hospital mortality (8.4% versus 16.5%) [10], and 30-day mortality (21.4% versus 26.3%) [11] appeared to favor the hypotensive group in two of the studies, of which one was conducted in the prehospital setting and one was performed in the hospital. Additionally, a subgroup analysis found the blunt trauma patients that received controlled resuscitation had decreased mortality compared to those with standard resuscitation (3.2% versus 17.7%; adjusted odds ratio: 0.17; 95% confidence interval: 0.03–0.92) [29]. Overall, it is hard to compare the mortality findings between studies, as each study assessed mortality at slightly different time points.

Secondary outcomes and complications were examined in four of the five randomized trials. In the three prehospital studies, Bickell et al. and Turner et al. found no difference between treatment groups in the rates of respiratory distress syndrome, sepsis, acute renal failure, coagulopathy, wound infection, or pneumonia [7, 8]; Schreiber et al. found no differences in the need for major surgical procedures, renal function, ICU-free days, or ventilator-free days [10]. In Carrick et al.’s in-hospital study, no differences were found in the rate of acute myocardial infarction, stroke, renal failure, hypotension, thrombocytopenia, coagulopathy, anemia, or infection between groups [11]. A longer length of stay [7] and increased acute renal injury [11] were found to be significantly higher in the groups that received more aggressive fluid administration.

It is challenging to determine whether the studies with prehospital interventions or in-hospital interventions produce better outcomes. As shown in Tables 1 and 2, each study within the prehospital time period and in-hospital time period was conducted in different populations and with different interventions. Yet there were also similarities across the groups. Additionally, each randomized controlled trial has limitations. In the Bickell et al. study, very short transport times were reported from the scene of the injury to the hospital, which may not be generalizable to all geographic locations [7]. The poor compliance by the paramedics to the protocols in the Turner et al. study may have contributed to the fact that no differences in mortality were observed. Also, though both blunt and penetrating traumas were included in the study design, the population consisted predominantly of blunt trauma injuries (98%) [8]. Dutton et al.’s study included all patients, not just those needing to undergo surgery; some of the patients (13.5%) were able to spontaneously undergo hemostasis without needing an operative procedure. Perhaps the injuries to these patients were not severe enough to need hypotensive resuscitation [9]. This limitation is echoed in the Schreiber et al. study who declared that the SBP of 90 mmHg or lower might not be low enough to exclude minimally injured patients since two-thirds of their patients had an Injury Severity Score lower than 15 [10]. Lastly, the randomized controlled trial by Carrick et al. was stopped early due to temporal changes in processes of care, lack of equipoise, slow accrual, and futility and therefore was not powered to see a difference in the primary outcome [11].

6. Changing Guidelines

Despite the limitations to each randomized controlled trial, the evidence is pointing towards lower blood pressure and less fluid administration, especially nonblood products. In 2013, the 9th edition of the Advanced Trauma Life Support (ATLS) course made content changes related to resuscitation strategies. The new content

(i) removed the phrase aggressive resuscitation and now advocates for permissive hypotension before the control of bleeding,

(ii) suggests less crystalloid use (1 L instead of 2) and early use of plasma and platelets in patients that require massive transfusion or in those with significant anticipated blood loss [33].

Similarly, an updated European guideline on the management of bleeding and coagulopathy following major trauma
### Table 1: Prehospital randomized controlled trials’ study criteria and outcomes.

<table>
<thead>
<tr>
<th>Study</th>
<th>Study years</th>
<th>Inclusion criteria</th>
<th>Exclusion criteria</th>
<th>Study arms</th>
<th>Outcomes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bickell et al. [7]</td>
<td>11/1/1989–12/22/1992</td>
<td>(i) Being ≥16 years (ii) GSW/stab wound to torso (iii) SBP ≤ 90 mmHg</td>
<td>(i) Being pregnant (ii) Revised Trauma Score = 0 (iii) Fatal GSW to head (iv) Minor injuries not requiring surgery</td>
<td>Immediate: rapid infusion of Ringer's solution in-route to hospital Delayed: no fluids in-route to hospital</td>
<td>(i) Increased survival to hospital discharge in delayed (70%) versus immediate (62%) group (ii) Shorter hospital LOS in delayed (11 ± 24 days) versus immediate (14 ± 24 days) groups (iii) No differences in RDS, sepsis, ARF, coagulopathy, wound infection, or pneumonia</td>
</tr>
<tr>
<td>Turner et al. [8]</td>
<td>5/1996–9/1997</td>
<td>(i) Adult trauma patients treated by randomized paramedic crew with at least one of the following: (a) Hospital LOS ≥ 3 days (b) Being admitted to ICU (c) Patients who died after paramedics arrived (d) Being transferred to another hospital (e) Death within 6 months of injury and cause of death was trauma from accident</td>
<td>(i) Being pregnant (ii) Poisonings, hangings, drownings, asphyxiation (iii) Being transported to hospital by helicopter (iv) Being treated by nonrandomized paramedic or doctor (v) Being dead before paramedics arrived at scene (vi) Superficial skin injuries (vii) Any patient with burns (viii) Having the following at admission: isolated fractured neck of femur, single pubic rami fracture, simple facial injury, simple spinal sprain (ix) Patients in “major incidents” (x) Being &lt;16 years (xi) Patients treated by EMT only (xii) Patients referred by GP</td>
<td>Protocol A: fluids started at the scene Protocol B: fluids withheld until hospital arrival</td>
<td>(i) No difference in mortality at 6 months for patients in Protocol A (10.4%) versus Protocol B (9.8%) (ii) No differences in the hospital or ICU LOS (iii) No differences in the proportion of patients with complications</td>
</tr>
<tr>
<td>Schreiber et al. [10]</td>
<td>3/2012–4/2013</td>
<td>(i) Blunt or penetrating trauma (ii) Being &gt;15 years (iii) SBP ≤ 90 mmHg (iv) No evidence of severe head injury (v) GCS &gt; 8</td>
<td>(i) Being pregnant (ii) Receiving &gt; 250 mL of fluid before randomization (iii) Receiving CPR by EMS (iv) Drowning (v) Asphyxia due to hanging (vi) Burns on &gt;20% of body (vii) Being incarcerated (viii) &gt;4 hours between call to dispatch and intervention (ix) Ground level falls* (x) Bilateral paralysis*</td>
<td>Standard: initial 2 L bolus of fluid with additional fluid to maintain SBP of 110 mmHg Controlled: 250 mL bolus of fluid to maintain SBP of 70 mmHg</td>
<td>(i) No differences in 24-hour mortality (5.2% versus 14.7%) or in-hospital mortality (8.4% versus 16.5%) for the controlled versus standard resuscitation groups, respectively (ii) Blunt trauma subgroup with controlled resuscitation had decreased mortality (3.2% versus 17.7%) (iii) No differences in major surgical procedures, renal function, ICU-free days, or ventilator-free days</td>
</tr>
</tbody>
</table>

*Exclusions added as the study progressed.
Italicized outcomes are statistically significant, *p* < 0.05.
ARF: acute renal failure; CPR: cardiopulmonary resuscitation; EMS: emergency medical service; EMT: emergency medical technician; GCS: Glasgow coma score; GP: general practitioner; GSW: gunshot wound; ICU: intensive care unit; LOS: length of stay; RDS: respiratory distress syndrome; SBP: systolic blood pressure.
Table 2: In-hospital randomized controlled trials’ study criteria and outcomes.

<table>
<thead>
<tr>
<th>Study</th>
<th>Study years</th>
<th>Inclusion criteria</th>
<th>Exclusion criteria</th>
<th>Study arms</th>
<th>Outcomes</th>
</tr>
</thead>
</table>
| Dutton et al. [9]         | 1996–1999          | (i) Arrival at hospital directly from scene  
(ii) Ongoing hemorrhage  
(iii) SBP < 90 mmHg in first hour after injury | (i) Being pregnant  
(ii) Central nervous system injury and altered consciousness or motor function  
(iii) Being >55 years  
(iv) History of diabetes or CAD | Conventional: received fluid to a target SBP > 100 mmHg  
Low: received fluid to a target SBP of 70 mmHg | (i) No difference in in-hospital mortality (7.3% in each group) |
(ii) SBP ≤ 90 mmHg  
(iii) Emergent laparotomy or thoracotomy to control bleeding | (i) Being pregnant  
(ii) Blunt trauma  
(iii) Being <14 years or >45 years  
(iv) Known or suspected head injury  
(v) Being incarcerated  
(vi) Those with “opt-out” bracelet | HMAP: targeted intraoperative minimum MAP = 65 mmHg  
LMAP: targeted intraoperative minimum MAP = 50 mmHg | (i) No differences in 30-day mortality (21.4% versus 26.3%) or 24-hour mortality (13% versus 20%) for LMAP and HMAP groups, respectively  
(ii) No differences in acute MI, stroke, renal failure, hypotension, coagulopathy, thrombocytopenia, anemia, or infection between groups  
(iii) Increased acute renal injury in the HMAP group (30% versus 13%) |

Italicized outcomes are statistically significant, \( p < 0.05 \).

CAD: coronary artery disease; HMAP: high mean arterial pressure; ICU: intensive care unit; LMAP: low mean arterial pressure; MAP: mean arterial pressure; MI: myocardial infarction; SBP: systolic blood pressure.
was published in 2013. These recommendations were formulated and graded according to the Grading of Recommendations Assessment, Development, and Evaluation (GRADE) hierarchy of evidence [34]. In this update, there were 37 recommendations covering initial resuscitation and prevention of further bleeding; diagnosis and monitoring of bleeding; tissue oxygenation, fluid, and hypothermia; rapid control of bleeding; and management of bleeding and coagulation. The recommendation specific to hypotensive resuscitation states the following:

(i) “We recommend a target systolic blood pressure of 80 to 90 mmHg until major bleeding has stopped in the initial phase following trauma without brain injury.” (Grade IC)

(ii) “We recommend that a mean arterial pressure ≥80 mmHg be maintained in patients with combined hemorrhagic shock and severe TBI (GCS ≤ 8).” (Grade IC)

These guidelines also provide a caveat in that patients with TBI and spinal injuries are contraindicated to the hypotensive approach, and careful consideration must be given when treating elderly patients or those with chronic arterial hypertension [35].

7. Conclusion

Optimal resuscitation strategies have been examined for nearly a century, more recently with several randomized controlled trials. The randomized controlled trials have demonstrated that aggressive fluid resuscitation in the prehospital and hospital setting leads to more complications than hypotensive resuscitation, with disparate findings on the survival benefit. Recent changes to the ATLS and European guidelines reflect the findings from the randomized controlled trials as well as observational studies and now advocate for lower target blood pressures in trauma patients. Still, since the populations studied in each trial are slightly different, as is the timing of intervention and the targeted vitals, there is still a need for a large, multicenter trial that can examine the benefit of hypotensive resuscitation in both blunt and penetrating trauma patients.

Competing Interests

The authors declare that there are no competing interests regarding the publication of this paper.

References


Research Article

The Effect of the Duration of Basic Life Support Training on the Learners’ Cardiopulmonary and Automated External Defibrillator Skills

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Background. Basic life support (BLS) training with hands-on practice can improve performance during simulated cardiac arrest, although the optimal duration for BLS training is unknown. This study aimed to assess the effectiveness of various BLS training durations for acquiring cardiopulmonary resuscitation (CPR) and automated external defibrillator (AED) skills.

Methods. We randomised 485 South Korean nonmedical college students into four levels of BLS training: level 1 (40 min), level 2 (80 min), level 3 (120 min), and level 4 (180 min). Before and after each level, the participants completed questionnaires regarding their willingness to perform CPR and use AEDs, and their psychomotor skills for CPR and AED use were assessed using a manikin with Skill-Reporter™ software.

Results. There were no significant differences between levels 1 and 2, although levels 3 and 4 exhibited significant differences in the proportion of overall adequate chest compressions \( p < 0.001 \) and average chest compression depth \( p = 0.003 \). All levels exhibited a greater posttest willingness to perform CPR and use AEDs \( \text{all, } p < 0.001 \). Conclusions. Brief BLS training provided a moderate level of skill for performing CPR and using AEDs. However, high-quality skills for CPR required longer and hands-on training, particularly hands-on training with AEDs.

1. Introduction

Bystander-initiated cardiopulmonary resuscitation (CPR) is critical to ensuring successful resuscitation in cases of out-of-hospital cardiac arrest [1]. Thus, layperson CPR training was initiated during the late 1970s by the American Heart Association, and many studies have highlighted that CPR education enhances the rates of bystander CPR [2, 3]. However, the bystander CPR rate remains relatively low and is a major obstacle to improving the survival rate for cases of out-of-hospital cardiac arrest [4, 5]. Several studies have indicated that a lack of CPR knowledge, anxiety regarding an adverse CPR outcome, and reluctance to perform mouth-to-mouth breathing all contribute to the low bystander CPR rate [6, 7]. Therefore, many efforts have been made to develop programs that provide basic life support (BLS) training. Recent studies have demonstrated the relative effectiveness of interactive computer- and video-based synchronous practice instruction, compared to conventional instructor-led courses [8, 9]. Furthermore, hands-only CPR is recommended for bystanders who are unwilling or unable to perform conventional CPR with mouth-to-mouth breathing [10]. Despite the effectiveness of BLS training for improving learners’ performance during simulated cardiac arrest, there are few studies regarding the optimal duration of BLS training [11]. Thus, the present study aimed to compare the effectiveness of various durations of BLS training, based on the acquisition of CPR- and automated external defibrillator (AED-) related skills, and the willingness and confidence of bystanders to perform CPR and apply an AED.
2. Materials and Methods

2.1. Study Design and Subjects. This study was funded by the Korean Centers for Disease Control & Prevention and approved by the institutional review board of Kangdong Sacred Heart Hospital. All participants were nonmedical college students who volunteered and provided their written informed consent. The participants received free BLS training between March 2015 and August 2015, as well as souvenirs that were worth approximately 10 American dollars.

During 2012, the Korean Centers for Disease Control & Prevention and the Korean Association of Cardiopulmonary Resuscitation (KACPR) developed four levels of BLS training for laypersons. For the present study, we randomly assigned participants to one of these four levels of BLS training: level 1 (hands-only CPR, 40 min), level 2 (hands-only CPR, 80 min), level 3 (conventional CPR, 120 min), and level 4 (conventional CPR, 180 min). Each course was administered to ≤35 participants, and a total of 16 courses (4 courses for each level) were provided during this study. Twenty-five instructors led these courses, and all instructors were doctors, nurses, or emergency medical technicians who were registered and certified as BLS instructors by the KACPR. All instructors were educated regarding the study's protocol. All BLS training courses were administered under instructor supervision, and training was provided using manikins and an AED-trainer; mouth-to-mouth breathing was performed using a face shield. All participants completed a questionnaire survey before and after each level of BLS training. At the end of each level, their CPR skills were also tested over 2 min using the Resusci Anne® manikin with Skill-Reporter software, and their AED-related skills were evaluated using a checklist. AED performance check list was authorized by KACPR. These tests were all supervised and conducted by certified BLS instructor.

2.2. BLS Course Format. The student-to-instructor ratio was 6:1, with at least one manikin and one AED for each group of two students. Each course was administered by first watching a video with the lead instructor and then practical training with a manikin (Little Anne®, Laerdal, Norway) and AED (AED Trainer2®, Laerdal, Norway). The specific contents of each program level are shown below and in Table I:

(i) Level 1 (hands-only CPR, 40 min): introducing the participants to the course, showing a case of cardiac arrest, recognizing cardiac arrest and asking for help, teaching chest compressions, hands-on practice for hands-only CPR, introducing an AED and how to use it, introducing mouth-to-mouth breathing, and a course summary.

(ii) Level 2 (hands-only CPR, 80 min): all level 1 contents, as well as hands-on practice with an AED and hands-on practice of hands-only CPR with an AED.

(iii) Level 3 (conventional CPR, 120 min): all level 2 contents, as well as hands-on practice of mouth-to-mouth breathing, hands-on practice of conventional CPR, and hands-on practice of conventional CPR with an AED.

(iv) Level 4 (conventional CPR, 180 min): all level 3 contents, as well as a BLS skill test using an AED, and providing feedback regarding CPR and AED skills.

2.3. Questionnaire. We modified a questionnaire from a previous study, which contained three parts: (a) the participant's demographics (age and sex) and experience with BLS training, (b) self-assessed confidence to perform bystander CPR and apply an AED, and (c) willingness to perform bystander CPR [6]. The self-assessed confidence to perform bystander CPR and apply an AED was evaluated using a visual analogue scale, with a score of 0 indicating "completely unable to perform CPR or use an AED" and a score of 100 indicating "able to confidently perform CPR or use an AED." The participants rated their willingness to perform CPR and use an AED using a 5-point Likert-type scale, with the scores categorized as "definitely no" (score 1), "no" (score 2), "not sure" (score 3), "probably yes" (score 4), and "definitely yes" (score 5).

2.4. Statistical Analysis. All statistical analyses were performed using SPSS software (version 19.0; SPSS Inc., Chicago, IL). Categorical variables were reported as number and percentage, and continuous variables were reported as mean and standard deviation (normal distribution) or median and interquartile range (IQR; nonnormal distribution). The willingness to perform CPR and use an AED before and after each level of the BLS training program was compared using the McNemar test, and confidence to perform CPR and use an AED was compared using the Wilcoxon signed rank test. Analysis of CPR quality among the four levels was performed using the chi-square test for categorical variables and using one-way analysis of variance (normal distribution) or the Kruskal-Wallis method (nonnormal distribution) for continuous variables. Post hoc paired comparisons between the levels were performed using the Mann-Whitney U test with Bonferroni corrections. All tests were two-tailed, and differences with a p value of <0.05 were considered statistically significant.
3. Results

3.1. Demographic Characteristics. A total of 502 participants signed up for and completed the BLS training. However, we excluded 10 participants who submitted incomplete questionnaires and 7 participants who had an error during the CPR quality check using the skill reporter. Therefore, 485 participants were included in the analyses. There was a significant, albeit small, difference when we compared the participants’ ages for the various levels (21 years for levels 1-2 and 20 years for levels 3-4). However, there were no significant differences in the participants’ sex, height, weight, body mass index, and prior BLS training. Among the 485 participants, 309 (63.7%) participants did not have prior BLS training experience (Table 2).

3.2. Analysis of CPR Quality according to Experience and Program Level. We analysed the CPR quality results among all participants and the novice participants. Among all participants, level 4 group had better CPR quality results (average compression depth and proportion of overall adequate compressions), compared to levels 1-3. There was no significant difference in the average compression rate, depth, and proportion of overall adequate compressions when we compared levels 1 and 2. However, the average compression depth exhibited a significant difference between level 3 (median: 51 mm, IQR: 44–57 mm) and level 4 (median: 55 mm, IQR: 50–59 mm; p = 0.003), and the proportion of overall adequate compressions also exhibited a significant difference between level 3 (median: 30.9%, IQR: 3.2–69.3%) and level 4 (median: 74.4%, IQR: 24.8–92.9%; p < 0.001). Post hoc paired comparison between levels 2 and 3 showed no difference in proportion of adequate compression depth (p = 0.119). The proportion of adequate recoils exhibited a significant difference among levels 1–4 (p = 0.006), and the post hoc paired comparison revealed a significant difference between level 1 and level 3 (p = 0.001). Only levels 3 and 4 involved mouth-to-mouth breathing, and there was no significant difference between level 3 (median: 25.0%, IQR: 0–44.4%) and level 4 (median: 20%, IQR: 0–50%; p = 0.825) (Table 3).

When we analysed only the novice participants, the proportion of overall adequate compressions exhibited a significant difference between level 3 (median: 29.8%, IQR: 2.4–67.8%) and level 4 (median: 56.7%, IQR: 9.8–88.9%; p = 0.008) (Supplemental Table 1 in Supplementary Material available online at http://dx.doi.org/10.1155/2016/2420568).

3.3. Analysis of AED Use according to Program Level. AED use was evaluated using a checklist at all steps for each level and between the various levels, with the highest performance observed in level 4. The correct location for the AED pads was observed for 85 (70.2%) participants in level 1, 107 (89.9%) participants in level 2, 114 (91.9%) participants in level 3, and 112 (92.6%) participants in level 4 (p < 0.001). The correct “immediate chest compression after shock” step was observed for 30 (24.8%) participants in level 1, 105 (88.2%) participants in level 2, 96 (77.4%) participants in level 3, and 110 (90.9%) participants in level 4 (p < 0.001). All participants successfully administered the shock within 90 s, although significant differences were observed when we compared to level 1 (median: 59 s, IQR: 55–65 s), level 2 (median: 53 s, IQR: 50–60 s), level 3 (median: 55 s, IQR: 50–60 s), and level 4 (median: 52 s, IQR: 48–56 s) (p < 0.001) (Table 4). The post hoc analysis revealed that level 1 participants exhibited poor performance for every step, except for “turn on the AED” step, compared to all other levels. The analysis of the novice group provided the same results as the analysis of all participants.

3.4. Effect of BLS Training on Willingness and Confidence to Perform Bystander CPR and Use an AED. The willingness to perform bystander CPR increased after BLS training, although there was no significant difference between the various levels. The willingness to use an AED also increased after BLS training, although there was no significant difference between the various levels. The self-assessed confidence in performing bystander CPR and using an AED increased after BLS training, although there was no significant difference between the various levels (Table 5). The analysis of the novice group provided the same results as the analysis of all participants.

4. Discussion

Our results confirmed that a relatively short duration of training improves CPR quality and the bystander’s attitude towards CPR and AED use, although a longer duration of training was needed to achieve optimal CPR quality and AED use. Similarly, several previous studies have reported that relatively short durations of training improved CPR quality. For example, Hirose et al. reported improvements in CPR quality after a 45 min CPR training program using a personal manikin [12]. In the present study, level 1 (hands-only, 40 min) achieved an average compression rate of 122/min and a median compression depth of 51 mm, although the median of proportion of overall adequate compressions was 27.0%, which was lower than those for the other levels. This difference may be due to improper positioning of the chest compression site. In contrast, Panchal et al. evaluated ultra-brief video training and found that the median compression depth was 37 mm, which was not significantly different from that in their control group [13]. This difference may indicate that BLS training is limited when it is not led by an instructor and that there is some baseline training duration that is needed to achieve a significant improvement. For example, levels 1 and 2 provided similar CPR quality-related outcomes, although level 2 provided better AED use scores. Thus, level 2 may be more appropriate for general training regarding CPR and AED use.

When we compared levels 3 and 4 (120 min and 180 min of conventional CPR), we observed that level 4 provided better CPR quality-related outcomes. Similarly, Andresen et al. have reported that a longer duration of training improves CPR quality [14]. In this context, level 3 included 70 min of hands-on training, and level 4 included 100 min of hands-on training; the 30 min difference included hands-on skills testing.
### Table 2: The characteristics of the 485 participants.

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Program level</th>
<th>1 (n = 121)</th>
<th>2 (n = 119)</th>
<th>3 (n = 124)</th>
<th>4 (n = 121)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (y/o)</td>
<td></td>
<td>21.0 (19.0–22.0)</td>
<td>21.0 (19.0–22.0)</td>
<td>20.0 (19.0–21.0)</td>
<td>20.0 (19.0–22.0)</td>
<td>0.003</td>
</tr>
<tr>
<td>Sex (male)†</td>
<td></td>
<td>55 (45.5%)</td>
<td>49 (41.2%)</td>
<td>52 (41.9%)</td>
<td>46 (38.0%)</td>
<td>0.707</td>
</tr>
<tr>
<td>Height (cm)</td>
<td></td>
<td>168.0 (162.5–175.0)</td>
<td>168.0 (162.0–174.0)</td>
<td>169.0 (163.0–174.8)</td>
<td>168.0 (163.0–175.0)</td>
<td>0.764</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td></td>
<td>59.0 (53.0–70.0)</td>
<td>56.0 (51.0–68.0)</td>
<td>57.0 (52.0–66.8)</td>
<td>57.0 (51.0–68.0)</td>
<td>0.616</td>
</tr>
<tr>
<td>Body mass index (kg/m²)</td>
<td></td>
<td>20.8 (19.6–23.2)</td>
<td>20.4 (19.2–22.2)</td>
<td>20.2 (19.2–22.1)</td>
<td>20.5 (19.3–22.1)</td>
<td>0.205</td>
</tr>
<tr>
<td>Prior BLS training†</td>
<td></td>
<td>48 (39.7%)</td>
<td>34 (28.6%)</td>
<td>46 (37.1%)</td>
<td>48 (39.7%)</td>
<td>0.231</td>
</tr>
</tbody>
</table>

All values were calculated using the Kruskal-Wallis method and expressed as median (interquartile range).

†Chi-square test (n, %).

BLS: basic life support.

### Table 3: Comparing cardiopulmonary resuscitation quality among all participants according to program level.

<table>
<thead>
<tr>
<th>Quality variables during CPR</th>
<th>Program level</th>
<th>1 (n = 121)</th>
<th>2 (n = 119)</th>
<th>3 (n = 124)</th>
<th>4 (n = 121)</th>
<th>Between 1 and 2‡</th>
<th>Between 3 and 4‡</th>
<th>Among 1–4†</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of total compressions</td>
<td></td>
<td>225.0</td>
<td>216.0</td>
<td>150.0</td>
<td>148.0</td>
<td>0.018</td>
<td>0.734</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Average compression rate (per min)</td>
<td></td>
<td>122.0</td>
<td>120.0</td>
<td>120.0</td>
<td>119.0</td>
<td>0.037</td>
<td>0.467</td>
<td>0.110</td>
</tr>
<tr>
<td>Average compression depth (mm)</td>
<td></td>
<td>51.0</td>
<td>52.0</td>
<td>51.0</td>
<td>55.0</td>
<td>0.367</td>
<td>0.003</td>
<td>0.001</td>
</tr>
<tr>
<td>Proportion of adequate compression depth (%)</td>
<td></td>
<td>63.2</td>
<td>82.5</td>
<td>68.1</td>
<td>91.7</td>
<td>0.252</td>
<td>0.023</td>
<td>0.053</td>
</tr>
<tr>
<td>Proportion of adequate recoil (%)</td>
<td></td>
<td>100.0</td>
<td>100.0</td>
<td>100.0</td>
<td>100.0</td>
<td>0.050</td>
<td>0.170</td>
<td>0.006</td>
</tr>
<tr>
<td>Proportion of overall adequate compression (%)</td>
<td></td>
<td>27.0</td>
<td>42.7</td>
<td>30.9</td>
<td>74.4</td>
<td>0.094</td>
<td>&lt;0.001</td>
<td>&lt;0.001**</td>
</tr>
<tr>
<td>Number of mouth-to-mouth breaths</td>
<td></td>
<td>—</td>
<td>—</td>
<td>8.0</td>
<td>8.0</td>
<td>—</td>
<td>0.368</td>
<td>—</td>
</tr>
<tr>
<td>Average ventilation volume (mL)</td>
<td></td>
<td>—</td>
<td>—</td>
<td>591.0</td>
<td>648.0</td>
<td>—</td>
<td>0.733</td>
<td>—</td>
</tr>
<tr>
<td>Proportion of adequate mouth-to-mouth breathing (%)</td>
<td></td>
<td>—</td>
<td>—</td>
<td>25.0</td>
<td>20.0</td>
<td>—</td>
<td>0.825</td>
<td>—</td>
</tr>
<tr>
<td>Hands-off time (s)</td>
<td></td>
<td>15.0</td>
<td>15.0</td>
<td>52.0</td>
<td>50.0</td>
<td>0.420</td>
<td>0.093</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

†Post hoc paired comparisons between the levels were performed using the Mann-Whitney U test with Bonferroni corrections (statistical significance was p < 0.0083).

‡Calculated using the Kruskal-Wallis method.

*Post hoc paired comparisons between levels 1 and 4 (p < 0.001) and levels 2 and 4 (p < 0.006).

**Post hoc paired comparisons between levels 1 and 4 (p < 0.001).

CPR: cardiopulmonary resuscitation.

### Table 4: Comparing automated external defibrillator application among all participants according to program level.

<table>
<thead>
<tr>
<th>Program level</th>
<th>1 (n = 121)</th>
<th>2 (n = 119)</th>
<th>3 (n = 124)</th>
<th>4 (n = 121)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Turn on the AED</td>
<td>Correct</td>
<td>115 (95.0%)</td>
<td>114 (95.8%)</td>
<td>119 (96.0%)</td>
<td>120 (99.2%)</td>
</tr>
<tr>
<td>Correct location of AED pads</td>
<td>Correct</td>
<td>85 (70.2%)</td>
<td>107 (89.9%)</td>
<td>114 (91.9%)</td>
<td>112 (92.6%)</td>
</tr>
<tr>
<td>Clear during analysis</td>
<td>Correct</td>
<td>50 (41.3%)</td>
<td>104 (87.4%)</td>
<td>104 (83.9%)</td>
<td>110 (90.9%)</td>
</tr>
<tr>
<td>Clear before shock</td>
<td>Correct</td>
<td>44 (36.4%)</td>
<td>95 (79.8%)</td>
<td>95 (76.6%)</td>
<td>108 (89.3%)</td>
</tr>
<tr>
<td>Immediate chest compression after shock</td>
<td>Correct</td>
<td>30 (24.8%)</td>
<td>105 (88.2%)</td>
<td>96 (77.4%)</td>
<td>110 (90.9%)</td>
</tr>
<tr>
<td>Time from AED arrival until shock†</td>
<td></td>
<td>59.0 (55.0–65.0)</td>
<td>53.0 (50.0–60.0)</td>
<td>55.0 (50.0–60.0)</td>
<td>52.0 (48.0–56.0)</td>
</tr>
</tbody>
</table>

†Calculated using the Kruskal-Wallis method and reported as median (interquartile range).

AED: automated external defibrillator.

Comparisons were performed using the chi-square test.

†Calculated using the Kruskal-Wallis method.
after completing the training in level 4. This additional testing and feedback appear to have helped achieve a significantly higher proportion of overall adequate compressions in level 4 (74.4%), compared to those in the other levels. Interestingly levels 2 and 3 showed similar CPR quality outcome. We assume that level 3 group had to learn mouth-to-mouth breath in their given time which could distract their concentration but, level 2 group can concentrate their skill on only compression. Therefore, these results suggest that prolonged hands-on practice and immediate instructor feedback help improve the quality of chest compressions after completing a BLS course.

Many recent studies’ results support the use of hands-only CPR for out-of-hospital CPR [15–17]. This is because hands-only CPR is as effective as conventional CPR and also because mouth-to-mouth breathing is a major barrier to bystander performance of CPR [6, 7]. Furthermore, our results indicate that levels 3 and 4 (conventional CPR training) achieved a poor quality of mouth-to-mouth breathing, even after 45 min of hands-on practice, and that the proportions of adequate mouth-to-mouth breathing were similar to the proportion in the novice group. This finding may indicate that it is important to emphasise hands-only CPR for laypersons, as a substantial amount of time would likely be needed to acquire an optimal level of skill in performing mouth-to-mouth breathing.

In the present study, we found that level 4 provided the highest score in applying an AED. In contrast, level 1 provided significantly lower scores in every step, with the exception of turning on the AED. This difference is likely related to the training in each level, as level 1 only introduced the participants to AEDs and did not include hands-on practice. Furthermore, many of the participants in level 1 did not say “clear” during their analysis and before the shock, which could lead to accidents when using AEDs, and three-quarters of the participants forgot to perform chest compressions after administering the shock. Although AEDs are intended for use by untrained laypersons [18], a short introduction without any hands-on practice does not appear to provide sufficient training for novices to adequately use these devices. Moreover, Gonzalez et al. have reported that two-thirds of laypersons can identify an AED and its purpose, although only approximately 50% of laypersons are willing to use AEDs [19]. Therefore, these results may indicate that relatively short BLS training with hands-on practice of AED is needed for laypersons to achieve satisfactory performance.

The present study demonstrated that improvements in willingness and confidence regarding CPR and applying an AED were independent of the BLS training duration. Similarly, Hirose et al. have reported that a simplified CPR training significantly increased the participants’ confidence in performing CPR and applying an AED after the training [12]. Another study has demonstrated that even self-training (by watching a 22 min video) improved willingness and confidence regarding bystander CPR [20]. Therefore, relatively short BLS training may be sufficient to improve the willingness to perform bystander CPR among the general public.

5. Study Limitations

This study has several limitations that warrant consideration when interpreting our findings. First, every BLS course was administered by a qualified BLS instructor, but different combinations of the instructors were assigned to the same level at each time. Therefore, the emphasis on the training content
may have varied according to each instructor’s lecturing style, although we attempted to minimise this effect by training the instructors regarding each level’s timeline. Second, the participants were all college student who were in their early twenties, which may have made them more capable of acquiring CPR and AED skills and more motivated to receive BLS training, than individuals from the general population. Therefore, the appropriate duration of BLS training may vary according to the laypersons’ demographic characteristics (e.g., age and education level).

6. Conclusions

Our results indicate that a relatively short duration of BLS training helped the participants acquire CPR- and AED-related skills. However, a longer duration of training and hands-on practice was needed to achieve a high quality of skills for performing CPR and using AEDs. Furthermore, BLS training increased the participants’ willingness and confidence to perform bystander CPR and to use an AED during cardiac arrest, regardless of the training duration.

Abbreviations

AED: Automated external defibrillator
BLS: Basic life support
CPR: Cardiopulmonary resuscitation
IQR: Interquartile range
KACPR: Korean Association of Cardiopulmonary Resuscitation

Disclosure

The Centers for Disease Control & Prevention of Korea did not have role in the study design, analysis, interpretation of the data, and the writing of the paper.

Competing Interests

The authors declare that no competing interests exist.

Authors’ Contributions

Jin Hyuck Lee and Youngsuk Cho contributed equally to this study.

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References


Research Article

Cardiopulmonary Resuscitation Pattern Evaluation Based on Ensemble Empirical Mode Decomposition Filter via Nonlinear Approaches

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Good quality cardiopulmonary resuscitation (CPR) is the mainstay of treatment for managing patients with out-of-hospital cardiac arrest (OHCA). Assessment of the quality of the CPR delivered is now possible through the electrocardiography (ECG) signal that can be collected by an automated external defibrillator (AED). This study evaluates a nonlinear approximation of the CPR given to the asystole patients. The raw ECG signal is filtered using ensemble empirical mode decomposition (EEMD), and the CPR-related intrinsic mode functions (IMF) are chosen to be evaluated. In addition, sample entropy (SE), complexity index (CI), and detrended fluctuation algorithm (DFA) are collated and statistical analysis is performed using ANOVA. The primary outcome measure assessed is the patient survival rate after two hours. CPR pattern of 951 asystole patients was analyzed for quality of CPR delivered. There was no significant difference observed in the CPR-related IMFs peak-to-peak interval analysis for patients who are younger or older than 60 years of age, similarly to the amplitude difference evaluation for SE and DFA. However, there is a difference noted for the CI ($p < 0.05$). The results show that patients group younger than 60 years have higher survival rate with high complexity of the CPR-IMFs amplitude differences.

1. Introduction

Cardiac disease and out-of-hospital cardiac arrest (OHCA) are the major healthcare problem internationally [1, 2]. Despite advances in medicine and cardiology, OHCA is still associated with a high mortality rate [3, 4]. One of the main causes of OHCA is severe ischemic heart disease, including the acute coronary artery occlusion [5–7]. According to Eisenberg et al., successful return of spontaneous circulation (ROSC) from OHCA is based on certain factors, such as the general condition of the patients, the type and vitality of the events, and the duration to bystander cardiopulmonary resuscitation (CPR) being delivered [8].

CPR is one of the fundamental links in the chain of survival in the management of the OHCA patients. When the connections between each other are well performed, the survival rate will increase significantly [9]. On the other hand, the unexpected cardiac rhythm can be escalated when one of these connections is postponed [10, 11]. An effective chest compression itself involves the application of the pressure to the sternum maintaining the flow of blood and oxygen to myocardium and brain [12]. The chest compression condition
is a dominant index of the CPR accomplishment [13–15]. In order to evaluate the CPR data, the noise is an essential concern. A filtering method can be performed in order to extract the correct information from the continuous signal. The use of empirical mode decomposition (EMD) filtering algorithm, proposed by Huang et al. [16, 17], has been used to filter signal problems, such as EMD-based filters which have also been used for narrow-band signals such as electrocardiography (ECG) [18] and blood pressure [19].

In advance, the filtered signal is extracted to achieve the information containing its characteristics. One of these methods, the entropy algorithm, was used in information theory [20] to address the nonlinearity problems. An entropy algorithm was also applied to the ECG signal studies [21, 22]. In a study by Costa et al., extended sample entropy was applied to evaluate the feature extraction of the ECG using multiscale entropy [23]. Another nonlinear method, detrended fluctuation analysis (DFA), was originally utilized for the DNA sequence [24].

Studies related to purifying the signal and extracting information for the cardiac arrest cases have been done for several years. A study utilizing a multichannel Wiener filter and a matching pursuit-like method is conducted to remove CPR artifact from the ECG trace [25]. Least mean-square (LSM) filtering has also been utilized to remove the CPR problem [26]. A new method combining the noise-assisted multivariable EMD (N-A MEMD) and LSM filtering was implemented by Lo et al. [27]. Furthermore, the application of the sample entropy has been utilized for shock outcome prediction [28] as well as multiscale entropy [29]. Detrended fluctuation analysis was utilized by Lin et al. for the study of ventricular fibrillation in OHCA cases [30]. The purpose of this study is to evaluate the CPR pattern by utilizing the EEMD to purify the CPR signal and the ECG data by applying the nonlinear algorithms to see the survival rate.

2. Data Acquisition and Algorithm

2.1. Data Acquisition. The dataset is retrospectively collected from the New Taipei City fire-based of emergency medical service (EMS). All the staff have been trained for the basic life support, early defibrillation, and advanced life support. All the ambulance units are equipped with a ForeRunner AED (Philips, Seattle, WA, USA). The ECG signal is logged into the AED card data, sampled for 200 Hz. The logging lead was placed on the patient chest [27].

This study has utilized data from the whole year of 2010. A total of 1207 patient ECGs are divided into two groups: trauma and non-trauma cardiac arrest. Focusing on the non-trauma patients only, the data is divided into another two groups: patients who had an AED shock and non-shock-able signal patients. In order to evaluate the pure CPR without any help of the AED, all the 1001 non-shock-able patients, which eventually becomes 951 sets after filtering for the quality of the data, are divided according to their age with the threshold of 60 years, as shown in Figure 1. The outcome of the patient is evaluated after 2 hours based on their conditions. The results are analyzed in MATLAB language (Mathwork Inc.).

![Figure 1: The flowchart of the CPR evaluation. *Note. The original 1001 ECG signals have to be reduced due to the quality of the data.](image-url)

2.2. Empirical Mode Decomposition-Based Filter

2.2.1. Empirical Mode Decomposition. EMD is an algorithm to decompose the specific frequency range of the data into a finite number of intrinsic mode functions (IMFs). These decomposed IMFs illustrate certain characteristics. However, for the real-world signals, the mode-mixing disturbs the regularity of the IMFs. For this reason, the ensemble empirical mode decomposition (EEMD) was proposed.

2.2.2. Ensemble Empirical Mode Decomposition. The intermittence corrupts the consistence of the IMFs. The subsequent mode function will be affected, hence the physical meaning of those IMFs that cannot be parted based on their characteristics. Wu and Huang [31] proposed EEMD using noise-assisted method to overcome this phenomenon. In EEMD, the white noise is added to the original signal to form a mixed combination of noise and signal in order to remove the intermittence and generate consistent IMFs. EEMD study was also conducted to an ECG noise filtering problem [32].

2.3. Feature Extraction Algorithms

2.3.1. Sample Entropy and Complexity Index. Entropy is known as a thermodynamics property in the evaluation of regularity. The higher the entropy means the less regular the pattern or the sequence to be recognized. For the multiscale entropy, the coarse grained time series is based on the scale factor [23]. The coarse grained time series will be evaluated by entropy algorithm. The result of the entropy corresponds to each scale which is called multiscale entropy. The complexity index (CI) is defined as measurement of the signal complexity. It is calculated by the evaluation of the area under curve of the multiscale entropy. The calculation from the recreated time series based on the coarse grained information will affect the area under the curve.

2.3.2. Detrended Fluctuation Analysis. Fractal analysis is one of the most prosperous methods to get the signal features. Detrended fluctuation analysis (DFA) is a nonstationary
algorithm for statistical analysis. A considerably physiology-related problem is a nonstationary time series one. This method is originally proposed by Peng et al. [24].

3. Results and Discussion

In this study, the original ECG logged from the AED machine was filtered by the EEMD algorithm, shown in Figures 2–4. From these figures, it can be seen that IMF 2 to IMF 4 are relatively similar to the CPR pattern having the dominant frequency as described in previous study conducted by Lo et al. [27]. Figures 5 and 6 also show the time-frequency evaluation; this shows the differences between the raw ECG and the reconstructed-CPR signal after the EEMD filter by combining the CPR-related IMFs. Figures 5(a) and 6(a) give the information about the time-frequency information. For Figure 5(a), the dominant signal occurs mostly below the CPR frequency ranges, lower than 0.5 Hz, indicated by the red area. Meanwhile, for Figure 6(a), after the EEMD filter, the dominant frequency shifts to the range of 2 Hz to 4 Hz, indicated by the red square. This filter also automatically reduces the baseline noise of the signal that can be seen by Figures 5(b) and 6(b).

All the maxima points are detected from the reconstructed IMFs that have the CPR frequency, by evaluating the changing of the slopes from positive to negative as shown in Figure 7. Furthermore, the maxima points are evaluated to obtain the maxima interval (I) and maxima amplitude differences (dA) from the IMF-combined CPR, shown in Figure 7. Furthermore, both signals, I and dA, are estimated by utilizing SE, CI, and DFA.

Evaluation of the results of the 951 ECGs from patients of non-trauma OHCA with a non-shock-able rhythm using a threshold of 60 years of age is shown in Table 1. A subgroup analysis is performed which begins for patients greater than 60 years of age: of this category 579 patients died and 116 patients survived. The mean SE value is $1.91 \pm 0.58$ and $1.87 \pm 0.56$ for dead and surviving patients, respectively ($p > 0.05$). CI for patients who died is $13.26 \pm 4.46$ and for those who survived is $13.48 \pm 4.67$ ($p > 0.05$). The DFA evaluation is $0.86 \pm 0.145$ for patients who have died and $0.833 \pm 0.136$ for those who have survived ($p > 0.05$).

A further subgroup analysis is performed for patients under 60 years of age. The total number of the patients for
Table 1: The statistical evaluation of the CPR IMFs result.

<table>
<thead>
<tr>
<th>Evaluation</th>
<th>Age</th>
<th>Feature</th>
<th>Status</th>
<th>Mean</th>
<th>Standard deviation</th>
<th>p value (p &lt; 0.05)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Interval</td>
<td>≥60 (579,116)</td>
<td>SE</td>
<td>Died</td>
<td>1.91</td>
<td>0.58</td>
<td>0.556</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Survival</td>
<td>1.87</td>
<td>0.56</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>CI</td>
<td>Died</td>
<td>13.26</td>
<td>4.46</td>
<td>0.62</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Survival</td>
<td>13.48</td>
<td>4.67</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>DFA</td>
<td>Died</td>
<td>0.86</td>
<td>0.145</td>
<td>0.06</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Survival</td>
<td>0.833</td>
<td>0.136</td>
<td></td>
</tr>
<tr>
<td>Interval</td>
<td>&lt;60 (215,41)</td>
<td>SE</td>
<td>Died</td>
<td>1.86</td>
<td>0.61</td>
<td>0.575</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Survival</td>
<td>1.81</td>
<td>0.6</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>CI</td>
<td>Died</td>
<td>13.12</td>
<td>4.9</td>
<td>0.234</td>
</tr>
<tr>
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<td></td>
<td></td>
<td>Survival</td>
<td>12.03</td>
<td>4.26</td>
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<td></td>
<td>DFA</td>
<td>Died</td>
<td>0.839</td>
<td>0.15</td>
<td>0.825</td>
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<tr>
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<td></td>
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<td>Survival</td>
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<td>0.12</td>
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<tr>
<td>Amplitude</td>
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<td>SE</td>
<td>Died</td>
<td>0.22</td>
<td>0.236</td>
<td>0.825</td>
</tr>
<tr>
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<td></td>
<td>Survival</td>
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<td>0.244</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>CI</td>
<td>Died</td>
<td>1.23</td>
<td>1.24</td>
<td>0.781</td>
</tr>
<tr>
<td></td>
<td></td>
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<td>Survival</td>
<td>1.195</td>
<td>1.184</td>
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<tr>
<td></td>
<td></td>
<td>DFA</td>
<td>Died</td>
<td>0.115</td>
<td>0.126</td>
<td>0.215</td>
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<tr>
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<td></td>
<td>Survival</td>
<td>0.099</td>
<td>0.1165</td>
<td></td>
</tr>
<tr>
<td>Amplitude</td>
<td>&lt;60 (215,41)</td>
<td>SE</td>
<td>Died</td>
<td>0.2</td>
<td>0.23</td>
<td>0.28</td>
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<tr>
<td></td>
<td></td>
<td></td>
<td>Survival</td>
<td>0.24</td>
<td>0.16</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>CI</td>
<td>Died</td>
<td>0.983</td>
<td>1.03</td>
<td>0.028*</td>
</tr>
<tr>
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<td></td>
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<td>Survival</td>
<td>1.378</td>
<td>1.173</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>DFA</td>
<td>Died</td>
<td>0.105</td>
<td>0.168</td>
<td>0.912</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Survival</td>
<td>0.1077</td>
<td>0.0983</td>
<td></td>
</tr>
</tbody>
</table>

Note. SE means sample entropy, CI complexity index, and DFA detrended fluctuation analysis; * significant different parameter.

Figure 6: EEMD-reconstructed CPR signal. (a) Time-frequency result; (b) the reconstructed signal.

Figure 7: CPR IMFs maxima information evaluation.

this class is less than half of the number of the patients older than 60 years. The observed SE is 1.86 ± 0.61 and 1.81 ± 0.6, respectively, for the patients who have died compared to those who have survived (p > 0.05). The CI is 13.12 ± 4.9 and 12.03 ± 4.26, respectively, for patients who have died compared to those who have survived. The DFA is 0.839 ± 0.15 and 0.845 ± 0.12, respectively, for patients who died and survived and also not significantly different.

On assessment of the amplitude difference, for patients aged 60 or over, patients who died had a mean SE value of 0.22 ± 0.236 and for the patients who have survived, the results are 0.226 ± 0.244 (p > 0.05). CI for patients who have died is 1.23 ± 1.24 versus 1.195 ± 1.184 for those who have survived (p > 0.05).

For cases of the category of age of less than 60 years, the SE has 0.2 ± 0.23 and 0.24 ± 0.16, respectively, of patients who have died and are alive and has no significant differences.
The CI has 0.983 ± 1.03 and 1.378 ± 1.173, respectively, for those who died and survived; this case is significantly different \( (p < 0.05) \). The DFA case creates 0.105 ± 0.168 and 0.107 ± 0.098 \( (p > 0.05) \).

In terms of the relationship of this result to the OHCA for the future applications, the focus is the automated CPR machine. According to a study by Steen et al., the automated CPR machine was very advantageous in performing the chest compression during transportation way [33]. The automated CPR also produced better pressure of end tidal carbon dioxide \( (P_{ET}\text{CO}_2) \) [34] and cortical blood flow [35] compared to the manual CPR. However, a study with 4471 patients conducted by Perkins et al., with the consistent rate and depth, shows the automated CPR is not significantly different from the manual CPR with the main outcome being the survival rate after 30 days of OHCA [36]. In another study by Smekal et al., evaluated automated and manual CPR for 75 and 73 patients, respectively, also provided no significant difference [37]. Also, Hallstrom et al. investigated a total of 554 and 517 for automated CPR and manual CPR, respectively. This study found that the automated CPR reduced the survival and made the neurological outcome worse [38]. The controversial results of the previous studies of automated and manual CPR may be due to the consistent amplitude of the automated CPR machines. By referring to our study’s results, not that consistent depth for the CPR amplitude, which can be implemented into the CPR machine for the future tests, may increase the survival rate.

### 4. Conclusions and Future Work

This study evaluates a total of 951 of the non-shock-able patient ECGs, using the ensemble empirical mode decomposition filtering and utilizing nonlinear approaches. The IMF-combined CPR maxima interval and the amplitude are evaluated. For most of the observations, there were no statistically significant differences observed. However, in the evaluation of CI for the maximal amplitude, a statistically significant difference was observed.

Based on the results, it can be concluded that for patients who are less than 60 years of age a higher survival rate was observed and was associated with more complexity in CPR amplitude differences. This result can have information that the automated CPR machine with the dynamic force may be a consideration.

This study has several limitations. Namely, when the noise interference occurred at the same frequency range of the CPR IMFs, they were included in the evaluation. This may somewhat affect the observations, especially for the slope evaluation. Furthermore, there were far more observations for patients who died than for those who survived.

For future study, the application of the advanced time-domain filter may be applied to purify the unfiltered noise on the frequency domain filter.

### Competing Interests

The authors declare no conflict of interests.

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### References


Evaluation of Bag-Valve-Mask Ventilation in Manikin Studies: What Are the Current Limitations?

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Introduction. Manikin-based studies for evaluation of ventilation performance show high heterogeneity in the analysis and experimental methods used as we pointed out in previous studies. In this work, we aim to evaluate these potential limitations and propose a new analysis methodology to reliably assess ventilation performance. Methods. One hundred forty healthcare providers were selected to ventilate a manikin with two adult self-inflating bags in random order. Ventilation parameters were analysed using different published analysis methods compared to ours. Results. Using different methods impacts the evaluation of ventilation efficiency which ranges from 0% to 45.71%. Our new method proved relevant and showed that all professionals tend to cause hyperventilation and revealed a significant relationship between professional category, grip strength of the hand keeping the mask, and ventilation performance (p = 0.0049 and p = 0.0297, resp.). Conclusion. Using adequate analysis methods is crucial to avoid many biases. Extrapolations to humans still have to be taken with caution as many factors impact the evaluation of ventilation performance. Healthcare professionals tend to cause hyperventilation with current devices. We believe this problem could be prevented by implementing monitoring tools in order to give direct feedback to healthcare professionals regarding ventilation efficiency and ventilatory parameter values.

1. Introduction

Bag-valve-mask (BVM) ventilation is mainly used in prehospital settings to ventilate patients in respiratory failure and/or cardiac arrest. This difficult procedure has attracted the attention of scientists since the eighties. Indeed, many studies have investigated factors such as ventilation techniques [1–6], ventilation devices [7–12], and operator characteristics and skills [6, 8, 9, 11] that may impact its performance. Most of them were carried out on manikin-based simulators. However, we previously reported that the use of this simulation tool might significantly impair peak pressure, tidal volume, and leakage measurements if the manikin intrinsic compliance and resistance are not properly considered when processing the recorded data. Indeed, we showed, on one of the most commonly used manikins, measurement biases of tidal volume ranging from 23 mL to 62 mL which could be the consequence of important inaccuracies which does not reflect exactly the human airway anatomy [13, 14]. Moreover, in a recent literature review we published, we noticed that scientists use different methodology to evaluate ventilation performance and we pointed out their heterogeneity in terms of both judgment criteria and analysis methods [15]. These methods do not consider ventilation variability within and between persons and do not give a relevant assessment of ventilation efficiency. Their potential impact on the evaluation of manual ventilation performance remains to be proved.

All these factors raise the question of the reliability of manikin-based studies. This research consists of an evaluation of the impact of these factors on manual ventilation
performance, in terms of analysis methodology, system-based simulations, or operator characteristics. We also propose a new analysis method, able to provide a chronological view of ventilation variability in order to accurately assess manual ventilation performance in bench conditions.

2. Materials and Methods

2.1. Protocol Design. We conducted this experimental trial at the Department of Emergency Medicine and Critical Care at the University of Franche-Comté Medical and Trauma Centre, Doubs Fire Department, and Jussieu Ambulance Services. The study protocol was submitted to the French data protection authority (Commission Nationale de l’Informatique et des Libertés, CNIL, registration number 1645179). The need for ethical approval was waived by the institutional ethics committee (Comité de Protection des Personnes CPP Est II). We enrolled healthcare professionals who were still in service, aged over 18 years, coming from different emergency structures (University of Franche-Comté Medical and Trauma Centre, Doubs Fire Department, and Jussieu Ambulance Services). Data from 140 volunteers were collected.

Prior to start, participants signed informed consent and fulfilled a questionnaire. We determined the size of the hand squeezing the bag and the grip strength of both hands using a tape measure and a Takei® dynamometer, respectively. Participants were instructed to ventilate with a bag-valve-mask a manikin simulating a 75 kg adult patient in respiratory arrest as they are used to do in their everyday practice. They were blinded regarding their ventilation performance. Because participants were not able to see the manikin chest rise, they were asked to ventilate the manikin for one minute before the tests in order to accustom themselves to the bench model. Then, participants manually ventilated the manikin with two adult self-inflating bags (Laerdal Bag® II and Ambu Spur® II with a reservoir volume of 2900 and 2600 mL, resp.) for five minutes each in a random order. Ventilation was performed in a standing position using a standard technique without chest compression; that is, one hand keeping the mask on the manikin’s face and the other hand squeezing the bag.

2.2. Experimental Bench Model. A Laerdal Airway Management Trainer manikin (Laerdal Medical, Stavanger, Norway) was installed on a stretcher. The manikin’s lungs were bypassed and directly connected to an ASL 5000® breathing simulator (IngMar Medical, Ltd., Pittsburgh, PA, USA) with a short respiratory hose (ID = 2.2 cm, L = 36 cm). A single compartment lung model was set with compliance of 70 mL/cmH₂O⁻¹ and resistance of 3.5 cmH₂O·L⁻¹·s. The intrinsic resistance and airway dead space of the manikin were evaluated for an accurate definition of our patient model [14]. Thus, the manikin’s dynamic airway resistance ranged from 2 to 5 cmH₂O·L⁻¹·s for peak flows ranging from 20 to 120 L·min⁻¹. Tidal volumes (\(V_T\)), lung peak flows (\(PF_{\text{lun}}\)), and inspiratory and expiratory times (\(I_{\text{time}}, E_{\text{time}}\)) were measured inside the ASL 5000 lung simulator and recorded for each ventilation cycle directly by the ASL SW3.3.106 software.

We also used two VTT® flowmeters (jeulin, MediaS-science, Haute-Normandie, France) to measure gastric and BVM insufflation flows.

2.3. Data Treatment. VTT sensor signals were triggered using MATLAB® (version R2008b, MathWorks, Natick, MA, USA) in order to detect each ventilation phase of each ventilatory cycle. Gastric tidal volumes (\(V_G\)) and BVM insufflation volumes (\(V_{\text{ins}}\)) were obtained through a time-related integral transformation of the flowmeters signals over the insufflation period of each cycle. Instantaneous ventilation rates (\(V_T\)) were calculated by measuring the period between each insufflation phase. We recalibrated tidal volume measurements according to peak insufflation flows obtained by the VTT sensor in order to compensate \(V_T\) deviation induced by the compliance of the dead space of the manikin [14].

2.4. Ventilation Performance Analyses. In a previous literature review, we showed a wide heterogeneity in the definition of successful ventilation, in terms of both analysis methods and judgment criteria [15]. In this paper, we aim to apply, on a unique database, the three main methods described below in order to study their impact on results:

(i) Method 1: an overall mean value analysis, that is, the analysis of the global mean value of each ventilatory parameter for all subjects combined together. This method does not take into account inter- and intravariability of ventilatory parameters.

(ii) Method 2: an individual mean value analysis, that is, the analysis of the mean value of each ventilatory parameter for each single subject. Compared to Method 1, it considers the variability between persons but not within person.

(iii) Method 3: a breath-by-breath analysis of each ventilatory parameter. This method takes into account variability between and within persons but it does not correlate it with time.

Although the main judgment criteria described in our review were tidal volume (\(V_T\)) and ventilation rate (\(V_R\)), different tolerance ranges were used to define ventilation efficiency (Table 1).

Finally, considering that none of these approaches is able to provide a clear understanding of ventilation variability [15], we worked out a new analysis approach. A specific algorithm has been designed to observe variations of a whole ventilation sequence. It consists in segmenting every ventilation test into sliding windows of one-minute length each with a shift of three ventilation cycles each time. This will enable us to consider intra- and interindividual and time variability of ventilatory parameters.

This algorithm evaluates the performance of a one-minute window depending on two judgment parameters: tidal volume (\(V_T\)) and ventilation rate (\(V_R\)). We previously reported on the lack of consensus regarding adequate \(V_T\).
Table 1: Different definitions and judgment criteria identified in the literature and ILCOR guidelines.

<table>
<thead>
<tr>
<th>Judgment criteria</th>
<th>Definition 1</th>
<th>Definition 2</th>
<th>Definition 3</th>
<th>Definition 4</th>
<th>Definition 5</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tidal volume</td>
<td>450–525 mL$^*$</td>
<td>400–600 mL</td>
<td>—</td>
<td>—</td>
<td>450–525 mL</td>
</tr>
<tr>
<td>Ventilation rate</td>
<td>—</td>
<td>—</td>
<td>8–10 bpm$^{**}$</td>
<td>10–15 bpm</td>
<td>8–10 bpm</td>
</tr>
</tbody>
</table>

$^*$ 6-7 mL·kg$^{-1}$, 75 kg of IBW; $^{**}$ bpm: breaths per minute.

Figure 1: Operating process of the new analysis algorithm. This figure shows the evaluation of one-minute sliding windows with a shift of three ventilation cycles. The 1st window is considered insufficient as there are only 5 adequate ventilation cycles. The 2nd window is excessive as mean $V_T > 600$ mL. The 3rd window is excessive as $V_R > 15$ bpm. Global ventilation performance of the whole test is considered excessive as the majority of sliding windows are excessive. * Adequate ventilation cycles.

However, a recent study by Lyazidi et al. led us to conclude that $V_T$ ranging from 4 to 8 mL·kg$^{-1}$ may be considered adequate, as long as they are measured inside the artificial lung [14, 16]. Thus, these threshold values were applied to our patient model (IBW: 75 kg) to define our tolerance range for adequate $V_T$ from 300 to 600 mL. Similarly, we considered $V_R$ between 8 and 15 bpm to be adequate regarding our patient model (no respiratory pathology). Therefore, we distinguish three situations to assess the performance of a sliding window according to $V_T$ and $V_R$ measurements during the one-minute period:

(i) 1st situation: $V_R \leq 15$ bpm, mean $V_T \leq 600$ mL, and/or there are at least 8 adequate ventilation cycles (with $V_R$ between 300 and 600 mL). This is considered to be efficient as there is no significant risk of dynamic hyperinflation.

(ii) 2nd situation: $V_R \leq 15$ bpm, mean $V_T \leq 600$ mL, and/or the number of adequate ventilation cycles $< 8$. This ventilation is considered insufficient as it may lead to poor tissue oxygenation.

(iii) 3rd situation: $V_R > 15$ bpm and/or mean $V_T > 600$ mL. This condition underlines global hyperventilation in the last minute period. In this case, where high $V_R$ and $V_T$ may increase intrathoracic pressure leading to pulmonary barotrauma and impairing haemodynamics, ventilation is considered excessive.

In order to explain how to implement this new analysis method, we tried to illustrate its operating process in Figure 1 by taking example on a ventilation curve.

The program appraises the global performance of the five-minute ventilation test by considering every sliding window performance and giving the general trend of the whole ventilation sequence. This novel method will be used to evaluate which factors influence manual ventilation performance of our healthcare professionals.

2.5. Statistical Analysis. Continuous data are expressed as mean ± SD. Results are presented as percentages for nominal variables. Chi2 and Fisher exact test were used to compare professional categories and experience, BVM type, hand size,
and hand grip strengths between the three different performance levels. Odds ratio, estimated by logistic regression, was used to analyse performance level for the multivariate model. A \( p \) value lower than 0.05 was considered to be statistically significant. Statistical analysis was performed with SAS 9.3 for Windows (SAS Institute Inc., Cary, NC, USA).

3. Results

Forty-five physicians (29 emergency medicine physicians and 16 anaesthesia/critical care physicians), forty-five nurses (27 anaesthesia nurses and 18 emergency medicine nurses), and fifty rescuers (31 firefighters, 17 emergency medical technicians, and 2 Red Cross first-aid rescuers) were enrolled in the study. Their professional experience ranged from less than one year to greater than 20 years. The mean population age was 37±9 years. One-third of the volunteers were women. Fifty-five participants thought that their performance was “good,” 83 thought that it was “medium,” and only one thought that it was “bad.” The detailed characteristics of the population are shown in Table 2.

3.1. Evaluation of the Different Analysis Methods and Definitions of Adequate Ventilation. Two hundred eighty ventilation tests have been recorded as each volunteer performed twice the five-minute ventilation test with two different BVM devices. Three different analysis methods and five definitions of ventilation efficiency were applied to this database to evaluate the manual ventilation performance of healthcare professionals. More than 54,000 ventilation cycles have been analysed. Ventilatory parameter values and manual ventilation performance results are reported in Tables 3 and 4.

Using the overall mean value analysis (Method 1), tidal volume was 333.94 ± 124.19 mL and ventilation rate was 24±9 bpm with 25% of the recorded \( V_{R} \) above 29 bpm (Table 3).

Whatever the definition used, mean values of \( V_{T} \) and \( V_{R} \) obtained with this method are not within the tolerance range, hence 0% of adequate ventilation (Table 4). Every ventilatory parameter seems to have high dispersion with a range, hence 0% of adequate ventilation. (Table 4). Every ventilatory parameter seems to have high dispersion with a range, hence 0% of adequate ventilation. (Table 4).
when comparing mean lung peak flow ($39.99 \pm 16.53$ L·min$^{-1}$) with mean BVM peak flow ($69.26 \pm 28.07$ L·min$^{-1}$).

Unlike Method 1, the influence of Methods 2 and 3 (the individual mean value analysis and the breath-by-breath analysis) on ventilation performance depends on the definition of adequate ventilation (Table 4). Indeed, for example, ventilation efficiency ranges from 0% to 45.71% and from 0.41% to 40.01% for Methods 2 and 3, respectively. Different definitions of efficient ventilation have thus an impact on results according to the analysis method used. Similarly, the analysis method can significantly impact performance results depending on the definition. For example, for Methods 2 and 3, Definition 4 gives, respectively, 25.71% and 14.35% of adequate ventilation ($p < 0.001$).

### 3.2. Ventilation Performance Results Using Different BVM Models

The results show that the use of different BVM models (Laerdal Bag II and Ambu Spur II) does not significantly affect manual ventilation performance ($p = 0.79$). Among 280 ventilation tests realized, 121 and 122 were inadequate for Ambu and Laerdal bags, respectively.

### 3.3. Ventilation Performance and Human Factors Using a New Analysis Method

Our new method showed only 21 (7.50%) efficient ventilation tests while 37 (13.21%) were insufficient and 222 (79.29%) were excessive.

Moreover, statistical analyses have revealed no effect of hand size ($p = 0.31$), professional experience ($p = 0.48$), and grip strength of the hand squeezing the bag ($p = 0.15$). However, a significant relationship between participants’ professional category and ventilation performance has been shown (Figure 2, $p = 0.0049$). While there is no statistical difference regarding the percentage of efficient ventilation, the proportion of excessive ventilation was significantly higher for rescuers (90%) than for nurses (74.44%) and physicians (72.22%) who consequently had higher percentages of insufficient ventilation (18.89% versus 3%).

Univariate analysis has revealed that the grip strength of the hand keeping the mask has an impact on ventilation performance (Figure 3, $p = 0.0297$). Indeed, excessive ventilation proportions are increasing with grip strength of the hand keeping the mask (70.97%, 77.21%, and 89.47% for weak, medium, and high grip strength, resp.) while insufficient ones are decreasing (22.58%, 13.24%, and 5.26%, resp.). Furthermore, ventilation efficiency is higher for participants with medium grip strength (9.56%) than for those with a high one (5.26%) or a weak one (6.45%). However, multivariate analysis shows that grip strength has less influence than professional category and only this last stays significant ($p = 0.0286$).

### Table 4: Manual ventilation efficiency ($n$ (%) using different analysis methods and definitions. $n = 140$ healthcare professionals for Methods 1 and 2; $n = 54,770$ ventilation cycles for Method 3.

<table>
<thead>
<tr>
<th>Analysis methods</th>
<th>Definition 1</th>
<th>Definition 2</th>
<th>Definition 3</th>
<th>Definition 4</th>
<th>Definition 5</th>
</tr>
</thead>
<tbody>
<tr>
<td>Method 1 (overall mean value analysis)</td>
<td>0 (0.00%)</td>
<td>0 (0.00%)</td>
<td>0 (0.00%)</td>
<td>0 (0.00%)</td>
<td>0 (0.00%)</td>
</tr>
<tr>
<td>Method 2 (individual mean value analysis)</td>
<td>27 (19.29%)</td>
<td>64 (45.71%)</td>
<td>0 (0.00%)</td>
<td>36 (25.71%)</td>
<td>0 (0.00%)</td>
</tr>
<tr>
<td>Method 3 (breath-by-breath analysis)</td>
<td>923 (16.86%)</td>
<td>2191 (40.01%)</td>
<td>188 (3.44%)</td>
<td>7860 (14.35%)</td>
<td>222 (0.41%)</td>
</tr>
</tbody>
</table>

![Figure 2: Percentage of excessive, efficient, and insufficient ventilation tests for professional categories (n = 280).](image)

![Figure 3: Percentage of excessive, efficient, and insufficient ventilation tests for grip strength categories of the hand keeping the mask (n = 274*, *6 missing values).](image)
4. Discussion

4.1. Factors Related to Analysis Methodology. In a previous manuscript, we identified three different analysis methods and five definitions of adequate ventilation used in several reviewed studies [15]. We have pointed out the heterogeneity of these approaches and their inability to consider ventilatory parameter variability within and between persons. We suggested that this could have a significant impact on results. Thus, this study was an opportunity to verify this hypothesis in a single database and to quantify its real impact on manual ventilation performance. Our findings showed that analysis methodology is the factor that has the most important effect on ventilation performance as it varies from 0% to 45.71% according to different analysis methods and definitions of ventilation efficiency. This would be due to the relative variability of $V_T$ and $V_R$ within persons which represents approximately 15% of the mean value of each and reached up to 86% and 66%, respectively, in some participants. Variability between persons was even more significant (about 38% of the mean value of each parameter) as mean $V_T$ and $V_R$ ranged from 47 to 877 mL and from 8 to 53 bpm.

For these reasons, we defined a new analysis method that allows a chronological evaluation of ventilatory parameters by segmenting a whole ventilation test into one-minute sliding windows. Figure 1 clearly shows the significance of ventilation variability and its impact on the evaluation of ventilation performance. In this example, our algorithm is able to detect a first period of insufficient ventilation with low tidal volumes (1st window) followed by a longer period of hyperventilation with excessive tidal volumes and ventilation rates (2nd and 3rd windows). This analysis method enables us to make a reliable assessment of the performance of the whole ventilation test. In this case, ventilation is considered excessive as there are a majority of excessive ventilation windows. However, if we had used one of the existing analysis methods that do not allow studying ventilation variability, this ventilation test would have been considered adequate. Indeed, Methods 1 and 2 would have found a mean $V_T$ of 523 mL and a mean $V_R$ of 14 bpm, which are both into their target range, and Method 3 would have resulted in 58% (14/24) of efficient ventilation cycles.

With our novel method, 280 ventilation tests realized by 140 healthcare professionals were analysed and we found that only 21 (7.50%) were efficient; the remaining 259 tests (92.50%) can be considered potentially deleterious. However, using the overall mean value analysis method, the BVM ventilation is ineffective with 0% of efficient ventilation tests according to different definitions reviewed.

Among the 92.50% of inadequate ventilation tests, 79.29% were excessive which may impair haemodynamics and induce pulmonary barotrauma, and 13.21% of them were insufficient which may cause hypoxia despite the fact that most of the participants thought their ventilation was adequate. This confirms on a larger sample size the results reported in previous studies [11, 17–20].

4.2. Factors Related to Manikin and BVM Models. Manikin-based simulations could influence manual ventilation performance as the anatomical design of facemasks is not particularly adapted to the manikin’s face shape [21]. Indeed, we found major differences between BVM insufflation volume and $V_T$, leading to a mean leak volume of 219 mL which represents $\approx$37% of the mean insufflation volume. This could be explained by the difficulty in keeping a real airtight seal [21]. Even if we avoided biases related to manikin compliance and resistance by recalibrating data, manikins used in ventilation studies cannot reflect exactly human respiratory mechanics. Another problem is the absence of chest movements which could disrupt healthcare professionals and their appreciation of ventilation quality provided. However, asking them to train on the bench model before tests may have minimized these biases. Although clinical trials and animal studies enable evaluating accurately ventilation efficiency by measuring physiological variables such as arterial blood gases, manikin-based studies remain the most widely used models as they are easy to implement with less stringent ethical rules and provide also the capability for standardization and isolation of key characteristics [13–15].

Furthermore, our study showed that the use of different BVM models has no impact on ventilation performance, although many healthcare professionals perform ventilation more with Ambu bags than with Laerdal ones (115 versus 42). A similar result was obtained by Augustine et al. who demonstrated that there was no obvious relationship between various BVM models used and the average tidal volume delivered [9]. We think that future development of new technologies may ensure a better control of manual ventilation efficiency.

4.3. Factors Related to Human Characteristics and Skills. In order to determine which human factors can affect manual ventilation performance, operator characteristics such as professional categories and experience, hand grip strength, and hand size have been evaluated.

There was no influence of professional experience and hand size on manual ventilation performance. These results were similar to those obtained by Otten et al. [4]. The fact that professional experience does not impact ventilation performance means that ventilation self-improvement is difficult to achieve with current devices. However, multivariate analysis has shown that the most influencing factor was professional category. While all healthcare workers tend to hyperventilate the manikin, physicians and nurses have lower rate of excessive ventilation. This may be related to higher expertise in physiology and respiratory care. This trend to perform hyperventilation has been shown in the literature [17, 19, 20]. High ventilation rates could also be due to the rapid refilling of the bag which can induce a reflex to squeeze and ventilate the manikin as soon as the bag reinflates [22, 23]. Hyperventilation is also accentuated by high grip strength of the hand keeping the mask. This can be explained by the greater ability to avoid leaks with high grip strength resulting in higher tidal volumes provided to the manikin. Keeping the mask on the manikin’s face with one hand is a difficult exercise requiring a strong effort, which may possibly cause hand muscles tetany and induce poor mask-to-face airtightness.
Therefore, professionals having high grip strength are more likely to hyperventilate patients than those with a weak one, for whom excessive insufflation volumes are compensated by large amounts of leaks [4]. Some studies have theorized that the difference in tidal volume is related to the ability to obtain a good mask-to-face seal [7, 9]. Conversely, Lee et al. and Augustine et al. showed that physical aspects including hand size, volume, and grip strength had no correlation with tidal volume [6, 9].

4.4. Limitations. We proposed a novel analysis method that is more relevant as it enables scientists to observe variability within and between persons, but it still has some limitations. Actually, only the correlation with clinical data, which remain the only real indicators of ventilation performance, will help to validate this new method. Therefore, we still cannot confirm that bag-valve-mask ventilation performance described in this study is a reliable representation of what could be obtained in clinical trials. Moreover, we only conducted this study in three different emergency structures. Even if a low ventilation performance rate has also been reported by other studies, diverse findings could be obtained in other centres where Basic Life Support training courses could differ.

5. Conclusion

Many factors may have an impact on manual ventilation performance. In order to accurately assess human factors, it is important to use adequate analysis methods to avoid biases related to methodology. The important variability within and between persons proves the relevance of our new analysis method, which allows observing ventilatory parameter variability on an entire ventilation period. We showed, with this novel method, that professional category and grip strength of the hand keeping the mask have a significant impact on manual ventilation performance. This study confirms that the evaluation of bag-mask ventilation performance is complex and cannot be fully determined on a manikin model. Extrapolations to humans have to be taken with caution. However, we can argue that healthcare professionals perform hyperventilation in most cases and have difficulties in performing adequate manual ventilation with current devices. We believe this problem could be prevented by implementing monitoring tools in order to give direct feedback to healthcare professionals regarding ventilation efficiency and ventilatory parameter values.

Competing Interests

The authors declare that there are no competing interests regarding the publication of this paper.

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References


Serum Procalcitonin and Procalcitonin Clearance as a Prognostic Biomarker in Patients with Severe Sepsis and Septic Shock

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1. Introduction

Sepsis is one of the leading causes of mortality in intensive care units (ICUs) [1]. The early detection of patients with sepsis in the ICU with worsening prognosis or with an increased risk of mortality is essential to prevent consequent organ dysfunction. Prompt diagnosis and administration of appropriate antimicrobial therapy are essential to reduce complications associated with sepsis-related organ failure and patient mortality; however, the individual response to sepsis is complex and not all patients with infections show signs or symptoms [2, 3]. In this context, it is useful to have biomarkers that can serve as predictors for sepsis in clinical practice.

Procalcitonin (PCT) is the 116-amino acid long precursor of calcitonin, which is elevated in sepsis [4, 5]. The degree of induction of PCT is associated with the severity of systemic infection and the presence of organ dysfunction. Thus, PCT is regarded as a useful biomarker for the diagnosis of sepsis.
and recent studies have suggested that dynamic changes of PCT could be predictive of certain outcomes in patients with severe sepsis and septic shock. Serum PCT can aid in the diagnosis of sepsis in critically ill patients; however, its prediction for survival is not well established, and a dynamic approach of assessing biomarkers may provide additional survival information of septic patients [4–6]. A concept of PCT clearance (PCTc) has been introduced in a pilot study as a tool for monitoring the evolution of PCT levels during severe sepsis [4–6]. PCTc measures the relative changes in PCT to the baseline PCT and is postulated to be a better predictor of outcome. Therefore, the hypothesis of this study is whether PCT levels and PCT clearance could serve as prognostic biomarkers for patients with severe sepsis and septic shock. The aim of the present study was to evaluate the usefulness of PCT levels and PCTc as biomarkers of prognosis in patients with severe sepsis and septic shock.

2. Materials and Methods

2.1. Patient Population. This is a prospective observational study conducted in the medical ICUs at a hospital in central Taiwan from July 2011 to June 2013. In the present study, all consecutive patients who fulfilled the criteria for sepsis were enrolled. Patients who underwent surgery or trauma or were aged less than 18 years were excluded from our series. The study was approved by the Institutional Review Board of the Taichung Tzu Chi Hospital, and a written informed consent was obtained from patients or patient representatives. Patients were treated according to the institutional protocol for the management of severe sepsis and septic shock, based on recommendations from the surviving sepsis campaign modified to meet recent evidence from the literature [7–9].

2.2. Study Design. This was a single-center, prospective observational study. All enrolled patients with sepsis or septic shock were managed based on the decision of the treating physicians in the ICU. In addition, the duration of antimicrobial therapy was guided by culture data, site of infection, and treating physician. The patients data included age, gender, vital signs, clinical status, Acute Physiology and Chronic Health Evaluation (APACHE II) score, Sequential Organ Failure Assessment (SOFA) score, site(s) of infection, laboratory tests findings (basic biochemistry, complete blood count, coagulation, and arterial blood gases), microbiological culture results, duration of hospitalization (length of stay in ICU and hospital), and clinical outcomes. Infection was diagnosed by standard clinical, laboratory, and microbiological parameters. APACHE II scores and SOFA scores on the first day after admission (day 1) and serum PCT levels on days 1, 3, and 5 of diagnosis of sepsis were calculated. The patients were followed up until hospital day 28, and the outcome at day 28 was noted as the primary outcome, defined as mortality related to sepsis within the first 28 days of admission to the ICU.

2.3. Measurement of Biomarkers. PCT was measured in serum samples that were collected on hospital days 1, 3, 5, and 7 in patients with sepsis and septic shock. The blood was drawn and centrifuged at 3,500 rpm for 5 min and

![Figure 1: Original sites of infection identified in patients with sepsis. The most common site of infection was bloodstream infection (75.0%), followed by lung (57.1%), urine (41.1%), abdomen (16.1%), and skin (14.3%).](image-url)

biochemistry markers were analyzed immediately. The serum samples were then stored at −80°C until further analysis. The concentration of PCT was measured by using a one-step immunoassay sandwich method with a fluorescent detection (ELFA). The PCT detection range is 0.05–200 ng/mL according to the manufacturer’s instructions (VIDAS II, Biomerieux Inc., France) [5–8]. Moreover, PCTc is calculated using the following formula [4]:

\[
\frac{(PCT_{day\ 3/day\ 5} - PCT_{day\ 1})}{PCT_{day\ 1}} \times 100\% = PCT_{day\ 3/day\ 5} \%
\]

PCTc on day 3 (PCTc-day 3) and that on day 5 (PCTc-day 5) was calculated based on this formula.

2.4. Statistical Analysis. Data of categorical variables were analyzed by the chi-square test or Fisher’s exact test, when appropriate. Continuous variables were analyzed by the Mann-Whitney U Test and Kruskal-Wallis Test. A p value less than 0.05 was considered to be statistically significant. Distributions of variables were reported as percentages and means ± standard deviation (SD). Statistical analyses were performed with SPSS software (version 15.0, SPSS, Inc., Chicago, IL, USA).

3. Results

3.1. Demographics and Clinical Presentations. During the study period, a total of 56 patients with sepsis and septic shock were admitted to the ICU at our hospital. Eight patients were excluded from the study because of incomplete clinical data, and 48 patients with sepsis were, thus, enrolled in our study. The mean age was 74 ± 12 years with 47.9% male and 52.1% female patients. On day 1, the mean APACHE II score was 22.9 ± 6.9 and the mean SOFA score was 7.2 ± 3.3. The positive blood culture rate was 60.4%. The average length of ICU stay was 12.5 ± 9.1 days, and the average total length of hospital stay was 23.0 ± 14.9 days. Ten patients required endotracheal tube insertion (20.8%), and the overall mortality was 16.7% (8 patients, 7 of whom had septic shock).

The original sites of infection are shown in Figure 1. Blood was identified as the most common site of infection...
Table 1: Microorganisms isolated from different sites in patients with sepsis or septic shock.

<table>
<thead>
<tr>
<th>Category (total positive isolations ( n = 87 ))</th>
<th>Blood</th>
<th>Urine</th>
<th>Sputum</th>
<th>Skin</th>
<th>Abdomen</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gram-positive bacteria ( (n = 16, 18.4%) )</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>\textit{Staphylococcus aureus}</td>
<td>0</td>
<td>0</td>
<td>1</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>Coagulase negative \textit{Staphylococci}</td>
<td>8</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>\textit{Streptococcus} spp.</td>
<td>2</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>\textit{Enterococcus} spp.</td>
<td>1</td>
<td>2</td>
<td>0</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>Gram-negative bacteria ( (n = 60, 69.0%) )</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>\textit{Escherichia coli}</td>
<td>7</td>
<td>10</td>
<td>2</td>
<td>2</td>
<td>1</td>
</tr>
<tr>
<td>\textit{Klebsiella pneumoniae}</td>
<td>8</td>
<td>4</td>
<td>5</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>\textit{Proteus mirabilis}</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>\textit{Salmonella D1}</td>
<td>1</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>\textit{Enterobacter} spp.</td>
<td>2</td>
<td>1</td>
<td>1</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>\textit{Haemophilus influenzae}</td>
<td>0</td>
<td>0</td>
<td>3</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>\textit{Pseudomonas aeruginosa}</td>
<td>1</td>
<td>1</td>
<td>2</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>\textit{Acinetobacter baumannii}</td>
<td>0</td>
<td>0</td>
<td>1</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Other \textit{Anarobes} spp.</td>
<td>2</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Fungus ( (n = 11, 12.6%) )</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>\textit{Candida albicans}</td>
<td>1</td>
<td>2</td>
<td>8</td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>

in patients with sepsis in the ICU. The majority of sepsis (75%) was because of bacteremia. The other original sites of infection were the lungs, urine, abdomen, and skin (57.1%, 41.1%, 16.1%, and 14.3%, resp.). The isolation rate of Gram-negative bacteria was 69%. \textit{Escherichia coli} (E. coli) and \textit{Klebsiella pneumoniae} (K. pneumoniae) were identified as the two most common microorganisms. Gram-positive bacteria and fungus composed 18.4% and 12.6%, respectively; coagulase negative \textit{Staphylococci} were identified as the most common Gram-positive bacteria, and \textit{Candida albicans} was the most common fungi isolated from sputum culture. A more detailed description of microorganisms isolated from different sites in patients with sepsis is presented in Table 1.

3.2. Clinical Factors Associated with Survival. The results of clinical factors between survivors and nonsurvivors of patients with sepsis or septic shock are listed in Table 2. The significant factors associated with survival in patients with sepsis included APACHE II scores, positive or negative sputum culture, and the length of ICU stay. Regarding the severity of illness, APACHE II and SOFA scores were compared in the two groups. Both scores were higher in the nonsurvivors, but only APACHE II scores showed a significant difference \( (p = 0.019) \). Among all the results of culture data, the presence of a positive sputum culture was significantly predominant in the nonsurvivor group \( (p = 0.01) \). In addition, we found that survivors tended to have shorter ICU stays but longer overall hospital stays than nonsurvivors. A shorter duration of ICU stay was also a significant factor associated with survival in patients with sepsis in the ICU \( (p = 0.040) \).

In patients with sepsis, however, serum PCT levels on days 1, 3, and 5 were not significant prognostic factors for survival. PCT concentration showed decay from baseline in the survivors, whereas it remained high in those who did not survive. Comparison between the changes in PCT levels in survivors and nonsurvivors is shown in Table 3. PCTc was also compared between the two groups. PCTc-day 3 and PCTc-day 5 were both significantly higher in patients who survived than in those who did not \( (p = 0.033, p = 0.002, \text{resp.}) \). The PCTc on day 3 and day 5 was associated with the prediction of survival in patients with sepsis in the ICU.

4. Discussion

Severe sepsis with septic shock is a major cause of morbidity and mortality in the ICU. Mortality increases with the severity of sepsis. In-hospital mortality rates for severe sepsis and septic shock are high, ranging between 18% and 50% \[10–12\]. In the present study, the mortality because of severe sepsis and septic shock was 22.9%, which is consistent with prior results \[10–12\]. Clinically, once the diagnosis of sepsis is made, the prediction of survival is important for the risk stratification of patients and in indicating the potential success or failure of treatment. We evaluated the predictive value of serum PCT for survival in patients with severe sepsis or septic shock. In this prospective study of patients with sepsis, we demonstrated that serum PCT measured on days 1, 3, and 5 of ICU stay was not predictive of mortality. Measurement of biomarkers at a single time point may be of limited value because of the large variability of biomarker secretion at different times during the progression of critical illness. Moreover, it is unclear how much time has lapsed between the initial onset of disease and the time of admission to the ICU. Nevertheless, in our study, PCTc increased progressively in surviving patients but decreased in nonsurvivors, with significant differences at 48 h and 96 h (PCTc-day 3 and PCTc-day 5). In patients with severe sepsis and septic shock, dynamic changes in PCTc-day 3 and -day 5 predicted survival. There was higher survival in septic patients with increased PCT clearance on day 3 of more than 38% compared to those below
Table 2: Comparisons of baseline characteristics between survivors and nonsurvivors in patients with sepsis or septic shock.

<table>
<thead>
<tr>
<th>Variables</th>
<th>All patients (n = 48)</th>
<th>Survivors (n = 40)</th>
<th>Dead (n = 8)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gender</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>19 (47.5)</td>
<td>4 (50.0)</td>
<td></td>
<td>0.897</td>
</tr>
<tr>
<td>Female</td>
<td>21 (52.5)</td>
<td>4 (50.0)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Culture results</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Blood culture</td>
<td></td>
<td></td>
<td></td>
<td>0.356</td>
</tr>
<tr>
<td>Positive</td>
<td>23 (57.5)</td>
<td>6 (75.0)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Negative</td>
<td>17 (42.5)</td>
<td>2 (25.0)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Urine culture</td>
<td></td>
<td></td>
<td></td>
<td>0.895</td>
</tr>
<tr>
<td>Positive</td>
<td>16 (40.0)</td>
<td>3 (37.5)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Negative</td>
<td>24 (60.0)</td>
<td>5 (62.5)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sputum culture</td>
<td></td>
<td></td>
<td></td>
<td>0.010</td>
</tr>
<tr>
<td>Positive</td>
<td>15 (37.5)</td>
<td>7 (87.5)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Negative</td>
<td>25 (62.5)</td>
<td>1 (12.5)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Endotracheal tube</td>
<td></td>
<td></td>
<td></td>
<td>0.204</td>
</tr>
<tr>
<td>Mean ± SD</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age (years)</td>
<td>75 ± 11</td>
<td>70 ± 14</td>
<td></td>
<td>0.355</td>
</tr>
<tr>
<td>Clinical scoring</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>APACHE II score (day 1)</td>
<td>21.9 ± 6.8</td>
<td>28.1 ± 5.2</td>
<td></td>
<td>0.019</td>
</tr>
<tr>
<td>SOFA score (day 1)</td>
<td>6.8 ± 3.2</td>
<td>9.0 ± 3.2</td>
<td></td>
<td>0.089</td>
</tr>
<tr>
<td>Laboratory tests</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Serum PCT (mg/dL)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Day 1</td>
<td>41.4 ± 54.7</td>
<td>37.4 ± 66.9</td>
<td></td>
<td>0.856</td>
</tr>
<tr>
<td>Day 3</td>
<td>28.5 ± 44.6</td>
<td>33.6 ± 48.0</td>
<td></td>
<td>0.773</td>
</tr>
<tr>
<td>Day 5</td>
<td>11.1 ± 22.6</td>
<td>11.8 ± 11.1</td>
<td></td>
<td>0.925</td>
</tr>
<tr>
<td>Blood sugar (mg/dL)</td>
<td>218.6 ± 153.9</td>
<td>241.7 ± 292.5</td>
<td></td>
<td>0.745</td>
</tr>
<tr>
<td>Blood pH</td>
<td>7.3 ± 0.1</td>
<td>7.3 ± 0.1</td>
<td></td>
<td>0.299</td>
</tr>
<tr>
<td>Blood bicarbonate</td>
<td>18.8 ± 5.8</td>
<td>19.0 ± 4.9</td>
<td></td>
<td>0.932</td>
</tr>
<tr>
<td>Duration of hospitalization</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>ICU stay (days)</td>
<td>11.2 ± 8.6</td>
<td>18.5 ± 9.6</td>
<td></td>
<td>0.040</td>
</tr>
<tr>
<td>Hospital stay (days)</td>
<td>23.9 ± 15.6</td>
<td>18.5 ± 9.7</td>
<td></td>
<td>0.352</td>
</tr>
</tbody>
</table>

Table 3: PCTc between survivors and nonsurvivors in patients with sepsis.

<table>
<thead>
<tr>
<th>Variables</th>
<th>Survivors (n = 37)</th>
<th>Dead (n = 11)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>PCTc-day 3</td>
<td>38.9 (−154.1 to 95.1)</td>
<td>11.6 (−533.6 to 34.0)</td>
<td>0.033</td>
</tr>
<tr>
<td>PCTc-day 5</td>
<td>80.3 (3.5 to 99.3)</td>
<td>43.2 (−85.2 to 83.4)</td>
<td>0.002</td>
</tr>
</tbody>
</table>

PCTc-day 3: PCT clearance at 48 h after admission (%); PCTc-day 5: PCT clearance at 96 h after admission (%).

In our study, the most common original site of infection in patients with sepsis was lung, followed by urinary tract and intra-abdominal infection. The majority of isolated microorganisms were Gram-negative bacteria, in which *E. coli* and *K. pneumoniae* were the most commonly identified strains. Among the isolated Gram-positive bacteria, coagulase negative *Staphylococci* were the most commonly identified strains. In our study, positive blood cultures were more common in dead patients than survivors (75% versus 57.5%), but the p value did not show significance. We think the results without statistically significant difference may be due to the small sample size. In addition, patients with increased PCT clearance on day 5 of more than 80% compared to those below 44% may have higher survival rate. As we know, a dynamic approach to biomarkers may capture the progression of disease and may be more useful in evaluating patients with sepsis. In this context, we observed that serum PCT levels measured at different time points after admission were not predictive of mortality; however, dynamic changes of PCT over 48 h and 96 h were predictive. The predictive significance for using PCT in prognosis may be apparent after determination of the progression of serial PCT concentrations relative to the baseline.
to the small sample size in our study. We believe that the difference of positive blood cultures between survivors and dead patients may be very important, but, in previous studies, culture positivity could not serve as a predictor of mortality in patients with sepsis [13–15]. In our study, the presence of a positive sputum culture was significantly more predominant in the nonsurvivors group. Thus, the positive sputum culture may appear to be a predictor of prognosis, whereas other culture results may or may not be associated with mortality in patients with sepsis.

Several prognostic indices are used in ICUs. The two most widely used are the APACHE II score and SOFA score; the utility of those is limited to the first 24 h of treatment in other studies [16, 17]. In our study, we found that while both APACHE II and SOFA scores were higher in the nonsurvivors than those in survivors, only APACHE II scores showed a significant difference between the two groups. The APACHE II score was a predictor of mortality in our analysis.

In conclusion, the prognosis of patients with severe sepsis and septic shock may be associated with PCTc. Dynamic changes of PCT reflected as PCTc at 48 h (day 3) and 96 h (day 5) after admission to the ICU may serve as a predictor of survival in critically ill patients with severe sepsis. This could assist primary care physicians in the risk stratification of critically ill patients with severe sepsis and septic shock.

**Competing Interests**

There are no competing interests related to this study.

**Authors’ Contributions**

Min-Yi Huang and Chun-Yu Chen reviewed the medical records, analyzed and interpreted the data, and drafted the paper; Kun-Hsi Wu and Ju-Huei Chien interpreted the data and drafted the paper. Kang-Hsi Wu and Yu-Jun Chang analyzed and interpreted the data. Han-Ping Wu designed and oversaw the study, interpreted the data, and revised the paper. All authors have read and approved the final paper for publication.

**References**


Role of Extracranial Carotid Duplex and Computed Tomography Perfusion Scanning in Evaluating Perfusion Status of Pericarotid Stenting

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Carotid stenting is an effective treatment of choice in terms of treating ischemic stroke patients with concomitant carotid stenosis. Though computed tomography perfusion scan has been recognized as a standard tool to monitor/follow up this group of patients, not everyone could endure due to underlying medical illness. In contrast, carotid duplex is a noninvasive assessment tool and could track patient clinical condition in real time. In this study we found that “resistance index” of the carotid ultrasound could detect flow changes before and after the stenting procedure, thus having great capacity to replace the role of computed tomography perfusion exam.

1. Introduction

Stroke is the fourth leading cause of death worldwide [1]. Among its various etiologies, carotid stenosis is the most well observed and accounts for 30 to 35 percent of total ischemic strokes [2]. Stenosis grading exceeding 70% lumen reduction doubles or triples the risk of stroke and its recurrence. Vascular neurologists have reported that prompt management of carotid stenosis through standard carotid stenting prevents stroke and its recurrence. In the pre-stenting phase, doctors routinely administer computed tomography (CT) perfusion scans to study the cerebral blood perfusion condition in the bilateral cerebral hemispheres.

Although CT perfusion scanning has several advantages and has been recognized as a standard tool for assessing cerebral perfusion in patients undergoing stenting, not all patients can tolerate it. This neuroimaging tool entails the use of a contrast medium, which is hazardous to patients, especially those with impaired renal function.

Extracranial carotid ultrasounding is noninvasive and requires no contrast mediums. Investigation and validation of the role of ultrasound in evaluating flow conditions in pre- and post-stenting phases are yet to be reported in the literature. This study utilizes a clinical parameter—resistance index (RI)—generated through carotid ultrasound exams and CT perfusion scans to investigate whether flow changes can be simultaneously observed in these two examinations.

2. Materials and Methods

2.1. Patient Identification. We consecutively recruited 15 patients scheduled to undergo carotid stenting. The patients were admitted to our outpatient clinics and emergency departments or transferred from our branch hospital; all patients had been hospitalized for examination and treatment. We included patients with age ≥18 years, with an initial ischemic or recurrent strokes, with angiographic evidence of >70% carotid stenosis, with no other etiology.
of stroke that could explain the index event, and with no evidence of recurrent stroke during the study period and followed up at least 6 months after the stenting treatment. Exclusion criteria were patients with cerebral hemorrhage, cerebral arteriovenous malformations, aneurysms, and bilateral moderate-severe carotid stenosis, and less than 6 months’ follow-ups. The enrolled patients were hospitalized for medical treatments along with baseline biochemistry work-ups. The ischemic stroke was confirmed by the diffusion weighted sequence of magnetic resonance imaging. The diagnostic digital subtraction angiography (DSA) was arranged during the hospitalization to gauge the degree of the carotid stenosis. The patients were stented one month after the index episode (stroke event). The participants were administered extracranial carotid ultrasound and CT angiography/perfusion (CTA/P) scanning simultaneously before carotid stenting. The above mentioned examinations were repeated simultaneously one month after stenting. This study was approved by the Institutional Review Board of Changhua Christian Hospital.

2.2. Baseline Clinical Characteristics. Baseline demographic data and clinical characteristics were collected including age, gender, and body mass index (BMI); baseline biochemistry data were collected on admission, such as low density lipoprotein (LDL) and glycated hemoglobin (HbA1c) levels and evidence or any major past history. Performance in activities of daily living was measured before stenting with the Barthel Index.

2.3. Cervical Carotid Ultrasound Examination. Cervical carotid artery examination was performed in our ultra-sonography laboratory by using a Philips iE33 7-Mhz linear transducer. Patients slightly tilted their head contralaterally, and the transducer was placed on their necks. First, cross-sectional B-mode scanning and longitudinal screening were performed to identify and confirm intraluminal plaques, respectively. Peak systolic velocity (PSV), end diastolic velocity (EDV), and resistance index (RI) of the CCA, internal carotid artery (ICA), and external carotid artery (ECA) were measured. RI is given by PSV – EDV/PSV. The degree of carotid stenosis was calculated using the European Carotid Surgery Trial method [3].

2.4. Computed Tomography Angiography/Perfusion Scan (CTA/P Imaging). CTA examinations were performed using a second-generation dual-source CT scanner (SOMATOM Definition Flash, Siemens Healthcare, Forchheim, Germany). Perfusion data sets were postprocessed using a Siemens Multimodality Workplace Workstation (Siemens Medical, Germany), which calculated mean transit time (MTT), cerebral blood volume (CBV), cerebral blood flow (CBF), and time to peak (TTP). The arterial input and venous outflow curves were analyzed to ensure data set completeness. The CTP parameters are defined as follows:

(1) dMTT: ipsilateral MTT – contralateral MTT.
(2) MTT ratio: ipsilateral MTT/contralateral MTT.
(3) MTT index: (ipsilateral MTT – contralateral MTT)/contralateral MTT.
(4) dCBV: ipsilateral CBV – contralateral CBV.
(5) CBV ratio: ipsilateral CBV/contralateral CBV.
(6) CBV index: (ipsilateral CBV – contralateral CBV)/contralateral CBV.
(7) dCBF: ipsilateral CBF – contralateral CBF.
(8) CBF ratio: ipsilateral CBF/contralateral CBF.
(9) CBF index: (ipsilateral CBF – contralateral CBF)/contralateral CBF.
(10) dTTP: ipsilateral TTP – contralateral TTP.
(11) TTP ratio: ipsilateral TTP/contralateral TTP.
(12) TTP index: (ipsilateral TTP – contralateral TTP)/contralateral TTP.

2.5. Magnetic Resonance Imaging and Angiography (MRI/A). Structural and functional MR imaging and angiographic examinations were performed using a 3-T (Magnetom Verio, Siemens Healthcare, USA) or a 1.5-T imager (Magnetom Aera, Siemens Healthcare) with a cervical coil. Standard protocol to evaluate a stroke including axial DWI, apparent diffusion coefficient, and fluid-attenuated inversion-recovery sequences was followed. Contrast-enhanced MR angiography was not routinely performed.

2.6. Digital Subtraction Angiography (DSA) and Stenting. Biplanar intra-arterial DSA was performed using a biplanar flap panel rotational angiography unit (Axiom Artis Zee, Siemens Healthcare) with an image intensifier matrix of 1024 × 1024 pixels and a final pixel size of 0.37 mm. A self-expandable carotid wallstent (7 mm × 30 mm) was delivered coaxially through the guiding catheter into the stenotic area (Figure 1).

2.7. Statistical Analyses. Continuous variables are presented as mean ± standard deviation (SD), median, percentile, minimal, and maximal values. Categorical variables are presented as numbers and percentages. Pre- and poststenting CT perfusion and carotid ultrasound variables were compared using Wilcoxon signed ranks test. 𝑃 < 0.05 was considered statistically significant. All statistical analyses were performed using SPSS for Windows (Version 16.0, SPSS Inc., Chicago, IL, USA).

3. Results
The baseline clinical characteristics of the 15 patients are summarized in Tables 1 and 2. Tables 3 and 4 report the flow changes reflected by the parameters of CT perfusion and carotid ultrasound examinations.
Ipsilateral mean values of MTT, CBV, and TTP decreased after stenting, whereas CBF increased slightly. The majority of patients exhibited decreased MTT, CBV, and TTP. Pre- and posttreatment TTP values differed significantly (𝑃 = 0.031, <0.05). Contralateral MTT, CBV, and TTP decreased,
Figure 1: An example of left side severe internal carotid artery stenosis undergoing carotid stenting treatment. An 85-year-old male patient presented with right side hemiparesis and aphasia 24 hours before admission to our neurology ward. (i) (a) denotes CTA scan showing >70% lumen reduction of left side proximal internal carotid artery and distal part of common carotid artery (black arrow). (ii) (b) shows the CT perfusion scan that suggests decreased blood perfusion to the left cerebral hemisphere indicating critical blood flow demand compared to the right side cerebral hemisphere. (iii) (c) presents the poststenting status with umbrella device that prevent embolus distal migration causing major subsequent stroke event (black arrow). (iv) (d) displays the follow-up cervical carotid ultrasound of normalized flow profile.

Table 1: Baseline patient features.

<table>
<thead>
<tr>
<th></th>
<th>Mean</th>
<th>SD</th>
<th>Median</th>
<th>Percentile 25</th>
<th>Percentile 75</th>
<th>Min</th>
<th>Max</th>
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</thead>
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<tr>
<td>Age</td>
<td>66.47</td>
<td>9.59</td>
<td>69.00</td>
<td>56.00</td>
<td>73.00</td>
<td>47.00</td>
<td>79.00</td>
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<tr>
<td>Grade of stenosis</td>
<td>0.71</td>
<td>0.10</td>
<td>0.74</td>
<td>0.67</td>
<td>0.78</td>
<td>0.53</td>
<td>0.84</td>
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<td>SBP</td>
<td>137.27</td>
<td>10.73</td>
<td>138.00</td>
<td>128.00</td>
<td>149.00</td>
<td>118.00</td>
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<td>DBP</td>
<td>77.47</td>
<td>8.33</td>
<td>80.00</td>
<td>74.00</td>
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<td>68.50</td>
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<td>8.33</td>
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<td>BMI</td>
<td>24.09</td>
<td>3.36</td>
<td>23.56</td>
<td>20.78</td>
<td>28.20</td>
<td>18.34</td>
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<tr>
<td>Barthel</td>
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<td>10.14</td>
<td>87.50</td>
<td>80.00</td>
<td>100.00</td>
<td>75.00</td>
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<td>29.41</td>
<td>121.00</td>
<td>97.90</td>
<td>134.00</td>
<td>86.40</td>
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<tr>
<td>HbA1c</td>
<td>6.94</td>
<td>1.89</td>
<td>6.65</td>
<td>5.70</td>
<td>7.30</td>
<td>5.30</td>
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<tr>
<td>Ac sugar</td>
<td>119.67</td>
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<td>96.00</td>
<td>94.00</td>
<td>128.00</td>
<td>80.00</td>
<td>227.00</td>
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<tr>
<td>Uric acid</td>
<td>6.25</td>
<td>1.43</td>
<td>6.35</td>
<td>5.40</td>
<td>7.00</td>
<td>4.10</td>
<td>9.20</td>
</tr>
</tbody>
</table>

Note. Min, minimum; Max, maximum; SBP, systolic blood pressure; DBP, diastolic blood pressure; BMI, body mass index; LDL, low density lipoprotein; SD, standard deviation.

whereas the mean CBF increased slightly. The ratio of patients exhibiting decreased and increased contralateral MTT, CBV, CBF, and TTP values is approximately 1 (Table 3).

Ipsilateral RI analyses showed that mean CCA RI reduced from 0.78 to 0.75, and most patients exhibited decreased CCA RIs. By contrast, mean ICA RI increased from 0.62 to 0.69, and most patients exhibited increased ICA RIs. Mean ECA RI decreased from 0.84 to 0.80; there are five and six patients, demonstrating decreased and increased ECA RIs, respectively (Table 3).

Contralateral RI analyses revealed that CCA, ICA, and ECA RIs increased after stenting, with most patients showing...


Table 2: Baseline patient demographics.

<table>
<thead>
<tr>
<th></th>
<th>N</th>
<th>%</th>
</tr>
</thead>
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<td>2</td>
<td>13.3</td>
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<td></td>
</tr>
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<td>9</td>
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<td><strong>Hypertension</strong></td>
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<td>3</td>
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<tr>
<td><strong>Hyperlipidemia</strong></td>
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<td>73.3</td>
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<td><strong>Prior stroke</strong></td>
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<td></td>
</tr>
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<td>8</td>
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<tr>
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<td>46.7</td>
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</table>

Increased mean CCA and ICA values; CCA RI increased from 0.73 to 0.77, ICA RI increased from 0.67 to 0.70, and ECA increased from 0.87 to 0.88 (Table 3).

The mean values of all other 12 CT perfusion scan parameters (Table 4) decreased after stenting. The majority of patients showed decreased values. Among the 12 parameters, MTT ratio, MTT index, and TTP ratio decreased significantly ($P = 0.013, 0.039$, and $0.017, <0.05$).

4. Discussion

Stroke is the fourth leading cause of death worldwide [1, 2], and, among its various etiologies, carotid stenosis accounts for the majority of strokes. Carotid stenting can effectively prevent stroke and its recurrence.

CT perfusion is a standard assessment routinely performed before carotid stenting because it provides vivid color images and several parameters that clarify the ipsilateral and contralateral cerebral hemispheres perfusion status, as well as identifying stroke location [4–9]. However, not all patients can undergo this assessment tool. This is because they entail the use of contrast mediums, which is hazardous to patients with impaired renal function. In addition, CT perfusion administration is restricted to medical facilities, thus requiring patients to visit the facility. Moreover, it requires multiple operators, making it time intensive and expensive for patients.

By contrast, carotid duplex is a mobile, single-operator, contrast-medium-free, and inexpensive examination. Although no studies have examined the role of RI in evaluating cerebral perfusion status after carotid stenting, RI has been widely used in nephrology. Derchi et al. tested RI in patients with renal dysfunction and reported that the risk of renal impairment increased twofold when renal RI was $>0.63$ [10]. In addition, RI is effective in predicting kidney transplant outcomes [11–13].

CT perfusion, by convention, is used to assess the cerebral artery perfusion status. The improvement of cerebral blood perfusion after stenting treatment can be indicated by a reduced MTT and an increased CBF within the ipsilateral carotid system [14, 15]. Our study is in accordance with these statements. The findings of MTT and CBF over the contralateral carotid system in the published papers [2, 16], however, have not come to general consensus. Our study shows that the MTT and CBF values decreased after treatment. Moreover, the absolute difference, ratio, and index values of bilateral cerebral hemispheres are also calculated. The results show a drop in values, particularly within the MTT ratio, MTT index, and TTP ratio.

RI, a clinical parameter generated from carotid ultrasound, represents the general downstream blood vascular bed resistance level [17]. RI $>0.75$ denotes increased downstream vascular bed, which can be due to various factors, including obstructions. Because CCA and ICA supply the majority of blood to the intracranial hemispheres, their RI values are lower than that of ECA in normal circumstances (CCA and ICA $<0.75$, ECA $>0.75$).

In our study, ipsilateral mean CCA RI values decreased from 0.78 to 0.75 after carotid treatment, indicating that ICA flow smoothened and resistance level decreased after treatment, subsequently drawing more blood to perfuse the same side of the cerebral hemisphere. The mean ipsilateral ICA RI value, however, rose from 0.62 to 0.69, elucidating the vasoconstriction mechanism after upstream dilation. Nevertheless, ipsilateral CCA and ICA returned to their normal values ($<0.75$). Conversely, on the contralateral side of the carotid system, mean RI rose in all carotid arteries (CCA, CA, and ECA), which explains the relatively low blood flow to the contralateral side of the vasculature because most of the blood was supplied to the ipsilateral side after stenting (Figure 2).

Our study has a few limitations. First, with only 15 patients, the sample size is small; the results must be...
Table 3: Changes in carotid duplex and CT perfusion parameters after carotid stenting.

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Time</th>
<th>Change status (number)</th>
<th>N</th>
<th>Mean</th>
<th>SD</th>
<th>Median</th>
<th>Q1</th>
<th>Q3</th>
<th>Min</th>
<th>Max</th>
<th>P value</th>
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<tbody>
<tr>
<td>MTT</td>
<td>Before treatment</td>
<td>13</td>
<td>7.06</td>
<td>3.33</td>
<td>6.27</td>
<td>4.29</td>
<td>10.16</td>
<td>3.28</td>
<td>13.06</td>
<td>10</td>
<td>3</td>
</tr>
<tr>
<td></td>
<td>After treatment</td>
<td>13</td>
<td>5.46</td>
<td>4.32</td>
<td>3.74</td>
<td>3.51</td>
<td>5.58</td>
<td>3.09</td>
<td>18.66</td>
<td>13</td>
<td>5.05</td>
</tr>
<tr>
<td>CBF</td>
<td>Before treatment</td>
<td>15</td>
<td>39.89</td>
<td>12.15</td>
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<td>24.30</td>
<td>36.93</td>
<td>13.93</td>
<td>61.56</td>
<td>8</td>
<td>7</td>
</tr>
<tr>
<td></td>
<td>After treatment</td>
<td>15</td>
<td>40.65</td>
<td>14.01</td>
<td>39.74</td>
<td>34.90</td>
<td>48.08</td>
<td>5.17</td>
<td>62.60</td>
<td>15</td>
<td>43.56</td>
</tr>
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<td>CBV</td>
<td>Before treatment</td>
<td>15</td>
<td>3.02</td>
<td>0.61</td>
<td>2.93</td>
<td>2.66</td>
<td>3.38</td>
<td>1.98</td>
<td>4.39</td>
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<tr>
<td></td>
<td>After treatment</td>
<td>15</td>
<td>2.63</td>
<td>1.23</td>
<td>2.33</td>
<td>2.15</td>
<td>2.87</td>
<td>1.57</td>
<td>6.73</td>
<td>11</td>
<td>4</td>
</tr>
<tr>
<td>TTP</td>
<td>Before treatment</td>
<td>15</td>
<td>18.89</td>
<td>10.50</td>
<td>12.78</td>
<td>10.08</td>
<td>28.63</td>
<td>8.44</td>
<td>39.28</td>
<td>15</td>
<td>17.91</td>
</tr>
<tr>
<td></td>
<td>After treatment</td>
<td>15</td>
<td>12.17</td>
<td>4.13</td>
<td>11.12</td>
<td>9.32</td>
<td>17.20</td>
<td>9.18</td>
<td>23.60</td>
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<tr>
<td>CCA RI</td>
<td>Before treatment</td>
<td>12</td>
<td>0.78</td>
<td>0.14</td>
<td>0.80</td>
<td>0.71</td>
<td>0.89</td>
<td>0.43</td>
<td>0.92</td>
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<tr>
<td></td>
<td>After treatment</td>
<td>12</td>
<td>0.75</td>
<td>0.08</td>
<td>0.76</td>
<td>0.76</td>
<td>0.79</td>
<td>0.55</td>
<td>0.88</td>
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<tr>
<td>ICA RI</td>
<td>Before treatment</td>
<td>12</td>
<td>0.62</td>
<td>0.19</td>
<td>0.62</td>
<td>0.52</td>
<td>0.73</td>
<td>0.24</td>
<td>0.91</td>
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<tr>
<td></td>
<td>After treatment</td>
<td>12</td>
<td>0.69</td>
<td>0.10</td>
<td>0.70</td>
<td>0.60</td>
<td>0.76</td>
<td>0.58</td>
<td>0.89</td>
<td>3</td>
<td>7</td>
</tr>
<tr>
<td>ECA RI</td>
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<td>0.12</td>
<td>0.85</td>
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<td>1.00</td>
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<td>6</td>
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<tr>
<td></td>
<td>After treatment</td>
<td>13</td>
<td>0.80</td>
<td>0.25</td>
<td>0.85</td>
<td>0.79</td>
<td>0.94</td>
<td>0.00</td>
<td>1.00</td>
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<td>6</td>
</tr>
</tbody>
</table>

Note: SD, standard deviation; CCA, common carotid artery; ICA, internal carotid artery; ECA, external carotid artery; RI, resistance index; MTT, mean transit time; CBF, cerebral blood flow; CBV, cerebral blood volume; TTP, time to peak.

Q1: percentile 25; Q3: percentile 75.

aP value by Wilcoxon signed ranks test.
### Table 4: CT perfusion parameters before and after stenting.

<table>
<thead>
<tr>
<th></th>
<th>Time</th>
<th>Change status (number)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Before treatment</td>
<td>After treatment</td>
</tr>
<tr>
<td></td>
<td>N</td>
<td>Mean</td>
</tr>
<tr>
<td>MTT ratio</td>
<td>13</td>
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</tr>
<tr>
<td>dMTT</td>
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<td>2.43</td>
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<tr>
<td>MTT index</td>
<td>13</td>
<td>0.44</td>
</tr>
<tr>
<td>CBV ratio</td>
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<td>1.11</td>
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<tr>
<td>dCBV</td>
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<tr>
<td>CBV index</td>
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<td>0.26</td>
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<tr>
<td>CBF ratio</td>
<td>15</td>
<td>1.13</td>
</tr>
<tr>
<td>dCBF</td>
<td>15</td>
<td>13.91</td>
</tr>
<tr>
<td>CBF index</td>
<td>15</td>
<td>0.44</td>
</tr>
<tr>
<td>TTP ratio</td>
<td>15</td>
<td>1.08</td>
</tr>
<tr>
<td>dTTP</td>
<td>15</td>
<td>2.10</td>
</tr>
<tr>
<td>TTP Index</td>
<td>15</td>
<td>0.14</td>
</tr>
</tbody>
</table>

Note: SD, standard deviation; dMTT, difference of mean transit time; dCBV, difference of cerebral blood volume; dCBF, difference of cerebral blood flow; dTTP, difference of time to peak.

Q₁: percentile 25; Q₃: percentile 75.

P value by Wilcoxon signed ranks test.
interpreted cautiously, and additional studies are necessary for confirming their applicability in various other conditions. Second, the carotid duplex and CT perfusion scans were conducted during persisting phases. Although the immediate effect of stenting can be detected, the long-term cerebral perfusion status is yet to be investigated. Finally, all immediate effect of stenting can be detected, the long-term were conducted during persisting phases. Although the findings of our RI study on carotid ultrasounding and CT perfusion scanning can provide important clinical information in evaluating the perfusion status in patients receiving stenting, especially if the patient condition is not suitable for repeated CT perfusion examinations.

5. Conclusions

The findings of our RI study on carotid ultrasounding and CT perfusion scanning can provide important clinical information in evaluating the perfusion status in patients receiving stenting, especially if the patient condition is not suitable for repeated CT perfusion examinations.

Conflict of Interests

The authors have no conflict of interests to declare.

Authors’ Contribution

Chih-Ming Lin was responsible for collecting data and study design. Yu-Jun Chang was responsible for biostatistical analysis. Chi-Kuang Liu was responsible for data collection. Cheng-Sheng Yu was responsible for data analysis. Henry Horng-Shing Lu was responsible for study design and data analysis.

Acknowledgments

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References


