Systems Analysis Comparing Physiologic Endpoints of Standard AHA and Compression-Only CPR

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Keywords

CPR, compression-only, emergency, resuscitation.

Abstract

Background

Several recent studies suggest that compression only CPR (C-CPR) has similar or superior outcomes to the standard AHA guidelines CPR (S-CPR). However, it has been difficult to rigorously study the key metabolic and hemodynamic endpoints in the acute clinical environment. A systems analysis approach employing a mathematical model of human physiology (Guyton/Coleman/Summers model) was used to compare the expected physiologic perturbations of S-CPR and C-CPR strategies.

Methods

The computer model contains over 5,000 variables of biologic interactions and encompasses a variety of physiologic processes of interest during the performance of CPR. The model is constructed on a foundation of basic physical principles and mass balances in an integrated scheme connected through algebraic loops and differential equations to create a global homeostatic system. A series of computer simulations recreated the protocols of S-CPR and C-CPR (100 compressions/minute). Critical physiologic endpoints predicted by the model for each of the strategies were compared during the performance of the initial four minutes of simulated high quality CPR.

Results

The S-CPR protocol resulted in a 34% lower average systemic blood flow as compared to a C-CPR strategy. The C-CPR produced a small increase in the blood and tissue acid load with a 10% higher serum lactate concentration and 3% lower ventricular tissue pH by comparison. However, the model also predicted that performing S-CPR could result in slightly better blood and tissue oxygen content (4% and 15% respectively).

Conclusions

There has been some debate concerning the operational strategy that should be used to optimize the patient's physiologic condition and potential for a favorable outcome during the performance of CPR. A theoretical systems analysis of the problem using a computer model of human physiology suggests that S-CPR provides slightly better oxygenation but at the cost of increasing the tissue acid burden as compared to C-CPR.

Introduction

Traditional cardiopulmonary resuscitation (CPR) methods with a combination of chest compressions and mouth-to-mouth ventilation as outlined by AHA guidelines (S-CPR) have been taught for decades as the unquestioned standard for patients with cardiac arrest.[1,2,3] This technique is familiar to many healthcare workers and has demonstrated some improvement in outcomes.[3,4] Recently, there has been a call for the adoption of a new standard for cardiopulmonary resuscitation with chest compressions only (C-CPR), also known as cardiocere-

bral resuscitation (CCR), with the goal of increasing the rate of bystander-initiated resuscitation efforts through the use of a simpler technique.[5,6,7] The idea remains controversial with some conflicting results reported in the literature when the two techniques are compared head-to-head.[7,8] However, most studies seem to suggest that there are little differences in clinical outcomes regardless of which technique is used.[9] The basis of the controversy centers on the definition of outcomes and the timing and operator-dependent factors surrounding the initiation of resuscitation efforts by bystanders.[10]

Regardless of the logistical considerations, what is still unclear is the explicit impact of the two separate techniques on the physiology of oxygen delivery and utilization and the potential resulting biochemical derangements that might prevent the spontaneous return of circulation and lead to an irreversible state. The difficulties in measuring these factors at the organ and cellular level in humans during a clinical setting of cardiac arrest has significantly limited our evaluation of the physiologic differences in the techniques. Computer models and simulation procedures have been proposed as a possible methodology to gain insight into clinical questions of this nature.[11,12]

The goal of the current study is to compare the outcomes of the two resuscitation techniques (S-CPR vs C-CPR) with regard to specific critical physiologic endpoints predicted for a virtual patient that has been integrated with a detailed computer model of human physiology.

Methods

A systems analysis approach employing a virtual patient integrated with a mathematical model of human physiology (Guyton/Coleman/Summers model) was used to predict the expected physiologic perturbations of the S-CPR and C-CPR strategies.[13,14,15] The model contains over 5,000 variables of biologic interactions and encompasses a variety of physiologic processes of interest to researchers and clinicians concerned with resuscitation issues. The model is constructed on a foundation of basic physical principles in a mathematical scheme of interconnections with a hierarchy of control that forms the overall model structure. Physiologic relationships derived from the evidence-based literature interconnect the body's physiologic systems and body organs through feedback and feedforward loops in the form of algebraic and differential equations to create a global homeostatic system. Through simulation studies, the investigators interact with the model using a computational interface that allows for the replication of the conditions of cardiac arrest and CPR interventions (chest compressions and ventilations) and a prediction of critical physiologic variables.

Model Validation

Model validation has been generally defined as the confirmation that a computer model possesses a satisfactory range of accuracy within its domain of applicability and is consistent with the intended use.[16] This emphasis on accuracy in the context of the clinical state of cardiac arrest and hemodynamic shock is

our approach to validation of the computational platform used in this study. Most important in this process is the comparison of physiologic endpoints that typify and define the clinical state to those predicted by the model. This model has previously undergone extensive validation of global hemodynamic and physiologic variables (of MAP, CO, SvO_2, etc) that are generally relevant to the pathologic state under study.[13,14] The overall dynamic performance of the model will be quantified by determination of the median performance error (MDPE = median {PE} over all data points as the percent of measured where PE= difference between measured and predicted values). MDPE has been considered as the measure of the *bias* and *inaccuracy* between the model's predictions and the corresponding experimental observations.[17,18]

In Silico Investigational Protocol

The investigational procedure using the computational platform and computer model involves recreating the experiment for a virtual subject in an *In Silico* environment.[13] This *In Silico* experiment is intended to simulate the common clinical context of bystanders or first responders performing CPR on a patient that has experienced an out-of-hospital cardiopulmonary arrest. This process requires a re-enactment of the pathologic event, which included the simulation of an abrupt cardiopulmonary arrest. The virtual subject used in the procedure is considered to be a normal 70 kilogram male with no previous pathology. The processes of high quality S-CPR and C-CPR were also simulated through the functionality of the model software interface for a period of four minutes. The simulation assumptions and their references origins are listed below.

Simulation Assumptions

- 70 kilogram man with spontaneous rhythm cardiac arrest
- Compression Rate of 100 compressions/minute[19]
- Compression Force of 350 newtons[20,21]
- S-CPR ventilated tidal volume is 500 ml[2,22]
- S-CPR ventilation rate is 30:2 compressions/ ventilations[2]
- C-CPR chest tidal volume is 50 ml/compression[23,24]

In this simulation experiment, the model predicted sequential changes in the prespecified variables, which were recorded during both CPR strategies for the same four-minute time points. These model-determined endpoints were compared as percentage differences. The blood and body tissue oxygen content, serum lactate levels, and ventricular myocardial tissue pHs were evaluated at the four-minute terminal point of the CPR process as an indicator of the relative effectiveness of the strategies to provide the needed oxygen delivery and support tissue metabolism. The cardiac output values averaged over the entire four minutes of the simulation were used as a comparative measure of the hemodynamic effectiveness.
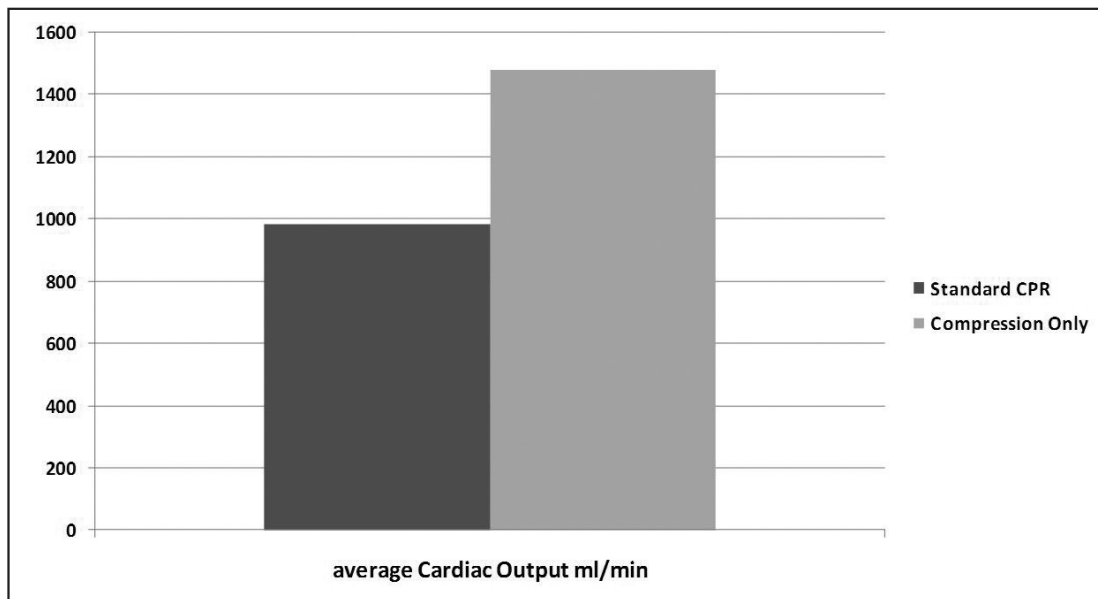
Figure 1: Comparison of the model predicted average cardiac output values generated over four minutes of the two simulated CPR strategies (Standard CPR vs Compression-Only CPR). The Standard CPR strategy produced a 34% lower average cardiac output.
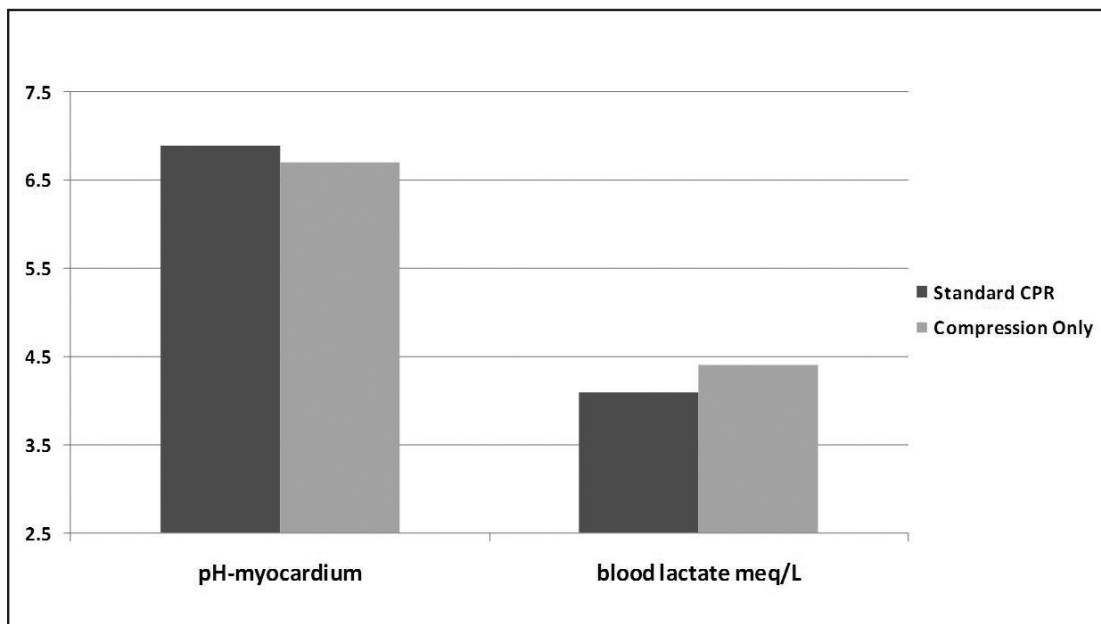

Figure 2: Comparison of the model predicted left ventricle myocardial tissue pH and blood lactate levels at the end of four minutes of the two simulated CPR strategies (Standard CPR vs Compression-Only CPR). This represents only a 3% lower tissue pH and 10% higher blood lactate level for the Compression-Only strategy by comparison.

Results

The application of the S-CPR protocol to the virtual cardiac arrest patient resulted in a 34% lower average systemic blood flow (cardiac output) as compared to a C-CPR strategy in the same patient (Figure 1). The C-CPR strategy produced a small increase in the blood and tissue acid load with a 10% higher serum lactate concentration and a 3% lower left ventricular myocardial tissue pH in contrast to S-CPR (Figure 2). However,

the model also predicted that performing S-CPR could result in a slightly better blood oxygen saturation (4%) and a mild increase in the overall body tissue oxygen content (15%) as compared to the C-CPR strategy (Figure 3).

Conclusions

For many years, the initiation of CPR by bystanders has been shown to have a significant impact on the outcomes of victims
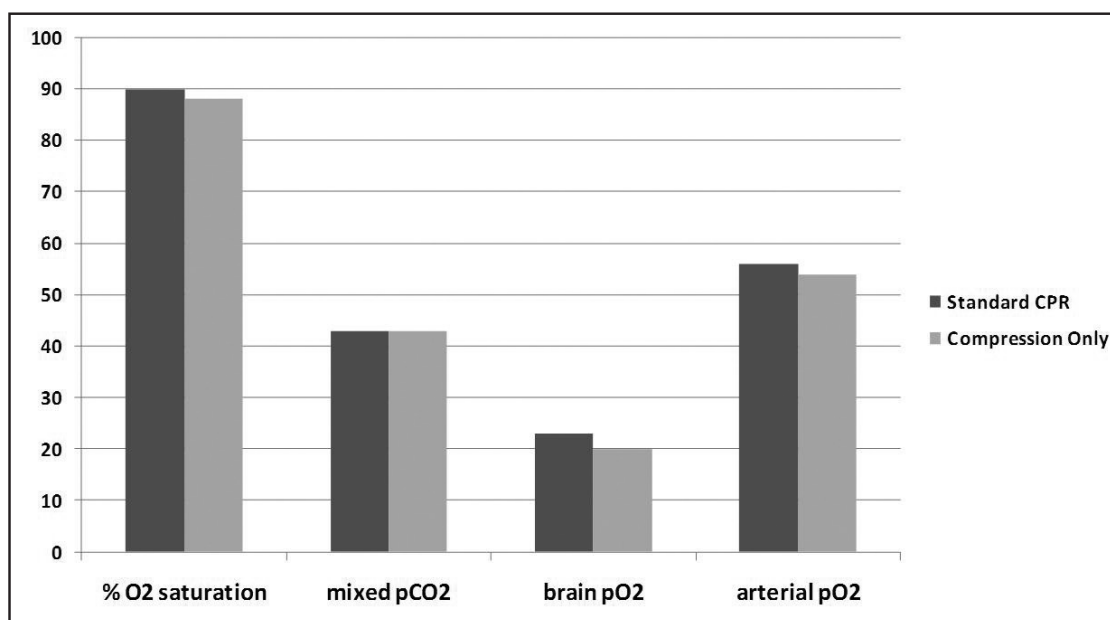
Figure 3: Comparison of the model predicted arterial oxygen saturation and pO$_2$, brain tissue pO$_2$, and the mixed venous pCO$_2$ at the end of 4 minutes of the two simulated CPR strategies (Standard CPR vs Compression-Only CPR). This suggests that there is only a small oxygenation advantage for the Standard CPR strategy over the Compression-Only strategy for the short period of the CPR.

of cardiac arrest.[1,3,4] However, despite dedicated public initiatives intended to educate the lay population in the techniques, CPR is performed in only about one-third of witnessed out-of-hospital arrests.[3,9,10,25] Simplifying the protocol of CPR to include a compressions-only methodology could potentially lower barriers to bystander initiation.[25] A move to shift management standards would be even more compelling if there was clear evidence of superior or equivalent outcomes for those patients in which a simpler C-CPR strategy was used. A number of current clinical trials provides evidence to support the use of C-CPR but are confounded by problems of experimental control obviously inherent in such studies.[6,7,8] There is also uncertainty with regard to the basic physiologic, hemodynamic, and metabolic advantages of one technique as compared to the other due to the difficulty in experimentally exploring these factors with standard clinical trials. In the current study, we employed the modern methodology of simulations studies using computer models of human physiology to provide some insight into the differentiation of these techniques from the basic physiologic perspective.

The results from this simulation study suggest that despite the very limited ventilation occurring during C-CPR, there is only a comparatively small oxygenation and metabolic advantage obtained through use of the customary S-CPR strategy. The level of oxygenation and metabolic derangement are commonly considered consequential in determining the chances for a spontaneous return of circulation and end-organ damage.[26] Therefore, this finding of the simulation study is consistent with the majority of clinical trials suggesting outcomes equivalent for the two techniques and provides support for those advocating a shift in CPR standards to the simpler technique. Systems analyses using the model can be used to help understand the seem-

ing paradox that the ventilations of S-CPR are not required to produce oxygenation similar to that found with compressions alone. Such an analysis reveals several key factors responsible for the results. The additional few compressions performed during C-CPR produce a third greater average blood flow. This technique also results in an uninterrupted continuity in oxygen delivery to vital organs. While the ventilation volumes found to be produced by chest compressions are less than dead space volumes and have limited value to provide oxygen, the blood present in the circulation at the time of cardiac arrest contains a reservoir of oxygen available for delivery over the short time period of the CPR. The simulation suggests that this blood oxygen reservoir may be important, since the tissue oxygenation is very similar for the two strategies. There is some experimental evidence in the literature to suggest that diffusion of oxygen from the dead spaces into the alveoli may find its way into the blood stream of even apneic patients, if there is a moving circulation.[27] Blood also provides a great source of buffers against the acidosis (hemoglobin, bicarbonate), and the continuous movement and greater average flow around the cardiovascular circuit of the C-CPR strategy also removes greater quantities of CO$_2$ from the body through the lungs. Evidence of this phenomenon can be seen within the simulation results with nearly identical mixed pCO$_2$ levels for the two strategies despite a somewhat higher blood and tissue acidosis with C-CPR.

There are several limitations to this study that should be noted. While the simulations incorporate the dynamics of a very complex and detailed model of human physiology, it is impossible to be sure that all the critical elements in play during CPR are represented correctly. However, the model has been shown to provide outputs as compared to human experimental studies of

hemodynamic shock. This suggests that the results should be at least directionally and semiquantitatively accurate for the study of cardiac arrest. The model also does not consider the practical logistical differences between the two differing strategies and assumes optimal high quality CPR. In actuality, delivery of nonstop compressions without fatiguing is quite difficult and could limit the effectiveness of that strategy. Likewise, a directive to provide ventilations could limit bystander engagement in the CPR process. The model also cannot predict the impact of the physiologic derangements on clinical outcomes. Those factors are beyond the intent of the current study and should be studied in clinical trials.

The initiation of bystander CPR is the vital initial link in the chain of survival in advanced cardiac life support (ACLS). Therefore, it is important that the best strategy is adopted to optimize patient outcomes. A determination of the superior strategy requires a concerted effort to study all the clinical and physiologic factors involved.

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