Out-of-hospital circulatory arrest: factors determining the outcome Amsterdam resuscitation study (ARREST) 2 and 3
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Chapter 7
Survival models for out-of-hospital cardiopulmonary resuscitation from the perspectives of the bystander, the first responder, and the paramedic

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Survival from out-of-hospital resuscitation depends on the strength of each component of the chain of survival. We studied on the scene, witnessed, nontraumatic resuscitations of patients older than 17 years. The influence of the chain of survival, and potential predictors on survival were analyzed by logistic regression modeling. From 1030 patients, 139 survived to hospital discharge. Three prediction models of survival were developed from the perspective of the different contributors active in out-of-hospital resuscitation: model I, bystanders; model II, first responders; and model III, paramedics. Predictors for survival (with odds ratio) were: in model I (bystanders) emergency medical service (EMS) witnessed arrest (0.50), delay to basic cardiopulmonary resuscitation (CPR) (0.74/min) and delay to EMS arrival (0.87/min); in model II (first responders): initial recorded heart rhythm (0.02 for nonshockable rhythm), delay to basic CPR (0.71/min and 0.87/min for shockable and nonshockable rhythms) and to defibrillation (0.83/min), and in model III (paramedics): need for advanced CPR (4.74 for advanced CPR not-needed), initial recorded heart rhythm (0.05 for nonshockable rhythm), and delay to basic CPR (0.77/min and 0.72/min for shockable and nonshockable rhythms), to defibrillation and to advanced CPR for shockable rhythms (0.89/min, and to advanced CPR for nonshockable rhythms (0.85/min). The area under the receiver-operator characteristic curve for model I was 0.763; for model II 0.848 and for model III 0.896. Of survivors 50% had restoration of circulation without need for advanced CPR. Three survival models for witnessed nontraumatic out-of-hospital resuscitation based on the information known by bystanders, first responders and paramedics explained survival with increasing precision. Early defibrillation can restore circulation without the need for advanced CPR. When advanced CPR is needed, its delay leads to a markedly reduced survival.

1. Introduction

The ‘chain of survival’ concept is an excellent way to describe the sequence of resuscitation actions after an out-of-hospital cardiac arrest; the chain includes: early access, early basic cardiopulmonary resuscitation (CPR), early defibrillation, and early advanced CPR. The links of the chain of survival, and the role of the factor time have been qualitatively and quantitatively studied in regression models. These models express survival as an outcome parameter, which depended on the independent components of the chain. However, apparently independent factors such as observation of ventricular fibrillation as the initial rhythm, and the need for advanced CPR are interlinked with earlier components in the chain. Basic CPR can maintain ventricular fibrillation and delays the transition into asystole, whereas early defibrillation can restore the circulation in patients without the need for advanced CPR. Previous studies described resuscitations where the initial recorded rhythm was ventricular fibrillation. From the community perspective, a model limited to a subgroup that cannot be identified from the onset of the collapse is not adequate, when other rhythms or asystole are not included in the model.

Our study was initiated to assess the effects, on survival, of the components of out-of-hospital resuscitations with information known by each of the three contributors to the care: the bystanders who can perform basic CPR, the first responders who can perform defibrillation, and the paramedics who can perform advanced CPR. Data collection was carried out by specially trained research personnel at the scene during resuscitation to ensure accurate determination of all critical time intervals and recorded activities.
2. Patients and Methods

2.1. Emergency Medical Service system

The emergency medical service (EMS) for Amsterdam and the surrounding region is a one-tiered system, which serves 1.3 million inhabitants. The service can be called via the national emergency telephone number 112, which is connected to the regional dispatch centers. The Dutch ambulance teams are qualified to perform advanced CPR according to the guidelines of the European Resuscitation Council.9

2.2. Study design

Between 1 June 1995 and 1 August 1997, all consecutive out-of-hospital witnessed, nontraumatic cardiac arrests of patients over 17 years of age were recorded. All patients were followed up to hospital discharge or up to death. For the definitions of terms we used ‘the Utstein Recommendations’.9 Ethics committees of the participating hospitals approved the study. A subset of the data, limited to cardiac origin of the arrest but including un witnessed arrests have previously been published in Utstein style.10

2.3. Data collection and time analysis

Specially trained research personnel collected data on the scene of the cardiac arrest as has been described in more detail previously.14 Briefly, when the dispatcher processed a call of a suspected arrest, EMS and research personnel were simultaneously activated. All information from the family, bystanders and EMS personnel was collected, with particular attention to accurately estimating the time of collapse, and the moments that basic and advanced CPR were started. The defibrillator ‘power on’ time was taken as the moment of arrival of the EMS personnel at the patient’s side. The ‘initial rhythm’ was the first recorded rhythm after collapse. If that rhythm was ventricular fibrillation or ventricular tachycardia, treated with a defibrillatory shock, it was classified as a shockable initial rhythm. All other rhythms, asystole included, were considered nonshockable initial rhythms. The time of defibrillation was automatically recorded, other events were manually marked on the defibrillator. The first advanced CPR intervention was endotracheal intubation, or the first administration of drugs. The difference between time stamps of defibrillators and other clocks were corrected to the clock of the dispatch center.

Information on the cause of death of the patients or hospital survival was obtained from the hospital’s medical records.

2.4. Time interval and definitions

‘Time to call’ was defined as the interval between the estimated moment of the collapse and the moment that the call reached the dispatch center. Similarly, ‘time to basic CPR’, ‘time to EMS arrival’, ‘time to first defibrillatory shock’ and ‘time to advanced CPR’ were all defined as intervals starting at the moment of collapse. When a patient collapsed after the call but before arrival of the EMS personnel, this was coded as ‘call before collapse’, a collapse after their arrival was coded as ‘EMS witnessed arrests’. When no bystander performed CPR, ‘time to basic CPR’ was the time up to EMS initiated basic CPR. ‘Advanced CPR not performed’ was defined when advanced CPR efforts were needed, but not accomplished. If after defibrillation, stable circulation returned immediately before advanced CPR measures (including intubation or intravenous drugs) were applied, this was defined as ‘advanced CPR not needed’. Survival was defined as discharge alive from hospital.
2.5. Statistical methods

In univariate analysis of survival, all system characteristics were categorized in discrete intervals for the calculation of odds ratios (OR) with 95% confidence interval (CI). The characteristics of the chain of survival: ‘time to call’, ‘time to basic CPR’, ‘time to first defibrillatory shock’, ‘time to advanced CPR’ were fitted univariate in a logistic model describing survival by time (min).

In multivariate analysis of survival, three models were designed to describe all witnessed arrests from the perspective of three different contributors active in resuscitation: model I, bystanders; model II, first responders; and model III, paramedics.

Model I concerned variables known before rhythm diagnosis, therefore we evaluated ‘EMS witnessed arrests’, ‘call before collapse’, ‘time to call’, ‘time to basic CPR’ and ‘time from basic CPR to EMS arrival’.

Model II added variables known at the time of rhythm diagnosis and the first defibrillatory shock: ‘time to basic CPR’*‘shockable initial rhythm’, ‘time to basic CPR’*‘nonshockable initial rhythm’ and ‘time from basic CPR to the first defibrillatory shock’.

Model III added variables known at the time advanced CPR was considered: ‘advanced CPR not needed’, ‘advanced CPR not performed’, ‘time from basic CPR to start advanced CPR’ for patient with a nonshockable initial rhythm and ‘time from the first defibrillatory shock to start advanced CPR’.

The logistic modeling is described in more detail in the appendix A. For the final models we used stepwise elimination of potential predictors and interaction terms. Elimination was based on the significance of each variable in the model and the significance in change of the log-likelihood, both were tested with the chi-square statistic and p-value < 0.05. The predictive ability of the three models was assessed with, the area under the receiver-operator characteristic (AUC_{ROC}) curve. The probability of observed survival versus expected survival was analyzed according to the Hosmer-Lemeshow Goodness-of-Fit test.\textsuperscript{11}

All statistics were performed in JMP 3.2 and the ROC analysis in SPSS 6.1 for the Apple Macintosh.\textsuperscript{12,13}

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**Figure 1.** Template of 1285 out-of-hospital resuscitation attempts in the Amsterdam area recorded in 26 months. Bystander CPR were basic CPR efforts done by lay persons before EMS arrived. EMS is emergency medical service; CPR is cardiopulmonary resuscitation.
3. Results

3.1. Study population

In the study period, 1285 patients had a resuscitation attempt by EMS personnel after a cardiac arrest; 255 did not meet the study criteria (Figure 1). Median time between collapse and call, initiation of basic CPR, first defibrillatory shock and advanced CPR measures were 1, 2, 11 and 13 minutes, respectively. Of the 1030 studied patients, 324 (31%) survived up to the time of hospital admission; 185 of these 324 patients (62%) died in the hospital, 115 patients as a direct consequence of the circulatory arrest (ischemic encephalopathy, multiple organ failure); 65 patients died of the primary cause of the arrest and 5 patients died of another cause. Eventually, 139 patients (13%) were discharged alive from the hospital.

Table 1. Univariate analysis of predictors of the system characteristics categorized in discrete intervals: time (min) to call, basic CPR, first defibrillatory shock, and advanced CPR (n = 1030).

<table>
<thead>
<tr>
<th>Time to call</th>
<th>survival (%)</th>
<th>alive / total (n / n)</th>
<th>odds ratio (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>EMS witnessed arrests</td>
<td>32</td>
<td>51 / 157</td>
<td>3.27 (2.10 - 5.11)</td>
</tr>
<tr>
<td>Call before collapse</td>
<td>15</td>
<td>13 / 86</td>
<td>1.21 (0.63 - 2.34)</td>
</tr>
<tr>
<td>0-1</td>
<td>13</td>
<td>51 / 398</td>
<td>*</td>
</tr>
<tr>
<td>2</td>
<td>10</td>
<td>17 / 173</td>
<td>0.74 (0.41 - 1.32)</td>
</tr>
<tr>
<td>&gt;2</td>
<td>3</td>
<td>7 / 216</td>
<td>0.23 (0.10 - 0.51)</td>
</tr>
<tr>
<td>Time to basic CPR</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>0-3</td>
<td>22</td>
<td>110 / 511</td>
<td>*</td>
</tr>
<tr>
<td>4-7</td>
<td>10</td>
<td>16 / 155</td>
<td>0.42 (0.24 - 0.73)</td>
</tr>
<tr>
<td>8-11</td>
<td>6</td>
<td>11 / 200</td>
<td>0.21 (0.11 - 0.40)</td>
</tr>
<tr>
<td>&gt;11</td>
<td>1</td>
<td>2 / 164</td>
<td>0.05 (0.01 - 0.18)</td>
</tr>
<tr>
<td>Time to first defibrillatory shock</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>0-4</td>
<td>72</td>
<td>51 / 71</td>
<td>*</td>
</tr>
<tr>
<td>5-8</td>
<td>30</td>
<td>16 / 54</td>
<td>0.17 (0.08 - 0.36)</td>
</tr>
<tr>
<td>9-12</td>
<td>17</td>
<td>34 / 197</td>
<td>0.08 (0.04 - 0.15)</td>
</tr>
<tr>
<td>13-16</td>
<td>10</td>
<td>17 / 169</td>
<td>0.04 (0.02 - 0.09)</td>
</tr>
<tr>
<td>&gt;16</td>
<td>6</td>
<td>5 / 87</td>
<td>0.02 (0.01 - 0.07)</td>
</tr>
<tr>
<td>Nonshockable initial rhythm</td>
<td>4</td>
<td>16 / 452</td>
<td>0.01 (0.01 - 0.03)</td>
</tr>
<tr>
<td>Time to advanced CPR</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Not needed</td>
<td>84</td>
<td>70 / 83</td>
<td>19.0 (8.35 - 43.4)</td>
</tr>
<tr>
<td>0-4</td>
<td>22</td>
<td>15 / 68</td>
<td>*</td>
</tr>
<tr>
<td>5-8</td>
<td>8</td>
<td>4 / 50</td>
<td>0.31 (0.10 - 0.99)</td>
</tr>
<tr>
<td>9-12</td>
<td>8</td>
<td>12 / 152</td>
<td>0.30 (0.13 - 0.69)</td>
</tr>
<tr>
<td>13-16</td>
<td>10</td>
<td>25 / 258</td>
<td>0.38 (0.19 - 0.77)</td>
</tr>
<tr>
<td>&gt;16</td>
<td>3</td>
<td>12 / 382</td>
<td>0.11 (0.05 - 0.26)</td>
</tr>
<tr>
<td>Not performed</td>
<td>3</td>
<td>1 / 37</td>
<td>0.20 (0.01 - 0.78)</td>
</tr>
</tbody>
</table>

* reference group, CI is confidence interval, EMS is emergency medical service, CPR is cardiopulmonary resuscitation.
3.2. Univariant prediction of survival

The system characteristics in relation to survival are presented in Table 1. The odds ratio for survival decreased when the time between collapse and each factor increased of the 783 bystander witnessed arrests. The call for assistance was delayed more than 2 minutes in 36% of these cases, with detrimental outcome. In 55% of the bystander witnessed arrests a bystander performed CPR, resulting in a survival of 66/476 (14%) compared to a survival of 22/397 (6%) when no bystander CPR was performed (RR 2.5, 95%CI: 1.6-4.0). Patients who needed no advanced CPR had the best chance to survive (84%). Fifty-two percent of the patients that did not need advanced CPR were defibrillated within 4 minutes. When advanced CPR was needed but not performed, survival was comparable to that of patients with the longest delays in advanced CPR.

Figure 2 shows the estimated survival as function of the time between collapse and each component of the chain of survival: (A) call, (B) basic CPR, (C) defibrillation, and (D) advanced CPR in a logistic univariate model. Each shows a marked decrease in survival with longer time intervals.

![Figure 2](image-url)

*Figure 2. Univariate logistic regression panels of the four components represent the chain of survival. (A) the time to call, (B) the time to basic CPR, (C) the time to the first defibrillatory shock, and (D) the time to advanced CPR. The intercept with the Y-axis represented the calculated survival when the time to the activity was 0 minutes. Survival was reduced by 50% (arrows) for each when the interval to the initiation was 2, 4, 7 and 9 minutes, respectively.*
Table 2. Prediction of survival from out-of-hospital resuscitations, from the perspective of the bystander (model I), the first responder (model II) and the paramedic (model III), (n = 1030).

<table>
<thead>
<tr>
<th>Predictors</th>
<th>Estimate</th>
<th>OR (95% CI)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Model I</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Intercept</td>
<td>-0.04</td>
<td></td>
<td>0.913</td>
</tr>
<tr>
<td>EMS witnessed arrests*</td>
<td>-0.70</td>
<td>0.50 (0.24-1.02)</td>
<td>0.057</td>
</tr>
<tr>
<td>Time to basic CPR†</td>
<td>-0.30</td>
<td>0.74 (0.68-0.81)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Time from basic CPR to EMS arrival†</td>
<td>-0.14</td>
<td>0.87 (0.81-0.92)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td><strong>Model II</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Intercept</td>
<td>1.13</td>
<td></td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Shockable initial rhythm*</td>
<td>-0.34</td>
<td>0.71 (0.66-0.76)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>time to basic CPR†</td>
<td>-0.18</td>
<td>0.83 (0.79-0.88)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Nonshockable initial rhythm*</td>
<td>-3.89</td>
<td>0.02 (0.01-0.04)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>time to basic CPR†</td>
<td>-0.13</td>
<td>0.87 (0.77-0.99)</td>
<td>0.035</td>
</tr>
<tr>
<td><strong>Model III</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Intercept</td>
<td>-0.29</td>
<td></td>
<td>0.447</td>
</tr>
<tr>
<td>Advanced CPR and shockable initial rhythm*</td>
<td>-0.26</td>
<td>0.77 (0.70-0.84)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>time to basic CPR†</td>
<td>-0.12</td>
<td>0.89 (0.84-0.94)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>time from basic CPR to advanced CPR†</td>
<td>-2.97</td>
<td>0.05 (0.02-0.16)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Advanced CPR and nonshockable initial rhythm*</td>
<td>-0.33</td>
<td>0.72 (0.51-1.01)</td>
<td>0.054</td>
</tr>
<tr>
<td>time to basic CPR†</td>
<td>-0.17</td>
<td>0.85 (0.73-0.98)</td>
<td>0.029</td>
</tr>
<tr>
<td>time from basic CPR to advanced CPR†</td>
<td>1.56</td>
<td>4.74 (1.76-12.7)</td>
<td>0.002</td>
</tr>
</tbody>
</table>

* Binary predictor coded 0 or 1. No estimate if the opposite predictor is also analyzed in each model.
† Continuous predictor per minute delay.
Cl is confidence interval, EMS is emergency medical service, CPR is cardiopulmonary resuscitation.

3.3. Multivariate prediction of survival

For model I (bystanders), factors that were known to the bystander up to the arrival of a first responder, and are significant predictors of survival are presented in Table 2. Per minute delay of initiating basic CPR, the odds of survival decreased with a factor 0.74. When basic CPR was performed before arrival of EMS, the odds of survival decreased by a factor of 0.87 per minute (Figure 3A). When EMS witnessed the arrest, the estimated survival was 32%, lower than the intercept of model I which represents the model-derived arrival of EMS without delay, with an estimated survival of 49%. ‘Time to call’ and ‘call before collapse’ were not significant predictors.

For model II (first responders), significant predictors of survival, known to the first responder, are presented in Table 2. Survival declined faster before (OR 0.71 per minute) than after basic CPR was started (OR 0.83 per minute) (Figure 3B). ‘Time to call’, ‘call before collapse’ and ‘EMS witnessed arrests’ were no significant predictors.

For model III (paramedics), significant predictive factors, known after arrival of the paramedics, are presented in Table 2. When advanced CPR was not needed, because spontaneous circulation returned immediately after the first defibrillations, survival was 84%. In the best imaginable situation in cases in which advanced CPR was needed, the survival was 57% (Figure 3, intercept of C). A shockable initial rhythm was superior in survival over a
Figure 3. Calculated survival as function of time to: EMS arrival (A): model I; first defibrillatory shock (B): model II; advanced CPR in patients with a shockable initial rhythm (C): model III; advanced CPR in patients with a nonshockable initial rhythm (D): model III. (A) The rapid decrease in survival when basic CPR is not started (bold line) and the less rapid decrease when basic CPR is initiated after 0, 2, 4, 6, 8 minutes (thin lines). (B) The large difference in survival between shockable (plain lines) versus nonshockable initial rhythm (dashed line). Again, there is a more rapid decrease in survival before basic CPR is started (bold line) than after basic CPR is initiated (thin lines). (C) The interval from basic CPR to shock, and the interval from shock to advanced CPR had a similar regression coefficient, so both intervals are merged into one curve (thin lines). For patients with a nonshockable initial rhythm, the next event after basic CPR will be advanced CPR (D). CPR is cardiopulmonary resuscitation.

nonshockable initial rhythm (Figure 3C,D). In the patients with a shockable initial rhythm, and when advanced CPR was necessary, three different time intervals occurred: ‘time to basic CPR’, ‘time from basic CPR to shock’ and ‘time from shock to advanced CPR’. The latter two time intervals had similar significant estimates (0.11 and 0.13) in the model, and were therefore
merged into a common interval from basic CPR to advanced CPR. ‘Time to call’, ‘call before collapse’, ‘EMS witnessed arrest’ and ‘advanced CPR not performed’ were not significant predictors of survival.

3.4. Testing of survival models

The predictive abilities of the three models were compared by comparing the area under the ROC curve. For model I, the AUC\textsubscript{ROC} was 0.763; for model II 0.848 and for model III 0.896. The calculated expected survival for the three models, and the observed survival are shown in Figure 4.

![Hosmer-Lemeshow graphs for the three models, comparing explained and observed survival, categorized in deciles. The graphs show more differentiation and a wider range in the survival categories from model I to model II, and to model III with better estimates in low and high probability; this indicates an increase in predictive power.]

4. Discussion

The aim of our study was to design comprehensive survival models for out-of-hospital resuscitations. Besides this, new findings in this study were the many calls with long delays after collapse with associated poor outcome, the independent effect of a delayed start of basic CPR on survival, and the observation that half of the survivors had restoration of circulation without the need for any advanced CPR measures after defibrillation.

**Early call.**

Since delay is the most important determinant of survival of out-of-hospital resuscitation, this study demonstrates that the time interval between collapse and call should not be ignored but be stressed in public education. Univariately there was a strong relation between the delay of the call and survival. However ‘time to call’ disappears in the multivariate analysis, probably because it effects the delay to defibrillation and advanced CPR together. For an accurate estimation of survival timing should start at the moment of collapse and therefore not ignoring the ‘time to call’, as is also required in the Utstein system of reporting out-of-hospital arrest.

**EMS witnessed arrest.**

If EMS personnel witnessed the arrest, survival was worse than with the model-extrapolated situation where EMS personnel could start resuscitation within half a minute. Explanation for this
apparent contradiction is that patients with pre-arrest symptoms who call for an ambulance before the arrest differ from those who had a sudden arrest without premonitory symptoms. When the EMS witnessed the arrest, 63% of the patients had a nonshockable initial rhythm, whereas in bystanders witnessed arrest this was only 40% (p < 0.001, Figure 1).

*Early basic CPR.*

Model I demonstrates that the delay to start of basic CPR has a great impact on survival. A delay in basic CPR of more than 3 minutes already results in decrease in survival of about 50%. This delay is the result of confusion and anxiety of the witness, attempts to alert neighbors, family, or the general practitioner and the call to the dispatch center before basic CPR is started. Although some of this delay is unavoidable, basic CPR teaching should pay attention to this. Studies should not only mention the mere performance of basic CPR, but also the delay to start of basic CPR to allow meaningful comparison between studies.

*Early defibrillation.*

We found a sometimes prolonged time delay between defibrillation and the first advanced CPR intervention. This enabled us to design survival models as if there was a two tiered EMS system, describing first responder defibrillation before arrival of the second tier. The importance of first responder defibrillation is demonstrated by model II. In the most ideal circumstances, defibrillatory shocks are given immediately after onset of ventricular fibrillation; in this case the outcome approaches that of the coronary care unit setting. Even without basic CPR, survival is expected to be 60% if the defibrillatory shocks is delivered after only 2 minutes.

*Early advanced CPR.*

Model III includes advanced CPR as the last part of the chain of survival. Generally, this is already a late intervention, but delay in advanced CPR resulted in a further reduction of survival. Advanced CPR was not required if the earlier components in the chain were delivered early, and were good indicators of survival. In 8% of the resuscitations (14% of all shockable initial rhythms), the circulation was restored immediately after defibrillation without the need for advanced CPR. Fifty percent of the survivors belonged to this group, which underscores the value of semi-automatic defibrillators in the hands of lay persons and the strategy of placing semi-automatic defibrillators in airliners and other places where defibrillation cannot be followed by advanced CPR.15,16 In a recent report 6 of the 13 patients (55%) who were defibrillated on board of an aircraft survived to discharge, supporting our observation.17 Frequently, advanced CPR measures might be necessary to stabilize the circulation and possibly to assist in neurologic recuperation.

The models adequately explain hospital survival, although we only included indicators of the prehospital phase, while many patients died after hospital admission. Their death was nearly always due to resuscitation related factors and was seldom due to an unexpected pathological condition. This is in agreement with other studies.18,19

*Comparison with earlier models.*

Comparing our models with the full and simplified models of Valenzuela, demonstrates two main differences.6 The AUC and our estimates for time from collapse to basic CPR and to defibrillation are higher than of their models. Both suggest an increase of accuracy of critical time events in our study, explained by less attenuation and by the use of research personnel at the scene who collected data prospectively. Correcting time-stamped data for drift of clocks and with time data from various sources proved particularly necessary. Mean time difference between defibrillator clocks and standard time was 0 minutes but the 90% percentile varied from -3 to +2 minutes, with extremes -19 to +17 minutes, similar to results from a previous study.20 Another explanation may be the difference in the models themselves, in particular that
our models recognize the dependence of seemingly independent factors, such as basic CPR and the initial recorded rhythm and that we separately incorporate the factor advanced CPR. When applying a selection of our data, according to their inclusion criteria, we found that their simplified model was comparable to our model I. However, their full model overestimated the low survival probabilities and underestimated the high survival probabilities compared with our models II and III. A reason for this is that their model is designed only for patients in ventricular fibrillation and that our prediction models II and III already incorporate some ‘outcome’ variables as initial rhythm and the necessity for advanced CPR. This is also clear in the Hosmer-Lemeshow graphic where the discrimination between the low and high survival probabilities improved from model I to model III.

Study limitations.

Not all time events during resuscitation were recorded, therefore these had to be estimated. Especially the time from collapse to call is difficult to determine accurately. Specially trained research personnel on the scene, who could fully concentrate on reconstructing the sequence of activities and its delays, estimated critical time events without bias but with uncertain precision. Ignoring the time interval from collapse to call probably leads to more inaccuracy in the prediction of survival of an out-of-hospital resuscitation. Our models are derived from one set of observations and not separately validated. Applicability of the models to data from other EMS systems must be verified.

Acknowledgements

The authors appreciate the dedicated support of all participating research personnel, dispatchers, ambulance and emergency room personnel in the Amsterdam Dispatch region.

Appendix A

A.1. Basic properties of the linear logistic model

The linear logistic model relates a probability (P) for developing the outcome event to the value of a baseline characteristic (X) using the linear logistic function: \( P = \frac{1}{1 + \exp^{-a+bX}} \). In constructing a model, the first step is to translate the observed baseline characteristics into a set of statistical variables \( X_1, X_2, ..., X_n \), which can be used in the regression model. As an example, the presence of a nonshockable heart rhythm (a baseline characteristic with only two categories, present or absent) is represented by an indicator variable assuming the value 1 if the paramedic diagnoses a nonshockable heart rhythm upon arrival and 0 if a shockable heart rhythm is found. This variable actually 'indicates' the presence of a nonshockable initial heart rhythm.

All dichotomous variables (with one exception: 'Advanced CPR not needed') were coded in such a way that the value 1 was assigned to the state that is associated with an increased risk of death. The quantitative variable time delay, for instance time to first CPR, was used in the model with its numeric value. All candidate variables were entered in the model and step-by-step eliminated until none of the remaining variables satisfied the removal criterion (p-value > 0.15).

A.2. Prediction models and time of baseline

The choice of the baseline point in time is essential in the construction of a prediction model. All information available at baseline can and should be used when one predicts the future occurrence of clinical events. In principle, none of the clinical information that becomes available later on should be used. In our study we chose three different baselines. The models for each of the baselines have their own interpretation and application.
First, we chose the witnessed moment of collapse as baseline. As a consequence, we only used the clinical information that was (in principle) available to the witness and/or bystander on scene. In addition, we used process characteristics of the subsequent care given to the patient, such as time until start of basic CPR and time until the arrival of the EMS. For this model (model I), we considered the following variables: cardiac arrest witnessed by EMS personnel (yes/no), call to the EMS already made when the cardiac arrest occurred (yes/no), time elapsed between cardiac arrest and call to the EMS (minutes), time elapsed between cardiac arrest and start of (lay) basic CPR (minutes), time elapsed between (lay) basic CPR and arrival of the EMS. Some of the time intervals were manually set to 0. For instance, when the EMS was already at the scene when the cardiac arrest occurred, the time to basic CPR and the time between basic CPR and the arrival of the EMS were both set to 0. Similarly, when the call to the EMS had already been made when the cardiac arrest occurred, the time to call was set to 0.

Second, we chose the time of arrival of the first responder as baseline. Here the 'first responder' refers to EMS personnel after checking the patient's heart rhythm. Again, we used process characteristics of the care given to the patient, but this only relates to basic CPR and the defibrillating capacity of the EMS personnel. Thus, the model is equally applicable to the first responder using an automatic external defibrillator without further advanced CPR capabilities. For this model (model II), we tested all variables of the previous model and added the presence of a shockable heart rhythm (yes/no). The analysis indicated that the predictive power of the time elapsed between the cardiac arrest and the start of basic CPR was substantially different between patients with and those without a shockable heart rhythm. As a result a so-called interaction-term was introduced in the statistical model. The statistical interaction translates into two (instead of one) odds ratios in Table 2. The last variable we evaluated was the time elapsed between the start of (lay) basic CPR and the delivery of the first defibrillatory shock. This variable was set to 0 for patients with a nonshockable heart rhythm.

Third, we chose the time of the decision of advanced CPR as baseline. This model (III) predicts the patient's probability of survival from the perspective of the paramedic who can deliver advanced CPR, and included all information available to the paramedic when advanced CPR was considered. All variables of the previous model were also used in this model and we added the variable 'advanced CPR not needed' indicating the lack of necessity to perform advanced CPR (yes/no), in the event of return of spontaneous circulation and sufficient respiration before advanced CPR could be given. For patients initially with a shockable heart rhythm who needed advanced CPR, we evaluated the time elapsed between the first defibrillatory shock and the start of advanced CPR. For patients with initially a nonshockable heart rhythm, we evaluated the time elapsed between the start of basic CPR and the start of advanced CPR.

A.3. Epidemiologic meaning of the regression coefficients

The regression coefficients have a direct epidemiological meaning: each coefficient represents the logarithm of the odds ratio of survival when all other factors are controlled. Its antilogarithm is the odds ratio of survival. As an example, the regression coefficient in model II for 'nonshockable rhythm' is -3.89; its antilogarithm (e^{-3.89}) is 0.02. This means that the odds of survival is approximately one-fiftieth of that of a patient with a shockable heart rhythm. In model I, the coefficient for time to basic CPR is -0.30 and that for the time from basic CPR to the arrival of the EMS is -0.14. The antilogarithms are 0.74 and 0.87 respectively. This means that the odds of survival is multiplied with 0.74 for every minute delay in the start of basic CPR. In other words, the patient turns in 26% of his chances of survival for every minute delay in basic CPR. Every minute delay in the arrival of the EMS, after the commencement of (lay) basic CPR is 'penalized' with a decrease of 13% in the odds of survival.
The coding for the models I and II was such that an increase in the value was associated with an increased risk of death. For model III this was true only for patients who needed advanced CPR. The intercept represents the logarithm of the odds of survival when all co-variables are set to 0. In models I and II (and in model III for patients requiring advanced CPR) this represents the best achievable probability of survival, graphically shown at time 0.

References


