

Original Article

The Effect of Ambulance Response Time on Survival Following Out-of-Hospital Cardiac Arrest

An Analysis from the German Resuscitation Registry

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Summary

Background: Out of hospital cardiac arrest (OHCA) is one of the more common causes of death in Germany. Ambulance response time is an important planning parameter for emergency medical services (EMS) systems. We studied the effect of ambulance response time on survival after resuscitation from OHCA.

Methods: We analyzed data from the German Resuscitation Registry for the years 2010–2016. First, we used a multivariate logistic regression analysis to determine the effect of ambulance response time (defined as the interval from the alarm to the arrival of the first rescue vehicle) on the hospital-discharge rate (in percent), depending on various factors, including resuscitation by bystanders. Second, we compared faster and slower EMS systems (defined as those arriving on the scene within 8 minutes in more than 75% of cases or in $\leq 75\%$ of cases) with respect to the frequency of resuscitation and the number of surviving patients.

Results: Our analysis of data from a total of 10 853 patients in the logistical regression model revealed that the rate of hospital discharge was significantly affected by the ambulance response time, bystander resuscitation, past medical history, age, witnessed vs. unwitnessed collapse, the initial heart rhythm, and the site of the collapse. The success of resuscitation was inversely related to the ambulance response time; thus, among patients who did not receive bystander resuscitation, the discharge rate declined from 12.9% at a mean response time of 1 minute and 10 seconds to 6.4% at a mean response time of 9 minutes and 47 seconds. Twelve faster EMS systems and 13 slower ones were identified, with a total of 9669 and 7865 resuscitated patients, respectively. The faster EMS systems initiated resuscitation more frequently and also had a higher discharge rate with good neurological outcome in proportion to the population of the catchment area (7.7 versus 5.6 persons per 100 000 population per year, odds ratio [OR] 0.72, 95% confidence interval [0.66; 0.79], $p < 0.001$).

Conclusion: Rapid ambulance response is associated with a higher rate of survival from OHCA with good neurological outcome. The response time, independently of whether bystander resuscitation measures are provided, has a significant independent effect on the survival rate. In drawing conclusions from these findings, one should bear in mind that this was a retrospective registry study, with the corresponding limitations.

Cite this as

Bürger A, Wnent J, Bohn A, Jantzen T, Brenner S, Lefering R, Seewald S, Gräsner JT, Fischer M: The effect of ambulance response time on survival following out-of-hospital cardiac arrest—an analysis from the German resuscitation registry. *Dtsch Arztebl Int* 2018; 115: 541–8.
DOI: 10.3238/arztebl.2018.0541

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With a mean annual incidence of 84 events per 100 000 population (range, 28–244), out-of-hospital cardiac arrest (OHCA) is one of the commonest causes of death in Germany and Europe (1). Approximately 50% of patients with sudden cardiac arrest die without any attempt being made at resuscitation, since either the event is not observed by bystanders or the emergency medical services (EMS) reach the scene of the emergency too late. The annual incidence of resuscitation is on average 49 per 100 000 population (range, 19–104) (1–6). EMS response time is an important planning factor for emergency medical services. A well-functioning chain of survival—starting with resuscitation by bystanders or the emergency control center dispatcher who takes the emergency call, up to the hospital team that provides the patient with intensive care treatment—is a prerequisite for good long-term results. In order to improve the treatment of patients with OHCA

BOX

Data and facts on the German resuscitation registry

The German resuscitation registry (*Deutsches Reanimationsregister*) was founded in 2002 by the German Society for Anesthesiology and Intensive Care (*Deutsche Gesellschaft für Anästhesiologie und Intensivmedizin*). It was officially launched at the 2007 German Anesthesia Congress in Hamburg. The registry is intended as a quality management tool designed to provide physicians and emergency medical services with the information needed to improve survival rates following cardiovascular arrest. Online evaluation is available to participants at all times for quality management purposes. They receive a monthly condensed report and an annual detailed quality report for their emergency medical and rescue services. Participants are offered coaching by resuscitation registry experts at annual meetings.

Data collection by the German Resuscitation Registry is voluntary and, naturally, takes place anonymously. Classification and evaluation in relation to individual patients is not possible.

At present, 134 of 241 emergency medical services and 145 hospitals in Germany participate in the registry. As of 1 May 2018, 162 276 records had been documented, of which 105 400 are resuscitation procedures and 13 204 are in-hospital emergency procedures without resuscitation, as well as 48 672 determinations of death by the emergency physician. A total of 134 emergency physicians and emergency medical services have documented 83 285 resuscitation procedures; they cover 30 560 680 inhabitants. In all, 41 centers meet the reference criteria and are able to provide not only emergency medical services data but also hospital data; these centers serve 11 743 850 inhabitants.

and integrate current research results, the European Resuscitation Council regularly publishes new guidelines on cardiopulmonary resuscitation (CPR) (7–11). Despite the implementation of these guidelines and EMS systems having comparable training and equipment, the results of out-of-hospital CPR are subject to considerable variation between the different EMS systems in Germany (12–14). The German Society for Anesthesiology and Intensive Care Medicine (*Deutsche Gesellschaft für Anästhesiologie und Intensivmedizin*) set up the German Resuscitation Registry (*Deutsches Reanimationsregister*) in 2007 as a comprehensive quality management instrument designed to measure and continuously improve treatment success. A number of studies suggest that the interval without CPR affects the outcome of resuscitation (18–22). To date, it has been demonstrated that the ambulance response time affects CPR incidence as well as short-term and long-term survival (14, 18). The aim of this study was to investigate the effect of ambulance response time on survival rates, particularly on neurological recovery following out-of-hospital cardiac arrest, in Germany

Methods

This cohort study was based on anonymized patient data from the German Resuscitation Registry for the period 1 January 2010 to 31 December 2016. All pre-hospital patients that had experienced out-of-hospital cardiac arrest were included, irrespective of whether CPR was initiated by trained emergency medical services personnel or by bystanders and, in particular, irrespective of the success of CPR. Data collection by the German Resuscitation Registry is voluntary and takes place anonymously. Data is entered by emergency physicians or emergency service personnel, and it is usually released by the medical directors of the emergency medical service or by persons assigned by them. EMS systems that had carried out resuscitation

treatment fewer than 100 times during the observation period and had less than 12 reporting months, as well as centers with incomplete documentation on follow-up treatment (response rate after hospital admission <80%), were excluded from the study, as were helicopter centers, since emergency medical service laws make no provision for these in terms of evaluating response time intervals. In addition, patients in whom the emergency medical services witnessed the collapse, a non-cardiac cause was responsible, or for whom the information on bystander CPR or on the “time to arrival of first vehicle” was lacking were excluded during the first part of the study.

The outcome measure was the success of resuscitation treatment administered by the emergency medical services. To this end, the following were each calculated as a percentage of resuscitated patients

- Return of spontaneous circulation (ROSC rate)
- Hospital admission rate
- Hospital discharge rate
- Discharge rate with good neurological outcome (CPC [cerebral performance categories] I or 2)

The second part of the study determined not only the effect of ambulance response time on survival rates as percentages, but also the annual number of resuscitated and surviving patients per 100 000 population, in two groups of faster and slower EMS systems (see the *eMethods* section for a detailed description).

The variable ambulance response time was measured as the time between “raising the alarm and arrival of the first vehicle at the scene.”

The first part of the study evaluated the effect of ambulance response time and bystander CPR on the dependent variable “discharge from hospital” by means of a multivariate logistic regression analysis. The following additional variables—based on the

TABLE

The effect of ambulance response time and bystander CPR on the percentage survival rate following out-of-hospital resuscitation

a) Bystander CPR						
Alarm raised to arrival of 1 st vehicle (min)	0–1–2	3–4–5	6–7–8	9–10–11	> 12	p-Value
Number of resuscitation patients (n)	445	1 496	1 412	656	351	
Alarm raised to arrival of 1 st vehicle (min:sec)	01:04 ± 00:53	04:11 ± 00:46	06:53 ± 00:48	09:47 ± 00:47	14:03 ± 02:21	
Alarm raised to 1 st defibrillation in VF (min:sec)	06:17 ± 10:35	08:11 ± 05:35	09:56 ± 04:40	12:41 ± 04:03	14:44 ± 05:37	
Alarm raised to 1 st vasopressor in non-VF (min:sec)	10:02 ± 04:52	11:17 ± 05:33	13:13 ± 05:38	15:48 ± 05:00	18:25 ± 07:27	
ROSC ever (%) [95% confidence interval]	56.0% * [51.2; 60.6]	53.3% * [50.7; 55.8]	46.4% * [43.8; 49.0]	46.3% * [42.5; 50.2]	43.3% * [38.1; 48.7]	<0.001
ROSC at hospital admission (%)	47.6% *	46.1% *	39.2% *	38.9% *	35.0% *	<0.001
Discharged alive (%)	22.0% *	20.3% *	15.7% *	14.0% *	13.1% *	<0.001
CPC 1 or 2 at discharge (%)	18.4% *	16.6% *	12.8% *	10.4% *	10.3% *	<0.001
ROSC expected according to RACA score	56.6% *	51.7% *	47.2% *	44.5% *	39.1% *	<0.001
Percentage of male patients	67.6%	66.2%	70.8% *	72.3%	69.0%	0.010
Age >80 years	25.8%	27.7% *	24.4% *	23.9% *	21.1%	0.117
Event occurred in public	40.0% *	32.9% *	26.5% *	24.4% *	28.5% *	<0.001
Percentage of shockable rhythms	42.9% *	41.6% *	38.1% *	36.9% *	30.8% *	<0.001
Adrenaline	78.9%	77.3% *	83.1%	84.5%	82.9%	0.018
Amiodarone	29.7% *	30.9% *	31.4% *	34.5% *	29.6%	0.096
Telephone-guided resuscitation	21.3%	29.8%	34.0%	34.3%	29.8%	<0.001
Endotracheal intubation performed	75.3% *	70.0%	68.1%	71.3%	68.7%	0.004

b) No bystander CPR						
Alarm raised to arrival of 1 st vehicle (min)	0–1–2	3–4–5	6–7–8	9–10–11	> 12	p-Value
Number of resuscitation patients (n)	660	2 449	2 122	851	411	
Alarm raised to arrival of 1 st vehicle (min:sec)	01:10 ± 00:52	04:10 ± 00:46	06:51 ± 00:48	09:47 ± 00:47	14:03 ± 02:12	
Alarm raised to 1 st defibrillation in VF (min:sec)	06:03 ± 03:37	08:37 ± 04:43	11:18 ± 04:31	14:25 ± 06:42	16:40 ± 09:41	
Alarm raised to 1 st vasopressor in non-VF (min:sec)	12:03 ± 06:43	12:48 ± 06:58	14:33 ± 06:04	15:45 ± 04:33	20:16 ± 08:05	
ROSC ever (%) [95% confidence interval]	44.1% [40.3; 48.0]	41.6% [39.7; 43.6]	42.0% [39.9; 44.1]	35.7% [32.5; 39.0]	32.1% [27.6; 36.9]	<0.001
ROSC at hospital admission (%)	37.4%	35.1%	34.7%	29.9%	25.1%	<0.001
Discharged alive (%)	12.9%	11.7%	9.1%	6.4%	7.3%	<0.001
CPC 1 or 2 at discharge (%)	10.2%	9.2%	6.6%	4.5%	6.3%	<0.001
ROSC expected according to RACA score	43.1%	39.4%	36.3%	33.9%	28.2%	<0.001
Percentage of male patients	67.9%	65.3%	64.1%	68.4%	67.6%	0.078
Age >80 years	29.9%	32.3%	30.6%	30.2%	25.8%	0.152
Event occurred in public	23.6%	17.7%	13.7%	13.4%	11.9%	<0.001
Percentage of shockable rhythms	29.4%	26.8%	22.8%	23.9%	17.5%	<0.001
Adrenaline	77.7%	82.2%	82.5%	83.0%	81.0%	0.006
Amiodarone	24.1%	23.8%	24.6%	24.8%	23.8%	0.752
Endotracheal intubation performed	66.8%	68.0%	68.9%	68.4%	64.2%	0.316

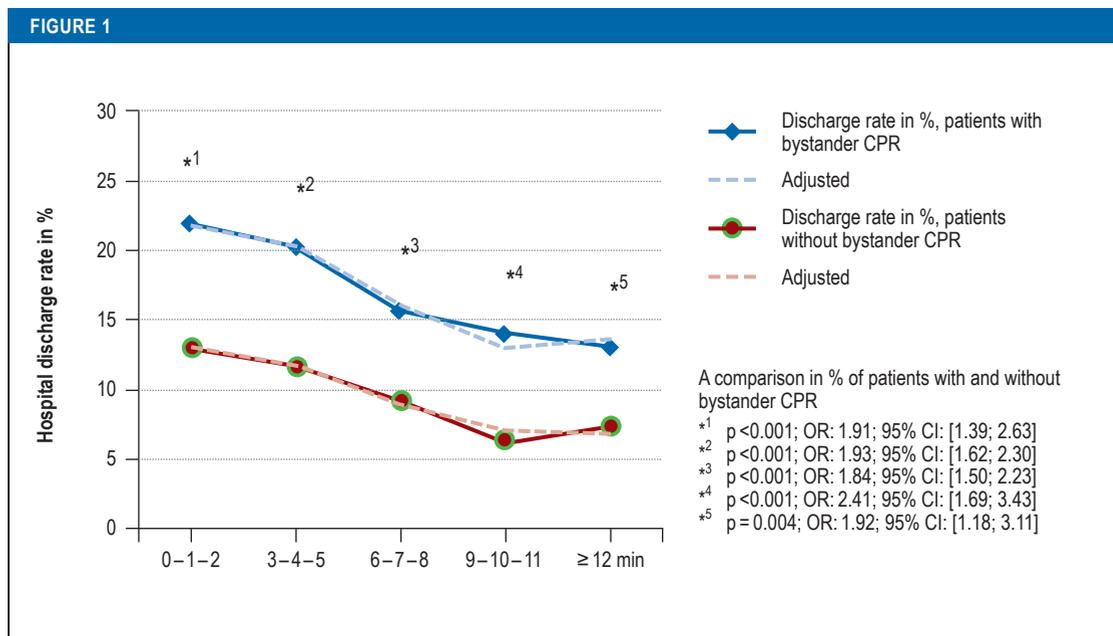
Raw data on 10 853 patients for multivariate logistic regression analysis with the outcome measure "discharge following OHCA."

Patients were assigned to five time categories.

Categories were defined according to the time interval between "raising of the alarm and arrival of the first vehicle."

Statistical analyses were performed using T-tests and chi-squared tests with Bonferroni correction; statistical significance was set at p<0.01.

There are significant differences between all data on patients marked with *, in whom bystander resuscitation was performed, compared with those in whom no bystander CPR was performed. CPC, cerebral performance categories; CPR, cardiopulmonary resuscitation; OHCA, out-of-hospital cardiac arrest; RACA, ROSC after cardiac arrest; ROSC, return of spontaneous circulation; VF, ventricular fibrillation



The effect of ambulance response time on the percentage hospital discharge rates of OHCA patients in emergency medical services (N = 10 853) depending on cardiopulmonary resuscitation performed by a bystander. Patients were assigned to five time categories; these categories were defined according to the time interval between “Raising of the alarm and arrival of the first vehicle.” The dashed lines show the discharge rates of these patients adjusted using a multivariate logistic regression model. Further statistical analyses was performed using the Chi² test with Bonferroni correction, odds ratio, and confidence interval; statistical significance was set at p<0.01. CPR, cardiopulmonary resuscitation; OHCA, out-of-hospital cardiac arrest; OR, odds ratio; 95% CI; 95% confidence interval

ROSC after cardiac arrest score (RACA score) (23, 24)—were included in the analysis: age, sex, location of cardiac arrest, event observed, first ECG rhythm, and pre-emergency status, which includes information on pre-existing diseases. Categorized variables were created for the multivariate logistic regression analyses: ambulance response time (0–2, 3–5, 6–8, 9–11, and ≥ 12 min), bystander CPR (without, with and without telephone assistance), age (<60, 60–69, 70–79, and ≥ 80 years), pre-existing diseases (unknown, without pre-existing disease, pre-existing disease without impairment, pre-existing disease with impairment, and pre-existing disease that renders normal life impossible), initial shockable rhythm (yes/no), witnessed event (yes/no), location of event: in public/medical practice (yes/no), and male sex (yes/no).

The Ethics Committee of the University of Lübeck, Germany, voted to approve structural analyses based on the German Resuscitation Registry (file number 12–226).

Data was processed using Excel 2017 software (Microsoft Corporation, Redmond, WA, USA) and IBM SPSS Statistics (IBM, Armonk, NY, USA). The multivariate logistic regression analysis was carried out in such a way that potential variables were included at p<0.05 and excluded at p>0.1. Regression coefficients, odd ratios, and confidence intervals were calculated for the variables included. Using the regression coefficients determined, a prediction model for the personalized probability of discharge was

created. This model was used to simulate the effects of shortened ambulance response times and increased rates of bystander CPR on the number of survivors. To this end, the potential ambulance response time was reduced on a percentage basis or the bystander CPR that had not been performed was randomized as performed in the respective datasets. The projection for Germany was based on the calculated or simulated discharge rates, an annual resuscitation incidence of 66/100 000 population (1), and a total population of 82.67 million.

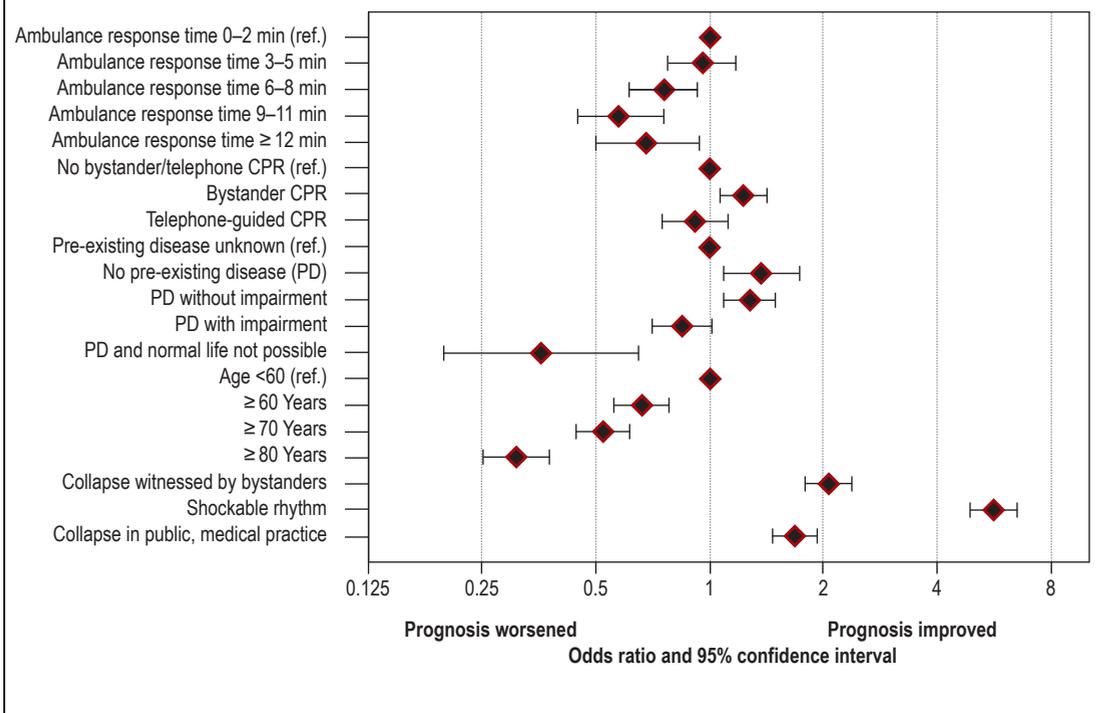
The tables show values as mean values or weighted mean values. Odds ratios and confidence intervals were calculated for group comparisons. Other statistical analyses were performed using T-tests, chi-square tests, and Bonferroni correction where required; statistical significance was set at p<0.05.

Results

According to the inclusion and exclusion criteria, 10 853 CPR patients from 25 emergency service areas were included in the first part of the study and 17 534 in the second part. Of these 17 534 data sets, the following were excluded from the multivariate logistic regression analysis:

- 3537 Patients due to non-cardiac cause
- 1036 Observed by emergency medical services (irrelevant to ambulance response time)
- 2108 Due to lack of information on individual ambulance response time

FIGURE 2



Multivariate logistic regression analysis with the binary outcome measure “Discharge following OHCA.” A total of 10 853 patients with OHCA that was not observed by the emergency medical services were included. Resuscitation success declines with increasing ambulance response time, higher age, and severe pre-existing disease. In contrast, bystander resuscitation, a shockable rhythm, or the fact that the collapse was witnessed or occurred in public or a medical practice, improve the prognosis following resuscitation by emergency medical services. CPR, cardiopulmonary resuscitation; OHCA, out-of-hospital cardiac arrest; ref., reference

The effect of ambulance response time on resuscitation success

The raw data showed that the rate of resuscitation success decreased with increasing ambulance response time (Table). The discharge rate fell from 22.0% to 14.0% if patients received bystander CPR and the mean ambulance response time rose from 1:04 to 9:47 min (odds ratio [OR]: 1.73; 95% confidence interval: [1.26; 2.37]; p<0.001). If no bystander CPR was performed, the discharge rate dropped from 12.9% to 6.4% if the mean ambulance response time rose from 1:10 to 9:47 min (OR: 2.18 [1.53; 3.12]; p<0.001).

On the other hand, the short-term and long-term survival after resuscitation was greater in both time groups if patients had received bystander/first responder resuscitation. For example, 18.4% of patients were discharged with good neurological outcome after an ambulance response time of 0–2 min if they had received bystander resuscitation and only 10.2% if bystander resuscitation had not been performed (OR: 2.0 [1.41; 2.83]; p<0.001). If the mean ambulance response time extended to 9:47 min, only 10.4% of patients with bystander resuscitation, and as little as 4.5% without bystander resuscitation, could be discharged with good neurological outcome (OR: 2.47 [1.64; 3.73]; p<0.001).

eTable 1 and Figure 1 show the results of the multivariate logistic regression analysis. In a seven-factor model, ambulance response time, bystander resuscitation, age, pre-existing disease, location of collapse, witnessed status, and initial heart rhythm significantly affect the probability of being discharged alive from the hospital following resuscitation by EMS systems. Sex has no effect on the discharge rate in this model. The model achieves a value of 0.296 according to Nagelkerke’s R squared. eTable 1 shows the corresponding regression coefficients, standard errors, and significance levels for this model. Figure 2 gives the odds ratio and confidence interval for each variable and category in a forest plot. Discharge rates according to the raw data on the 10 853 patients and adjusted by the regression model are shown in Figure 1.

eFigure 1 gives the number of patients that survive annually following resuscitation by emergency medical services as a projection and simulation on the basis of the logistic regression model. At a measured discharge rate of 13%, this means that 7091 patients survive per year in Germany. By reducing the individual ambulance response times by 10%, 20%, or 30%, the number of survivors increases annually by 370, 515, or 634 patients, respectively. If the rate of

bystander resuscitation could be raised by 20 or 40 percentage points to 47% or 67%, an additional 245 or 426 patients could be saved each year. By simulating a 20% reduction in ambulance response time combined with an increase in the rate of bystander resuscitation to 47%, as many as 771 more patients/year could be saved, amounting to an annual total of 7862 patients saved in Germany by EMS systems following sudden cardiac arrest and resuscitation

The effect of ambulance response time on the EMS system level

The 12 faster (n = 9669) and 13 slower (n = 7865) EMS systems reached 85.8% versus 67.9% of patients, respectively, with the first vehicle arriving within 8 min. Slower emergency medical services initiated resuscitation significantly more rarely, i.e., with an annual incidence of 59.3 compared with 70.3 patients/100 000 population (OR = 0.84 [0.82; 0.87]; p < 0.001) (eFigure 2).

The effect of ambulance response time on resuscitation success

Short-term resuscitation success is greater in faster EMS systems (eTable 2):

- All-time incidence of ROSC: 26.7 patients/100 000 population/year (slower EMS systems) versus 32.9 (OR: 0.81 [0.78; 0.85]; p < 0.001)
- Incidence of hospital admission: 22.6 patients/100 000 population/year (slower EMS systems) versus 27.9 (OR: 0.81 [0.77; 0.85]; p < 0.001).

More patients show good long-term results in faster EMS systems:

- Incidence of patients discharged alive: 7.3 patients/100 000 population/year (slower EMS systems) versus 9.7 (OR: 0.75 [0.69; 0.82]; p < 0.001)
- Incidence of discharge with good neurological outcome (CPC 1/2): 5.6 patients/100 000 population/year (slower EMS systems) versus 7.7 (OR: 0.72 [0.66; 0.79]; p < 0.001).

Discussion

The results of the multivariate logistic regression analysis showed that ambulance response time and bystander resuscitation significantly affect survival following out-of-hospital cardiac arrest, in addition to age, pre-existing disease, witnessed status, location of collapse, and initial heart rhythm. The simulation showed that both reduced ambulance response times and higher bystander resuscitation rates can significantly increase the number of patients that survive. Categorizing the variable “ambulance response time” confers the advantage that non-linear associations can also be readily modeled. When considered as a continuous variable, on the other hand, one calculates an effect “per minute.” However, in further logistic regression analyses, the effect of ambulance response time—also as a continuous

variable—on both the probability of discharge and on good neurological recovery was the same; there was a reduction in the probability of survival of 5% per minute prolongation of ambulance response time (eTables 4a and 4b).

The second part of the study additionally showed that faster EMS systems—standardized to the number of inhabitants—perform CPR on more patients and that more patients leave the hospital with good neurological outcome following OHCA. This is all the more remarkable given that the likelihood of ROSC did not differ between faster and slower EMS systems and that the quality of medical treatment was comparable

Therefore, it is highly likely that shorter ambulance response time intervals result in higher survival rates, individually and as a planning factor, since shorter response time intervals enable trained emergency service personnel to carry out optimal chest compression earlier, ensure oxygenation earlier by means of airway management, O₂ administration, and ventilation, and administer vasopressors earlier. In addition, more patients are found to be in a shockable rhythm at shorter ambulance response times, and defibrillation is performed earlier (21, 27–29). In summary, these measures result in better oxygen supply to the heart and brain, earlier defibrillation, and therefore to better resuscitation outcomes.

In line with this, a recent study based on the Danish resuscitation registry showed that, with increasing ambulance response times, the 30-day survival rate drops comparably fast as does the discharge rate in this study (18). In both studies, bystander resuscitation doubled the chances of survival at ambulance response times of under 5 min (OR: 1.8–2.4). In contrast to the data in this study, the Danish study showed that bystander resuscitation no longer conferred a significant benefit at an ambulance response time of 13 min. It was possible to simulate for Denmark, with a population of around 5.75 million, that shortening the average ambulance response time from 7 to 5 min could save 119 lives or 2.1 lives/100 000 population per year. This is higher than the simulation here and comparable to our data at the emergency medical services level, which showed an increase of 2.4 patients discharged alive/100 000 population per year at shorter EMS system response time intervals

The results of the two studies highlight the fact that short ambulance response times are vital and that further efforts need to be made to shorten both ambulance response times and the time to resuscitation (30–32). The German Resuscitation Council (*Deutscher Rat für Wiederbelebung*) White Paper on resuscitation management calls for ambulance response times within 8 min to be achieved in 85% of cases uniformly across Germany (33). Due to different legislations in the German federal states, there are 16 regulations on ambulance response times in Germany to date, the significance and influence of

Key messages

- With 100 000 patients affected in Germany every year, sudden out-of-hospital cardiac arrest is a frequent event and a logistical and medical challenge for emergency physicians and emergency medical services.
- Ambulance response time is an important planning factor for emergency medical services systems. This study investigated the effect of ambulance response time on resuscitation outcome.
- Multivariate logistic regression analysis showed that shorter ambulance response times and bystander resuscitation increase the percentage discharge rate following OHCA and resuscitation.
- Faster emergency medical services begin resuscitation more often and more patients can be admitted to hospital following out-of-hospital cardiac arrest, although the risk at the start of resuscitation and the quality of care provided by the emergency physician and emergency medical services are comparable.
- For the first time, it was possible to show for Germany that emergency medical services with shorter ambulance response times, as well as a higher rate of bystander resuscitation, enable more patients to leave hospital following OHCA and resuscitation with good neurological recovery.

which have been subjected to only scant scientific examination. Shortening ambulance response times is needed and also feasible by increasing the provision of emergency service units and optimizing logistics (e.g., location optimization or a “comprehensive next vehicle strategy”).

Since the considerable importance of bystander CPR has been demonstrated, the rate and quality of bystander resuscitation needs to be improved. Emergency medical services are called upon to implement telephone-guided CPR throughout Germany (7, 34, 35). Emergency medical services can also introduce new systems that use smartphone location data to guide pre-registered and trained laypersons to CPR patients (36, 37). The performance of resuscitation by bystanders should become a matter of course. To achieve this, training should be provided as early on as at school age (11). Since cardiac arrest occurs more frequently in the homes of older people, all age groups need to be mobilized to perform bystander resuscitation. Initiatives such as the German “*Woche der Wiederbelebung*” (“Resuscitation Week”) are designed to encourage ever more individuals to save lives in cases of out-of-hospital cardiac arrest (38).

The study clearly highlights the positive effect of shorter ambulance response times and bystander resuscitation on survival following out-of-hospital cardiac arrest and resuscitation. Further joint efforts need to be made to broadly disseminate resuscitation knowledge in the general population and to bring ambulance response times in line with medical requirements.

Limitations

Limitations need to be taken into account when evaluating results. The German Resuscitation Registry operates on a voluntary basis, which explains why 134 of 241 emergency medical services in Germany currently submit data to the registry. At present, only 41 emergency medical services are able to supply follow-

up data on hospital treatment for the evaluation of long-term outcomes, in part due to data protection requirements. This limits representativeness as a result. Participants are responsible for ensuring data quality; this can no longer be verified following data entry, since data are transmitted to the registry in anonymized form. Resuscitation outcome is affected by the quality of chest compression (frequency, depth, pauses), on which the resuscitation registry does not collect data. As such, it is possible that unrecorded variables and confounders might have affected the outcome.

Conflict of interests

Dr. Wnent, Dr. Bohn, Prof. Jantzen, Mrs. Brenner, Prof. Gräsner, Dr. Seewald und Prof. Fischer are members of the steering committee of the German Resuscitation Registry.

The remaining authors state that they have no conflicts of interest.

Manuscript submitted on 30 December 2017, revised version accepted on 22 May 2018

Translated from the original German by Christine Schaefer-Tsorpatzidis

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► **Supplementary material**
eMethods, eTables, eFigures:
www.aerzteblatt-international.de/18m0541

Erratum

In the article entitled “Bowlegs and Intensive Football Training in Children and Adolescents” by Peter Helmut Thaller et al. in issue 24 of *Deutsches Ärzteblatt International*, the abbreviation MPTA in the legends of *Figure 2* and the *Figure* was erroneously explained as “medial proximal femoral angle.” In both instances, it should have read “medial proximal tibial angle.”

MWR

Supplementary material to:

The Effect of Ambulance Response Time on Survival Following Out-of-Hospital Cardiac Arrest

An Analysis from the German Resuscitation Registry

by Andreas Bürger, Jan Wnent, Andreas Bohn, Tanja Jantzen, Sigrid Brenner, Rolf Lefering, Stephan Seewald, Jan-Thorsten Gräsner, and Matthias Fischer

Dtsch Arztebl Int 2018; 115: 541–8. DOI: 10.3238/arztebl.2018.0541

eTABLE 1

Multivariate logistical regression analysis of the effect of ambulance response time “raising of the alarm to arrival of the 1st vehicle” and bystander cardiopulmonary resuscitation (CPR) on the percentage discharge rate following out-of-hospital resuscitation

Discharge	Regression coefficient B	Standard error	Wald	df	p-value	Exp(B)
Ambulance response time 0–2 min (ref.)			30.194	4.000	0.000	
Ambulance response time 3–5 min	–0.045	0.105	0.186	1.000	0.667	0.956
Ambulance response time 6–8 min	–0.276	0.109	6.402	1.000	0.011	0.759
Ambulance response time 9–11 min	–0.544	0.133	16.806	1.000	0.000	0.581
Ambulance response time ≥ 12 min	–0.379	0.162	5.487	1.000	0.019	0.685
No bystander or telephone-guided CPR (ref.)			11.471	2.000	0.003	
Bystander CPR	0.206	0.073	8.034	1.000	0.005	1.229
Telephone-guided CPR	–0.088	0.102	0.739	1.000	0.390	0.916
Age <60 (ref.)			140.402	3.000	0.000	
≥ 60 Years	–0.411	0.086	23.026	1.000	0.000	0.663
≥ 70 Years	–0.644	0.084	59.381	1.000	0.000	0.525
≥ 80 Years	–1.173	0.105	125.866	1.000	0.000	0.309
Pre-existing disease unknown (ref.)			38.266	4.000	0.000	
Without pre-existing disease (PD)	0.314	0.116	7.301	1.000	0.007	1.368
PD without impairment	0.244	0.079	9.501	1.000	0.002	1.276
PD with impairment	–0.174	0.091	3.691	1.000	0.055	0.840
PD and normal life not possible	–1.027	0.303	11.466	1.000	0.001	0.358
Collapse witnessed by bystanders	0.724	0.074	97.021	1.000	0.000	2.063
Shockable rhythm	1.730	0.070	604.915	1.000	0.000	5.639
Collapse in public, medical practice	0.521	0.069	56.515	1.000	0.000	1.685
Constant	–2.757	0.129	459.321	1.000	0.000	0.063

Multivariate logistic regression analysis with the outcome measure “discharge after prehospital resuscitation.”

A total of 10 853 patients with sudden cardiac arrest that was not observed by the emergency medical services were included. Regression coefficient, standard error, Wald statistics, degrees of freedom (df) and the exponential function of the regression coefficient to the basis e (odds ratio) are shown. The regression coefficient shows that resuscitation success declines with increasing ambulance response time, higher age, and severe pre-existing disease. In contrast, bystander resuscitation, a shockable rhythm, or the fact that the collapse was witnessed or occurred in public or in a medical practice, improve the prognosis following resuscitation by emergency medical services. The regression coefficients were used to formulate the regression model.

eTABLE 2

The effect of ambulance response time at the emergency medical services (EMS) systems level on survival rates (incidence and percent) following pre-hospital resuscitation: a comparison of fast versus slow EMS systems

	Faster EMS systems RTR >75%	Slower EMS systems RTR ≤ 75%	p-value	Odds ratio [95% confidence interval]
a)				
Population	3 513 900	2 991 290		
Size of region covered (km ²)	5618	9213		
Population density (per km ²)	1153	620		
Person years	13 750 030	13 259 021		
Patients with cardiac arrest (CA) (n)	15 012	14 714		
CA Incidence (1/100 000 l/year)	109	111	0.159	1.02 [0.99; 1.04]
CA mortality (1/100 000 l/year)	101.4	105.4	<0.001	1.04 [1.02; 1.07]
CA lethality (%)	92.9	95.0	<0.001	1.37 [1.26; 1.50]
Number of resuscitation patients (n)	9669	7865		
RTR (response time reliability) (%)	85.8	67.9	<0.001	0.35 [0.33; 0.38]
Raising of alarm to arrival of 1 st vehicle (min:sec)	05:45 ± 02:56	07:00 ± 04:06	<0.001	t-Test
CPR Incidence (1/100 000 l/year)	70.3	59.3	<0.001	0.84 [0.82; 0.87]
b)				
Incidence of ROSC ever (1/100 000 l/year)	32.9	26.7	<0.001	0.81 [0.78; 0.85]
Incidence of hospital admission (1/100 000 l/year)	27.9	22.6	<0.001	0.81 [0.77; 0.85]
Incidence of discharge alive (1/100 000 l/year)	9.7	7.3	<0.001	0.75 [0.69; 0.82]
Incidence of CPC 1/2 at discharge (1/100 000 l/year)	7.7	5.6	<0.001	0.72 [0.66; 0.79]
ROSC ever (%) [95% confidence interval]	46.8 [45.8; 47.8]	45.1 [44.0; 46.2]	0.025	0.93 [0.88; 0.99]
ROSC expected according to RACA score (%)	43.0	42.5	0.505	1.02 [0.96; 1.08]
ROSC at hospital admission (%)	39.7	38.1	0.036	0.94 [0.88; 1.00]
Discharged alive (%)	13.8	12.4	0.004	0.88 [0.80; 0.96]
CPC 1/2 at discharge (%)	11.0	9.4	<0.001	0.84 [0.76; 0.93]

	Faster EMS systems RTR >75%	Slower EMS systems RTR ≤ 75%	p-value	Odds ratio [95% confidence interval]
c)				
Male patients (%)	63.8	66.3	<0.001	1.12 [1.05; 1.19]
Age (mean)	69.2 ± 16.8	67.8 ± 17.0	<0.001	t-Test
Age >80 years (%)	28.4	25.4	<0.001	0.86 [0.80; 0.92]
Cardiac cause (%)	63.2	66.2	<0.001	1.14 [1.07; 1.21]
Witnessed by bystanders (%)	44.3	45.9	0.031	1.07 [1.01; 1.14]
Witnessed by professionals (%)	12.2	13.0	0.109	1.08 [0.98; 1.18]
Event occurred in public (%)	16.1	17.1	0.091	1.07 [0.99; 1.16]
Event not in public (%)	73.8	71.2	<0.001	0.88 [0.82; 0.94]
Shockable rhythms (%)	26.2	24.1	0.002	0.90 [0.84; 0.96]
Pulseless electrical activity (%)	19.2	20.0	0.217	1.05 [0.97; 1.13]
Asystole (%)	53.4	52.0	0.060	0.95 [0.89; 1.00]
CPR prior to arrival of emergency medical services (%)	34.1	34.1	0.949	1.00 [0.94; 1.07]
Telephone-guided resuscitation (%)	13.3	9.7	<0.001	0.71 [0.64; 0.78]
Time from alarm raised to start of CPR by ES ≤ 8 min (%)	57.1	52.3	<0.001	0.83 [0.78; 0.88]
Time from alarm raised to 1 st defibrillation in VF/VFL ≤ 8 min (%)	33.7	27.9	<0.001	0.76 [0.71; 0.81]
Adrenaline (%)	79.3	80.9	0.007	1.11 [1.03; 1.20]
Amiodarone (%)	22.5	22.1	0.483	0.98 [0.91; 1.05]
Endotracheal intubation performed (%)	69.3	67.0	<0.001	0.90 [0.84; 0.96]
Emergency physician requested by AC (%)	13.2	12.3	0.064	0.92 [0.84; 1.01]

A comparison of the effect of ambulance response time at the emergency medical services level between 12 fast and 13 slow EMS systems in Germany. A faster EMS system reaches >75% of patients with the first vehicle within 8 min after raising of the alarm, a slower EMS system reaches ≤ 75% of patients (response time reliability, RTR >75% versus RTR ≤ 75%). Incidences and mortality were calculated per 100 000 population/year; percentages relate to the number of resuscitation patients. Statistical analysis was performed using the Chi² test, odds ratio, and confidence interval; statistical significance was set at p<0.05.

CPC, cerebral performance categories; CPR, cardiopulmonary resuscitation; I, inhabitants; RACA, ROSC after cardiac arrest; EMS, emergency medical services; ROSC, return of spontaneous circulation; RTR, response time reliability; AC, ambulance crew; VF/VFL, ventricular fibrillation/flutter

eTABLE 3

Survival rates for index patients (VF + CA): a comparison of fast versus slow EMS systems

	Faster EMS systems RTR > 75%	Slower EMS systems RTR ≤ 75%	p-value	Odds ratio [95% confidence interval]
Index patients (n)	1657	1306		
Frequency of index patients (%)	17.1%	16.6%	0.350	0.96 [0.89; 1.04]
CPR incidence in index patients (1/100 000 I/year)	12.1	9.8	<0.001	0.82 [0.76; 0.88]
ROSC ever in index patients (%)	76.0%	74.4%	0.324	0.92 [0.78; 1.09]
ROSC at hospital admission in index patients t (%)	68.7%	68.1%	0.756	0.98 [0.83; 1.14]
Index patients discharged alive (%)	39.0%	36.1%	0.105	0.88 [0.76; 1.03]
CPC 1/2 at discharge in index patients (%)	33.2%	29.5%	0.031	0.84 [0.72; 0.99]
CPC 3/4 at discharge in index patients (%)	3.6%	3.1%	0.454	0.86 [0.56; 1.31]

Resuscitation incidence and percentage results for resuscitation in index patients, i.e., patients with observed cardiovascular arrest of cardiac origin with initial ventricular fibrillation; a comparison of 12 fast and 13 slow physician-staffed EMS systems in Germany. Incidence was calculated as number/100 000 population/year; the percentages relate to all resuscitations initiated in index patients; statistical analysis was performed using the Chi² test, odds ratio, and confidence interval; statistical significance was set at p<0.05.

CPC, cerebral performance categories; CPR, cardiopulmonary resuscitation; CA, cardiac arrest; EMS, emergency medical services; ROSC, return of spontaneous circulation; RTR, response time reliability; VF, ventricular fibrillation

eTABLE 4

Prognosis following pre-hospital resuscitation by emergency medical services

	Regression coefficient B	Standard error	Wald	df	p-value	Exp(B) [95% confidence interval]
a) Outcome measure “Discharge following pre-hospital resuscitation”						
Ambulance response time per minute	-0.050	0.010	25.773	1.000	0.000	0.951 [0.93; 0.97]
No bystander/telephone-guided CPR (ref.)			11.953	2.000	0.003	
Bystander CPR	0.208	0.073	8.205	1.000	0.004	1.231 [1.07; 1.42]
Telephone-guided CPR	-0.095	0.102	0.859	1.000	0.354	0.91 [0.74; 1.11]
Age <60 (ref.)			141.459	3.000	0.000	
≥ 60 Years	-0.413	0.086	23.343	1.000	0.000	0.661 [0.56; 0.78]
≥ 70 Years	-0.649	0.084	60.417	1.000	0.000	0.522 [0.44; 0.62]
≥ 80 Years	-1.175	0.104	126.526	1.000	0.000	0.309 [0.25; 0.38]
Pre-existing disease unknown (ref.)			38.145	4.000	0.000	
No pre-existing disease (PD)	0.317	0.116	7.458	1.000	0.006	1.373 [1.09; 1.72]
PD without impairment	0.245	0.079	9.619	1.000	0.002	1.278 [1.09; 1.49]
PD with impairment	-0.169	0.091	3.477	1.000	0.062	0.845 [0.71; 1.01]
PD and normal life not possible	-1.025	0.303	11.447	1.000	0.001	0.359 [0.20; 0.65]
Collapse witnessed by bystanders	0.724	0.073	97.106	1.000	0.000	2.062 [1.79; 2.38]
Shockable rhythm (VF/VFL)	1.726	0.070	603.119	1.000	0.000	5.617 [4.89; 6.45]
Collapse in public, medical practice	0.522	0.069	56.760	1.000	0.000	1.685 [1.47; 1.93]
Constant	-2.651	0.111	568.062	1.000	0.000	0.071
b) Outcome measure “Discharge with good neurological outcome CPC 1 or 2”						
Ambulance response time per minute	-0.051	0.011	21.992	1.000	0.000	0.95 [0.93; 0.97]
No bystander/telephone-guided CPR (ref.)			10.895	2.000	0.004	
Bystander CPR	0.214	0.079	7.350	1.000	0.007	1.239 [1.06; 1.45]
Telephone-guided CPR	-0.101	0.113	0.797	1.000	0.372	0.904 [0.73; 1.13]
Age <60 (ref.)			110.795	3.000	0.000	
≥ 60 Years	-0.422	0.093	20.567	1.000	0.000	0.656 [0.55; 0.79]
≥ 70 Years	-0.702	0.092	57.911	1.000	0.000	0.495 [0.41; 0.59]
≥ 80 Years	-1.086	0.114	90.387	1.000	0.000	0.338 [0.27; 0.42]
Pre-existing disease unknown (ref.)			28.823	4.000	0.000	
No pre-existing disease (PD)	0.323	0.124	6.739	1.000	0.009	1.381 [1.08; 1.76]
PD without impairment	0.257	0.086	8.903	1.000	0.003	1.294 [1.09; 1.53]
PD with impairment	-0.070	0.100	0.488	1.000	0.485	0.933 [0.77; 1.13]
PD and normal life not possible	-1.375	0.420	10.721	1.000	0.001	0.253 [0.11; 0.58]
Collapse witnessed by bystanders	0.779	0.083	88.183	1.000	0.000	2.179 [1.85; 2.56]
Shockable rhythm (VF/VFL)	1.760	0.080	483.193	1.000	0.000	5.811 [4.97; 6.80]
Collapse in public, medical practice	0.597	0.075	63.641	1.000	0.000	1.817 [1.57; 2.10]
Constant	-3.088	0.125	606.778	1.000	0.000	0.046

Multivariate logistic regression analysis with (a) the outcome measure “discharge following OHCA” and (b) outcome measure “discharge with good neurological outcome CPC 1 or 2” and the continuous variable ambulance response time. The regression coefficient shows that resuscitation success declines with increasing ambulance response time, higher age, and severe pre-existing disease. In particular, one sees a 5% reduction in survival probability per minute of prolonged ambulance response time. In contrast, bystander resuscitation, a shockable rhythm, or the fact that the collapse was witnessed or occurred in public or a medical practice, improve the prognosis following pre-hospital resuscitation by emergency medical services

CPC, cerebral performance categories; CPR, cardiopulmonary resuscitation; ref., reference; OHCA, out-of-hospital cardiac arrest; PD, pre-existing disease; VF/VFL, ventricular fibrillation/flutter

eMETHODS

The second part of the study determined the effect of ambulance response time on survival incidence and rates on the emergency medical services level. A group of faster emergency medical services (EMS) systems was compared with a group of slower EMS systems. An EMS system was considered faster (F-EMS) if more than 75% of patients were reached by the first vehicle at the latest within 8 min of being alerted (response time reliability, RTR >75%). Slower EMS systems (S-EMS) reached fewer than 75% of patients within 8 min of being alerted (RTR ≤ 75%).

On the EMS system level, not only the survival rate percentages, but also the number of resuscitated and surviving patients per 100 000 population/year were determined. The following incidences were calculated as additional criteria:

- CPR incidence (CPR, cardiopulmonary resuscitation)
- Incidence of ROSC (return of spontaneous circulation) ever
- Incidence of hospital admission
- Incidence of discharge alive
- Incidence of CPC (cerebral performance category) 1 or 2 at hospital discharge.

The number of respective patients was divided by person years and standardized per 100 000 population. The person years were obtained from the total number of person years per EMS system, which is calculated by multiplying the number of population and the years of the reporting period per EMS system.

The success of resuscitation can be determined by the variables mentioned above, as well as by the quality of medical care. One can assume comparable quality of medical care in emergency medical service groups if the proportion of ROSC rates predicted using the RACA (ROSC after cardiac arrest) score tallies with the observed rates (23, 24), or if resuscitation results in index patients do not differ (1). Index patients are patients with observed cardiac arrest that are found in a shockable rhythm (1).

The power analysis for part 2 yielded a sample size of 3837 patients per sample for the outcome measure discharge rate of 10% or 12% at an alpha error of 5% and a power of 80%.

The effect of ambulance response time at the emergency medical services level

Factors affecting population geography and process quality are presented in *eTable 2a*. The population covered totals 3 513 000 in the faster and 2 991 290 in the slower emergency medical services; the investigation covers 13 750 030 person years in the faster and 13 259 021 person years in the slower EMS systems.

Faster EMS systems initiated resuscitation significantly more frequently: CPR incidence S-EMS = 59.3 versus F-EMS = 70.3 patients/100 000 population/year (OR: 0.84; 95% confidence interval: [0.82; 0.87]; $p < 0.001$).

Short-term resuscitation success is greater in faster EMS systems (*eTable 2*):

- Incidence of ROSC ever: 26.7 patients/100 000 population/year (slower EMS systems) versus 32.9 (OR: 0.81 [0.78; 0.85]; $p < 0.001$)
- Incidence of hospital admission: 22.6 patients/100 000 population/year (slower EMS systems) versus 27.9 (OR: 0.81 [0.77; 0.85]; $p < 0.001$).

More patients show good long-term results in faster EMS systems:

- Incidence of patients discharged alive: 7.3 patients/100 000 population/year (slower EMS systems) versus 9.7 (OR: 0.75 [0.69; 0.82]; $p < 0.001$)
- Incidence of discharge with good neurological outcome (CPC 1/2): 5.6 patients/100 000 population/year (slower EMS systems) versus 7.7 (OR: 0.72 [0.66; 0.79]; $p < 0.001$).

There was no significant difference in the likelihood of resuscitation in faster and slower emergency medical services as calculated using the RACA score: RACA F-EMS = 43.0% versus RACA S-EMS = 42.5% (OR: 1.02 [0.96; 1.08]; $p = 0.505$).

Quality of resuscitation

A comparison of the 95% confidence interval for ROSC ever with the “expected ROSC rate” shows comparable CPR quality in faster and slower EMS systems, since the actual ROSC rate was significantly higher compared with the expected rate (*eTable 2*).

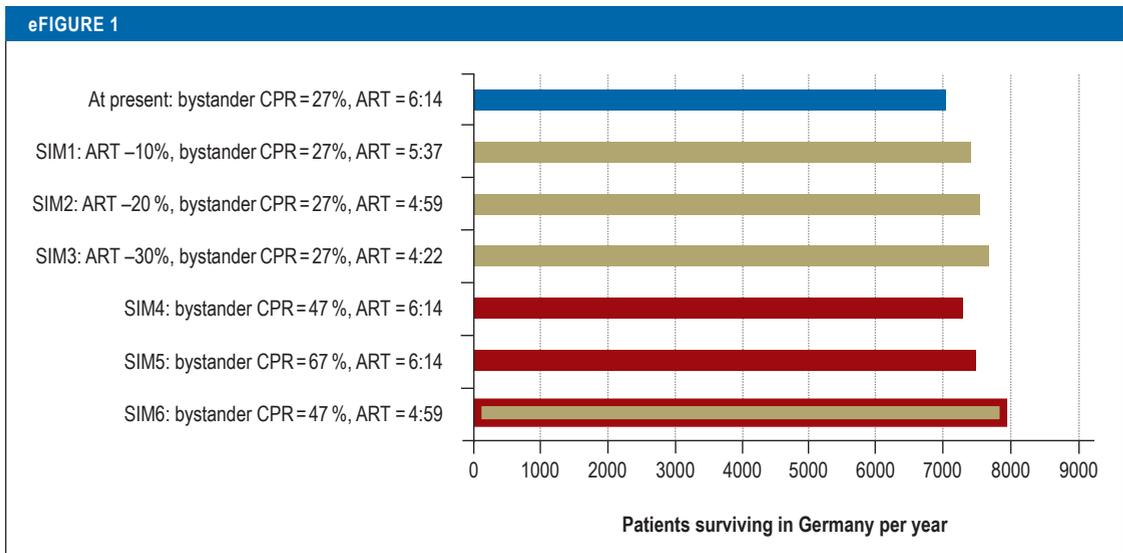
This is similarly apparent when looking at the rate of resuscitation success in index patients (*eTable 3*), since there is no difference between faster and slower EMS systems in the endpoints “ROSC ever,” “ROSC on admission,” and “discharged alive.”

Resuscitation interventions (*eTable 2c*)

With regard to bystander resuscitation prior to arrival of the EMS systems, there was no difference between faster and slower EMS systems; telephone-guided resuscitation was carried out more frequently in faster EMS systems.

Faster emergency medical services initiated resuscitation attempts earlier. CPR initiation by emergency medical services within 8 min: S-EMS = 52.3 % versus F-EMS = 57.1 % (OR: 0.83 [0.78; 0.88]; $p < 0.001$).

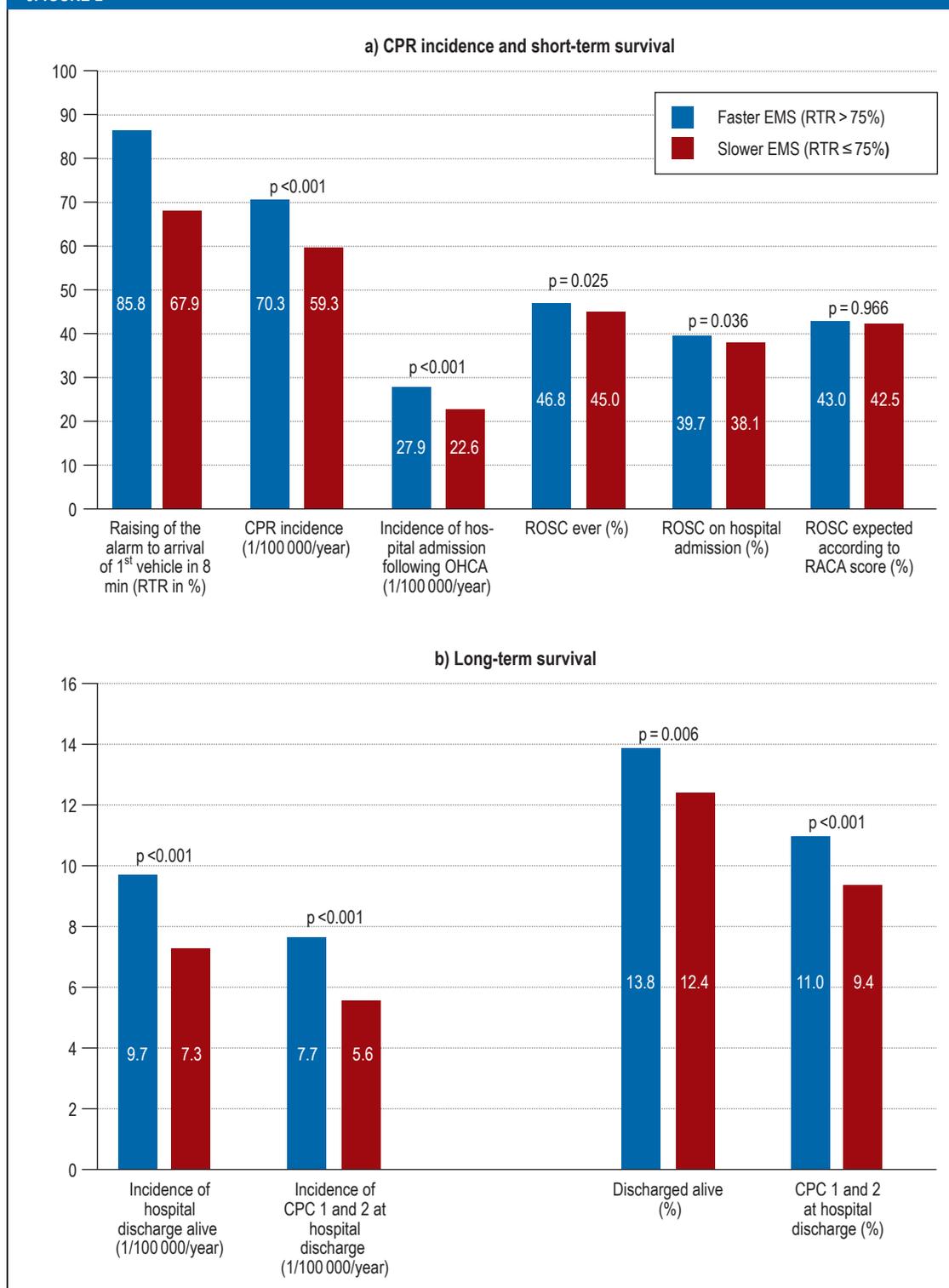
A shockable rhythm was found significantly more frequently on initial rhythm analysis in faster emergency medical services: S-EMS = 24.1 % versus F-EMS = 26.2 % (OR: 0.90 [0.84; 0.96]; $p = 0.002$); significantly more patients were defibrillated within 8 min: S-EMS = 27.9 % versus F-EMS = 33.7 % (OR: 0.76 [0.71; 0.81]; $p < 0.001$).



The number of patients that survive annually following resuscitation by EMS systems as a projection and simulation on the basis of the logistic regression model. At a measured hospital discharge rate of 13%, this means that 7091 patients survive per year in Germany. By reducing the individual ambulance response times by 10%, 20%, or 30%, the number of survivors increases annually by 370, 515, or 634 patients, respectively. If the rate of bystander CPR could be raised by 20 or 40 percentage points to 47% or 67%, an additional 245 or 426 patients could be saved every year. By simulating a 20% reduction in ambulance response time combined with an increase in the rate of bystander CPR to 47%, as many as 771 more patients/year could be saved, amounting to an annual total of 7862 patients saved in Germany by EMS systems following sudden OHCA and resuscitation.

ART, ambulance response time; CPR, cardiopulmonary resuscitation; EMS, emergency medical services; OHCA, out-of-hospital cardiac arrest; SIM, simulation

eFIGURE 2



The effect of ambulance response time at the EMS systems level on CPR incidence and resuscitation success in a comparison of 12 faster (9669 resuscitation patients) and 13 slower (7865 resuscitation patients) EMS systems. A faster EMS system reaches >75% of patients with the first vehicle within 8 min after raising of the alarm, a slower system reaches ≤ 75% of patients. The incidences and mortality were calculated as number/100 000 population/year; the percentages given relate to the number of resuscitation patients; statistical analysis was performed using the Chi² test; and statistical significance was set at p<0.05.

CPC, cerebral performance categories; CPR, cardiopulmonary resuscitation; EMS, emergency medical services; OHCA, out of hospital cardiac arrests; RACA, ROSC after cardiac arrest; ROSC, return of spontaneous circulation; RTR, response time reliability