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Clinical paper

Study of risk factors for injuries due to cardiopulmonary resuscitation with special focus on the role of the heart: A machine learning analysis of a prospective registry with multiple sources of information (ReCaPTa Study)

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Abstract

Background: The study of thoracic injuries and biomechanics during CPR requires detailed studies that are very scarce. The role of the heart in CPR biomechanics has not been determined. This study aimed to determine the risk factors importance for serious ribcage damage due to CPR.

Methods: Data were collected from a prospective registry of out-of-hospital cardiac arrest between April 2014 and April 2017. This study included consecutive out-of-hospital CPR attempts undergoing an autopsy study focused on CPR injuries. Cardiac mass ratio was defined as the ratio of real to expected heart mass. Pearson's correlation coefficient was used to select clinically relevant variables and subsequently classification tree models were built. The Gini index was used to determine the importance of the associated serious ribcage damage factors. The LUCAS® chest compressions device forces and the cardiac mass were analyzed by linear regression.

Results: Two hundred CPR attempts were included (133 manual CPR and 67 mechanical CPR). The mean age of the sample was 60.4 ± 13.5, and 56 (28%) were women. In all, 65.0% of the patients presented serious ribcage damage. From the classification tree build with the clinically relevant variables, age (0.44), cardiac mass ratio (0.26), CPR time (0.22), and mechanical CPR (0.07), in that order, were the most influential factors on serious ribcage damage. The chest compression forces were greater in subjects with higher cardiac mass.

Conclusions: The heart plays a key role in CPR biomechanics being cardiac mass ratio the second most important risk factor for CPR injuries.

Keywords: Heart, Cardiopulmonary resuscitation, Biomechanics, Cardiac arrest, Thoracic injuries

Introduction

Chest compressions are the key maneuver responsible for driving flow to the brain and heart during cardiopulmonary resuscitation (CPR). Since this maneuver was first described in 1960, the chest compressions technique has not changed significantly.[1] In the latest CPR guidelines, the recommended compression depth is between 50 and 60 mm for an average-sized adult.[2] The maximum compression depth was limited to 60 mm because of the increased risk of injury.[3] The incidence of serious ribcage damage (SRD) ranges between 39.8% and 63.3%.[4,5] Increasing age, female sex and the thoracic perimeter as anthropometrical variable are the intrinsic factors, and the compression depth, mechanical compressions

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and CPR time the main extrinsic factors associated with CPR injuries.[4,6,7]

Chest injuries caused by CPR have recently been described as an independent factor in 30-day mortality following out-of-hospital cardiac arrest (OHCA).[8] Theoretically, it is explained by the analysis of the pressure–volume curves of the Campbell diagram, which shows how thoracic molding secondary to serious CPR injuries impairs venous return and favors dynamic obstruction of the left ventricular outflow tract (LVOT).[9] LVOT obstruction was observed in 11 of 19 patients undergoing extracorporeal membrane oxygenation (ECMO) and was associated with poor prognosis.[10] Moreover, data from a series of OHCAs treated with mechanical CPR show that the loss of thoracic elastic properties secondary to CPR-related injuries is associated with decreased survival.[11]

Establishing a one-size-fits-all chest compression depth would be beneficial for providing recommendations at the population level. However, specialized resuscitation teams need data to personalize the compression depth to patients of different sizes, and mechanical compressors are not designed to preserve the elastic properties of the thorax, which could be helpful to improve hemodynamics during prolonged CPR as a bridge to ECMO.[12] Chest biomechanics during CPR depends on two forces, the elastic force of the cartilaginous-bone system of the rib cage and the damping force exerted by the intrathoracic viscera.[13] Changes in thoracic geometry, such as in obesity and age, are the main factors affecting the elastic force, increasing the rib cage stiffness and the risk of CPR injuries.[4,14] However, there are very limited data on the role of the anthropometrical variables and specifically of the heart in chest stiffness, which is necessary to understand the chest biomechanics during CPR.[11] This study aimed to determine the risk factors importance for serious ribcage damage in deceased subjects who had undergone manual and mechanical CPR.

Data and methods

Study design and setting

The data analyzed were provided by the ReCaPTa study, an OHCA prospective registry of Tarragona (Catalonia, Spain), with multiple information sources and focused on sudden cardiac death and CPR-related injuries.[15] This study was approved by the Ethical Clinic Research Committee of the University Hospital Joan XXIII in Tarragona (Ref: CI 65/2014), which waived the need for informed consent from participants.

Participants, clinical and autopsy variables

The study included autopsied patients who underwent a prehospital CPR attempt from April 2014 to March 2017. This set included both manual and mechanical CPR performed with the mechanical chest compressor device LUCAS®. Patients under 18 years, CPR > 100 min duration, cases with extreme body mass index and those with a traumatic cause of death were excluded. For each patient, the EMS team collected all data regarding CPR assistance, such as the CPR type and duration. The LUCAS® device was used based on the clinical decision of the EMS team and following the manufacturer's recommendations. The primary care research team collected the medical background data on the subject. In Spain a forensic autopsy is required for all sudden and unexpected natural death in non-hospitalized persons. All patients underwent subsequent autopsy by the forensic medical personnel of the Institut de Medicina Legal i Ciències Forenses de Catalunya (IMLCFC) in Tarragona, to determine CPR-associated injuries following a protocol focused on the study of CPR injuries described previously.[16] Only injuries secondary to CPR according to forensic criteria were considered.

The damage variables were defined as follows. Bilateral rib fracture was defined as the presence of at least one fracture on each side of the thorax. Serious visceral damage was considered when hemopericardium, epicardial contusion, thoracic aorta dissection or hematoma, pneumothorax, hemothorax, hepatic laceration, hepatic subcapsular hematoma, spleen injury, or pulmonary hematoma was observed.[16] Serious ribcage damage (SRD) was defined as the presence of a sternum fracture and/or >6 rib fractures if unilateral or >4 rib fractures if at least one rib was bilateral, as described previously.[5]

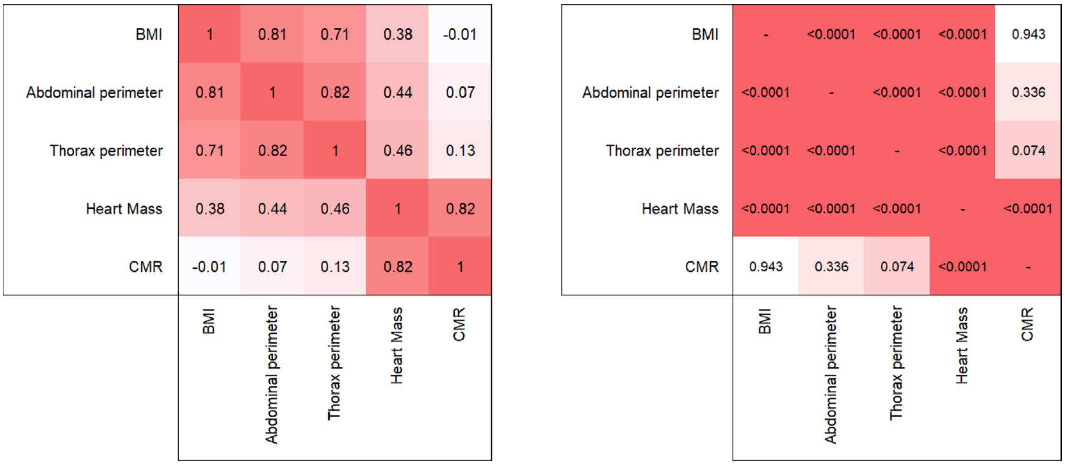
The autopsy protocol included the collection of variables as gender, age, and cause of death and anthropometric variables as weight, height, and thorax and abdominal perimeter. In addition, cardiac variables were determined, including the heart mass. The heart is weighed as part of the usual forensic macroscopic study. To analyze the influence of heart increase on serious ribcage damage, an additional variable was defined, called the cardiac mass ratio (CMR). The CMR is calculated as $CMR = rcm/ecm$, were rcm is the measured cardiac mass and ecm the expected cardiac mass value based on sex and weight data published from forensic autopsies of Caucasian patients.[17] Thus, patients with CMR values higher than 1 present a heart mass higher than those expected based on their sex and weight.

Regarding medical histories, the variables collected were hypertension, diabetes, dyslipidemia, and the presence of a cardiac pathology defined as a previous coronary disease, heart failure history, or cardiomyopathy.

The collected study data consisted of both cases treated with manual and mechanical CPR performed with the LUCAS® device. 37 of the LUCAS®-treated cases were published in a previous study.[11] The device automatically applies the force required to achieve a compression depth of 53 mm with an accuracy of ± 2 mm. The force exerted by the device at the point of maximum compression depth with a maximum accuracy of ± 100 newtons (N) was measured, and these force values were used to define the maximum force (Fmax) and the mean force (Fmean) of the treatment period.

Model development

In order to study the factors associated with serious ribcage damage, we considered all the factors described in the literature and we defined them as clinically relevant variables. The extrinsic factors such as CPR time, mechanical compressions and the intrinsic factors such as age and sex were included in the classification tree. However, due to the interdependence between the different anthropometric variables (BMI, heart mass, CMR, abdominal perimeter and thoracic perimeter) a correlation study was performed. CMR was chosen among the anthropometric variables because it presented the lowest correlation with the rest, as shown in Fig. 1. This is because CMR considers the increase ratio in heart mass with respect to the expected mass value as a function of the subject's size (weight, height, BMI and total body surface area), in contrast to heart mass or thoracic perimeter. The correlation between all the variables considered is shown in a heat map, available in the supplementary material in Fig. 1S.



	BMI	Abdominal perimeter	Thorax perimeter	Heart Mass	CMR
BMI	1	0.81	0.71	0.38	-0.01
Abdominal perimeter	0.81	1	0.82	0.44	0.07
Thorax perimeter	0.71	0.82	1	0.46	0.13
Heart Mass	0.38	0.44	0.46	1	0.82
CMR	-0.01	0.07	0.13	0.82	1

	BMI	Abdominal perimeter	Thorax perimeter	Heart Mass	CMR
BMI	-	<0.0001	<0.0001	<0.0001	0.943
Abdominal perimeter	<0.0001	-	<0.0001	<0.0001	0.336
Thorax perimeter	<0.0001	<0.0001	-	<0.0001	0.074
Heart Mass	<0.0001	<0.0001	<0.0001	-	<0.0001
CMR	0.943	0.336	0.074	<0.0001	-

Fig. 1 – Correlation plot of all the anthropometric variables.

Finally, the clinically relevant variables sex, age, CMR, total CPR duration and mechanical compressions, were introduced into the classification tree to analyze the ranges of values in which variables influence the serious ribcage damage incidence. Other methodologies, such as random forest or artificial neural networks (ANN), were not considered because they require a larger sample and are less directly interpretable than the classification tree. In this case classification tree algorithm uses Gini impurity as criterion to select the most informative feature for node splitting. Specifically, the feature with the lowest impurity is chosen to make the best classification at each node of the tree. Based on the Gini indexing feature, importance of different variables for serious ribcage damage and non-serious ribcage damage classification were also calculated and results were visualized as bar plot. In addition, several hyperparameters were considered for constructing the classification tree, including setting the tree depth at three levels, specifying the minimum number of samples for node splitting to be 30, and the minimum number of samples for leaf splitting to be four. Other classification trees were explored. A tree was constructed including thoracic perimeter or heart mass instead of CMR among the clinically relevant variables to compare the importance of these anthropometric variables as shown in Fig. 2S and 3S of the supplementary material. Other variable selection strategies for the classification tree are shown in Fig. 4S. However, given the objectives of this research and the correlation exhibited by the variables analyzed, the tree of greatest interest and applicability is presented in the result section.

Statistical analysis

Quantitative variables are shown using the mean and standard deviations (SD) or median and interquartile range (25th and 75th centiles). Categorical or binary values are expressed as the percentage and number of cases (count). An univariate analysis between serious ribcage damage and non-serious ribcage damage patients was performed by means of the chi-square (χ^2) test for categorical variables and the Student´s T or Mann-Whitney test for quantitative variables. All tests were two-tailed, and p-values lower than 0.05 were considered statistically significant. Analysis was performed using scikit-learn, an open-source Python-based machine learning library,[18] while descriptive plotting of the classification tree was conducted using the dtreeviz library.[19]

Results

The initial data set consisted of 237 consecutive cases studied by the focused CPR injuries autopsy protocol during the study period. Eight patients with traumatic cardiac arrest, eight subjects under 18 years old, three CPR events longer than 100 minutes, and one case with an extreme BMI value were excluded to ensure a proper analysis. Moreover, 17 cases were resuscitated with the Autopulse® compression device and were therefore excluded. Thus, the final study data consisted of 200 resuscitation attempts assisted by the EMS.

Characteristics of the study population and injuries

Characteristics of the study population, are shown in Table 1. Of all the studied cases 65.0% presented serious ribcage damage. The injuries in the total study population and in the groups of serious ribcage damage and non-serious ribcage damage cases are shown in Table 2. The percentage distribution of fractures in the thorax is represented in Fig. 5S. Nineteen percent of the study population presented serious visceral damage. Among them 18 (9%) cases presented epicardial contusion, 15 (7.5%) anterior mediastinal hematoma, 9 (4.5%) hemopericardium and 4 (2%) hematoma or dissection of the thoracic aorta. Regarding medical backgrounds, 56% of the sample presented hypertension, 39.4% diabetes, 37.9% dyslipidemia, and 25% a previous known cardiac pathology.

The classification tree results

The relevant clinical variables selection was made after correlation variables study, as shown in Fig. 1 and Fig. 1S. Among anthropometric variables (BMI, thorax perimeter, abdominal perimeter, heart mass and CMR) all variables excepting CMR are highly correlated ($p < 0.0001$), whereas CMR is strongly correlated with heart mass, with a ρ coefficient of 0.82 ($p < 0.0001$) and is nearly related to thorax perimeter ($\rho = 0.069$, $p = 0.074$). Thus, CMR was chosen as an anthropometric variable, as it explains additional information with respect to heart mass. Fig. 2A showed the clinically relevant variables included in the classification tree were age, sex, CPR time, mechanical compressions and CMR. Fig. 2B showed that age (0.44), CMR (0.26), CPR time (0.22), and mechanical CPR (0.07) are, in that order, the most influential variables in the occurrence of serious ribcage damage, according to the Gini significance. The

Table 1 – Characteristics of the study population.

Variables	
N	200
Age, y	60.4 (13.6)
Female	56 (28.0)
CPR Characteristics	
Total CPR duration	37.9 (16.1)
Basic support duration, min, median (IQR)	8.0 (3.0–14.0)
Advance support duration, min, median (IQR)	27.5 (17.0–39.0)
Treated with mechanical compressions	67 (33.5)
Anthropometric Variables	
BMI (kg/m^2)	29.9 (5.7)
Thorax perimeter (mm)	102.7 (12.2)
Abdominal perimeter (mm)	102.5 (14.5)
Heart mass (g)	480.5 (140.3)
Septointerventricular wall thickness (mm)	16.2 (3.9)
LV posterior wall thickness (mm)	15.7 (3.4)
Cardiac mass ratio	1.33 (0.29)
Cause of death	
Cardiac cause of death	**105 (52.5)**

Data are expressed as mean and SD for normally distributed variables and median and interquartile range (IQR) for quantitative variables and frequency (N) and percentage for categorical variables.

Abbreviations: CPR = cardiopulmonary resuscitation; LV = left ventricular.

The data set has 10 missing values for total CPR duration, basic support duration, and advance support duration and 8 missing values for Cardiac mass ratio.

results of classification trees with other selected anthropometric variables can be consulted in the supplementary material (Fig. 2S and 3S).

Given the role of the CMR in the classification tree, its relation with possible previous pathologies has been investigated. CMR was higher in patients who had a previous cardiac pathology than in those without (1.429 ± 0.295 vs 1.309 ± 0.290, $p = 0.038$). Moreover, subjects who died due to a cardiac cause had a higher CMR value than those who died due to other causes (1.40 ± 0.30 vs 1.25 ± 0.26, $p < 0.001$).

The force applied by the LUCAS device during the whole CPR period for the 37 cases was analyzed. It was observed that both the mean force ($p = 0.022$) of all the maneuver and the maximum force ($p = 0.021$) exerted by the mechanical compressor were higher when the heart mass of the subjects was greater, as shown in Fig. 3, being the heart mass highly correlated with CMR in this set of cases ($p < 0.001$).

Discussion

This prospective study focused in CPR injuries using clinically validated data from multiple sources and analyzes the causality of intrinsic and extrinsic factors in the CPR injury risk. To our knowledge, this is the first study using machine learning techniques investigating the role of intrinsic and extrinsic factors together on CPR injury. This study allowed us to compare the weight of different anthropometric variables, confirming a specific weight of the CMR compared to other known factors as thoracic perimeter. A classification tree analyze the influence of specific ranges of these variables on the occurrence of serious ribcage damage, which may not be found in a regression analysis. Age and CMR are the main risk factors, followed by CPR duration and mechanical compressions.

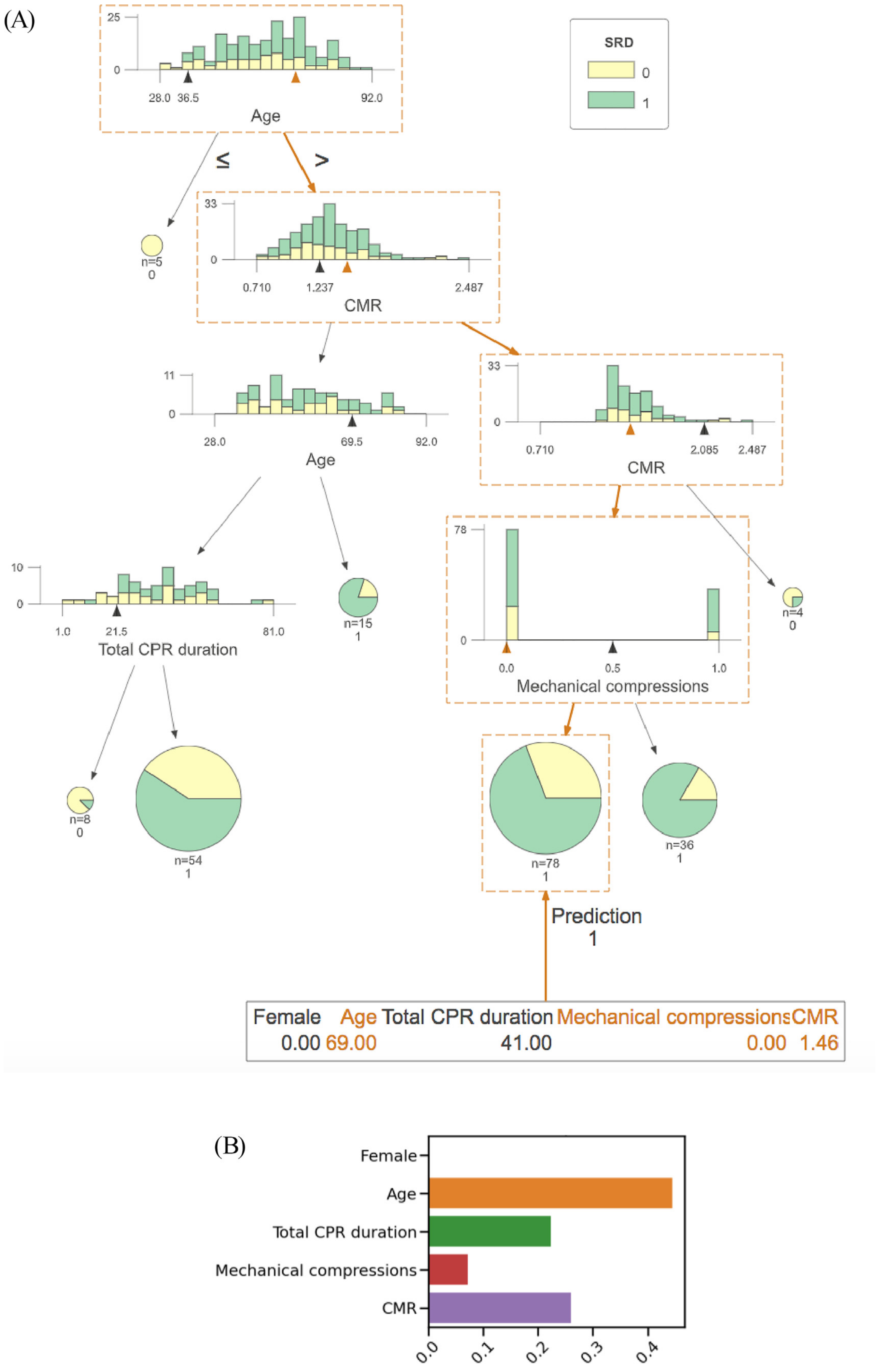
To our knowledge, this is the first description of the heart role as an injury risk factor. However, age, CPR time, and mechanical compressions are also known risk factors.[20,21,7] Gender-related risk has been associated with elderly women mainly.[22] Further, CMR is the ratio of the real heart mass and the expected heart mass, based on sex and weight of the subjects. Thus, the CMR is a normalized value that somehow isolates the sex and weight effects to focus only on the heart mass increase with respect to those heart mass that the subject should have due to its anthropometric characteristics. The injuries incidence described in our study, as expected, was higher than that in other series of survivors, but lower than that in other series of autopsied non-survivors.[5,23] It is noteworthy that the age, medical history, and the incidence of injuries described in our series were similar to those in a series of cases of prolonged CPR included in an ECMO CPR protocol, so our findings could be extrapolated to this type of patients.[24] Furthermore, this study highlights the importance of an increase in cardiac mass with respect to the expected heart mass in the emergence of serious ribcage damage. Specifically, a heart with a mass 24% greater than expected has been associated with an increased risk of serious ribcage damage. Moreover, a relationship between mean and peak compression force and cardiac mass has also been found, confirming the important role of the heart in the intra-thoracic damping force occurring during chest compressions. The increased damping force occurring in cases with higher CMR increases total thoracic stiffness. When this is plotted on a force vs. displacement curve, the increase in thoracic stiffness results in higher force requirements to achieve the same displacement so that the fracture limit is easily reached increasing the risk of serious thoracic damage.[9]

The heart is deformed at each chest compression as can be visualized in a recent 4D simulation.[25] In general, the heart increases in size and horizontalizes with age and with the development of heart

Table 2 – Injuries of the study population with serious and non-serious ribcage damage.

Variables	Total	Non serious ribcage damage	Serious ribcage damage
N	200	70 (35.0)	130 (65.0)
Sternum fracture	92 (46)	0 (0.0)	92 (70.8)
Rib fractures	155 (77.5)	28 (40.0)	127 (97.7)
Number of rib fractures	6.0 (1.0–10.0)	1.4 (0.0–2.0)	8.4 (6.0–11.0)
Bilateral rib fractures	120 (60)	4 (5.7)	116 (89.2)
Sternum and bilateral rib fractures	78 (39)	0 (0.0)	78 (60.0)
Flail chest	10 (5)	0 (0.0)	10 (7.7)
Serious visceral damage	38 (19)	5 (7.10)	33 (25.4)

Data are expressed as Frequency (N) and percentage for categorical variables and median and interquartile range (IQR) for quantitative variables.


(A)
SRD
0
1
25
0
28.0
36.5
92.0
Age
≤
>
n=5
0
33
0
0.710
1.237
2.487
CMR
11
0
28.0
69.5
92.0
Age
33
0
0.710
2.085
2.487
CMR
10
0
1.0
21.5
81.0
Total CPR duration
n=15
1
78
0
0.0
0.5
1.0
Mechanical compressions
n=4
0
n=8
0
n=54
1
n=78
1
n=36
1
Prediction
1
Female Age Total CPR duration Mechanical compressions CMR
0.00 69.00 41.00 0.00 1.46
(B)
Female
Age
Total CPR duration
Mechanical compressions
CMR
0.0
0.1
0.2
0.3
0.4

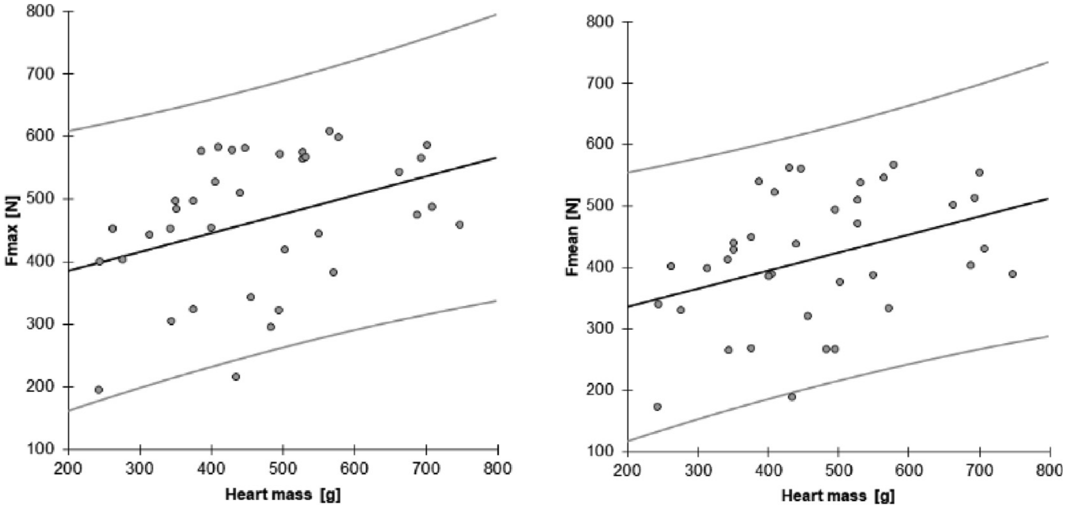


Fig. 3 – Variation of maximum force and mean force of the mechanical chest compressions with heart mass. ***Linear regression analysis was performed. The light gray lines show the 95% confidence interval. Abbreviations: Fmax = maximum force of mechanical chest compression; Fmean = mean force of mechanical chest compression.***

disease. The left ventricular outflow tract (LVOT) was found more frequently under the center of the sternum with increasing age and in patients with previous heart disease which has an impact on hemodynamics.[26–28] When the area of maximum thoracic compression is located near the LVOT, it is obstructed, resulting in a dramatic fall of the ventricular stroke volume.[29] Serious ribcage damage molds the thorax producing a posterior fall of the sternum and aggravating the LVOT obstruction, which would justify a worse survival in cases with a higher serious ribcage damage incidence, as previously described by our research group.[11] Additionally, during prolonged CPR, the heart becomes stiffer due to the stone heart phenomenon and more horizontalized as it increases in size, thus increasing the chest stiffness during CPR.[30,31]

Moreover, the classification tree showed that, for patients with and increased CMR, the mechanical CPR increases the serious ribcage damage risk with respect to the manual CPR. This suggests that performing a mechanical maneuver of a constant compression depth induces an increase in injury risk in these type of patients, and the heart size should be taken into account to personalize the CPR. Besides, it can be hypothesized that manual CPR led to less serious ribcage damage ratio cases, as the force applied could be limited because the rescuer can feel the thoracic stiffness.

These findings are important for clinical practice to move toward more personalized CPR. In this regard, it would be advisable to consider the influential factors in serious ribcage damage, especially in mechanical CPR, to reduce CPR-associated injuries focusing on preserving the biomechanical properties of the thorax and avoiding LVOT during CPR. This is particularly necessary for patients undergoing prolonged mechanical CPR, which should be more protective. From our point of view, decreasing the compression depth between 5 and 10 mm in patients at higher risk of serious ribcage damage could be one of the most effective strategies to avoid injuries in prolonged mechanical CPR.[32,33] It should be borne in mind that the highest survival has been associated with compression depth ranges between 40.3 and 55.3 mm and between 45 and 50 mm, depending on the study.[34,35] Another protective strategy would be to ensure that the mechanical compressor piston is placed in the lower third of the sternum, especially in larger patients, and to avoid caudal or cephalic migration of the piston.[9,20,36] Personalizing CPR, a more caudal compression at the sternum or even a leftward and caudally displaced chest compression may be safe in terms of risk of ribcage damage and has been associated with better hemodynamic outcomes.[37–40] As lines of future research, more data on the correlation between LVOT during chest compressions and anthropometric variables or history of heart disease are needed to help guide a more personalized CPR.

This study has some limitations. One is the relatively small sample but the difficulty of obtaining the sample with these specific variables must be taken into account. This study does not include survivors. The sample of this study only recruited patients from

Fig. 2 – Classification tree scheme and risk factors importance. A. The optimal path for serious ribcage damage prediction. Yellow colour indicates cases with non-serious ribcage damage (SRD = 0) due to CPR. Light green colour indicates cases with serious ribcage damage (SRD = 1) due to CPR. The number under the circular diagram shows the predominant cases according to serious ribcage damage. The optimal path for serious ribcage damage prediction is highlighted in orange corresponding to a particular case. The value of this particular case is in the bottom box of figure. Abbreviations: CMR = cardiac mass ratio; CPR = cardiopulmonary resuscitation. B: Risk factors importance following Gini index bar plot. Abbreviations: CMR = cardiac mass ratio; CPR = cardiopulmonary resuscitation.

one Spanish region. It is difficult to determine the exact role of mechanical CPR as a risk factor for injury because all patients received manual compressions beforehand. In addition, the depth of compression performed during manual CPR was not measured. The mechanical compressor manufacturer's recommendations include a contraindication to use in cases where the patient's size is too small or too large to fit the piston, which could be a potential bias. Not all patients who died in the field after a CPR attempt were studied by autopsy, which may lead to a possible selection bias, but the ratio of autopsies performed in our setting is high compared to that in other countries. [41]

Conclusions

The heart plays a key role in CPR biomechanics. The increase in the cardiac mass over the expected mass has been described as the second most important risk factor for CPR injuries. This study analyses together the intrinsic and extrinsic factors for serious ribcage damage due to CPR providing new evidence for further progress toward a personalized CPR.

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CRediT authorship contribution statement

Silvia García-Vilana: Writing – review & editing, Writing – original draft, Software, Investigation, Formal analysis, Data curation, Conceptualization. **Vikas Kumar:** Writing – review & editing, Writing – original draft, Formal analysis, Data curation. **Saurav Kumar:** Writing – review & editing, Writing – original draft, Formal analysis, Data curation. **Eneko Barberia:** Writing – review & editing, Writing – original draft, Supervision, Investigation, Funding acquisition, Data curation. **Inés Landín:** Writing – review & editing, Writing – original draft, Investigation, Data curation. **Ester Granado-Font:** Writing – review & editing, Writing – original draft, Investigation, Data curation. **Silvia Solà-Muñoz:** Writing – review & editing, Writing – original draft, Software, Investigation, Formal analysis, Data curation, Conceptualization. **Xavier Jiménez-Fàbrega:** Writing – review & editing, Resources, Investigation, Funding acquisition, Data curation. **Alfredo Bardají:** Writing – review & editing, Resources, Investigation, Funding acquisition, Data curation. **Bjarne Madsen Hardig:** Methodology, Software, Data curation, Writing – original draft, Visualization, Investigation, Writing – review & editing. **Youcef Azeli:** Writing – review & editing, Writing – original draft, Validation, Supervision, Resources, Methodology, Investigation, Data curation, Conceptualization.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Appendix A. Supplementary material

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