



Number of Prehospital Defibrillation Shocks and the Return of Spontaneous Circulation in Out-of-Hospital Cardiac Arrest

Hastane Dışı Kardiyak Arrest Durumunda Uygulanan Hastane Öncesi Defibrilasyon Şoklarının Sayısı ve Spontan Dolaşımın Geri Dönüşü

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Objective: It has not been determined yet whether the number of defibrillation shocks delivered over the first 30 min of cardiopulmonary resuscitation (CPR) impacts the rate of successful return of spontaneous circulation (ROSC) in out-of-hospital cardiac arrest (OHCA).

Methods: We conducted a retrospective observational study in non-traumatic OHCA. Patients who were administered defibrillation shocks using a public automated external defibrillator (AED) were consecutively enrolled in the study. We assessed the relationship between ROSC and the number of prehospital defibrillation shocks and constructed a receiver operating characteristic (ROC) curve to illustrate the ability of repeated defibrillation shocks to predict ROSC over the first 30 min of CPR.

Results: Increasing the number of defibrillation shocks progressively decreased the probability to achieve ROSC. The highest rate of ROSC (33%) was observed when four shocks were delivered. The ROC curve illustrated that the fourth shock maximised sensitivity and specificity (area under the curve [AUC]=0.72). The positive and negative predictive values for ROSC reached 82% and 48%, respectively, when <4 shocks were delivered.

Conclusion: The delivery of four defibrillation shocks in OHCA most related to ROSC. The evaluation of the number of delivered shock during the first 30 min of CPR is a simple tool that can be used for an early decision in OHCA patient.

Keywords: Number of defibrillation shocks, shockable rhythm, out-of-hospital cardiac arrest, resuscitation, outcome.

Amaç: Hastane dışı kardiyak arrest (HDKA) geçiren hastalarda kardiyopulmoner resüsitasyonun (CPR) ilk 30 dakikasında uygulanan defibrilasyon şok sayısının spontan dolaşımın başarılı bir şekilde geri dönüşü (SDGD) üzerindeki etkisi halen belirlenmemiştir.

Yöntemler: Non-travmatik HDKA hakkında retrospektif bir gözlem çalışması yapıldı. Otomatik eksternal defibrilatör (OED) kullanılarak defibrilasyon şoku uygulanan hastalar ardışık olarak çalışmaya dahil edildiler. SDGD ile hastane öncesi defibrilasyon şoku sayısı arasındaki ilişki değerlendirildi ve CPR'nin ilk 30 dakikasındaki SDGD'yi öngörmede tekrarlanan defibrilasyon şoklarının etkisini göstermek amacıyla alıcı işletim karakteristik (ROC) eğrisi oluşturuldu.

Bulgular: Defibrilasyon şok sayısının giderek artırılması SDGD'ye ulaşma olasılığını azalttı. En yüksek SDGD oranının (%33) dört şok uygulandığında olduğu görüldü. ROC eğrisine göre, dördüncü şok duyarlılık ve özgüllük oranını maksimuma çıkardı (eğri altındaki alan [AUC]=0,72). Dördün altında şok uygulandığında pozitif ve negatif SDGD değerleri sırasıyla %82 ve %48'e ulaştı.

Sonuç: HDKA'da dört defibrilasyon şokunun uygulanması daha çok SDGD ile ilişkilidir. CPR'nin ilk 30 dakikasında uygulanan şok sayısının değerlendirilmesi, HDKA hastalarında erken karar vermek için kullanılabilir basit bir yöntemdir.

Anahtar Sözcükler: Defibrilasyon şok sayısı, şoklanabilir ritim, hastane dışı kardiyak arrest, resüsitasyon, sonuç

Introduction

Since the first description of cardiopulmonary resuscitation (CPR) in 1960 (1), continuous research and development has been performed to improve care efficiency in the management of cardiac arrest (CA). Currently, the state of scientific knowledge is summarised in the guidelines for advanced life support (ALS) published by national and international societies, such as the American Heart Association and European Resuscitation Council (2). Despite fundamental research and clinical studies in CA, the outcomes of applying basic life support and ALS remain poor, with survival rates of 8.2%–22% for hospitalised patients and of 6%–11% for critically ill patients (3-6).

Out-of-hospital CA (OHCA) is often due to ventricular fibrillation with an incidence varying from 18% to 63% (7). Interestingly, recurrent ventricular fibrillation during CPR (8) and thus repeated defibrillation shocks associated with prolonged CPR has been reported to negatively impact survival (9, 10). In fact, a rapid decline in the survival rate was noticed when ALS was prolonged for more than 10-15 min, with no return of spontaneous circulation (ROSC) (11-13).

Resuscitation failure constrains the emergency medical services (EMS) at the scene to decide between implementation of extracorporeal life support (ECLS) out- or in-hospital, organ donation after eligibility or termination of ALS. In fact, extracorporeal CPR (ECPR) improved the outcome of refractory OHCA (14).

In France, refractory CA is defined as a failure in ROSC upon 30 min of ALS (15), while other countries do not clearly define this entity. Consequently, time-to-ROSC is a key element to predict patient outcome and to decide for early implementation of ECPR.

To our knowledge, no study focused on the association between the number of delivered defibrillation shocks and the ROSC. In this study, we propose to describe the relationship between the number of delivered defibrillation shocks and ROSC.

Methods

Methodology

A retrospective observational cohort study in OHCA was performed between 1 January 2007 and 31 December 2013 in Paris, France. All consecutive non-traumatic OHCA were identified. Patients with no attempt at resuscitation were excluded from the study. All OHCA patients who received prehospital defibrillation shocks with a public automated external defibrillator (AED) performed by emergency medical teams (EMTs) or mobile intensive care units (MICUs) were enrolled in the study. The study population included patients aged >18 years who underwent OHCA from either cardiac or non-cardiac aetiology, excluding traumatic causes.

The number of delivered defibrillation shocks was collected for each patient by extraction from medical reports. In France, for each EMT or MICU intervention, a medical report collecting medical history of patient and therapeutic interventions (drugs administration, tracheal intubation and number of delivered defibrillation) is generated. Thereafter, these data are reported in a computer file from which database for this study was extracted and analysed. In this medical report, schedules are also mentioned. When the EMT or the MICU is at the scene, a member of the team named the 'time keeper' is designed. His role is to collect hours of each intervention (defibrillation, tracheal intubation and drugs administration with dose). The time of each shock has been collected. The defibrillator was only used by EMT or MICU (depending who was the first arrived at the scene): semi-AED for EMT, whereas a manual external defibrillator with an intensity of 200J for MICU.

All data were obtained from the registry database of the service d'aide médicale d'urgence (SAMU) 15 of Paris.

In France, the management of out-of-hospital emergencies is based on the EMS (SAMU), with a national access number of 15 (16). The identification of patients occurs through a te-

lephonic call to a call centre, named the regulation call centre. Patients are evaluated over the telephonic call based on their medical history and symptoms. The appropriate orientation of patients relies on an efficient anamnestic evaluation that allows the regulation call centre to dispatch the appropriate care support. When an OHCA is suspected, an EMT is dispatched on the scene, followed by an MICU.

All patients were treated according to the 2000 (17) and 2005 (18) French guidelines based on the European Resuscitation Council guidelines. In France, the OHCA benefit from CPR during 30 min after which the OHCA is considered refractory and the physician should decide between implementation of extracorporeal life support, organ donation after eligibility or termination of CPR.

The main outcome was ROSC after the delivery of defibrillation shocks during the first 30 min of CPR. The start of CPR began when the EMT or MICU arrived at the scene. Professional rescuers and members of Paris fire brigade, who benefit from an annual training, only performed chest compressions. The victim was also ventilated using a facemask by an EMT, which was switched to a tracheal tube after MICU arrival.

The 'no-flow' corresponds to the period before all CPR by EMT, MICU or a layperson. It does not correspond to the period when nobody touches the victim for shock delivery. The 'low-flow' corresponds to the period between the beginning of CPR and the ROSC occurrence (15).

Return of spontaneous circulation was defined as a palpable pulse in any vessel. Patients were categorised by their initial rhythm. Patients with initial shockable rhythms included ventricular fibrillation, pulseless ventricular tachycardia and unclassified rhythms that were shocked with the AED. Initial non-shockable rhythms included pulseless electrical activity, asystole and unclassified rhythms that were not shocked by the AED.

According to the French law, the local ethical committee considered that consent of patients was waived for participation in this observational study.

Statistical analysis

The Kaplan-Meier curve was used to illustrate the relationship between the number of electric shocks and ROSC during the first 30 min of ALS.

Receiver operating characteristic (ROC) curve analyses was used to determine the diagnostic performance of the number of delivered defibrillation shocks to predict ROSC during the first 30 min of CPR.

The quantitative variable 'number of defibrillation shocks' was then dichotomised into a binary variable. Sensitivity (Se), specificity (Sp) and positive (PPV) and negative (NPV) predictive values were calculated for the optimal cut-off.

All variables for the primary outcome were first analysed using a univariate method. The statistical significance of the variables was determined using Chi-square tests. The multivariate model included all parameters with a p value of <0.05 in the univariate analysis. A multivariate analysis using a logistic regression model was then performed to determine the odds ratio (OR) with 95% confidence interval.

Data are presented as either absolute numbers (percentages), medians with range or mean with standard deviation (SD). The data analysis was performed using R[®] version 3.2.3.

Results

A total of 1,532 OHCA patients were included in the study between 1 January 2007 and 31 December 2013. In total, 756 (49%) OHCA patients presented with initial shockable rhythms and 776 (51%) with non-shockable rhythms (Figure 1).

An overview of the demographic and clinical characteristics of patients with initial shockable rhythms is presented in Table 1. Among the 756 patients with initial shockable rhythms, 562 (74%) were males with a mean age of 59±16 years (Table 1).

Table 1. Demographic and clinical characteristics of OHCA with shockable rhythms. Data are expressed as mean values with standard deviation (±SD) and as absolute numbers with percentage	
Mean age (years)	59±16
Male gender, n (%)	562 (74%)
No-flow (minutes)	6±6
Low-flow (minutes)	19±14
OHCA: out-of-hospital cardiac arrest	

Figure 2 illustrates the decrease of ROSC according to the number of delivered defibrillation shocks. The median value of delivered electric shocks was 3 (Figure 2). When four shocks were delivered, ROSC was achieved in 33% patients with OHCA during the first 30 min of CPR (Figure 2).

Receiver operating characteristic analyses indicated a cut-off point of four shocks for identifying a patient with ROSC in OHCA events with initial shockable rhythms, with an area under the curve (AUC) of 0.72 (Figure 3). The sensitivity and specificity were 80% and 52%, respectively (Table 2). With a number of delivered shock threshold at 4, the PPV was 82% and NPV reached 48% (Table 2).

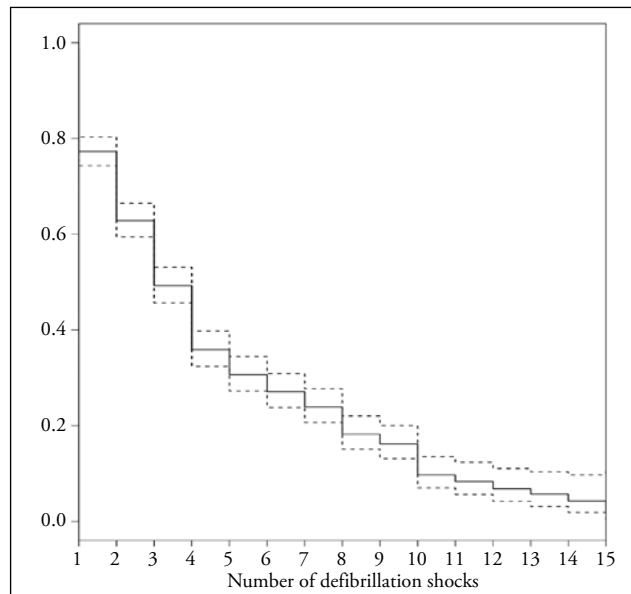


Figure 2. Association between the number of defibrillation shocks and ROSC. The relationship between the number of delivered shocks and ROSC is illustrated using a Kaplan–Meier curve. Values for electric shocks are given as absolute number and ROSC is expressed as the percentage of success. ROSC: return of spontaneous circulation

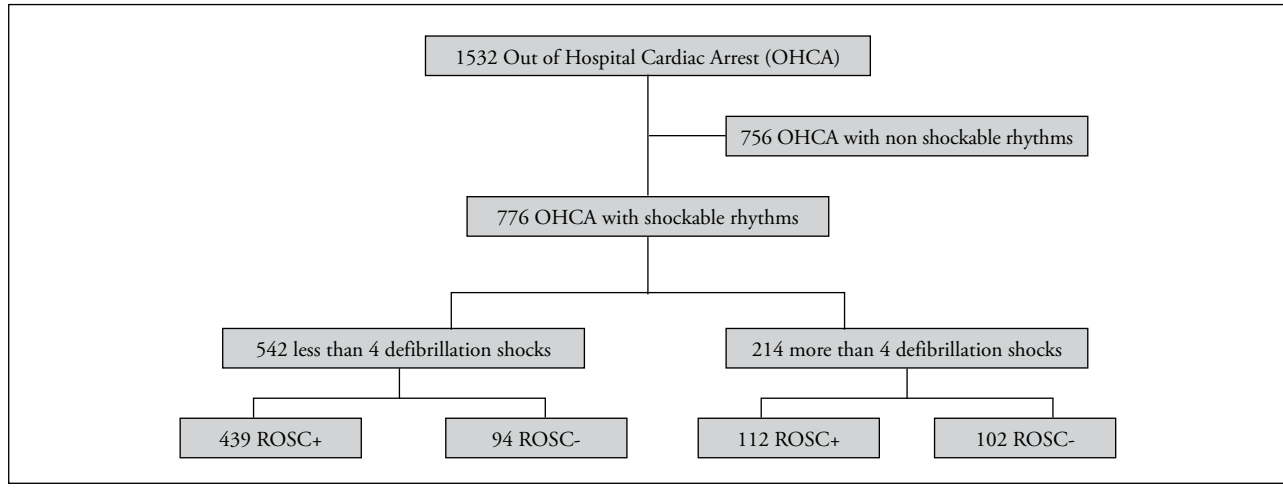


Figure 1. Flow chart of OHCA in the study
OHCA: out-of-hospital cardiac arrest

The statistical relationship between the number of delivered defibrillation shocks and ROSC was significant ($p=8.10-10$, Table 3). This association was found for both delivery of less or more than 4 shocks. To compensate for the confounding effect of the duration of no-flow, we regressed the effect of no-flow from ROSC and found that the association of the delivery of <4 shocks with no-flow-corrected ROSC remained (5.10-12, Table 3). No significant association was found between the age and ROSC and between gender and ROSC (Table 3).

Discussion

This study attempted to identify the optimal number of out-of-hospital defibrillation shocks associated with ROSC during on-scene resuscitation of initial shockable rhythms in OHCA.

Shockable rhythms are one of the presentations of OHCA (19) and are associated with better outcomes when reinforced by temperature control after ROSC (20, 21). ROSC in OHCA remains poor despite recent progress in the management of CA (3-6).

In this study, we determined the threshold number of delivered defibrillation shocks for the diagnosis of ROSC during the first 30 min of CPR. Choosing the best threshold value at 4, the delivery of <4 shocks predicted ROSC with useful PPV for practice. Indeed, efficient defibrillation and survival were reported to decline upon four shocks (8). According to

the guidelines on CA, a defibrillation shock can be delivered every 2 min. Taking into account our observations and the guidelines over the study period, four shocks would be delivered in a delay of 8-10 min. Consequently, our data are in agreement with the previously reported data by Reynolds et al. (22).

In France, the definition of refractory CA is a failure in ROSC upon 30 min of ALS (15). Thereafter, three options are available for the physician in the absence of ROSC. ECLS implemented out- or in-hospital is a possible option to gain time and allow further aetiological investigation. Organ donation upon hospital admission after eligibility is another alternative. At last, the termination of ALS might be another option when the first two options are not considered feasible. Importantly, ECLS showed an improved outcome (survival or organs quality) when implemented precociously (23-25). The French definition of refractory CA could potentially be re-thought according to the data presented here. This study illustrated that the fourth shock maximised the sensitivity and specificity (AUC=0.72). A high sensitivity (80%) reduced the risk of false negative, i.e., patients who were de-

Table 2. Contingency table designed for the number of delivered shocks threshold for the diagnosis of ROSC

	ROSC +	ROSC -	
Less than 4 shocks	439	94	533
More than 4 shocks	112	102	214
	551	196	747

Data are expressed as absolute values. ROSC: return of spontaneous circulation

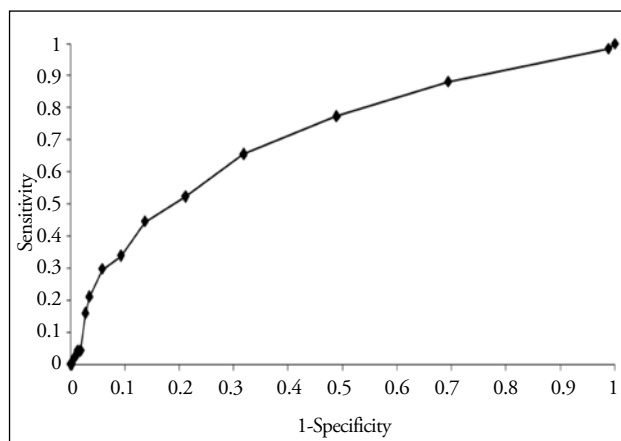


Figure 3. Receiving operator characteristics of external shocks for ROSC
ROSC: return of spontaneous circulation

Table 3. Results of univariate and multivariate analyses between ROSC and others variables. Data are expressed with odds ratio (OR; 95% CI) and OR adjusted (ORa) with (95% CI). The association was considered significant when the p value was <0.05

Variable	OR [95% CI]	p	ORa [95% CI]	p
Age	1.00 [0.99-1.01]	0.56	1.01 [1.00-1.02]	0.23
Gender	1.12 [0.82-1.56]	0.55	1.06 [0.72-1.58]	0.81
No-flow	0.92 [0.89-0.94]	7.10-7	0.91 [0.89-0.94]	8.10^-7
Defibrillation shocks	0.84 [0.80-0.88]	8.10-10	1.14 [1.03-1.28]	0.04
Defibrillation shocks <4	4.26 [3.18-5.72]	4.10-16	4.19 [2.98-5.92]	5.10^-12
Defibrillation shocks >4	0.23 [0.17-0.31]	4.10-16	0.12 [0.06-0.23]	1.08^-7

ROSC: return of spontaneous circulation; OR: odds ratio

livered more than 4 shocks presented reduced probability to achieve ROSC. However, a specificity of 52% underlined a high false positive rate. The corresponding AUC showed that the number of delivered defibrillation shocks as a marker has a predictive ability to discriminate ROSC from non ROSC in OHCA patients. This association was most interesting for its high PPV (82%). Alternatively, patients who received <4 shocks were very likely to achieve ROSC. However, the delivery of >4 shocks was a bad indicator of the patient outcome suggesting that CPR had to be pursued as ROSC was achieved in 50% of cases.

The number of defibrillation shocks is a simple parameter to obtain and might be an interesting tool in deciding not to pursue CPR upon four shocks and instead to anticipate the next step. However, this parameter should not be considered as a marker for the cessation of CPR, as ROSC can be observed beyond the fourth defibrillation shock.

In CA, the important prognostic factors are the no-flow and low-flow values (15). The low-flow duration was not included in the analyses as it is considered an equivalent of the outcome (ROSC). However, no-flow was considered a confounding factor and explains the results obtained here. Our results showed that the number of delivered defibrillation shocks could predict ROSC even after the adjustment on the no-flow.

Several limitations can be mentioned when interpreting the results presented herein. Despite similarities in the organisation of prehospital EMT and MICU and clear guidelines on the management of CA, differences in the clinical management of prehospital OHCA may have affected patient outcomes in this study. Moreover, this study was conducted in Paris where emergency services are efficient, which may limit the extrapolation of our results to other cities. Indeed, in Paris, an MICU or EMT needs an average of 9 min to reach a patient (26).

The therapeutic support was left to the physician's discretion and to bedside judgement. In addition, patients were followed up only for the first 30 min of CPR, beyond which CA is usually considered refractory in normothermic patients (15). Temperature was not monitored for all patients.

Moreover, the definitive aetiology of CA was not collected. Our study focused on the relationship between the number of delivered defibrillation shocks and ROSC, and we did not measure the impact on survival, as previously described (27), and on the neurological outcome.

Conclusion

These data describe an interesting association between the number of delivered defibrillation shocks and ROSC over the first 30 min of CPR in OHCA due to shockable rhythms. We found a threshold of four shocks to predict ROSC with high sensitivity. This threshold can be used for early implementa-

tion of ECLS or organ donation in such patients. However, further prospective multicentre randomised studies are needed to establish an international standardised definition of refractory CA.

Ethics Committee Approval: Authors declared that the research was conducted according to the principles of the World Medical Association Declaration of Helsinki "Ethical Principles for Medical Research Involving Human Subjects", (amended in October 2013).

Informed Consent: According to the French law, the local ethical committee considered that consent of patients was waived for participation in this observational study.

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Hasta Onamı: Fransız kanunlarına göre, yerel etik komite, hastaların rızalarının bu gözlemsel çalışmaya katılmaktan feragat edildiğini düşünüyor.

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