

Current trends in the management of out of hospital cardiac arrest (OHCA)

Michal Plodr^{1,2}, Eva Chalusova¹

Sudden cardiac arrest remains a relevant problem with a significant number of deaths worldwide. Although survival rates have more than tripled over the last 20 years (4% in 2001 vs. 14% in 2020), survival rates with good neurological outcomes remain persistently low, representing a major socioeconomic problem. Every minute of delay from patient collapse to start cardiopulmonary resuscitation (CPR) and early defibrillation reduces the chance of survival by approximately 10–12%. Therefore, the time to treatment is a crucial factor in the prognosis of patients with out-of-hospital cardiac arrest (OHCA). Research teams working in the pre-hospital setting are therefore looking for ways to improve the transmission of information from the site of an emergency event and to make it easier for emergency medical dispatch centres (EMDC) to recognise life-threatening conditions with minimal deviation. For emergency unit procedures already at the scene of the event, methods are being sought to efficiently and temporarily replace a non-functioning cardiopulmonary system. In the case of traumatic cardiac arrest (TCA), the focus is mainly on effective affecting non-compressible haemorrhage.

Key words: OHCA, drones and AED, video emergency calls, artificial intelligence, ECPR, REBOA, pre-hospital blood transfusion

Received: October 4, 2023; Revised: February 27, 2024; Accepted: February 27, 2024; Available online: March 4, 2024

<https://doi.org/10.5507/bp.2024.006>

© 2024 The Authors; <https://creativecommons.org/licenses/by/4.0/>

¹Department of Emergency Medicine and Military General Medicine, Military Faculty of Medicine, University of Defence, Hradec Kralove, Czech Republic

²Emergency Medical Services of the Hradec Kralove Region, Hradec Kralove, Czech Republic

Corresponding author: Michal Plodr, e-mail: plodrmic@seznam.cz

INTRODUCTION

It has been more than 60 years since the development of the modern conception of resuscitation principles, as we know them today. Research teams expended considerable efforts to increase the number of survivors primarily with good neurological outcome over these years. However, there has been only a little change on the prognosis of the OHCA patients even after this time. Sudden cardiac arrest is the third most often cause of death in Europe. Annual OHCA incidence in Europe impacts between 67 to 170/100000 inhabitants, the percentage of survivals until discharging from hospital is 8% on average (varying from 0% to 18%) (ref.¹). Aspects influencing the prognosis of patients are multifactorial and include especially early recognition of cardiac arrest by EMDC, application of the telephone-assisted cardiopulmonary resuscitation (TA-CPR), early defibrillation by lay responders, until appropriate transport of a patient to a cardiac arrest centre besides others. Over time considerable effort to improve individual aspects of resuscitation, a part of chain of survival has been made. Success of implementation shows a large variability though – i.e., TA-CPR is applied in the range of 3.2–87.8%, bystanders or lay responders CPR varies from 13 to 82.6% (ref.¹). It can be seen from the above mentioned that the differences in the care of patients are given among others also by demographic and socio-economic conditions affecting the organisational structure of pre-hospital care and the

possibility of applying up-to date knowledge and technology. A whole range of different resuscitation techniques and methods were explored in an effort to improve the results after OHCA and, at the same time, make the individual steps of the decision-making process easier. Some of them are relatively easy and they are aimed at a change in thinking or perception of the circumstances of cardiac arrest and the consequences. The aim is to increase the awareness of cardiac arrest symptoms – CA recognition and early initiation of quality basic life support and early defibrillation by lay responders. CPR guidelines from 2021 present the Top 5 messages in the Systems Saving Lives chapter, where among others it calls on educational events and awareness campaigns for both adults and the children (kids save lives programme) (ref.^{2,3}).

One of the key moments in CA patients is the implementation of early defibrillation. Although there is continuous spreading of the automated external defibrillators (AED) network, the device may not always be available at the scene. An option for timely delivery is the use of a drone as an AED carrier. Although the usage of this flying technology with remote control itself is burdened by a number of limitations, simulation studies show promising results and the publication about first real usage is available. The progress in the field of artificial intelligence is unstoppable and there is noticeable penetration into the environment of emergency services as well. A communication machine learning model (MLM) platform can be a suitable instrument for dispatchers. Correctly

“trained“ machines are able to help during the recognition of OHCA identifiers during the call and to draw attention to this risk to the dispatcher. The possibility of making a video of the situation from the point of injury can be another support for correct decision making regarding the urgency of the condition and its nature and of the resources sent. Currently, applications which enable the transfer of a situational video with the help of smartphones after activation of the caller are available. So far, possible consequences connected with GDPR or archiving such a record have not been completely resolved. Another procedure currently of interest to research teams in both the pre-hospital and early hospital phases and allowing temporary bridging of nonfunctioning circulation is extracorporeal cardiopulmonary resuscitation (ECPR). This procedure for indicated patients uses transport into a cardiac arrest centre under continuous resuscitation where connection to extracorporeal membrane oxygenation (ECMO) follows. Trauma patients are at risk of the consequences of especially non-compressible bleeding in the cavities or retroperitoneum. The solution for such conditions may be the use of resuscitative endovascular balloon occlusion of the aorta (REBOA) or pre-hospital administration of blood transfusions.

It is necessary to be aware the fact that none of the above-mentioned sophisticated procedures is a “one size fits all” method. However, for the indicated groups of patients, they can undoubtedly improve the prognosis and increase survival rates, especially with good neurological outcome.

Drones and AED

One of the most important factors influencing the prognosis of the patient is shortening the time from the collapse to early defibrillation. Prognosis of the survival drops with every minute of delay of the defibrillation by 10–12% (ref.^{1,4}). One of the tempting ideas of how to bring AED to the afflicted concerns the possibility of using drones or unmanned aerial vehicles (UAV) as AED carriers. A student of Delft University of Technology, Netherlands, Alec Momont, showed the first possible realization in 2014. It was a project with an ambitious goal to increase the survival rate from 8 to 80% (ref.⁵). A range of research teams which started simulation studies of feasibility while using “flying“ AED in particular were interested in this idea. Considerations about drone usage were first aimed at remote areas, with a low density of population and scarce network of stationary AED locations. Simulation studies also in suburban areas at a distance of 5 to 10 km from the AED base were performed over time. The results were promising and research teams showed the feasibility of drone usage also in these conditions^{6,8}. One of the few prospective studies on this theme was led by colleagues from Karolinska Institute. The results were published in 2022 and drone usability with AED for urban areas was assessed. 53 potentially suitable OHCA activations with the drone used as an AED carrier were listed in the studies. The drone took off 12 times in reality, AED was brought to the point of injury 11 times and 7 times before the Emergency medical service (EMS) arrival. 74%

of potentially suitable flights were not realized especially due to unfavourable meteorological conditions (wind, rain), sunset, impossibility of drone usage at the point of injury (no-flight zones) or great distance (ref.⁹). The median of the interval of reaching the place before the EMS crew arrival was 1:52 min⁹. The University Medicine of Greifswald team presented the latest simulation study. To evaluate the feasibility of AED transport to already intervening first responders (FR) was the aim. Each action was started by a simulated emergency call, on the basis of which both local FR and a drone with AED were activated. The time from accepting the call to the defibrillation with the help of AED taken by a drone varied between 6 and 16 min which was shorter than the average defibrillation time of the emergency services which is 19:48 min in the given rural region. All drone landings including the AED reception were conducted safely. Organization during the drone landing and AED delivery were evaluated as satisfactory and did not influence the quality of resuscitation. The authors conclude that simulated operations confirmed the feasibility of the suggested model in low population density areas with poor accessibility of emergency services in particular. On the other hand, they draw attention to the amount of legislation and logistical questions, including the necessity of educating the population in the area of the assumed deployment¹⁰.

The conclusions of simulation studies presented are promising at first sight and it would appear there is nothing to stop drone introduction to pre-hospital practice. However, a rarely discussed area is the cost-benefit ratio. One of the paper looking at this question comes from North Carolina. The authors calculate the costs of building the networks of docking stations for the drones with AED on the territory of North Carolina with the presumption of reaching a patient within 5 min. Calculations of optimum coverage model (96.5%) of areas are covered within 5 min, a drone lifetime is 4 years) mean building 1015 docking stations at an estimated cost of 26.5 millions USD (based on calculations from 2019) (ref.¹¹). Regarding the calculated costs and a wide range of limiting logistic questions (drone traffic control and limitations arising from that, specialised personnel, running and audit costs) a legitimate question comes up if this trend can be expected in the near future and if it is not more suitable to invest in the building of a network of first responders equipped with a standard AED device. Nevertheless, using a drone with AED can be a solution for the most inaccessible areas which are not possible to cover by FR with AED. Also, it can work for low suburban development where manoeuvring among tall building and consequent risks are not involved. Given the assumed costs not only for the operation activation but also for maintenance, a drone with AED usage will be the privilege of rich states in particular. Only 8 years after the first reference concerning the possibility of using a drone as an AED carrier, the first real action was published in The New England Journal of Medicine (NEJM). It was a 71-year-old man with OHCA for whom also a drone with AED and EMS was sent. It reached the scene – in an area of low suburban development – after 670 metres

of flight 3:19 min after its activation and 1:19 min before a ground-based ambulance arrived. A defibrillation on scene was performed and the patient survived with a good neurological outcome¹².

Artificial intelligence and machine learning models

Artificial intelligence (AI) is a summary term which includes all the technologies where a computer or a system appears to be intelligent. This could be anything from recognizing a picture up to an aircraft autopilot system. Machine learning model (MLM) is a subset of artificial intelligence and is focussed on the ability of the device to obtain the information from data. A chain of words or links related to a certain activity or a condition can form this data. The work of a modern “call-centre” is an inspiration where devices working as a filter can identify from a call which service is required and they can redirect a call to a particular service provider prospectively. Computers during answering and evaluating emergency calls could behave in a similar way. Such systems estimate the probability of defined conditions based on formulas of voiced words which a dispatcher could potentially mishear.

However, it is necessary to mention that an emergency call has a whole range of specifics: the callers are often under stress, they are not specialists in medical terminology and do not use standard communication. The dispatcher must examine the broader context of the whole call to evaluate medical difficulties of the caller correctly. To teach a computer to recognize for example OHCA with acceptable reliability requires relatively great effort.

Moreover, patients with OHCA can have gasping or hypoxic spasms which make final correct decision difficult. The median correct recognition of OHCA based on an emergency call is 74% (range 14 to 97%) (ref.¹³⁻¹⁶). Dispatch centres with correctly set methodology of conducting emergency calls have a higher level of correct recognition, however there is still some room for improvement¹³⁻¹⁶. The first reports on the topic of AI or MLM as a tool for emergency calls are no older than 2 years. In 2021 a research team from Denmark published the first randomized clinical study. More than 100 000 emergency calls were analysed in the first phase of the study, where there were about 2 000 calls concerning cardiac arrest among them. False positive calls were eliminated from the file and, on the other hand, false negative calls were added. This file of calls was analysed by a computer based on a machine learning model (MLM). All the links and chains relating to a correct recognition of OHCA were selected. MLM evaluated a group of 169 049 calls in a following phase. Calls evaluated as suspicious of the presence of OHCA (n=5.242) were randomized into two groups – an experimental one where MLM support was available, and a control group, without support. The aim was to compare correct identification of OHCA in both the groups. In the experimental group – with MLM support – OHCA was correctly identified in 93.1%, MLM without support in 90.5%. MLM raised the success rate of recognition by 2.6%, however, without statistical significance. The time until OHCA was recognized was practically the same in both groups (1.72 min, resp. 1.70 min). When data from

all OHCA were evaluated, MLM showed better results – OHCA was recognised with a sensitivity of 85%, while a dispatcher reached a value of 77.5%. This success rate was though burdened by a worse positive predictive value (PPV), which reached only 18% in MLM in comparison with 56% in dispatchers (ref.¹⁷). MLM recognised a few more cardiac arrests, however, at the cost that it identified many calls as arrests when there were no OHCA). In 2023 the team of Stig Blomberg published another study on this theme, this time with the aim to identify key points when there is MLM failure in terms of false negative or false positive evaluation of the call in the OHCA identification context. Machine learning model (MLM) identified correct OHCA incidence with a sensitivity of 84.5% (95% CI: 82.2; 86.6) and specificity 97.1% (95% CI: 97.1; 97.2) from the group of analysed calls. MLM did not recognize OHCA in 15.5% cases, it identified false positivity in 2.4% (ref.¹⁸). A large group of callers from the unrecognized OHCA group were callers with a language barrier, therefore one of the conclusions of the authors of the study is to widen the pool of language patterns for MLM (ref.¹⁸). That MLM is able to analyse in advance learnt patterns sufficiently quickly was also confirmed by the study of authors from Sweden. Both MLM and dispatcher success rate in OHCA recognition (without limiting the length of the call) was nearly the same (86 resp. 84%), however, MLM was 28 seconds faster on average, time median of call processing 72 seconds (IQR, 40–132 s), resp. 94 seconds (IQR, 51–174 s) for dispatchers (ref.¹⁹). The results of MLM usage are promising and it would appear machines will replace human resources soon. However, the reality is more complicated and a well-educated dispatcher will not have to worry about losing their job for a long time. It is also worth mentioning in the context of further MLM usage that the above-mentioned studies come from very well-set systems and the level of OHCA recognition is around 90%. Although not in all the regions (median sensitivity 73.9%; range: 14.1–96.9%) (ref.¹⁹).

It was proved that MLM can work adequately quickly and is able to recognize a high proportion of cardiac arrest at the same time. On the other hand, it still shows a significant tendency to overtriage with the border level of false positive indications. It appears suboptimal at the moment because the reaction of the system to the activation during OHCA is massive and there is a risk of limiting or exhausting resources due to a non-acceptable value of false positive activations. However, MLM could be a suitable instrument for those dispatch centres where the level of OHCA recognition is lower, furthermore, for starting dispatch centres and for dispatch centres where answering emergency calls is processed by dispatchers who are not medical specialists.

Videocalls – visuals from the point of injury

One of the biggest challenges which the witnesses of the collapse face, is cardiac arrest recognition. After receiving an emergency call with symptoms of cardiac arrest, the dispatcher specifically asks about the state of vital signs – consciousness and breathing. If the fact that

it is or could be OHCA arises from the call, they initiate instructions on the phone (TA-CPR). The structure of these instructions is defined by an international guidelines framework²⁰. The entire information transfer from the scene and also to scene is conducted by voice. Although the dispatchers are educated how to use the communication channel correctly, OHCA recognition based on a phone call varies over a wide range²¹. Absence of visual cognitive perception of the current situation led research teams to the idea of a video sent from the place of injury. A dispatcher can verify current conditions thanks to a direct on scene visual check. He can correct the performed activity and increase the quality of the methods used for the resuscitation thanks to a visual check and he is also a psychological support for the lay responders. It is possible to use visual situational awareness also during other events besides OHCA, i.e., during a traffic accident. This way a dispatcher can also coordinate accessible human resources on the basis of a direct picture broadcast. The broadcast of the video by phone requires sufficient capacity of the networks and these were carried out by the introduction of 3G technology. One of the first studies with video was conducted in Norway during an OHCA simulation²¹. University students were divided into groups based on the fact whether CPR was conducted on the basis of standard TA-CPR or video-assisted CPR (VA-CPR). A statistically significant difference in favour of VA-CPR was shown in hands-off time, i.e., the time until the first compression was performed. A statistically significant difference was not shown in other values. However, it is necessary to mention probands in both the groups had 70–73% training in CPR basics (ref.²¹). The above-mentioned understanding and perceiving the instructions both by lay bystanders and an easier way of explaining instructions by dispatchers was an additional finding also in other studies. Later the VA-CPR issue was the focus of attention of mainly Asian authors. They were interested in the analysis of simulation models solely in the context of instructions connected with OHCA and comparison of efficiency of TA-CPR and VA-CPR. In their meta-analysis of simulation studies Lin et al. showed a better VA-CPR effect in terms of maintaining the demanded frequency of compressions (105 vs. 81) and keeping correct hand position on the chest – odds-ratio for correct position was 0.8 (95% CI: 0.53–1.30) in comparison with TA-CPR. Delaying VA-CPR (median 31.5 s; 95% CI: 10.94–52.09) was a secondary result²². A South Korean team led by H. S. Lee published results of retrospective clinical studies led in Seoul. 2109 calls in total were included (TA-CPR 1722, resp. 387 for VA-CPR). A statistically significant difference in the parameter of survival to hospital discharge was shown (12.3% vs. 27.1%; $P < 0.0001$). Significance in the parameter of a satisfactory neurological condition (CPC 1,2) in favour of VA-CPR (6.8% vs. 19.4%; $P < 0.0001$) was shown at the same time. The fact that VA-CPR forms up to 13% of all calls with OHCA is interesting (ref.²³). A simulated study by the team of authors Linderot et al. comes from Europe. 3 groups of probands were created who accepted instructions in the following forms: TA-CPR; VA-CPR and resuscitation without dispatcher

support. The VA-CPR group showed a tendency towards better results in the following parameters: the depth of compressions, maintaining the frequency and correct hand positioning, however without statistical significance. This was shown in the parameter of total ratio of correctly performed compressions in favour of VA-CPR in comparison with TA-CPR and a group without support (82.6% vs. 75.4%, resp. 77.3%). Similarly, significant improvement in the following parameters: hand positioning, frequency of compressions, depth of compressions and the level of arms stretched during compressions in favour of VA-CPR were shown by the team from Copenhagen (ref.²⁴). As has already been mentioned, the support of the callers by videocall does not have to be only in the cases with OHCA. The team of authors from the Czech Republic published results of the study, where results of video consultations in the conditions with low priority were evaluated. Such events were attended by a non-medical crew and some patients could be left at home after consultation with a doctor. Usage of videocalls in practice did not lead to a significantly higher number of patients kept at home (failure rate indicator was a repeated departure to the patient within 48 h). However, the consequent investigation of all the participants proved subjectively a better perception of both the process of passing on information of medical staff, and satisfaction with the course of actions and treatment of the patients²⁵. An amalgamation of two innovative methods were introduced by colleagues from a university from Korean Jecheon. In their simulation study they combined AED transport by a drone to the point of injury and a video call with the VA-CPR application was activated at the same time. The reality that the parameter of frequency of the compressions, depth of the compression and hands-off time had significantly better results was confirmed. Qualitative evaluation of work with a drone, AED take over and perception of both the methods of instructions (VA-CPR and TA-CPR) was conducted at the same time. Experience was mostly positive and the VA-CPR group perceived better support in the form of visual contact. A matter of interest was the discovery of a certain amount of concern caused by the landing of the drone to the bystanders providing CPR, which made them aim their attention to their own safety more than to the correct CPR (ref.²⁶).

Transmission of video is becoming an easier matter with technological development and expanding capacity of mobile networks (4G, 5G). Video implementation from smart phones into the software of the dispatch centre requires some measures. The videocall implementation itself must not delay the primary function of the dispatch centre – to accept an emergency call, localize an event and set priorities based on input information. Only after that is it possible to be interested in the activation of the videocall. Activation is carried out by sending a link from the dispatch centre to the mobile phone of the lay bystander, he will confirm it and thus he activates the camera of the mobile phone. It is clear from the above-described process of activation that a video call will play its role in cases where there are more lay bystanders at the scene. This reality was confirmed also in the studies mentioned

where the highest frequency of the VA-CPR activation was in a public space with a higher presence of people. The age of the lay bystander will also play its role, as will lay bystander compliance connected with stress or panic at the point of injury. There can be obstacles from the side of the dispatcher (for example incomplete knowledge of the process of VA-CPR activation or other obstacles during directions accompanied by the video – an unpleasant view of the OHCA victim) to a lesser extent. Questions concerning the necessity of archiving videocalls as a part of medical documentation will be the subject of national legislative measures and recommendations.

Extracorporeal cardiopulmonary resuscitation (ECPR)

The idea of a heart-lung machine was realized by John Gibbon as a means for blood oxygenation during long term cardio-surgical operations in the 50's of the 20th century. The principle of the process designated as Extracorporeal Life Support (ECLS), later as Extracorporeal Membrane Oxygenation (ECMO), lies in blood transfer to a membrane oxygenator, where oxygenation occurs and is later transported back into the blood circulation. Thus, replacing the function of heart and lungs. In the 80's of the last century a certain stagnation occurred in the use on adult patients and ECMO was used mainly for child patients and only a small number of highly specialized centres focused on ECMO for adult patients for the next 30 years. On the basis of the described principle of ECMO it was only a question of time before research teams concentrated on using the method on patients with cardiac arrest. ECPR uses ECMO connection for patients with cardiac arrest when conventional CPR (CCPR) is ineffective. ECMO provides adequate perfusion in vital organs (heart, lungs, brain) and for a selected group of patients enables the low flow time to be bridged until potentially reversible causes of cardiac arrest are solved. The cause of cardiac arrest in adult patients is coronary artery disease in 75–80% cases, with the possibility of percutaneous coronary intervention (PCI) (ref.²⁷⁻²⁹). ECMO connection is performed mostly after admission into the cardiac arrest centre; however, studies on the use of ECMO in the pre-hospital sector are already available. This kind of news started to occur in 2000 in observational studies or in case reports, and the conclusions were promising²⁷⁻²⁹. A massive development of ECPR indications has been recorded in the last decade. For example, from 2007 until 2014 there was a 30 times growth of ECMO activation in Germany³⁰.

A key question remains whether ECPR has benefits over CCPR performed in the standard way for confirming the efficiency of the method. Although ECPR might seem to be a groundbreaking method in care of OHCA patients, the conclusions of the research are not definite. For example, a randomized, single centre ARREST study showed the benefit of an early initiated ECPR at OHCA with refractory ventricular fibrillation (14 patients in ECPR group, 15 patients in CCPR group; survival to hospital discharge ECPR group 6; CCPR group 1; survival to 3 and 6 months: ECPR group 6; CCPR group 0; $P:0.0063$)³¹. On the other hand, in 2022 colleagues from Prague con-

ducted a Prague OHCA trial sub-analysis and compared the value of statistical significance between ECPR and CCPR in patients with defibrillated rhythm at admission, i.e., one of the main criteria during consideration of ECPR activation. 256 patients in total (124 in ECPR group, 132 in CCPR group, low-flow time 61 min; IQR 55–70) was listed in the study. Regressive analysis proved that initial defibrillated rhythm is an independent predictor of successful survival, regardless of using ECPR or CCPR (49% vs. 33%). A 16% difference is noticeable in favour of ECPR, however without a proven statistical significance³². Analyses of the performed studies proved unambiguously that the value of survival drops with extended low-flow interval. In patients with defibrillated rhythm at admission in the ECPR group the percentage of survival drops from 37.2% in 15 min low-flow interval down to 19.1% in 60 min (in CCPR group, which is 36.8% in the 15th minute and 0.3% in the 60th minute) (ref.³³). Recent meta-analysis from 2023 conducted by Holmberg et al. evaluated conclusions of research conducted on the ECPR issue. Results of 27 observation studies and particularly conclusions of three randomized studies were included^{31,34,35}. The result of the conclusion is that ECPR showed a potential benefit, however the certainty of the evidence remains low. A similar result was found by one of the last multicentric randomized studies from the Netherlands where the authors came to the conclusion that in patients with refractory OHCA, ECPR and CCPR had a similar influence on survival with a favourable neurological outcome³⁶. In that case it is obvious this method requires a strict selection of patients who will have the highest chance to profit from ECPR activation. One of the suggested indication criteria can be a “Rhythm check three – A2BCDE3” acronym: Rhythm check three – three defibrillation charges at maximum – if still unsuccessful, think of ECPR!); A2: 1 Age ≤ 70 years, 2 Activity (signs of life, cardiac motion in ultrasound); B: Bystander witnessed arrest; C: CPR started within 5 min after arrest; D: Defibrillation (max 3 $\times$); E3: 1 Endstage disease excluded (applies also to “do not resuscitate” orders, major comorbidities), 2 Endtidal CO₂ 10 mmHg (1.3 kPa), 3 Estimated time to ECPR (e.g., <60 min) (ref.³⁷).

In view of the crucial importance of the length of low-flow interval a tempting idea arises whether or not to decrease this interval by ECMO procedure “transferring” into pre-hospital phase, as close as possible to the patient with collapse. Nevertheless, the conclusions of reviews involved in this method did not show a clear benefit. Low-flow time during the implementation of pre-hospital ECMO was 61 min (95% CI: 45–77) which practically is the same time as during connection to ECMO after arrival at the centre (Yannopoulos: 59 ± 28 min, Belohlavek: 61 min; IQR 55–70). There is a lack of reliable evidence at the present time whether use of ECMO in the pre-hospital setting can be recommended³⁸. Broad accessibility of ECMO, the lack of information concerning input criteria for selection of patients and false expectations could lead to non-selective indications, ineffective treatment with the wasting of precious resources and risk of closing a promising way for patients who could profit

from this method. The device for ECMO itself is not the most expensive item. The costs lie in keeping the whole system of expert workers on stand-by. A strict selection of patients following the above-mentioned criteria will be necessary for reliable confirmation of the efficiency of the method. Results of randomized studies initiated in the Netherlands (ON-SCENE: NCT04620070) are expected in 2026 where the results of pre-hospital ECPR and CCPR after Helicopter emergency medical service (HEMS) on arrival at the scene will be compared. Unambiguous indication for ECPR initiation is currently in hypothermic patients with risk factors facing heart arrest (i.e., core temperature <30 °C, ventricular arrhythmia, blood pressure <90 mmHg) (ref.³⁹).

TRAUMATIC CARDIAC ARREST (TCA)

Traumatic cardiac arrest makes up approximately 4% of all OHCA, the value of survival varies between 0–5%. Accidents are the most common cause of death in the age group up to 45 years old. 55–70% patients die before reaching definite care. Continuous bleeding (40–60%) is the most often cause of TCA and of these up to 90% patients die as the results of non-compressible haemorrhage into cavities as a result of injury of the thoracic and abdominal organs, bleeding into retroperitoneum and as the results of pelvic injury or injury of large blood vessels. If patients survive, 1/3 arrive at hospital with a coagulation disorder (ref.⁴⁰⁻⁴²). Simultaneous treatment of reversible causes – hypovolemia, hypoxia, tension pneumothorax, tamponade is a priority in the care of TCA patients (*“do not pump an empty heart”*) (ref.^{39,40-42}). It is necessary to admit that analyses of injuries from war conflicts bring certain progress or change of view of methodology of patients' trauma. Usage of tourniquet and its role in extremity massive bleeding is a good example. The Royal Army Medical Corps Journal published a statement in 1916: *“We are inclined to think that tourniquets are an invention of the Evil One”*. Later, experience with tourniquet usage practically have not been discussed any deeper in specialist press since 1940, and as for indication, the formerly expressed opinion originating especially from the fear of possible complications (acute compartment syndrome, irreversible nerve injury, ischemic damage) persisted⁴³. Analyses from the conflict in Vietnam showed that 9% of deaths were due to insufficiently treated extremity bleeding and the opinion of tourniquet usage started to change. However, analyses of injuries from the conflicts in Iraq and Afghanistan still showed an unnecessarily high number of deaths of preventable bleeding and the rate of extremity bleeding was at 7.8% consistently until 2005 (ref.⁴⁴). In the Tactical Combat Casualty Care (TCCC) programme a massive promotion for using tourniquets in extremity trauma occurred based on this experience and positive results followed. The number of deaths from bleeding from extremity traumas dropped by 67% from 2006 to June 2011 (ref.^{45,46}). Tourniquet usage, together with local compression or with haemostatic bandages, are recommended for extremity compressible bleeding also

in civilian life based on this experience⁴⁷. Possibilities of affecting non-compressible haemorrhage in pre-hospital care were zero or at best very limited until recently and such patients were transported as fast as possible (load and go). The organisation of rapid transport is still a key factor, however, methods are available to enable the initiation of advanced trauma resuscitation in the pre-hospital sector. Resuscitative endovascular balloon occlusion of the aorta (REBOA) and pre-hospital blood transfusion (PHBT) are the methods currently receiving the most attention.

Resuscitative endovascular balloon occlusion of the aorta (REBOA)

The method was described for the first time during the Korean war in the 50's and it remained without gaining a greater interest for a relatively long time despite its promising results due to the high number of undesirable complications. However, with progression of technological development in the area of production of catheters, REBOA expanded gradually into a wide range of clinical conditions connected with bleeding, for example ruptured abdominal aortic aneurysm, post-partum haemorrhage and gastrointestinal tract bleeding and also in patients with bleeding as a result of trauma⁴⁸⁻⁵⁰. Temporary occlusion of the aorta retrogradely with an inserted balloon from the common femoral artery is the principle of this method. Aortic occlusion causes increase of diastolic heart filling, improvement of perfusion of myocardium and stopping bleeding distally from occlusion. The course of aorta is divided into 3 zones for the purposes of REBOA. Zone I: from the origin of left subclavian artery to the origin of celiac artery, a section which is approximately 20 cm long. It corresponds externally to the distance from ligamentum inguinale to xiphoid; Zone II: from celiac artery to the origin of more distally renal artery, of the length of about 3 cm; Zone III: from the origin of renal arteries to the aortic bifurcation of the length of approximately 10 cm, externally from ligamentum inguinale to umbilicus. Indication for REBOA usage in zone I is a haemorrhagic shock as a result of non-compressible abdominal-pelvic haemorrhage and in Zone III pelvic injury or non-compressible haemorrhage from junctional zones (groin) in particular. Zone II is a no-occlusion zone for REBOA implementation^{51,52}. It is important to realize that REBOA is not a definitive solution but only an instrument for bridging and gaining time until surgical treatment is performed. Given the mechanism of functioning – obturation of aortic lumen – the method is burdened by a relatively high level of mortality. Amputation of a leg (3.6–5.3%), acute kidney injury (10.7–22.8%), balloon-related thromboembolic events (3.5–4.3%) and acute compartment syndrome (0.7–3.5%) are the most common complications (ref.^{53,54}). Input results were very promising and a significantly higher level of survival (16.7% non-REBOA group vs. 62.5% REBOA; $P<0.001$) was shown (ref.⁵⁵). The first systemic review and meta-analysis were available with an increasing number of observation studies in particular. However, expectations in terms of definite confirmation of REBOA importance was

not shown and as for quality evidence concerning REBOA efficacy on the level of mortality or survival, these are still missing and current conclusions are contradictory. Population studies in particular using national trauma registers make up the current evidence base. The study of Nori and his colleagues, using a Japanese trauma data bank, showed a threefold higher level of mortality in patients with REBOA in comparison to a control group⁵⁶. Another study used the national file of the American College of Surgeons Trauma Quality Improvement Program (ACS-TQIP) data. Adequate REBOA ($n=140$) and non-REBOA groups ($n=280$) were compared. There was a higher level of mortality in REBOA group in comparison with non-REBOA group (50 [35.7%] vs. 53 [18.9%]; $P=0.01$). The patients in the REBOA group had also a higher incidence of complications – acute kidney injury (15 [10.7%] vs. 9 [3.2%]; $P=0.02$) and also, they underwent an amputation of a extremity more often, too (5 [3.6%] vs. 2 [0.7%]; $P=0.04$) (ref.⁵⁷). On the other hand, the team from the University of Maryland compared followed parameters in REBOA group and a control one, contemporary, and showed a significant difference only in in-hospital mortality and the length of stay in hospital (19.3% vs. 35.1%; $P=0.024$). The other followed parameters (24-hour mortality, 30-day mortality, acute kidney injury) showed better tendency in the favour of REBOA group, though without proven significance (ref.⁵³). The aim of currently the most extensive systemic review with meta-analysis of 11 included observation studies from 2021 under the leadership of Greta Castellini was to identify whether REBOA is an effective method in large blood loss management as a result of trauma. The conclusion is as follows: with low quality of evidence, adjusted overall estimates found a difference in favour of REBOA when compared to resuscitative thoracotomy (RT) (aOR 0.38; 95% CI: 0.20–0.74). With very low quality of evidence, REBOA when compared to no-REBOA (aOR 1.40; 95% CI: 0.79–2.46) did not show a significant difference in outcomes (ref.⁵¹). The authors call for a need for a randomized controlled trial (RCT) in a comprehensive conclusion, where a group of patients who underwent REBOA and a group where REBOA was not performed would be clearly compared. It could be argued that performance of such an RCT would be contested in cases of life-threatening conditions.

The greatest enemy for patients after trauma with continuous bleeding is time and the first peak of death was identified within 30 minutes after the trauma⁵⁸. Options have been explored to reduce this peak as much as possible. One promising way is to transfer the methods for management of bleeding directly to the pre-hospital sector. The first case of pre-hospital REBOA usage was performed by London Air Ambulance (LAA) in 2016. REBOA was implemented on a 32-year-old man after a fall from height with a pelvic injury and a subsequent good prognosis⁵⁹. Other outcomes have not been convincing yet despite the first success of pre-hospital REBOA. A team of authors from Birmingham published outcomes of a current systemic review concerning pre-hospital REBOA usage both in civilian and military sectors. Regarding the

inconsistencies of input and consequently followed parameters only 6 studies, 3 military and 3 civilian ones, were included – with the number of patients ranging from 1 to 21, with a total number of 48. Non-compressible haemorrhage, blunt or penetrating injury and shock (defined as $SBP \leq 90$ mmHg) were input criteria. The authors state in the conclusion that due to substantial heterogeneity across included studies and the missing data, the true effect of pre-hospital REBOA is still unclear. The causality between REBOA and its effectiveness was not illustrated and conclusions cannot be generalized. 30-day survival was evaluated only by 2 studies (non-REBOA group 38% vs. REBOA group 67%). However, a high level of thromboembolic complications demanding thrombectomy (77%) was recorded. Predominant performance of occlusion in Zone I was in military studies (85%). Occlusion in Zone III (93%) prevailed in civilian studies. The time of occlusion varied 21–36 min in Zone I, 9–18 min in Zone III (ref.⁶⁰). The HEMS team from German Halle published an interesting consideration. In retrospective analysis, trauma of the patients who were treated by 29 HEMS teams I total, only 1.3% patients were identified as eligible for REBOA performance (ref.⁶¹). The attention is drawn to disunity in indication criteria. $SBP \leq 90$ mmHg is used as one of the main input values by one of the teams. The values of the circulation might change dynamically in time though. A range of quickly evaluable symptoms and data generating a complex view confirming a current condition and a possible development of dynamics: pallor, clammy skin, “air-hunger,” venous collapse, hypotension (low volume or absent peripheral pulses), low/falling EtCO₂, tachy- or bradycardia, and altered mental status are used by LAA as indication criteria, point-of-care ultrasonography (POCUS) usage could be suitable as well. The possible requirement of national guidelines which will be adjusted to particular individual systems are highlighted by the authors. The necessary need of continuous REBOA simulators training is emphasized as well⁶¹.

The latest news are reports on the use of REBOA in patients with non-traumatic OHCA. Occlusion of the aorta at the level of Zone I will, cause an increased redistribution of blood above the occlusion balloon and perfusion of the heart, lungs, and brain will be improved. Aortic pressure, cerebral perfusion pressure, and cerebral blood flow will increase with a simultaneous provision of heart compressions and better neurological status after CPR, if ROSC is applied returns, can be assumed. The method is an equivalent of ECPR and similarly, it represents a bridging therapeutic method with the main goal to shorten low-flow time. So far published conclusions are more or less the experience of the authors and they cannot be assumed as recommendations for practice⁶². Conclusions of the first observational study on pre-hospital REBOA usage with OHCA patients were published in 2019 by colleagues from Trondheim, Norway. The HEMS team used REBOA with 10 OHCA patients where CPR was initiated within 10 minutes after the onset of heart arrest. The first rhythm was asystole in 60%, 6 patients were transported to hospital with ROSC and one patient (10%) had a 30-day survival. Confirmation of REBOA feasibility

ity in the pre-hospital area was the main conclusion, not affecting the survival level⁶³. A retrospective analysis of OHCA patients with the aim of predicting the ratio of patients suitable for pre-hospital REBOA comes from the same medical centre. Age of 18–75, low comorbidity, witnessed collapse or response time (time interval between first call received at dispatch centre to the time when the first EMS was on scene) within 15 min and the duration of CPR ≥ 30 min were the input criteria. 8.6% patients were selected based on these criteria (ref.⁶⁴). The team under the leadership of Jostein R. Brede profiled in REBOA with OHCA very intensively. He has prepared a prospective randomized REBOARREST study which will last for 3 years. Comparing results of a control group of patients (standard CPR) and an intervention group (standard CPR and REBOA as an adjunctive treatment) will be the primary goal. To follow the percentage of patients who will reach ROSC lasting at least 20 min, and to measure the percentage of patients who will survive up to 30 days with a good neurological outcome will be a secondary aim. Describing hemodynamic physiology of aortal occlusion during the procedure and monitoring all adverse effects will be other goals. Significant conclusions for further implementation, especially an indication criteria can be expected considering the plan to involve 200 patients⁶⁵.

Pre-hospital blood transfusion (PHBT)

As has already been mentioned, war conflicts might be a source of precious experience and a lesson learned. It is no different regarding a PHBT project. This concept is based on experience from the Vietnam war and has been optimized during further conflicts. The decrease in long-term mortality has been confirmed compared to patients who did not receive PHBT or received a late transfusion⁶⁶. There are still controversies concerning the issue of whether early initiated administration of blood products means initiation as early as in a pre-hospital setting and whether this method is effective due to input limitations (logistic background, storage conditions and equipment, limited accurate diagnostic possibilities at the location of the incident with a risk of unnecessarily administered blood products). Although it is possible to assume intuitively PHBT improves survival, published data on this theme have not shown enough evidence so far. Observational studies which show promising results are available. Improved patient outcome including decreased blood product use, reduced early in-hospital mortality, more efficient intravascular volume expansion and reduced risk of early trauma induced coagulopathy have been proven. PHBT is an appropriate and safe intervention based on these findings⁶⁷⁻⁶⁹. Two randomized studies from 2018 comparing the effect of pre-hospital administration of blood products and a standard fluid resuscitation (0.9% chloride saline) showed contradictory results. Moore et al. did not prove that pre-hospital plasma administration was connected with better survival (ref.⁷⁰). On the other hand, conclusions of Sperry et al. proved in injured patients with a risk of haemorrhagic

shock that pre-hospital plasma administration was safe and it was connected with a lower 30-day mortality and decreasing prothrombin time ratio in comparison with a standard fluid resuscitation^{70,71}. The latest randomized RePHILL trial compared a pre-hospital use of PRBC and lyophilised plasma (LyoPlas) group to a 0.9% chloride saline group. The trial did not show, that pre-hospital PRBC-LyoPlas was superior to 0.9% sodium chloride for adult patients with trauma-related haemorrhagic shock. This study is often quoted as a PHBT concept inconclusiveness. However, the authors applied to each group 422, resp. 437 mL 0.9% saline chloride on average at the scene initially before the decision about randomization to groups (PRBc and lyophilised plasma group vs. 0.9% sodium chloride group). Early administration of blood products is understood as administration of products as soon as possible without previous haemodilution by crystalloids. In addition, separated blood components (packed red blood cells – PRBc and plasma) were compared, not whole blood (Low Titre O-type Whole Blood – LTOWB) use of which has been on the rise in recent years (ref.⁷²). Whole blood usage has been experiencing a renaissance in recent years and it is possible to say, again, this is a classic case of experience transfer from war conflicts. Whole blood was used as early as during the first world war and later during the Korean war. At the beginning of the early 60's a gradual development of technologies for blood separation into individual components with the possibility of storage it for a long time continued. Using these components found its unique place in haematology and in other internal specializations in particular while whole blood usage was diminishing. It became clear during the wars in Afghanistan and Iraq, that supplying individual blood components bring logistic difficulties, in particular the lifespan of blood platelets whose shelf life is shorter than with other components. Storage and manipulation with three units of blood components (PRBc, plasma and platelets) was more difficult than manipulation with one unit of whole blood. Therefore, those responsible returned to the idea of using whole blood and so-called walking blood banks were created. Besides that, there was a progression in processing and in particular keeping whole blood which is possible to keep up until 21 days without influence of function of the platelets or coagulation factors⁷³. With more than 8 thousand administered transfusion units of whole blood, data indicates equivalent, if not better results for combat injuries in comparison with separate components⁷⁴⁻⁷⁶. LTOWB thanks to a low non-therapeutic fluid (i. e., preservative solution) content and a low haemodilution effect can improve relevance of shock condition, post traumatic coagulopathy and decrease post traumatic mortality in comparison with the usage of separate blood components. Although the significance of usage of whole blood was proved under military conditions, the level of knowledge in the civilian pre-hospital sector has not brought the necessary level of evidence yet. However, the first observational studies provide promising results. Scandinavian countries are traditional leaders in following progress in pre-hospital care.

Conclusions of their experience with whole blood administration was published by a team from Bergen, Norway in 2022. LTOWB was applied to 15 patients with non-trauma bleeding and 37 with trauma bleeding. Their experience indicated that whole blood usage is feasible and safe despite more demanding management. The same experience was previously published by colleagues from Israel on a cohort of 27 patients⁷⁷⁻⁷⁹. Pleasing news is, also the Czech Republic via HEMS of the Hradec Kralove region, Czech Republic (author's experience) joined these countries in 2021 as one of the first central European countries. The decision to start the transfusion is a key moment. The EMS/HEMS teams have only limited amount of input information concerning the severity of bleeding at the scene. Not all the teams are in the possession of on-site laboratory testing or sonography, whose final interpretation can be burdened by the professional experience of the user. A unified algorithm with indication criteria would be optimal. However, vital parameters show dynamics and variability and are dependent on many factors (age, comorbidity). The question is whether it is possible to create such an algorithm at all. Nowadays PHBT indication criteria differ between countries. Based on the survey conducted among European countries, the main identifier for PHBT is major trauma, shock, and prolonged entrapment in unstable patients⁸⁰. According to the review, which involved 22 PHBT studies by Shand et al., the physiological criterion most frequently assessed is systolic blood pressure (SBP) (varied between < 70 and < 90 mmHg), tachycardia (varied between > 108 and > 130 /min) or no radial pulse. The mechanism of injury (penetrating injury or amputation above the knee/elbow) was included in 5 studies as an indication criterion. In 4 studies, the criteria for PHBT were not identified and in six studies, the criteria for PHBT were not quantified⁸¹. Usage of score systems using basic vital functions easily detectable and countable at the point of injury, i.e., shock index (SI) or pulse pressure (PP) could be assisting and specifying indication criteria. These indexes showed optimal ratio of sensitivity and specificity: SI AUC 0.88; 95% CI (0.82-0.93), cut-off 0.85; PP AUC 0.85 with 95% CI (0.79-0.91), cut-off 40 in retrospective analysis of PHBT patients (n=76) (ref.⁸²).

DISCUSSION

Despite continuous progress in the area of emergency conditions, including those affected by OHCA, still a low level of patients who survive the event with a good neurological outcome remains. Despite continuous progress in the emergency area, there is still a low level of patients who survive cardiac arrest with a good neurological outcome. Authorities responsible for producing guidelines pay attention to the broadest awareness in the field of OHCA, particularly to recognize cardiac arrest symptoms and start quality basic life support. Therefore, an appeal to a wide range of specialists is addressed to spread their knowledge as much as possible in a comprehensive form

among lay public. Children are an important part of the chain of survival in the level of quality performed in basic life support. It is possible to make them excited using attractive education methods and they can spread this excitement to their families where there is the most common incidence of OHCA. Awareness about AED usage can be listed among basic technical skills as well. Local EMDC are urged to create a clear network of AED location, both stationary and mobile ones. There is also a demand for training the maximum possible number of first responders who are educated in basic resuscitation skills. A network of these first responders is a part of operational dispatch centre control programmes and when in need they can be dispatched to the point of injury if a longer-range EMS time is estimated^{2,3}. Also technical, invasive methods are going through a boom besides these non-technical methods. Present level of knowledge has not reached statistically significant values in most of them, however, conducted studies show promising results in relation to the level of mortality and survival. Regardless, it is necessary to realize these techniques, even though they can give rise to the impression of a revolutionary method, are designated in pre-hospital sector in particular for gaining time until definitive care in specialized centres. Only a certain group of patients who follow more or less defined input criteria before the decision itself can profit from their activation in the long term^{31,32,36,38,60-62}. A decision-making process shortly after reaching the scene is a crucial moment for activation of the consequent procedure. EMS/HEMS teams only have a limited amount of information about the current condition of vital functions and severity of bleeding at their disposal. Indication criteria for activation of some procedures are more or less defined (ECPR, REBOA) (ref.^{37,51,52}). Input criteria of other procedures can vary based on local providers' definition and a clinical gestalt (PHBT) also plays a role in the decision-making process^{80,81}. As they are not only technically but also financially demanding methods, they will apparently remain in the area of interest and development of financially stable states and regions. Financial demands are placed not only on getting own technical equipment for a particular method but especially by the sustainability of the functioning of the whole system. High-tech operators require costs on personnel sources, training of personnel and keeping functionality of the whole system in 24/7 mode. Therefore, it is necessary to look for an acceptable cost-benefit compromise. Whether there are conditions for valid confirmation of effectiveness of invasive methods in well set up systems with a dense structure of pre-hospital EMS/HEMS networks and availability of specialized centres (cardiac arrest centres, trauma centres) is arguable. Transport time with the performance itself should not exceed 60 minutes while considering activation of this procedure^{37,38,61}. This is all pre-hospital time (the interval from the incident to admission at emergency department) in quality set up systems, which undoubtedly the EU countries or north America countries are. Patients are given to emergency departments of specialized centres (trauma centres, cardiac arrest centres) in this inter-

val and the invasive method itself can be performed still within an acceptable time window, in a more comfortable environment, with usage of supporting lab and imaging methods and possibility of early intervention during possible complications, which invasive methods are burdened with. Of course, this consideration is not intended for remote areas, where it will probably be more difficult to get sufficiently big cohorts of patients in comparison to city and suburban areas.

CONCLUSION

Newly introduced non-invasive and invasive methods for patients with out of hospital cardiac arrest have the potential to improve rates of survival with a good neurological outcome. For evidence confirmation it is necessary to continue in conducting prospective randomized trials on sufficiently large cohorts of patients. Continued scientific efforts with the submission of evidence and definitive recommendations can be expected, especially in high- and middle-income countries due to the financial demands of high-tech technologies.

Search strategy and selection criteria

Our search strategy aimed to evaluate studies on current trends in the management of OHCA – traumatic and non-traumatic aetiology. Scientific articles were retrieved using the PubMed and Web of Science databases. All searches were up to January 2023, papers relating to current knowledge on individual methods not older than 5 years. Search terms corresponding to the text chapters “drones and AEDs”, “video emergency call”, “machine learning models”, “ECPR”, “REBOA” and “pre-hospital blood transfusion” were used. Only the full texts of the articles in English were reviewed or the papers were requested through personal communication with the corresponding authors.

Acknowledgements: The work was supported by the Ministry of Defence of the Czech Republic “Long Term Organization Development Plan 1011” – Clinical disciplines II of the Military Faculty of Medicine Hradec Kralove, University of Defence, Czech Republic (Project No: DZRO-FVZ22-KLINIKA II)

Author contributions: MP: concept, literature search, manuscript writing; ECH: literature search, critical revision.

Conflict of interest statement: None declared.

REFERENCES

- Gräsner JT, Wnent J, Herlitz J, Perkins GD, Lefering R, Tjelmeland I, Koster RW, Masterson S, Rossell-Ortiz F, Maurer H, Böttiger BW, Moertl M, Mols P, Alihodžić H, Hadžibegović I, Ioannides M, Truhlář A, Wissenberg M, Salo A, Escutnaire J, Nikolaou N, Nagy E, Jonsson BS, Wright P, Semeraro F, Clarens C, Beesems S, Cebula G, Correia VH, Cimpoesu D, Raffay V, Trenkler S, Markota A, Strömsöe A, Burkart R, Booth S, Bossaert L. Survival after out-of-hospital cardiac arrest in Europe - Results of the EuReCa TWO study. *Resuscitation* 2020;148(1):218-26.
- Gräsner JT, Herlitz J, Tjelmeland IBM, Wnent J, Masterson S, Lilja G, Bein B, Böttiger BW, Rosell-Ortiz F, Nolan JP, Bossaert L, Perkins GD. European Resuscitation Council Guidelines 2021: Epidemiology of cardiac arrest in Europe. *Resuscitation* 2021;161(4):61-79.
- Semeraro F, Greif R, Böttiger BW, Burkart R, Cimpoesu D, Georgiou M, Yeung J, Lippert F, S Lockey A, Olasveengen TM, Ristagno G, Schlieber J, Schnaubelt S, Scapigliati AG, Monsieurs K. European Resuscitation Council Guidelines 2021: Systems saving lives. *Resuscitation* 2021;161(4):80-97.
- Chai J, Fordyce CB, Guan M, Humphries K, Hutton J, Christenson J, Grunau B. The association of duration of resuscitation and long-term survival and functional outcomes after out-of-hospital cardiac arrest. *Resuscitation* 2023;182:109654.
- Delft University of Technology. Ambulance Drone [article on Internet]. 2014 [cited 2023 Aug 20]. Available from: <https://www.tudelft.nl/io/onderzoek/research-labs/applied-labs/ambulance-drone>.
- Sanfridsson J, Sparrevik J, Hollenberg J, Nordberg P, Djärv T, Ringh M, Svensson L, Forsberg S, Nord A, Andersson-Hagiwara M, Claesson A. Drone delivery of an automated external defibrillator - a mixed method simulation study of bystander experience. *Scand J Trauma Resusc Emerg Med* 2019;27(1):40.
- Boutillier JJ, Brooks SC, Janmohamed A, Byers A, Buick JE, Zhan C, Schoellig AP, Cheskes S, Morrison LJ, Chan TCY, Rescu Epistery Investigators. Optimizing a Drone Network to Deliver Automated External Defibrillators. *Circulation* 2017;135(25):2454-65.
- Lim JCL, Loh N, Lam HH, Lee JW, Liu N, Yeo JW, Ho AFW. The Role of Drones in Out-of-Hospital Cardiac Arrest: A Scoping Review. *J Clin Med* 2022;11(19):5744.
- Schierbeck S, Hollenberg J, Nord A, Svensson L, Nordberg P, Ringh M, Forsberg S, Lundgren P, Axelsson C, Claesson A. Automated external defibrillators delivered by drones to patients with suspected out-of-hospital cardiac arrest. *Eur Heart J* 2022;43(15):1478-87.
- Baumgarten MC, Röper J, Hahnenkamp K, Thies KC. Drones delivering automated external defibrillators-Integrating unmanned aerial systems into the chain of survival: A simulation study in rural Germany. *Resuscitation* 2022;172(3):139-45.
- Bogle BM, Rosamond WD, Snyder KT, Zègre-Hemsey JK. The Case for Drone-assisted Emergency Response to Cardiac Arrest: An Optimized Statewide Deployment Approach. *N C Med J* 2019;80(4):204-12.
- Schierbeck S, Svensson L, Claesson A. Use of a Drone-Delivered Automated External Defibrillator in an Out-of-Hospital Cardiac Arrest – letter to editor. *N Engl J Med* 2022;386:1953-4.
- Holmén J, Herlitz J, Ricksten SE, Strömsöe A, Hagberg E, Axelsson C, Rawshani A. Shortening Ambulance Response Time Increases Survival in Out-of-Hospital Cardiac Arrest. *J Am Heart Assoc* 2020;9(21):1-12.
- Viereck S, Möller TP, Ersbøll AK, Bækgaard JS, Claesson A, Hollenberg J, Folke F, Lippert FK. Recognising out-of-hospital cardiac arrest during emergency calls increases bystander cardiopulmonary resuscitation and survival. *Resuscitation* 2017;115(1):141-7.
- Plodr M, Truhlár A, Krenciková J, Praunova M, Svaba V, Masek J, Bejrova D, Paral J. Effect of introduction of a standardized protocol in dispatcher-assisted cardiopulmonary resuscitation. *Resuscitation* 2016;106(2):18-23.
- Kurz MC, Bobrow BJ, Buckingham J, Cabanas JG, Eisenberg M, Fromm P, Panczyk MJ, Rea T, Seaman K, Vaillancourt C; American Heart Association Advocacy Coordinating Committee. Telecommunicator Cardiopulmonary Resuscitation: A Policy Statement From the American Heart Association. *Circulation* 2020;141(12):686-700.
- Blomberg SN, Christensen HC, Lippert F, Ersbøll AK, Torp-Petersen C, Sayre MR, Kudenchuk PJ, Folke F. Effect of Machine Learning on Dispatcher Recognition of Out-of-Hospital Cardiac Arrest During Calls to Emergency Medical Services: A Randomized Clinical Trial. *JAMA Netw Open* 2021;4(1):1-7.
- Blomberg SN, Jensen TW, Porsborg Andersen M, Folke F, Kjær Ersbøll A, Torp-Petersen C, Lippert F, Collatz Christensen H. When the machine is wrong. Characteristics of true and false predictions of Out-of-Hospital Cardiac arrests in emergency calls using a machine-learning model. *Resuscitation* 2023;183(2):1-7.
- Viereck S, Möller TP, Rothman JP, Folke F, Lippert FK. Recognition of out-of-hospital cardiac arrest during emergency calls - a systematic review of observational studies. *Scand J Trauma Resusc Emerg Med* 2017;25(1):2-12.

20. Panchal AR, Berg KM, Cabañas JG, Kurz MC, Link MS, Del Rios M, Hirsch KG, Chan PS, Hazinski MF, Morley PT, Donnino MW, Kudenchuk PJ. 2019 American Heart Association Focused Update on Systems of Care: Dispatcher-Assisted Cardiopulmonary Resuscitation and Cardiac Arrest Centers: An Update to the American Heart Association Guidelines for Cardiopulmonary Resuscitation and Emergency Cardiovascular Care. *Circulation* 2019;140(24):895-903.
21. Bolle SR, Scholl J, Gilbert M. Can video mobile phones improve CPR quality when used for dispatcher assistance during simulated cardiac arrest? *Acta Anaesthesiol Scand* 2009;53(1):116-20.
22. Lin YY, Chiang WC, Hsieh MJ, Sun JT, Chang YC, Ma MH. Quality of audio-assisted versus video-assisted dispatcher-instructed bystander cardiopulmonary resuscitation: A systematic review and meta-analysis. *Resuscitation* 2018;123(2):77-85.
23. Lee HS, You K, Jeon JP, Kim C, Kim S. The effect of video-instructed versus audio-instructed dispatcher-assisted cardiopulmonary resuscitation on patient outcomes following out of hospital cardiac arrest in Seoul. *Sci Rep* 2021;11(1):1-9.
24. Linderöth G, Lippert F, Østergaard D, Ersbøll AK, Meyhoff CS, Folke F, Christensen HC. Live video from bystanders' smartphones to medical dispatchers in real emergencies. *BMC Emerg Med* 2021;21(1):2-10.
25. Sykora R, Renza M, Ruzicka J, Bakurova P, Kukacka K, Smetana J, Duska J. Audiovisual Consults by Paramedics to Reduce Hospital Transport After Low-Urgency Calls: Randomized Controlled Trial. *Prehosp Disaster Med* 2020;35(6):656-62.
26. Kim HJ, Kim JH, Park D. Comparing audio- and video-delivered instructions in dispatcher-assisted cardiopulmonary resuscitation with drone-delivered automatic external defibrillator: a mixed methods simulation study. *Peer J* 2021;15(9):2-8.
27. Younger JG, Schreiner RJ, Swaniker F, Hirschl RB, Chapman RA, Bartlett RH. Extracorporeal resuscitation of cardiac arrest. *Acad Emerg Med* 1999;6(7):700-7.
28. Maekawa K, Tanno K, Hase M, Mori K, Asai Y. Extracorporeal cardiopulmonary resuscitation for patients with out-of-hospital cardiac arrest of cardiac origin: a propensity-matched study and predictor analysis. *Crit Care Med* 2013;41(5):1186-96.
29. Mosier JM, Kelsey M, Raz Y, Gunnerson KJ, Meyer R, Hypes CD, Malo J, Whitmore SP, Spaite DW. Extracorporeal membrane oxygenation (ECMO) for critically ill adults in the emergency department: history, current applications, and future directions. *Crit Care* 2015;17(12):1155-7.
30. Wengenmayer T, Rombach S, Ramshorn F, Biever P, Bode C, Duerschmied D, Staudacher DL. Influence of low-flow time on survival after extracorporeal cardiopulmonary resuscitation (eCPR). *Crit Care* 2017;21(1):1744-8.
31. Yannopoulos D, Bartos J, Raveendran G, Walser E, Connett J, Murray TA, Collins G, Zhang L, Kalra R, Kosmopoulos M, John R, Shaffer A, Frascone RJ, Wesley K, Conterato M, Biros M, Tolar J, Aufderheide TP. Advanced reperfusion strategies for patients with out-of-hospital cardiac arrest and refractory ventricular fibrillation (ARREST): a phase 2, single centre, open-label, randomised controlled trial. *Lancet* 2020;396(10265):1807-16.
32. Havranek S, Fingrova Z, Rob D, Smalcova J, Kavalkova P, Franek O, Smid O, Huptych M, Dusik M, Linhart A, Belohlavek J. Initial rhythm and survival in refractory out-of-hospital cardiac arrest. Post-hoc analysis of the Prague OHCA randomized trial. *Resuscitation* 2022;181(12):289-96.
33. Mandigers L, Boersma E, den Uil CA, Gommers D, Bělohávek J, Belliato M, Lorusso R, Dos Reis Miranda D. Systematic review and meta-analysis comparing low-flow duration of extracorporeal and conventional cardiopulmonary resuscitation. *Interact Cardiovasc Thorac Surg* 2022;35(4):1-5.
34. Hsu CH, Meurer WJ, Domeier R, Fowler J, Whitmore SP, Bassin BS, Gunnerson KJ, Haft JW, Lynch WR, Nallamothu BK, Havey RA, Kidwell KM, Stacey WC, Silbergleit R, Bartlett RH, Neumar RW. Extracorporeal Cardiopulmonary Resuscitation for Refractory Out-of-Hospital Cardiac Arrest (EROCA): Results of a Randomized Feasibility Trial of Expedited Out-of-Hospital Transport. *Ann Emerg Med* 2021;78(1):92-101.
35. Holmberg MJ, Granfeldt A, Guerguerian AM, Sandroni C, Hsu CH, Gardner RM, Lind PC, Eggertsen MA, Johannsen CM, Andersen LW. Extracorporeal cardiopulmonary resuscitation for cardiac arrest: An updated systematic review. *Resuscitation* 2023;182(1):1-9.
36. Suverein MM, Delnoij TSR, Lorusso R, Brandon Bravo Bruinsma GJ, Otterspoor L, Elzo Kraemer CV, Vlaar APJ, van der Heijden JJ, Scholten E, den Uil C, Jansen T, van den Bogaard B, Kuijpers M, Lam KY, Montero Cabezas JM, Driessen AHG, Rittersma SZH, Heijnen BG, Dos Reis Miranda D, Bleeker G, de Metz J, Hermanides RS, Lopez Matta J, Eberl S, Donker DW, van Thiel RJ, Akin S, van Meer O, Henriques J, Bokhoven KC, Mandigers L, Bunge JHH, Bol ME, Winkens B, Essers B, Weerwind PW, Maessen JG, van de Poll MCG. Early Extracorporeal CPR for Refractory Out-of-Hospital Cardiac Arrest. *N Engl J Med* 2023;388(4):299-309.
37. Mueller M, Magnet IAM, Poppe M, Mitteregger T, Krammel M. Rhythm check three - A2BCDE3! - A new acronym to select eligible patients for extracorporeal cardiopulmonary resuscitation (eCPR). *Resuscitation* 2022;171(2):30-2.
38. Kruit N, Rattan N, Tian D, Dieleman S, Burrell A, Dennis M. Prehospital Extracorporeal Cardiopulmonary Resuscitation for Out-of-Hospital Cardiac Arrest: A Systematic Review and Meta-Analysis. *J Cardiothorac Vasc Anesth* 2023;37(5):748-54.
39. Lott C, Truhlář A, Alfonzo A, Barelli A, González-Salvado V, Hinkelbein J, Nolan JP, Paal P, Perkins GD, Thies KC, Yeung J, Zideman DA, Soar J; ERC Special Circumstances Writing Group Collaborators. European Resuscitation Council Guidelines 2021: Cardiac arrest in special circumstances. *Resuscitation* 2021;161(4):152-219.
40. Vianen NJ, Van Lieshout EMM, Maissan IM, Bramer WM, Hartog DD, Verhofstad MHJ, Van Vledder MG. Prehospital traumatic cardiac arrest: a systematic review and meta-analysis. *Eur J Trauma Emerg Surg* 2022;48(4):3357-72.
41. Engdahl J, Holmberg M, Karlson BW, Luepker R, Herlitz J. The epidemiology of out-of-hospital 'sudden' cardiac arrest. *Resuscitation* 2002;52(3):235-45.
42. van Oostendorp SE, Tan EC, Geeraedts LM Jr. Prehospital control of life-threatening truncal and junctional haemorrhage is the ultimate challenge in optimizing trauma care: a review of treatment options and their applicability in the civilian trauma setting. *Scand J Trauma Resusc Emerg Med* 2016;24(1):1-9.
43. Lee C, Porter KM, Hodgetts TJ. Tourniquet use in the civilian prehospital setting. *Emerg Med J* 2007;24(8):584-7.
44. Kelly JF, Ritenour AE, McLaughlin DF, Bagg KA, Apodaca AN, Mallak CT, Pearse L, Lawnick MM, Champion HR, Wade CE, Holcomb JB. Injury severity and causes of death from Operation Iraqi Freedom and Operation Enduring Freedom: 2003-2004 versus 2006. *J Trauma* 2008;64(2 Suppl):S21-6; discussion S26-7. doi: 10.1097/TA.0b013e318160b9fb
45. Eastridge BJ, Mabry RL, Seguin P, Cantrell J, Tops T, Uribe P, Mallett O, Zubko T, Oetjen-Gerdes L, Rasmussen TE, Butler FK, Kotwal RS, Holcomb JB, Wade C, Champion H, Lawnick M, Moores L, Blackburne LH. Death on the battlefield (2001-2011): implications for the future of combat casualty care. *J Trauma Acute Care Surg* 2012;73(6 Suppl 5):S431-437.
46. Kragh JF Jr, Littrel ML, Jones JA, Walters TJ, Baer DG, Wade CE, Holcomb JB. Battle casualty survival with emergency tourniquet use to stop limb bleeding. *J Emerg Med* 2011;41(6):590-7.
47. Grottko E, Grønlykke L, Harrois A, Hunt BJ, Kaserer A, Komadina R, Madsen MH, Maegele M, Mora L, Riddez L, Romero CS, Samama CM, Vincent JL, Wiberg S, Spahn DR. The European guideline on management of major bleeding and coagulopathy following trauma: sixth edition. *Crit Care* 2023;27(1):2-45.
48. Manzano Nunez R, Naranjo MP, Foianini E, Ferrada P, Rincon E, García-Perdomo HA, Burbano P, Herrera JP, García AF, Ordoñez CA. A meta-analysis of resuscitative endovascular balloon occlusion of the aorta (REBOA) or open aortic cross-clamping by resuscitative thoracotomy in non-compressible torso hemorrhage patients. *World J Emerg Surg* 2017;14(7):1-8.
49. Hughes CW. Use of an intra-aortic balloon catheter tamponade for controlling intra-abdominal hemorrhage in man. *Surgery* 1954;36(1):65-8.
50. Howard ER, Young AE. Control of aortic haemorrhage by balloon catheter. *Br Med J* 1971;17(3):161.
51. Castellini G, Gianola S, Biffi A, Porcu G, Fabbri A, Ruggieri MP, Coniglio C, Napoletano A, Cocclite D, D'Angelo D, Fauci AJ, Iacorossi L, Latina R, Salomone K, Gupta S, Iannone P, Chiara O; Italian National Institute of Health guideline working group on Major Trauma. Resuscitative endovascular balloon occlusion of the aorta (REBOA) in patients with major trauma and uncontrolled haemorrhagic shock: a systematic review with meta-analysis. *World J Emerg Surg* 2021;16(1):2-12.

52. Jamal L, Saini A, Quencer K, Altun I, Albadawi H, Khurana A, Naidu S, Patel I, Alzubaidi S, Oklu R. Emerging approaches to pre-hospital hemorrhage control: a narrative review. *Ann Transl Med* 2021;9(14):2-10.
53. Harfouche MN, Madurska MJ, Elansary N, Abdou H, Lang E, DuBose JJ, Kundi R, Feliciano DV, Scalea TM, Morrison JJ. Resuscitative endovascular balloon occlusion of the aorta associated with improved survival in hemorrhagic shock. *PLoS One* 2022;17(3):1-10.
54. Cantle PM. REBOA utility. *Surg Open Sci* 2022;18(8):50-5.
55. Moore LJ, Brenner M, Kozar RA, Pasley J, Wade CE, Baraniuk MS, Scalea T, Holcomb JB. Implementation of resuscitative endovascular balloon occlusion of the aorta as an alternative to resuscitative thoracotomy for noncompressible truncal hemorrhage. *J Trauma Acute Care Surg* 2015;79(4):523-30.
56. Norii T, Crandall C, Terasaka Y. Survival of severe blunt trauma patients treated with resuscitative endovascular balloon occlusion of the aorta compared with propensity score-adjusted untreated patients. *J Trauma Acute Care Surg* 2015;78(4):721-8.
57. Joseph B, Zeeshan M, Sakran JV, Hamidi M, Kulvatunyoun N, Khan M, O'Keeffe T, Rhee P. Nationwide Analysis of Resuscitative Endovascular Balloon Occlusion of the Aorta in Civilian Trauma. *JAMA Surg* 2019;154(6):500-8.
58. Alarhayem AQ, Myers JG, Dent D, Liao L, Muir M, Mueller D, Nicholson S, Cestero R, Johnson MC, Stewart R, O'Keefe G, Eastridge BJ. Time is the enemy: Mortality in trauma patients with hemorrhage from torso injury occurs long before the "golden hour". *Am J Surg* 2016;212(6):1101-5.
59. Sadek S, Lockey DJ, Lendrum RA, Perkins Z, Price J, Davies GE. Resuscitative endovascular balloon occlusion of the aorta (REBOA) in the pre-hospital setting: An additional resuscitation option for uncontrolled catastrophic haemorrhage. *Resuscitation* 2016;107(10):135-8.
60. Chan CN, Kadir B, Ahmed Z. The Role of Prehospital REBOA for Hemorrhage Control in Civilian and Military Austere Settings: A Systematic Review. *Trauma Care* 2022;2(1):63-78.
61. Hilbert-Carius P, Schmalbach B, Wrigge H, Schmidt M, Abu-Zidan FM, Aschenbrenner U, Streibert F. Do we need pre-hospital resuscitative endovascular balloon occlusion of the aorta (REBOA) in the civilian helicopter emergency medical services (HEMS)? *Intern Emerg Med* 2023;18(2):627-37.
62. Nowadly CD, Johnson MA, Hoareau GL, Manning JE, Daley JI. The use of resuscitative endovascular balloon occlusion of the aorta (REBOA) for non-traumatic cardiac arrest: A review. *J Am Coll Emerg Physicians Open* 2020;1(5):737-43.
63. Brede JR, Lafrenz T, Klepstad P, Skjærseth EA, Nordseth T, Søvik E, Krüger AJ. Feasibility of Pre-Hospital Resuscitative Endovascular Balloon Occlusion of the Aorta in Non-Traumatic Out-of-Hospital Cardiac Arrest. *J Am Heart Assoc* 2019;8(22):2-10.
64. Brede JR, Kramer-Johansen J, Rehn M. A needs assessment of resuscitative endovascular balloon occlusion of the aorta (REBOA) in non-traumatic out-of-hospital cardiac arrest in Norway. *BMC Emerg Med* 2020;20(28):2-9.
65. Brede JR, Skulberg AK, Rehn M, Thorsen K, Klepstad P, Tylleskär I, Farbu B, Dale J, Nordseth T, Wiseth R, Krüger AJ. REBOARREST, resuscitative endovascular balloon occlusion of the aorta in non-traumatic out-of-hospital cardiac arrest: a study protocol for a randomised, parallel group, clinical multicentre trial. *Trials* 2021;22(1):511.
66. Shackelford SA, Del Junco DJ, Powell-Dunford N, Mazuchowski EL, Howard JT, Kotwal RS, Gurney J, Butler FK Jr, Gross K, Stockinger ZT. Association of Prehospital Blood Product Transfusion During Medical Evacuation of Combat Casualties in Afghanistan With Acute and 30-Day Survival. *JAMA* 2017;318(16):1581-91.
67. van Turenhout EC, Bossers SM, Loer SA, Giannakopoulos GF, Schwarte LA, Schober P. Pre-hospital transfusion of red blood cells. Part 2: A systematic review of treatment effects on outcomes. *Transfus Med* 2020;30(2):106-33.
68. Brown JB, Sperry JL, Fombrona A, Billiar TR, Peitzman AB, Guyette FX. Pre-trauma center red blood cell transfusion is associated with improved early outcomes in air medical trauma patients. *J Am Coll Surg* 2015;220(5):797-808.
69. Rijnhout T, Wever KE, Marinus R, Hoogerwerf N, Geeraedts L, Tan E. Is pre-hospital blood transfusion effective and safe in haemorrhagic trauma patients? A systematic review and meta-analysis. *Injury* 2019;50(5):1017-27.
70. Moore HB, Moore EE, Chapman MP, McVane K, Bryskiewicz G, Blechar R, Chin T, Burlew CC, Pieracci F, West FB, Fleming CD, Ghasabyan A, Chandler J, Silliman CC, Banerjee A, Sauaia A. Plasma-first resuscitation to treat haemorrhagic shock during emergency ground transportation in an urban area: a randomised trial. *Lancet* 2018;28(10144):283-91. doi: 10.1016/S0140-6736(18)31553-8
71. Sperry JL, Guyette FX, Brown JB, Yazer MH, Trulzi DJ, Early-Young BJ, Adams PW, Daley BJ, Miller RS, Harbrecht BG, Claridge JA, Phelan HA, Witham WR, Putnam AT, Duane TM, Alarcon LH, Callaway CW, Zuckerbraun BS, Neal MD, Rosengart MR, Forsythe RM, Billiar TR, Yealy DM, Peitzman AB, Zenati MS; PAMPer Study Group. Prehospital Plasma during Air Medical Transport in Trauma Patients at Risk for Hemorrhagic Shock. *N Engl J Med* 2018;379(4):315-26. doi: 10.1056/NEJMoa1802345
72. Crombie N, Doughty HA, Bishop JRB, Desai A, Dixon EF, Hancox JM, Herbert MJ, Leech C, Lewis SJ, Nash MR, Naumann DN, Slinn G, Smith H, Smith IM, Wale RK, Wilson A, Ives N, Perkins GD; RePHILL collaborative group. Resuscitation with blood products in patients with trauma-related haemorrhagic shock receiving prehospital care (RePHILL): a multicentre, open-label, randomised, controlled, phase 3 trial. *Lancet Haematol* 2022;9(4):e250-e261. doi: 10.1016/S2352-3026(22)00040-0
73. McCoy CC, Brenner M, Duchesne J, Roberts D, Ferrada P, Horer T, Kauvar D, Khan M, Kirkpatrick A, Ordonez C, Ferreira B, Priouzzam A, Cotton BA. Back to the Future: Whole Blood Resuscitation of the Severely Injured Trauma Patient. *Shock* 2021;56(1S):9-15.
74. Nessen SC, Eastridge BJ, Cronk D, Craig RM, Berséus O, Ellison R, Remick K, Seery J, Shah A, Spinella PC. Fresh whole blood use by forward surgical teams in Afghanistan is associated with improved survival compared to component therapy without platelets. *Transfusion* 2013;53(51):107-13.
75. Gurney J, Staudt A, Cap A, Shackelford S, Mann-Salinas E, Le T, Nessen S, Spinella P. Improved survival in critically injured combat casualties treated with fresh whole blood by forward surgical teams in Afghanistan. *Transfusion* 2020;60(53):180-8.
76. Spinella PC, Perkins JG, Grathwohl KW, Beekley AC, Holcomb JB. Warm fresh whole blood is independently associated with improved survival for patients with combat-related traumatic injuries. *J Trauma* 2009;66(4 Suppl):69-76.
77. Sunde GA, Bjerkvig C, Bekkevold M, Kristoffersen EK, Strandenes G, Bruserud Ø, Apseth TO, Heltne JK. Implementation of a low-titre whole blood transfusion program in a civilian helicopter emergency medical service. *Scand J Trauma Resusc Emerg Med* 2022;30(1):2-9.
78. Levin D, Zur M, Shinar E, Moshe T, Tsur AM, Nadler R, Yazer MH, Epstein D, Avital G, Gelikas S, Glassberg E, Benov A, Chen J. Low-Titer Group O Whole-Blood Resuscitation in the Prehospital Setting in Israel: Review of the First 2.5 Years' Experience. *Transfus Med Hemother* 2021;48(6):342-9.
79. Shea SM, Staudt AM, Thomas KA, Schuerer D, Mielke JE, Folkerts D, Lowder E, Martin C, Bochicchio GV, Spinella PC. The use of low-titer group O whole blood is independently associated with improved survival compared to component therapy in adults with severe traumatic hemorrhage. *Transfusion* 2020;60(53):2-9.
80. Thies KC, Truhlář A, Keene D, Hinkelbein J, Rützler K, Brazzi L, Vivien B. Pre-hospital blood transfusion - an ESA survey of European practice. *Scand J Trauma Resusc Emerg Med* 2020;28(1):79. doi: 10.1186/s13049-020-00774-1
81. Shand S, Curtis K, Dinh M, Burns B. What is the impact of pre-hospital blood product administration for patients with catastrophic haemorrhage: an integrative review? *Injury* 2019;50(2):226-34.
82. Plodrm M, Berková J, Hyšpler R, Truhlář A, Páral J, Kočí J. Prediction of pre-hospital blood transfusion in trauma patients based on scoring systems. *BMC Emerg Med* 2023;23(1):2-9.