Available online at www.sciencedirect.com

Resuscitation

journal homepage: www.elsevier.com/locate/resuscitation

Clinical paper

Association between left ventricular outflow tract opening and successful resuscitation after cardiac arrest

Emanuele Catena, Davide Ottolina, Tommaso Fossali, Roberto Rech, Beatrice Borghi, Andrea Perotti, Elisa Ballone, Paola Bergomi, Alberto Corona, Antonio Castelli, Riccardo Colombo *

Department of Anesthesia and Intensive Care Unit, ASST Fatebenefratelli Sacco, Luigi Sacco Hospital, Polo Universitario, University of Milan, Milan, Italy

Abstract

Background: Survival after cardiac arrest depends on adequate cardiopulmonary resuscitation (CPR). Manual or mechanical external chest compression may be ineffective to restore circulation: structures subjected to external chest compression may differ in forces transfer to intrathoracic structures due to anatomic characteristics and physiological changes.

This clinical study aims to assess the association of trans-oesophageal findings during CPR and successful resuscitation.

Methods: Retrospective cohort study. Trans-oesophageal assessment of right ventricular fractional area change, right ventricular outflow tract fractional shortening, left ventricular volumes, ejection fraction, and aortic diameters were performed in refractory out-of-hospital cardiac arrest patients admitted to emergency department for extracorporeal CPR.

Results: 19 patients were analyzed. 15 of 19 patients (79%) received venous-arterial extracorporeal membrane oxygenation support. Resuscitation was successful with return of spontaneous circulation or electromechanical activity in 7 patients (group-SUXX) and failed in 12 patients (group-FAIL). 6 patients (32%) were alive at 24 h from the cardiac arrest, one patient (5%) survived to hospital discharge. Left ventricular outflow tract (LVOT) was open during CPR in all patients in group-SUXX and in 1 patient in group-FAIL (p 0.0002). None of the patients with closed LVOT had successful resuscitation. Patients in group-SUXX had a higher ejection fraction (p 0.03), ascending aortic diameter (p 0.04), and survival rate than those in group-FAIL (p 0.015). In a multiple variable Cox's proportional model LVOT opening was the only variable associated with successful resuscitation.

Conclusions: Trans-oesophageal echocardiography can be useful in the emergency setting of cardiopulmonary arrest for discriminating between successful and failing resuscitation.

Keywords: cardiac arrest, cardiopulmonary resuscitation, transesophageal echocardiography, left ventricular outflow tract, mechanical circulatory support, external cardiac massage

Abbreviations: ACLS, advanced cardiac life support; CPR, cardiopulmonary resuscitation; DC shock, direct-current defibrillation; ECMO, extracorporeal membrane oxygenation; ECPR, cardiopulmonary resuscitation with extracorporeal life support; ED, emergency department; EF, ejection fraction; IABP, iantra-aortic balloon pump; LVOT, left ventricular outflow tract; OHCA, out-of-hospital cardiac arrest; REMA, return of electrical and mechanical activity; ROSC, return of spontaneous circulation; RVFAC, right ventricular fractional area change; RVOT, right ventricular outflow tract; RVOT-fs, right ventricular outflow tract fractional shortening; TEE, trans-oesophageal echocardiography; VF, ventricular fibrillation; VT, ventricular tachycardia.

* Corresponding author at: ASST Fatebenefratelli Sacco, Luigi Sacco Hospital, Via G.B. Grassi 74, 20157 Milan, Italy.
E-mail address: riccardo.colombo@asst-fbf-sacco.it (R. Colombo).

https://doi.org/10.1016/j.resuscitation.2019.02.027
Received 2 August 2018; Received in revised form 31 January 2019; Accepted 20 February 2019
0300-9572/© 2019 Elsevier B.V. All rights reserved.

Introduction

Survival after cardiac arrest is influenced by prompt and effective cardiopulmonary resuscitation (CPR). Forward blood flow during CPR is provided by compression of the heart between the sternum and the thoracic vertebrae (cardiac pump theory) and by intra-thoracic pressure fluctuations (thoracic pump theory).[1–4] According to the cardiac pump theory, chest compression is the essential factor in supplying blood to the vital organs.[5]

Deep compressions followed by full-chest recoil performed at an adequate rate affect survival rate and neurologic outcomes.[6,7] The American Heart Association's CPR guidelines emphasize the importance of delivering high-quality compressions and minimizing interruptions.[8,9] For these reasons, mechanical devices, which can compress the chest with constant depths and rates for prolonged periods without decline in quality, are routinely used by the emergency teams.[10,11]

Sometimes, manual or mechanical chest compression may be ineffective to provide anterograde blood flow: anatomical disposition and mechanical properties of the structures subjected to external compression may vary among individuals.[12] Moreover, it is not fully established how the force of chest compression is transferred to intrathoracic structures.[13] Study on chest computed tomography scans and cardiac magnetic resonance imaging found that the left ventricle is rarely beneath the centre of sternum - the point of maximal compression - whereas the left ventricular outflow tract (LVOT), aortic valve, or aortic root are located in that position in 50%–80% of the patients with cardiac disease.[13,14] Hwuang suggested that LVOT compression may impede left ventricular ejection, whereas compression of both ventricular chambers without LVOT compression may be more effective.[12] This hypothesis could explain the effectiveness heterogeneity of chest compressions sometimes clinically observed.[13]

This clinical study aims to assess the association of trans-oesophageal findings during CPR and successful resuscitation.

Methods

A retrospective cohort study was conducted between July 2015 and November 2017 on patients between 18–70 years old, consecutively admitted to the emergency department of the Luigi Sacco Hospital in Milan, a tertiary referral centre, for witnessed refractory out-of-hospital cardiac arrest (OHCA) with criteria for extracorporeal cardiopulmonary resuscitation (ECPR). The publication of these data has been authorized by Institutional Ethical Committee (Comitato Etico Milano Area 1, ASST Fatebenefratelli Sacco, approved on 20th June 2018).

All patients with out-of-hospital witnessed cardiac arrest, time from the event to CPR start ("no flow time") $<$6 min, absence of major comorbidities or terminal illness, unsuccessful 20 min ACLS treatment and expected event to hospital arrival (event-to-door) time $<$65 min were carried under mechanical ventilation to the Emergency Department of our hospital to perform ECPR. On the patient arrival at the emergency department, a fast-focused two-dimensional TEE exam was performed by an ICU physician (EC) expert in echocardiography. The multiplane trans-oesophageal probe (Philips X7-2 t TEE transducer on Philips Epiq 7 ultrasound system, Philips Healthcare, Andover, MA) was introduced into the oesophagus, the heart and ascending aorta were briefly examined to search for possible causes of the cardiac arrest and to rule out aortic dissection. Chest compression was continued during introduction of the probe and the examination. Images and video clips were stored digitally and analyzed off-line (Philips QLAB, Philips Healthcare, Andover, MA).

After implantation of venous-arterial extracorporeal membrane oxygenation (ECMO) or restoration of spontaneous circulation all patients underwent emergency coronary angiography. Post-resuscitation care was performed in a standardized protocol, with target temperature management (internal body temperature was maintained at 36 °C), sedation, and inotropic support (epinephrine) if necessary. In case of ECPR intra-aortic balloon pump (IABP) (Maquet Datascope Corp, Mahwah, NJ) was positioned in the contra-lateral femoral artery and anticoagulation was performed using unfractionated heparin, with the goal of an activated clotting time of 180–220 s.

Echocardiographic measurements and electromechanical definitions

The following parameters were collected in all patients:

- *Right ventricular outflow tract fractional shortening (RVOT-fs),* (end-diastolic diameter – end-systolic diameter)/end-diastolic diameter × 100.[15,16]

Under external cardiac massage the "systolic diameter" was defined as the minimal diameter of RVOT measured at the end of compression phase on sub-pulmonary region in midoesophageal aortic valve short axis view, using multiplane angle of approximately 45–65°.[17] The "diastolic diameter" was defined as the maximal diameter of right ventricular outflow tract measured at the end of relaxation phase.

- *Right ventricular fractional area change (RVFAC),* (end-diastolic area – end-systolic area)/end-diastolic area × 100.[18]

Under external cardiac massage the "systolic area" was defined as the area of maximal compression of the right ventricle measured at the end of compression phase on midoesophageal four-chambers view. The "diastolic area" was defined as the maximal area of the right ventricle measured at the end of relaxation phase. The endocardial border was traced from the tricuspid annulus along the free wall to the apex, then back to the annulus, along the interventricular septum at point of end-compression and end-relaxation.

- *Left ventricular outflow tract (LVOT),* diameter measured at the end of compression phase from midoesophageal long-axis view of aortic valve, on angle of approximately 110–135°, using inner edge to inner edge technique.[19]
- *Aortic root diameters and tubular portion of the ascending aorta,* measured at the end of compression phase from midoesophageal long-axis view of aortic valve, on angle of approximately 110–135°, using inner edge to inner edge method.[17] The aortic annular diameter was measured between the hinge points of the aortic valve leaflets, sino-tubular junction at point of transition between the sinuses of Valsalva and the tubular portion of the ascending aorta, ascending aorta approximately 5 cm away from aortic valve annulus plane.
- *Left ventricular volumes and ejection fraction*, using monoplane method of disks (modified Simpson's rule) in four-chambers view for volume calculations at end-diastole and at end-systole.[17] A

single plane method was used for measurements and the area of the disk was then assumed to be circular as two adequate orthogonal views for biplane method were not available. Frames showing the left ventricle at end-relaxation ("end-diastolic") and at end-compression ("end-systolic) were selected for measurements of end-diastolic volume (EDV) and end-systolic volume (ESV). Ejection fraction (EF) was calculated as follows: Ejection fraction = (EDV–ESV)/EDV.

- *Return of electro-mechanical activity (REMA)* was defined as the return of QRS complexes on ECG associated with longitudinal left ventricular diameter systolic shortening of at least 5 mm, measured from the mitral plane to the apical endocardial border in the four-chambers view.
- *Return of spontaneous circulation (ROSC)* was defined according to the American Heart guidelines.[8,9]

Outcome

The primary outcome of this study was to assess if TEE variables measured during CPR for refractory cardiac arrest were associated with successful resuscitation. Successful resuscitation was defined as return of electro-mechanical activity (REMA) while the patients were in ECMO or ROSC without ECMO.

Statistics

The normality distribution of variables was checked with D'Agostino–Pearson test. Comparison of demographic and baseline clinical parameters was performed by Student's t-test for unpaired samples for variables normally distributed, and the Mann–Whitney rank sum test for variables not normally distributed. Comparison of qualitative variables was performed by the Fisher-s exact test. Data are shown as median (IQR). The survival was analysed using Kaplan–Meier log-rank survival analysis (calculating the cumulative probability of patients remaining alive after hospital arrival). A Cox's Proportional Hazard Regression model was fitted, using a step-by-step enter approach, to identify independent predictors of failed resuscitation. Statistical significance was defined as $p < 0.05$ for two-tails test.

Analysis was performed by using SigmaPlot software (Systat Software, San Jose, CA, USA) and SAS 9.2 software for Windows (SAS Institute, Cary, NC).

Results

19 patients consecutively admitted to the Emergency Department for non-traumatic OHCA were studied. Advanced cardiac life support (ACLS) was performed by the physicians of the emergency medical system according to the current guidelines.[20] Automatic and mechanical chest compression device (LUCAS 2; Jolife AB, Lund, Sweden) was used in 15 (79%) patients. The presumed cause of arrest was unknown; none of patients had a history of pre-existing cardiac disease.

15 of 19 patients (79%) were treated with ECPR by venous-arterial ECMO. Four patients were excluded from mechanical circulatory support: one because of ROSC occurred following CPR, one because of unsuccessful cannulation due to technical problems, and two because of prolonged event-to-door time (>65 min). All ECMO patients were cannulated via the femoral artery and the femoral vein.

The resuscitation was successful with return of sinus rhythm in seven patients (37%) (group-SUXX) and failed in 12 patients (group-FAIL). REMA occurred in five patients in group-SUXX within the first 30 min of ECMO support, and ROSC occurred in two patients following CPR only.

After 24 h from the cardiac arrest six patients (32%) survived, and one patient (5%) survived to hospital discharge after ECMO support. Characteristics and echographic findings of the studied patients are shown in Table 1.

Echocardiographic parameters during CPR and outcome

The average time from patient arrival to completion of the TEE exam was 8 (5–12) min. TEE probe insertion into the oesophagus was not difficult and did not impede the resuscitation manoeuvres. Image quality was good in all patients. Pericardial effusion, cardiac tamponade and valvular alterations were rapidly excluded. LVOT opening was significantly different between the two groups. It occurred in seven (100%) patients in group-SUXX and in one patient (8%) of group-FAIL (p 0.0002). Diameter of ascending aorta, and ejection fraction values were significantly different between groups. In all patients under the compression phase the right ventricular free wall was displaced towards the interventricular septum resulting in a marked reduction in cavity size. Similarly, this was accompanied by a significant compression of RVOT (Fig. 1).

Time-course of the event from cardiac arrest to hospital admission did not differ between the groups. Emergent coronary angiographic study was performed in all resuscitated patients in group-SUXX, and in eight patients in group-FAIL. The remaining four patients died early due to exclusion from ECMO. Culprit lesion was found in four patients in group-SUXX and in seven patients in group-FAIL. It was successfully treated by angioplasty and drug eluting stent implantation.

At 24 h after the event the survival rate in group-SUXX was 71%, and in group-FAIL 8% (p 0.009). Two patients in the group-SUXX became organ donors. The median survival time after the cardiac arrest was 35 (18–223) h and 6 (2–20) h for group-SUXX and group-FAIL respectively (p 0.015). The survival time was significantly higher in patients with LVOT opening during chest compression (p 0.007) (Fig. 2).

After check of the hazards' proportionality, we entered three variables in the Cox's proportional model: (i) LVOT opening, (ii) use of mechanical chest compression and (iii) no flow time. Their hazards associated with primary outcome were respectively (i) 0.205 (95%CI 0.05–0.794), (ii) 3.154 (95%CI 0.724–13.73), and (iii) 0.872 (95%CI 0.703–1.081).

Discussion

The main finding of our study is that LVOT opening during CPR is significantly associated with the probability of successful resuscitation in patients with witnessed cardiac arrest refractory to ACLS treatment.

Previous studies emphasized the advantages of bedside echocardiography in the emergency setting of cardiopulmonary arrest.[2,21] TEE offers some advantages: the probe may be easily placed after tracheal intubation and left in site during CPR. Neither the enlarged lungs of chronic obstructive pulmonary disease patients nor the adipose tissue impairs the TEE imaging. The effectiveness of chest compression can be assessed by the real time views of the heart

Table 1 – Characteristics and echocardiographic findings of the studied patients.

	Group-SUXX Successful resuscitation (n = 7)	Group-FAIL Failed resuscitation (n = 12)	*p*
Age years	52 (51–65)	50 (43.5–64.5)	*0.7*
M:F	6:1	12:0	*0.37*
Body Mass Index (kg. m^{-2})	28 (23–29)	29 (26.5–31)	*0.36*
Witnessed cardiac arrest (n)	7 (100%)	12 (100%)	–
VF or VT at presentation (n)	6 (86%)	9 (75%)	*1*
Number of DC shock (n)	5 (1–6)	4.5 (3–6)	*0.8*
By-stander CPR (n)	4 (57%)	10 (83%)	*0.3*
Automatic chest compression (n)	6 (86%)	9 (75%)	*1*
Time event to ACLS (min)	11 (2–18)	14 (12–17)	*0.64*
Time event to DC shock (min)	5 (1.7–8.5)	7.5 (4.3–12)	*0.32*
Time event to Hospital (min)	53 (39–56)	52.5 (42.7–63)	*0.6*
No Flow Time (min)	2 (0–5)	0 (0–4)	*0.99*
Low Flow Time (min)	87 (66–88)	75 (68.3–85.7)	*0.43*
ECMO (n)	6 (86%)	9 (75%)	*1*
REMA (n)	5 (71%)	0	–
ROSC (n)	2 (29%)	0	–
Post-resuscitation coronaric angiography			
n	7 (100%)	8 (66%)	*0.25*
revarscularization (n)	4 (57%)	7 (58%)	*1*
24 h survival (n)	5 (71%)	1 (8%)	*0.009*
Hospital survival (n)	1 (14%)	0	–
Organ donor (n)	2 (29%)	0	–
Ecocardiographic parameters			
RVFAC (%)	61.8 (57.7–65.2)	57.2 (51.6–65.6)	*0.42*
RVOT-fs (%)	47.9 (29.3–64.2)	42.7 (22.8–55.3)	*0.63*
LVOT			
Open (n)	7 (100%)	1 (8%)	*0.0002*
Diameter (cm)	1.3 (1.15–1.63)	0 (0–0)	–
Aortic diameter			
Annulus (cm)	1.7 (1.4–2)	1.5 (1.2–1.9)	*0.15*
Sino-tubular junction (cm)	2 (1.8–2.3)	1.6 (1.4–2)	*0.31*
Ascending aorta (cm)	2.3 (1.8–2.5)	1.5 (0.8–2)	*0.04*
LVEDV (ml)	67.5 (51.3–107.7)	80.6 (55.4–99.6)	*0.55*
LVESV (ml)	23.9 (20.4–34.5)	37.9 (31.5–55)	*0.06*
EF (%)	60 (55–70.2)	47 (43–59)	*0.03*

For definition and calculation of the variable see the text. ACLS, advanced cardiac life support; DC shock, direct-current defibrillation; ECMO, extracorporeal membrane oxygenation; EF, ejection fraction; LVOT, left ventricular outflow tract; REMA, return of electrical and mechanical activity; ROSC, return of spontaneous circulation; RVFAC, right ventricular fractional area change; RVOT, right ventricular outflow tract; RVOT-fs, right ventricular outflow tract fractional shortening. Data are expressed as median (IQR), or n and (%) when appropriate.

during resuscitation efforts: the ventricular walls should move inward, LVOT should open during compression, and ventricular chambers should change in size to guarantee their filling and emptying during CPR.[22] Finally, TEE may allow the resuscitation team to diagnose the cause of cardiac arrest (i.e. aortic dissection, pericardial effusion, cardiac tamponade, valvular dysfunction, free wall rupture, or pulmonary embolism). In our series, the TEE assessment was easily performed by an expert physician, was not time consuming, didn't delay resuscitation manoeuvres, and provided a useful guide during cannulation for ECMO.

The TEE was able to discriminate between successful and failing cardiopulmonary resuscitation. In our study, none of the patients with closed LVOT during chest compression and relaxation phases had successful resuscitation. No blood can be pushed into the aortic root and systemic circulation without the LVOT opening. These findings corroborate the hypothesis of previous studies about the adverse effect of LVOT obstruction on the efficacy of CPR by increasing the resistance to forward blood flow from the left ventricle.[12] Sternal compressions may be more or less effective as a results of chest characteristics and distribution of compressive forces into intrathoracic structures.[23] In the 11 patients with LVOT obstruction, the LVOT was compressed between the interventricular septum and the anterior leaflet of the mitral valve. This resulted in a significantly reduced ejection fraction of the left ventricle. Cardiac arrest and CPR manoeuvres might cause modification in left ventricular chamber shape and in the spatial relations between mitral valve, subvalvular apparatus, left ventricular septum, outflow tract, and aortic root. Moreover, positive pressure ventilation might further dislocate intrathoracic structures. The anterior leaflet of the mitral valve may be moved toward the septum by the not-physiologic blood flow produced by chest compressions. The mitral-septal contact may be increased in patients with anatomic or functional substratum: small and hypertrophic left ventricle, hypovolemia, sigmoid-shape septum, fibrotic septal changes at the level of leaflet-septal contact, anomalous

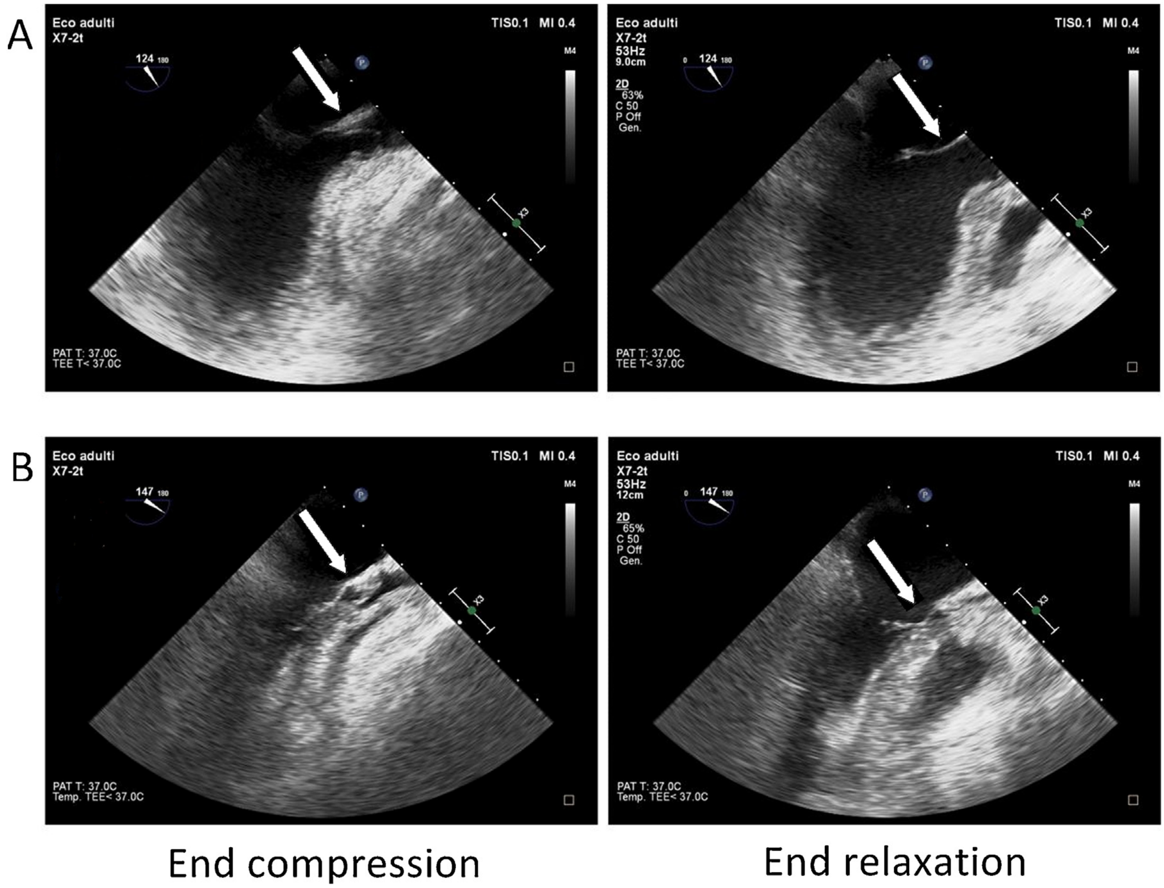

Fig. 1 – Midoesophageal long-axis view of aortic valve and ascending aorta shows: (A) patient with open LVOT and (B) patient with closed LVOT during compression (left) and relaxation (right) phases. White arrows indicate the LVOTs.

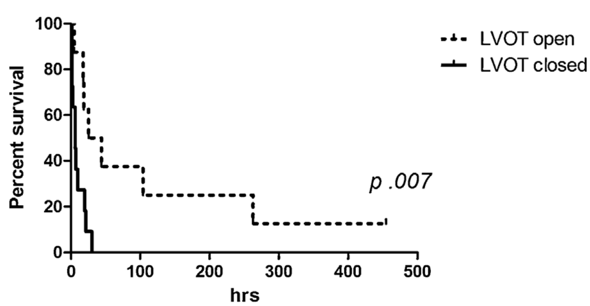

Fig. 2 – Kaplan-Meyer curves represent the percentage of patient remaining alive after hospital admission according to LVOT pattern.

papillary muscle insertion, and abnormalities of the mitral subvalvular apparatus.

During external cardiac massage probably both cardiac and thoracic pump mechanisms coexists.[24] During the decompression the chest recoil reduces intrathoracic pressure which improves venous blood flow to the heart. Squashing the right ventricle by chest compressions generates a blood flow towards pulmonary circulation. Positive pressure ventilation during CPR increases the intrathoracic pressure and lungs' volume squeezing the blood from the pulmonary capillary bed towards the left atrium. The oesophagus and the descending thoracic aorta lie posteriorly to the left atrium, it is unknown whether blood stagnation into the left atrium may cause further compression of the under-filled aorta worsening further the tissue perfusion.

Some authors suggest that the currently recommended compression point[9] may not be effective in generating forward blood flow during CPR and that compression of the sternum with hand placement more caudal may avoid compression of the left ventricular outflow.[25]

Authors suggest as alternative location the area on the sternum between the standard position and the xiphoid process.[12] Our study was not designed to investigate this hypothesis, more evidences are needed to determine whether LVOT opening can be altered by CPR positioning. Our study found that LVOT pattern during CPR was associated with the resuscitation outcome.

All patients enrolled in this study were admitted to the emergency department to be treated by ECPR. Venous-arterial ECMO is an useful tool in properly selected patients as rescue strategy for out-of-hospital refractory cardiac arrest.[26–28] ECPR is expensive and source demanding. In our series one patient survived to hospital discharge and two patients became organ donors out of seven patients in group-SUXX, respect to none in group-FAIL. Our results suggest that TEE assessment during CPR might improve the selection criteria of patients to be liable to mechanical circulatory support. This hypothesis should be tested prospectively in future studies and, if confirmed, TEE could be useful to reallocate resources in the emergency resuscitation. To our knowledge, this is the first study that shows the significant association of a single echocardiographic parameter with successful CPR.

The studied patients had a low survival rate of about 5%. It could be argued about the real efficacy of resuscitation efforts by ECPR. These results are like those found by other authors.[28] The core of the question is not if the ECPR is efficient, but if there are alternatives to it. ECPR is performed in *refractory* cardiac arrests in whom ACLS efforts by emergency medical system have been ineffective. Nowadays, the only alternative to ECPR attempt in this setting is, reasonably, the cemetery.

Our study has some limitations. It is a retrospective analysis of case series and includes a small number of subjects. These findings must be verified prospectically. Most patients were treated by mechanical external chest compression. Although this study provides informative data regarding the role of TEE in cardiac arrest, it is not a randomized trial and does not compare mechanical vs. manual chest compressions. Furthermore, after the resuscitation manoeuvres and implantation of ECMO it is very difficult to obtain cardiac and thoracic CT scan images, thus our TEE findings lack a CT confirmation. Moreover, it is well known that positive pressure ventilation influences the return of blood to the heart and eventually the forward flow during CPR.[29] We controlled the respiratory rate according to the guidelines, but we cannot argue about the intrathoracic pressures generated in our patients.

Whether our data, obtained in a quite young population, could be generalized to elderly patients is unknown. Anatomical thoracic differences are attributed to various body types, sex and age of individuals. Some pleural, pulmonary, or cardiovascular diseases can also alter the relative position of the heart and sternum. Therefore, further prospective studies on different case-mix are required to confirm our findings.

Conclusions

The trans-oesophageal echocardiographic examination can be performed in the emergency setting during cardiopulmonary resuscitation. In these young populations with out-of-hospital witnessed refractory cardiac arrest, LVOT opening was associated with successful CPR.

Conflicts of interest

Authors have no conflict of interests.

Funding

Intramural source only.

Acknowledgments

None.

REFERENCES

1. Redberg RF, Tucker KJ, Cohen TJ, Dutton JP, Callaham ML, Schiller NB. Physiology of blood flow during cardiopulmonary resuscitation. A transesophageal echocardiographic study. Circulation 1993;88:534–42 PubMed PMID: 8339415.
2. Pell AC, Guly UM, Sutherland GR, Steedman DJ, Bloomfield P, Robertson C. Mechanism of closed chest cardiopulmonary resuscitation investigated by transoesophageal echocardiography. J Accid Emerg Med 1994;11:139–43 PubMed PMID: 7804575. Pubmed Central PMCID: 1342417.
3. Criley JM, Blaufuss AH, Kissel GL. Cough-induced cardiac compression. Self-administered from of cardiopulmonary resuscitation. JAMA 1976;236:1246–50 PubMed PMID: 989068.
4. Rudikoff MT, Maughan WL, Effron M, Freund P, Weisfeldt ML. Mechanisms of blood flow during cardiopulmonary resuscitation. Circulation 1980;61:345–52 PubMed PMID: 7351060.
5. Hwang SO, Lee KH, Cho JH, Yoon J, Choe KH. Changes of aortic dimensions as evidence of cardiac pump mechanism during cardiopulmonary resuscitation in humans. Resuscitation. 2001;50:87–93 PubMed PMID: 11719134.
6. Cunningham LM, Mattu A, O'Connor RE, Brady WJ. Cardiopulmonary resuscitation for cardiac arrest: the importance of uninterrupted chest compressions in cardiac arrest resuscitation. Am J Emerg Med 2012;30:1630–8 PubMed PMID: 22633716.
7. Georgiou M, Papathanassoglou E, Xanthos T. Systematic review of the mechanisms driving effective blood flow during adult CPR. Resuscitation. 2014;85:1586–93 PubMed PMID: 25238739.
8. Kleinman ME, Goldberger ZD, Rea T, Swor RA, Bobrow BJ, Brennan EE, et al. 2017 American Heart Association focused update on adult basic life support and cardiopulmonary resuscitation quality: an update to the American Heart Association Guidelines for cardiopulmonary resuscitation and emergency cardiovascular care. Circulation 2018;137:e7–e13 PubMed PMID: 29114008.
9. Kleinman ME, Brennan EE, Goldberger ZD, Swor RA, Terry M, Bobrow BJ, et al. Part 5: adult basic life support and cardiopulmonary resuscitation quality: 2015 American Heart Association guidelines update for cardiopulmonary resuscitation and emergency cardiovascular care. Circulation 2015;132:S414–35 PubMed PMID: 26472993.
10. Gates S, Quinn T, Deakin CD, Blair L, Couper K, Perkins GD. Mechanical chest compression for out of hospital cardiac arrest: systematic review and meta-analysis. Resuscitation 2015;94:91–7 PubMed PMID: 26190673.
11. Couper K, Smyth M, Perkins GD. Mechanical devices for chest compression: to use or not to use? Current opinion in critical care 2015;21:188–94 PubMed PMID: 25887299.
12. Hwang SO, Zhao PG, Choi HJ, et al. Compression of the left ventricular outflow tract during cardiopulmonary resuscitation. Acad Emerg Med 2009;16:928–33 PubMed PMID: 19732038.

13. Nestaas S, Stensaeth KH, Rosseland V, Kramer-Johansen J. Radiological assessment of chest compression point and achievable compression depth in cardiac patients. Scand J Trauma Resusc Emerg Med 2016;24:54 PubMed PMID: 27103035. Pubmed Central PMCID: 4840890.
14. Shin J, Rhee JE, Kim K. Is the inter-nipple line the correct hand position for effective chest compression in adult cardiopulmonary resuscitation? Resuscitation 2007;75:305–10 PubMed PMID: 17590258.
15. Lindqvist P, Calcutteea A, Henein M. Echocardiography in the assessment of right heart function. Eur J Echocardiogr 2008;9:225–34 PubMed PMID: 17588498.
16. Lindqvist P, Henein M, Kazzam E. Right ventricular outflow-tract fractional shortening: an applicable measure of right ventricular systolic function. Eur J Echocardiogr 2003;4:29–35 PubMed PMID: 12565060.
17. Lang RM, Badano LP, Mor-Avi V, et al. Recommendations for cardiac chamber quantification by echocardiography in adults: an update from the American Society of Echocardiography and the European Association of cardiovascular imaging. Eur Heart J Cardiovasc Imaging 2015;16:233–70 PubMed PMID: 25712077.
18. Rudski LG, Lai WW, Afilalo J, et al. Guidelines for the echocardiographic assessment of the right heart in adults: a report from the American Society of Echocardiography endorsed by the European Association of Echocardiography, a registered branch of the European Society of Cardiology, and the Canadian Society of Echocardiography. J Am Soc Echocardiogr 2010;23:685–713 quiz 86-8. PubMed PMID: 20620859.
19. Nishimura RA, Otto CM, Bonow RO, et al. AHA/ACC guideline for the management of patients with valvular heart disease: executive summary: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines. J Am Cardiol 2014;63:2438–88 PubMed PMID: 24603192.
20. Link MS, Berkow LC, Kudenchuk PJ, et al. Part 7: adult advanced cardiovascular life support: 2015 American Heart Association guidelines update for cardiopulmonary resuscitation and emergency cardiovascular care. Circulation 2015;132:S444–64 PubMed PMID: 26472995.
21. Tucker KJ, Redberg RF, Schiller NB, Cohen TJ, Cardiopulmonary Resuscitation Working Group. Active compression-decompression resuscitation: analysis of transmitral flow and left ventricular volume by transesophageal echocardiography in humans. J Am Coll Cardiol 1993;22:1485–93 PubMed PMID: 8227809.
22. Blaivas M. Transesophageal echocardiography during cardiopulmonary arrest in the emergency department. Resuscitation 2008;78:135–40 PubMed PMID: 18486300.
23. Qvigstad E, Kramer-Johansen J, Tomte O, et al. Clinical pilot study of different hand positions during manual chest compressions monitored with capnography. Resuscitation 2013;84:1203–7 PubMed PMID: 23499897.
24. Nassar BS, Kerber R. Improving CPR performance. Chest 2017;152:1061–9 PubMed PMID: 28499516.
25. Cha KC, Kim YJ, Shin HJ, et al. Optimal position for external chest compression during cardiopulmonary resuscitation: an analysis based on chest CT in patients resuscitated from cardiac arrest. Emerg Med J 2013;30:615–9 PubMed PMID: 22833601.
26. Johnson NJ, Acker M, Hsu CH, et al. Extracorporeal life support as rescue strategy for out-of-hospital and emergency department cardiac arrest. Resuscitation 2014;85:1527–32 PubMed PMID: 25201611.
27. Le Guen M, Nicolas-Robin A, Carreira S, et al. Extracorporeal life support following out-of-hospital refractory cardiac arrest. Crit Care 2011;15:R29 PubMed PMID: 21244674. Pubmed Central PMCID: 3222065.
28. Lamhaut L, Hutin A, Puymirat E, et al. A pre-hospital extracorporeal cardio pulmonary resuscitation (ECPR) strategy for treatment of refractory out hospital cardiac arrest: an observational study and propensity analysis. Resuscitation. 2017;117:109–17 PubMed PMID: 28414164.
29. Sigurdsson G, Yannopoulos D, McKnite SH, Lurie KG. Cardiorespiratory interactions and blood flow generation during cardiac arrest and other states of low blood flow. Curr Opin Crit Care 2003;9:183–8 PubMed PMID: 12771667.