ELSEVIER

Resuscitation 54 (2002) 37–45

RESUSCITATION

www.elsevier.com/locate/resuscitation

Low chance of survival among patients requiring adrenaline (epinephrine) or intubation after out-of-hospital cardiac arrest in Sweden

Mikael Holmberg *, Stig Holmberg, Johan Herlitz

Department of Cardiology, Sahlgrenska University Hospital, SE-413 45 Göteborg, Sweden

Received 5 March 2001; received in revised form 9 April 2001; accepted 14 March 2002

Abstract

Aim: To relate the outcome of out-of-hospital cardiac arrest to whether medication with adrenaline (epinephrine) was given and whether patients were intubated. *Patients:* A national survey in Sweden between 1990–1995 among patients suffering out-of-hospital cardiac arrest and in whom resuscitation was attempted. Sixty per cent of ambulance organisations in Sweden participated. *Design:* Prospective evaluation. Survival was defined as survival 1 month after cardiac arrest. *Results:* In all, 14 065 patients were included in the evaluation. Of these, resuscitation was attempted in 10 966 cases. Among these adrenaline (epinephrine) was given in 42.4 and 47.5% were intubated. In an univariate analysis treatment with adrenaline (epinephrine) and intubation was associated with a lower survival when all patients were evaluated. In a multivariate analysis including age, sex, place of arrest, bystander-CPR, initial arrhythmia, arrest being witnessed and aetiology, treatment with adrenaline (epinephrine) (OR 0.43, CI 0.27–0.66) and intubation (OR 0.71, CI 0.51–0.99) were both independent predictors of a lower chance of survival. When separately analysing patients with bystander witnessed cardiac arrest found in ventricular fibrillation and requiring more than 3 defibrillatory shocks neither treatment with adrenaline (epinephrine) nor intubation was associated with survival. Among patients with a non-shockable rhythm treatment with adrenaline (epinephrine) was a significant independent predictor for lower survival (OR 0.30, CI 0.07–0.82). *Conclusion:* In a national survey in Sweden including 10 966 cases of out-of-hospital cardiac arrest the outcome was related to whether medication with adrenaline (epinephrine) was given and whether patients were intubated. Neither in total nor in any subgroup did we find results indicating beneficial effects of any of these two interventions. Whether treatment with adrenaline (epinephrine) or intubation will increase survival after out-of-hospital cardiac arrest needs to be confirmed in prospective randomised trials. © 2002 Published by Elsevier Science Ireland Ltd.

Keywords: Adrenaline; Ventricular fibrillation; Cardiac arrest

1. Introduction

Although, adrenaline (epinephrine) and tracheal intubation are recommended as treatment by the American Heart Association (AHA) and the European Resuscitation Council (ERC) at cardiac arrest (CA) there are no studies supporting their positive effect on survival in humans [1,2]. This lack of information has implications for planning and maintenance of EMS systems around the world.

Most of the patients with heart disease and cardiac arrest suffer from initial ventricular fibrillation (VF) as shown in prospective, non-randomised trials and observational studies that early defibrillation could save a large proportion of these patients and that early CPR further increases survival [3].

In the current algorithm from the ERC and AHA both adrenaline (epinephrine) and intubation are recommended in every prolonged resuscitative procedure both for patients in VF and for patients with non-VF. Patients in cardiac arrest who require prolonged, complex treatment have a very poor prognosis and have low survival rates associated with neurological deficits. It has been hard to find support for improved survival with adrenaline (epinephrine) and intubation in these

* Corresponding author. Tel.: +46-31-3421000; fax: +46-31-416640

E-mail address: mikael.holmberg@vgregion.se (M. Holmberg).

0300-9572/02/$ - see front matter © 2002 Published by Elsevier Science Ireland Ltd.
PII: S0300-9572(02)00048-5

patient groups in prospective, non-randomised trials as this would require large numbers of patients. Randomised-controlled trials have also been difficult to perform on ethical grounds.

The recommendations from ERC and AHA have organisational and economic implications as both intubation and medication requires a complicated and costly training and control system. If these interventions are without effect on survival, they should be removed from the recommendations of standard treatment of cardiac arrest. This should simplify training programmes and allow the ambulance staff to concentrate on the treatments known to increase survival.

In Sweden since 1990 there is an ongoing national registry of out-of-hospital cardiac arrests where patients from all over Sweden are included. The emergency medical systems have variable proficiency and means of resuscitation. These differences have led to a registry where it was possible to analyse the association between the use of adrenaline (epinephrine) and intubation and survival.

The aim of this study was to investigate (a) the proportion of patients with out-of-hospital cardiac arrest who were given adrenaline (epinephrine) and intubation (b) the association between the use of adrenaline (epinephrine) and intubation and survival.

2. Methods

2.1. Statistical methods

All analyses were performed using statistical analysis system. Pitman's non-parametric test was used. In evaluations of dichotomous variables Fisher's exact test, a special form of Pitman's test was used. A P-value of less than 0.05 was regarded as significant. Two-tailed tests were applied. For multivariate analysis, a stepwise logistic regression procedure was used.

2.2. Ambulance registry

This study was based on material collected within the Swedish ambulance cardiac arrest registry. The registry started in 1990 with a few ambulance systems. It has been joined by more systems subsequently and by 1995 the registry was based on reports from approximately 60% of the ambulance systems. These systems cover 5 million inhabitants out of the total 8.7 million in Sweden.

Most of the ambulance organisations included serve smaller communities with less than 100 000 inhabitants, and only recently have the larger cities, i.e. Stockholm, Göteborg and Malmö, joined the registry. Approximately 25% of all case reports included emanate from these cities.

All parts of Sweden are served by ambulance dispatch centres with similar protocols for interviewing and responding to those who call for ambulances. All interviews are always begun with a few simple questions to identify suspected cardiac arrest victims. In such cases an ambulance is immediately dispatched before the interview is continued.

2.3. Ambulance organisations

Sweden is sparsely populated, but approximately 80% of the population live in cities or community centres. Most of these, but not all, have their own ambulance station.

Approximately 100 ambulance organisations operate in Sweden. They all have a physician as a medical director. Sixty percent of the ambulances are based at hospitals and the other 40% are co-ordinated with, and based at, the fire brigade stations.

In some ambulance systems, the only treatment for cardiac arrest victims would be CPR and defibrillation, while in others a full ALS protocol can be applied including early intubation and drug treatment. In Sweden since 1987 there is an ALS protocol developed by the Scandinavian Resuscitation Council. This protocol was revised in 1992 according to ERC recommendations. In these protocols rapid defibrillation with three shocks preceding intubation and medication was advocated thus creating an unchanged ACLS algorithm during the study period.

2.4. CPR-training systems

In 1983 the Swedish Society of Cardiology created a national CPR-training programme based on AHAs guidelines. The programme was revised in 1987 and again in 1993, this time according to guidelines from the ERC. In 1987 a similar programme on ALS was launched based on AHA guidelines. The programme was revised 1992 according to ERC. A programme for AED-defibrillation was created in 1993.

2.5. Study design

For each case of out-of-hospital cardiac arrest the ambulance crew filled in a form with demographic information such as age, place of arrest, probable background of the arrest, by-stander occupation and standardised description of the resuscitation procedure including intervention times and interventions such as bystander-CPR (B-CPR), defibrillation, intubation, drug treatment and status at first contact. (Bystander was defined as someone who was not on healthcare duty performing CPR on duty.)

In ambulances with manual defibrillators the initial rhythm was defined as VF, pulseless electrical activity

Table 1
Bystander characteristics for all patients in relation to adrenaline (epinephrine) and intubation

		Adrenaline			Intubation		
	n	Yes	No	*P*	Yes	No	*P*
Age (mean, years)	10.500	67.1	67.5		67.1	67.6	
Place of arrest (home), %	10.837	62.9	61.6		62.5	61.8	
Gender (male), %	10.437	73.5	71.3	0.015	72.5	71.8	
VF (at first ECG), %	10.966	51.0	60.9	< 0.0001	53.5	59.6	< 0.0001
Witnessed, %	9.878	70.0	64.4	< 0.0001	68.8	65.0	< 0.0001
B-CPR, %	9.371	34.6	30.5	< 0.0001	33.7	30.9	0.004
CA-call (mean, min)	7.542	8.5	11.4	< 0.0001	8.2	12.0	< 0.0001
CA-arrival (mean, min)	7.371	16.0	19.3	< 0.0001	15.5	20.1	< 0.0001
Call-first ECG (mean, min)	9.580	11.7	11.8		11.7	11.8	

The different *n* values represent different levels of missing data.

(PEA) or asystole. For AEDs the rhythm was defined as VT/VF (i.e. shockable rhythm) and other. The initial rhythm was based on information both from the first ECG recording after arrival of the ambulance crew and whether the patient was defibrillated or not.

The time of arrest was estimated by interviewing the bystander. Thereafter the ambulance crew recorded the time of arrival at the patient's side, the time of start of B-CPR, the time of first defibrillation, the time of palpable pulsations, the time of start of transport to hospital and arrival at hospital. The number of DC shocks was recorded.

Immediate outcome was reported as dead on arrival, dead in emergency room or admitted to hospital alive.

The form was completed during and immediately after the acute event. The medical director reviewed each form and a copy was sent to a central registry. After one month another copy was sent with the additional information of outcome after 1 month, dead or alive.

3. Results

Between January 1990 and May 1995 14 065 reports on cardiac arrest were collected. Resuscitation was attempted in 10 966 cases. In the remaining 3099 cases no resuscitation was attempted and the patient was transported to hospital only to be declared dead.

In 60.2% of the patients the cardiac arrest was witnessed by bystanders and in 9.9% by ambulance crew. In 29.9% cases the arrest was unwitnessed. In 43.3% of the patients the presenting ECG showed a shockable rhythm and in 56.7% a non-shockable rhythm.

Survival to 1 month was 9.6% for patients with bystander witnessed arrest and VF, 31.9% for crew witnessed arrest and VF, 4.0% for unwitnessed arrests with VF and 0.9% for patients with non-shockable rhythms.

3.1. Adrenaline (epinephrine)

Adrenaline (epinephrine) was given in 4566 (42.4%) of the cases and 156 (3.4%) patients survived to 1 month compared to 388 (6.3%) of the 6207 patients who were not given adrenaline (epinephrine) ($P < 0.0001$). Characteristics in terms of age, place of arrest, gender and various factors at resuscitation are described in Table 1. Significant differences were found when comparing those who received adrenaline (epinephrine) with those who did not. Thus, patients who received adrenaline (epinephrine) included more males, less frequently showed VF at first recording, more frequently had a witnessed arrest, more frequently received B-CPR, had a shorter interval between CA and call for ambulance and a shorter interval between CA and arrival of ambulance. Among patients having a bystander witnessed CA being found in VF and requiring more than 3 defibrillations no significant difference was found between patients given adrenaline (epinephrine) and not (Table 2).

In Table 3 is shown mortality among patients who were and were not treated with adrenaline (epinephrine) in relation to initial arrhythmia, witnessed status and number of defibrillations. The survival rate was significantly lower for those given adrenaline (epinephrine) in the subgroup being found with VF and given 1–3 defibrillatory shocks. This was true both for the crew witnessed cardiac arrests, the bystander witnessed cardiac arrest and the non-witnessed cardiac arrests.

In the subgroups being found with VF and given 4 defibrillations or more the survival rate for those given adrenaline (epinephrine) was 5.9% and for those with no adrenaline (epinephrine) 8.9%, but the difference was not statistically significant.

In the subgroup of patients with non-VF the survival rate was significantly lower in the adrenaline (epinephrine) group only for the crew witnessed cardiac arrests. Among the bystander witnessed and non-witnessed cardiac arrests there was no significant difference in

Table 2
Bystander characteristics for the patients with shockable rhythm receiving 4 or more defibrillations in relation to adrenaline (epinephrine) and intubation

		Adrenaline			Intubation		
	n	Yes	No	*P*	Yes	No	*P*
Age (mean, years)	1.001	67.5	68.5		67.8	68.0	
Place of arrest (home), %	1.002	57.0	59.7		57.3	60.2	
Gender (male), %	986	79.9	81.1		78.9	83.0	
B-CPR, %	1.008	44.3	38.0		42.7	41.1	
CA-call (mean, min)	909	4.2	3.7		4.7	4.2	
CA-arrival (mean, min)	894	11.6	10.3		11.6	10.2	
Call-first ECG (mean, min)	1.004	10.5	9.1		10.6	9.0	

The different *n* values represent different levels of missing data.

survival rate between adrenaline (epinephrine) and non-adrenaline (epinephrine) groups.

3.2. Intubation

Trachheal intubation was attempted in 5118 (47.5%) cases in who 183 (3.6%) patients survived to 1 month compared to 361 (6.4%) of 5655 patients who were not intubated ($P < 0.0001$). Those patients who were intubated differed from those who were not by being less likely to have presented in VF, more likely to have a witnessed arrest, more likely to receive B-CPR, more likely to have a shorter interval between CA and call for ambulance and more likely to have a shorter interval between CA and arrival of the ambulance (Table 1). Among patients having a bystander witnessed CA being found in VF and requiring more than 3 defibrillations no significant difference was found between patients who were intubated and those who were not (Table 2).

Table 4 shows the mortality among patients who were and were not intubated in relation to initial arrhythmia, witnessed status and number of defibrillatory shocks.

In the subgroup of patients with a bystander witnessed cardiac arrest being found in VF and who required more than 3 defibrillatory shocks there was a significantly worse outcome for patients who were intubated compared to those who were not.

The survival rate was significantly lower for crew witnessed and bystander witnessed cardiac arrests in the subgroup being found in VF and given 1–3 defibrillatory shocks and who were intubated compared to those who were not.

In the subgroups found in VF and given 4 defibrillations or more the survival rate for those who were intubated was 6.4% and for those who were not it was 8.0%. Survival was significantly less for the crew witnessed patients who were intubated than those who were not.

Table 3
Number and proportion of patients surviving to 1 month in relation to adrenaline (epinephrine), presenting rhythm, number of shocks and witnessed status

	Adrenaline				
	Yes		No		*P*
Ventricular Fibrillation					
⩽3 Shocks delivered					
Crew witnessed	11/69[a]	16.2%	75/186[a]	43.4%	< 0.0001
Bystander witnessed	49/713[a]	6.9%	156/930[a]	17.0%	< 0.0001
Not witnessed	4/220[a]	1.8%	19/302[a]	6.3%	0.020
Ventricular fibrillation					
⩾4 Shocks delivered					
Crew witnessed	6/48[a]	12.8%	10/33[a]	32.3%	
Bystander witnessed	41/681[a]	6.1%	27/347[a]	7.9%	
Not witnessed	6/175[a]	3.5%	7/112[a]	6.3%	
No ventricular fibrillation					
Crew witnessed	3/289[a]	1.2%	22/463[a]	5.3%	0.006
Bystander witnessed	19/1048[a]	1.8%	32/1493[a]	2.2%	
Not witnessed	5/824[a]	0.6%	9/1451[a]	0.6%	

[a] Number of survivors/number of patients.

Table 4
Number and proportion of patients surviving to 1 month in relation to intubation, presenting rhythm, number of shocks and witnessed status

	Intubation				
	Yes		No		*P*
Ventricular fibrillation ⩽3 Shocks delivered					
Crew witnessed	7/54[a]	13%	79/201[a]	42.3%	<0.0001
Bystander witnessed	61/788[a]	7.8%	144/855[a]	17.0%	<0.0001
Not witnessed	9/262[a]	3.5%	14/260[a]	5.4%	
Ventricular fibrillation ⩾4 Shocks delivered					
Crew witnessed	3/42[a]	7.3%	13/39[a]	35.1%	0.005
Bystander witnessed	45/682[a]	6.6%	23/346[a]	6.8%	
Not witnessed	9/170[a]	5.3%	4/117[a]	3.5%	
No ventricular fibrillation					
Crew witnessed	2/314[a]	0.7%	23/438[a]	5.9%	0.0001
Bystander witnessed	27/1237[a]	2.2%	24/1304[a]	1.9%	
Not witnessed	7/972[a]	0.7%	7/1303[a]	0.5%	

[a] Number of survivors/number of patients.

For the subgroup of patients with non-VF the survival rate was significantly lower in the intubated group only for the crew witnessed cardiac arrests. Among the bystander witnessed and non-witnessed cardiac arrests there was no significant difference in survival rate between those intubated and not.

3.3. Logistic regression analysis

A logistic regression analysis was performed to identify variables with independent effect on survival to 1 month. The variables included were age (over vs. under median age), gender (male vs. female), place of arrest (not at home vs. at home), witnessed CA (yes vs. no), shockable presenting rhythm (yes vs. no), heart disease (yes vs. no), B-CPR (yes vs. no), intubation (yes vs. no), adrenaline (epinephrine) (yes vs. no) and interval between call and first ECG (over vs. under median time).

When all patients were included treatment with adrenaline (epinephrine) and intubation were both independently associated with a lower chance of survival if time intervals were not included in the analysis (Table 5). If time intervals were included, the sample size became somewhat smaller and then treatment with adrenaline (epinephrine) but not intubation remained as an independent predictor of a lower chance of survival (Table 6). Among patients found in VF requiring more than 3 defibrillations neither adrenaline (epinephrine), nor intubation, was associated with survival (Table 7). Among patients found in a non-shockable rhythm treatment with adrenaline (epinephrine) was associated with a lower survival (Table 8).

4. Discussion

Adrenaline (epinephrine) and intubation have been included in the AHA algorithm of resuscitation since 1974 and when AHA reintroduced the concept of 'chain of survival' in 1991 there was consensus on the positive effect of the three first links of the chain namely early

Table 5
Independent factors for survival to 1 month in a logistic regression analysis for all patients with time intervals not included ($n = 6607$)

	OR	95% CI
Adrenaline (yes/no)	0.43	0.27–0.66
Intubation (yes/no)	0.71	0.51–0.99
Place of CA (not at home/home)	2.71	2.12–3.50
Witnessed (yes/no)	0.46	0.33–0.63
Gender (male/female)	1.51	1.15–1.96
VT/VF (yes/no)	4.80	3.55–6.59
B-CPR (yes/no)	2.06	1.60–2.66
Age (>71/<71)	0.98	0.98–0.99

Values beneath 1.0 indicates negative effect.

Table 6
Independent factors for survival to 1 month in a logistic regression analysis for all patients with time intervals included ($n = 6408$)

	OR	95% CI
Adrenaline (yes/no)	0.50	0.31–0.79
Time: call-first ECG (yes/no)	0.86	0.83–0.87
Place of CA (not at home/home)	2.16	1.67–2.82
Witnessed (yes/no)	0.47	0.33–0.65
Gender (male/female)	1.46	1.10–1.92
VT/VF (yes/no)	5.00	3.64–6.97
B-CPR (yes/no)	2.45	1.88–3.19
Age (>71/<71)	0.98	1.60–2.66

Values beneath 1.0 indicates negative effect.

Table 7
Independent factors for survival to 1 month in a logistic regression analysis for patients with shockable rhythm given four shocks or more

	OR	95% CI
Heart disease (yes/no)	0.32	0.09–0.88
Place of CA (not at home/home)	3.53	2.03–6.32
Age (> 71/ < 71)	0.95	0.93–0.97

With time intervals not included ($n = 922$). Values beneath 1.0 indicates negative effect.

Table 8
Independent factors for survival to 1 month in a logistic regression analysis for patients with non-shockable rhythm

	OR	95% CI
Adrenaline (yes/no)	0.30	0.07–0.82
Place (not at home/home)	3.25	2.12–5.03
Age (> 71/ < 71)	0.99	0.98–0.996

With time intervals not included ($n = 4971$). Values beneath 1.0 indicates negative effect.

access, early CPR and early defibrillation, where positive effects on survival has been demonstrated in numerous non-randomised prospective and observational studies. The fourth link (early ACLS, i.e. drugs and intubation) in the chain was much debated and has only been shown theoretically to be beneficiary [4]. Research in this field has been hard to carry out both on practical and ethical grounds and so far no positive randomised-controlled trial with survival as endpoint has been presented [5].

The use of adrenaline (epinephrine) in resuscitation is based on experimental studies on healthy animals with intravascular pressure and regional blood flows as endpoints [6,7]. No prospective study in adult humans have demonstrated survival advantages and there is only one study (with serious limitations) which has compared adrenaline (epinephrine) to no adrenaline (epinephrine) [8]. This study showed no significant difference in hospital discharge rate. Also when standard doses of adrenaline (epinephrine) were compared to very high doses of adrenaline (epinephrine) there were no significant increases in survival [9–13]. Lately it has even been suggested that high doses of adrenaline (epinephrine) produced impaired neurological outcome [14].

Neither has any randomised-controlled study been performed to demonstrate increased survival for patients treated with tracheal intubation as opposed to other airway treatment. Only one prospective study with a small number of patients, has a positive survival to discharge when comparing tracheal intubation to oropharyngeal airway and oesophageal obturator airway [15]. In several other observational studies there was a negative correlation between its use and survival [16,17].

Among patients with out-of-hospital cardiac arrest some patients will only need a few defibrillatory shocks, while the majority also will receive more complex treatment with drugs and intubation.

Efforts to establish the effect of drugs or intubation on survival by a simple comparison of survival rates for patients with and without such treatment, might give misleading results. Most survivors are found among patients with VF that respond to the first 1–2 shocks and hence need no drugs or intubation and therefore such comparisons will be biased and show a higher survival rate for patients not given drugs or being intubated.

The Swedish Cardiac Arrest Registry offers a specific opportunity to assess the association between the use of adrenaline (epinephrine) and intubation and survival. Among the participating ambulance organisations only some ambulance crews are trained in ALS i.e. are authorised to give drugs and to intubate. Thus, there is one patient group that according to guidelines should have been treated with adrenaline (epinephrine) and intubation, but where the ambulance crew had no training and delegation to give that treatment, and another group where the correct treatment was given. If the patient groups with and without such treatment were identical in all other respects the survival rates for the two groups should give an indication of the effect of adrenaline (epinephrine) and intubation on survival.

For such analysis our patients were divided into 3 groups. Those being found in VF and given 1–3 defibrillations, those being found in VF and given more than 3 defibrillations and those not being found in VF.

The most interesting group was the one with patients being found in VF and given 4 defibrillations or more. According to guidelines all these patients should have been given adrenaline (epinephrine) after the third defibrillatory shock. However, it was given only to 65% of the patients in this group suggesting that in 35% of the patients the ambulance crew was not allowed to give drugs. No significant difference was found between the two patients groups for any variables prior to treatment in the comparison. It could thus be assumed that differences in survival rate would reflect the effect of adrenaline (epinephrine) on survival. This comparison could then, with all its limitations, be regarded as a surrogate for a randomised trial.

The survival rate for patients given adrenaline (epinephrine) was 5.9% (53/905) vs. 8.9% (44/492) for those not given adrenaline (epinephrine). The survival rates were not significantly different and do not support any benefit for adrenaline (epinephrine).

A corresponding analysis for intubation demonstrated that 64% were intubated. Of those where the guidelines required intubation the survival rates were 6.4% for those intubated and 8.0% for those not

intubated, suggesting no survival benefit of early intubation.

The data from the next patient group, those being found in VF given 1–3 defibrillations are more difficult to interpret. Only 45% of all such patients were given adrenaline (epinephrine). According to guidelines no adrenaline (epinephrine) should be given between the three first defibrillatory shocks. However, the majority of the patients in our study died outside hospital and thus had their rhythm transformed into asystole or PEA by the defibrillatory shocks. According to guidelines they should then be given adrenaline (epinephrine) alternating with CPR until the resuscitation procedure was stopped.

Most of the patients with VF that survived belong to this group and therefore needed no adrenaline (epinephrine).

Yet another and larger group of patients had a temporary return of spontaneous circulation (ROSC) after one or more these shocks and hence needed no adrenaline (epinephrine).

The patient group not given adrenaline (epinephrine) thus do not only include patients where the ambulance crew was not allow to give adrenaline (epinephrine), but also most of the patients with ROSC and among them most of the survivors.

For the patient group given 1–3 defibrillations a comparison of survival rates between those with and without adrenaline (epinephrine) will therefore give grossly misleading results.

When patients are further divided into cardiac arrests that are crew witnessed, bystander witnessed and not witnessed it could be demonstrated that for each of these groups there was a significantly higher survival for patients not receiving adrenaline (epinephrine). As already pointed out, this could not be taken as an indication of negative effect of adrenaline (epinephrine), but rather a consequence of a selection bias of surviving patients.

An analysis of relation between survival and intubation for this patient group shows similar results. 46% of the patients are intubated and there are highly significant differences in survival with 7.0% survival for the intubated and 18.0% for non-intubated patients.

The third patient group presenting with a non-shockable rhythm on the first ECG is of special interest as it has been argued that the reason for their survival there must be some ALS procedures, most likely administration of adrenaline (epinephrine) and intubation [18]. In several studies including our own, this patient group compromises approximately 20% of all patients surviving to 1 month. The over all survival rate for this group is very low, 1.6% and only 39% of the patients were given adrenaline (epinephrine). It could only be speculated on why such a low percentage was given adrenaline (epinephrine). One probable reason was that many of these patients were considered to be beyond revival and that only half-hearted resuscitation was started. There was no significant difference in survival rate with 1.2% survival among those given adrenaline (epinephrine) and 1.8% among those without adrenaline (epinephrine).

In one small subgroup, those that were crew witnessed, there was a significantly negative correlation between adrenaline (epinephrine) and survival.

The data on intubation for this group were similar, 45% were intubated and there was no significant differences in survival rate for those intubated and not.

In a multiple logistic regression analysis including all patients both adrenaline (epinephrine) and intubation were independently and negatively associated with survival. Whether these results are caused by a negative influence of these treatments on survival or whether there are other confounding factors not being recorded that explain these data can only be speculated upon. It is, however tempting to assume that patients who received either adrenaline (epinephrine) or intubation or both were the sickest, and that all factors reflecting this were not included in the multivariate model.

In that respect this type of analysis appear more meaningful among patients being found in VF and requiring more than 3 defibrillations and among patients being found in a non-shockable rhythm, because here we defined subgroups with a known more adverse prognosis. However, neither these analyses indicated any favourable effect on survival of adrenaline (epinephrine) and intubation.

5. Limitations of the study

Our study has severe limitations and the data must be interpreted with caution. In contrast to a randomised trial we cannot assume that the patient groups with and without treatment with adrenaline (epinephrine) and intubation are comparable. In fact, it is demonstrated that for the total patient group there are significant differences in a number of variables between those with and without treatment with adrenaline (epinephrine) and intubation.

Even for the most well defined group in our study, those being found in VF given 4 or more defibrillations we can only speculate that patient groups are comparable. Even if we found no differences between the groups there could, however, be differences for variables not analysed that could influence survival and confound our results.

We have no information on the proficiency of ambulance crews to intubate.

Furthermore, we have no information on the compliance of ambulance crews to the guidelines. The record form does not allow any control of whether the patient

was given adrenaline (epinephrine) on the correct indication.

6. Conclusion

In our prospective observational study we have not found any data indicating a positive effect of adrenaline (epinephrine) or intubation on survival. Randomised-controlled studies are needed.

Appendix A

Participating ambulance district physicians; Å Andren-Sandberg MD, L-Å Augustsson MD, S Berglind MD, J Bennis MD, U Björnstig MD, K Brunnhage MD, J Castenhag MD, B Eriksson MD, A Elvin MD, B Engerström MD, L Engerström MD, M Erlandsson MD, L Fernandez MD, J Fischer MD, B Gustavsson MD, S Hagman MD, M Helfner MD, H Huldt MD, M Johansson MD, R Johansson MD, M Kjeldgaard MD, M Larsson MD, Ö Lennander MD, S Leward MD, T Lindgren MD, T Lorentz MD, G Morin MD, J Olsson MD, PO Persson MD, T Samuelsson MD, M Schwartz MD, B Sjölund MD, A Skjöldebrand MD, E Skole MD, G Skoog MD.

References

[1] Guidelines for cardiopulmonary resuscitation and emergency cardiac care. Emergency Cardiac Care Committee and Subcommittees, American Heart Association. Part III. Adult advanced cardiac life support. JAMA 1992;268:2199–241.
[2] The 1998 European Resuscitation Council guidelines for adult advanced life support. Advanced Life Support Working Group of the European Resuscitation Council. BMJ 1998;316:1863–9.
[3] Cummins R.O., et al. Improving survival from sudden cardiac arrest: the 'chain of survival' concept. Circulation 1991;83:832–1847.
[4] Larsen M., Eisenberg M., Cummins R., Hallstrom A.. Predicting survival from out-of-hospital cardiac arrest: a graphic model. Ann Emerg Med 1993;22:1652–8.
[5] Callaham M.. Quantifying the scanty science of prehospital emergency care. Ann Emerg Med 1997;30:785–90.
[6] Pearson J., Redding J.. The role of epinephrine in cardiac resuscitstion. Anesth Analg 1963;42:599–606.
[7] Redding J., Pearson J.. Resuscitation from ventricular fibrillation. Drug therapy. JAMA 1968;203:255–60.
[8] Woodhouse S., Cox S., Boyd P., Case C., Weber M.. High dose and standard dose adrenaline do not alter survival, compared with placebo, in cardiac arrest. Resuscitation 1995;30:243–9.
[9] Callaham M., Madsen C., Barton C., Saunders C., Pointer J.. A randomized clinical trial of high-dose epinephrine and norepinephrine vs standard-dose epinephrine in prehospital cardiac arrest. JAMA 1992;268:2667–72.
[10] Brown C., Martin D., Pepe P., et al. A comparison of standard-dose and high-dose epinephrine in cardiac arrest outside the hospital. The Multicenter High-Dose Epinephrine Study Group. N Engl J Med 1992;327:1051–5.
[11] Stiell I., Hebert P., Weitzman B., et al. High-dose epinephrine in adult cardiac arrest. N Engl J Med 1992;327(15).
[12] Herlitz J., Ekstrom L., Wennerblom B., Axelsson A., Bang A., Holmberg S.. Adrenaline in out-of-hospital ventricular fibrillation. Does it make any difference? Resuscitation 1995;29:195–201.
[13] Gueugniaud P., Mols P., Goldstein P., et al. A comparison of repeated high doses and repeated standard doses of epinephrine for cardiac arrest outside the hospital. European Epinephrine Study Group. N Engl J Med 1998;339:1595–601.
[14] Behringer W., Kittler H., Sterz F., et al. Cumulative epinephrine dose during cardiopulmonary resusciation and neurologic outcome. Ann Int Med 1998;129:450–6.
[15] Hillis M., Sinclair D., Butler G., Cain E.. Prehospital cardiac arrest survival and neurologic recovery. J Emerg Med 1993;11:245–52.
[16] Adams J., Sirel J., Marsden K., Cobbe S.. Heartstart Scotland: the use of paramedic skills in out of hospital resuscitation. Heart 1997;78:399–402.
[17] Guly U., Mitchell R., Cook R., Steedman D., Robertson C.. Paramedics and technicians are equally successful at managing cardiac arrest outside hospital. BMJ 1995;310:1091–4.
[18] Pepe P.E., Levine R.L., Fromm R.E.J., Curka P.A., Clark P.S., Zachariah B.S.. Cardiac arrest presenting with rhythms other than ventricular fibrillation: contribution of resuscitative efforts toward total survivorship. Crit Care Med 1993;21:1813–4.

Portuguese Abstract and Keywords

Objectivo: Relatar o resultado da paragem cardíaca extra-hospitalar quando foi administrada adrenalina (epinefrina) e os doentes foram intubação. *Doentes:* Uma pesquisa nacional na Suécia entre 1990-1995 em doentes que sofreram paragem cardíaca extra-hospitalar e em quem foi tentada a reanimação. Participaram sessenta por cento das organizações de ambulâncias da Suécia. *Método:* Avaliação prospectiva. Sobrevida foi definido como sobrevivência 1 mês após a paragem cardíaca. *Resultados:* No total, foram incluídos no estudo 14065 doentes. Destes, a reanimação foi tentada em 10966. Adrenalina (epinefrina) foi administrada em 42.4% e 47.5% foram intubados. Numa análise univariada o tratamento com adrenalina (epinefrina) e intubação estava associado com menor sobrevida quando todos os doentes eram avaliados. Numa análise multivariada, incluindo idade, sexo, local da paragem, reanimação por transeunte, arritmia inicial, paragem testemunhada e etiologia, o tratamento com adrenalina (epinefrina) (OR 0.43, CI 0.27–0.66) e a intubação (OR 0.71, CI 0.51–0.99) eram ambos factores predictivos independentes de menor probabilidade de sobrevida. Quando se analisava separadamente doentes com paragem cardíaca testemunhada em fibrilhação ventricular e que necessitaram de mais de três choques, nem o tratamento com adrenalina (epinefrina) nem a intubação estavam associadas com sobrevida. Entre os doentes com ritmo não desfibrilável, o tratamento com adrenalina (epinefrina) era um factor predictivo significativo para menor sobrevida (OR 0.30, CI 0.07–0.82). *Conclusão:* Num estudo nacional na Suécia que incluiu

10966 casos de paragem cardíaca extra-hospitalar, o prognóstico estava relacionado a administração de adrenalina (epinefrina) e com a intubação dos doentes. Não encontramos resultados indicadores de um efeito benéfico de nenhuma destas atitudes no grupo do total dos doentes ou em qualquer subgrupo considerado. Se o tratamento com adrenalina (epinefrina) ou intubação irá aumentar a sobrevida após paragem cardíaca extra-hospitalar precisa de ser confirmado em estudos prospectivos randomizados.

Palavras chave: Adrenalina; Fibrilação ventricular; Paragem cardíaca

Spanish Abstract and Keywords

Objetivo: Relacionar el resultado del paro cardíaco prehospitalario con el uso del medicamento adrenalina (epinefrina) y con la intubación de los pacientes. *Pacientes*: Encuesta nacional en suecia entre 1990–1995 entre los pacientes que sufrieron un paro cardíaco extrahospitalario en quienes se intentó resucitación. Participaron 60% de las organizaciones de ambulancias de Suecia. *Diseño*: Evaluación prospectiva. Se definió sobrevida como sobrevida un mes después del paro cardíaco. *Resultados*: Se incluyeron en total 14065 pacientes en la evaluación. De estos , se intentó la tesucitación en 10966 casos. Entre estos se usó adrenalina en el 42.4 % y fueron intubados en la tráquea un 47.5%. En un análisis unidireccional del tratamiento con adrenalina (epinefrina) e intubación estos tratamientos se asociaron con menor sobrevida cuando se evaluaban todos los pacientes. En un analisis multivariable que incluye edad, sexo, lugar del paro cardíaco, presencia de reanimación por testigos, arritmias iniciales, paro presenciado y etiología, tratamiento con adrenalina(epinefrina) (OR 0.43, CI 0.27–0.66) y con intubación (OR 0.71, CI 0.51–0.99) siendo ambos predictores independientes de una baja peobabilidades de sobrevida. Cuando se analiza separadamente los pacientes con paro presenciado encontrados en fibrilación ventricular que requirieron mas de tres descargas desfibriladoras no se asoció ni la sobrevida con tratamiento con adrenalina(epinefrina) ni con intubación traqueal. Entre los pacientes con ritmo inicial no desfibrilable el tratamiento con adrenalina (epinefrina) fue un factor de prediccion para baja sobrevida (OR 0.30, CI 0.07–8.82). *Conclusión*: En una encuesta nacional en suecia,que incluía 10966 casos de paro cardíaco prehospitalario se relacionó con el curso. No encontramos resultados que mostraran beneficios de cualquiera de estas 2 intervenciones. Si acaso el tratamiento con adrenalina (epinefrina) o la intubación traquel mejoran la sobrevida después de un paro cardíaco pre hospitalario deberá ser confirmado con estudio prospectivo randomizado.

Palabras clave: Adrenalina; Fibrilación ventricular; Paro cardíaco