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Articles

Estimating Effectiveness of Cardiac Arrest Interventions

A Logistic Regression Survival Model

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Abstract

Background The study objective was to develop a simple, generalizable predictive model for survival after out-of-hospital cardiac arrest due to ventricular fibrillation.

Methods and Results Logistic regression analysis of two retrospective series (n=205 and n=1667, respectively) of out-of-hospital cardiac arrests was performed on data sets from a Southwestern city (population, 415 000; area, 406 km^2) and a Northwestern county (population, 1 038 000; area, 1399 km^2). Both are served by similar two-tiered emergency response systems. All arrests were witnessed and occurred before the arrival of emergency responders, and the initial cardiac rhythm observed was ventricular fibrillation. The main outcome measure was survival to hospital discharge. Patient age, initiation of CPR by bystanders, interval from collapse to CPR, interval from collapse to defibrillation, bystander CPR/collapse-to-CPR interval interaction, and collapse-to-CPR/collapse-to-defibrillation interval interaction were significantly associated with survival. There was not a significant difference between observed survival rates at the two sites after control for significant predictors. A simplified predictive model retaining only collapse to CPR and collapse to defibrillation intervals performed comparably to the more complicated explanatory model.

Conclusions The effectiveness of prehospital interventions for out-of-hospital cardiac arrest may be estimated from their influence on collapse to CPR and collapse to defibrillation intervals. A model derived from combined data from two geographically distinct populations did not identify site as a predictor of survival if clinically relevant predictor variables were controlled for. This model can be generalized to other US populations and used to project the local effectiveness of interventions to improve cardiac arrest survival.

Key Words:
- cardiopulmonary resuscitation
- death, sudden
- defibrillation
- survival

Survival rates after out-of-hospital cardiac arrest vary widely across the United States.[1] Although survival rates of 30% to 35% have been reported for those patients whose initial cardiac electrical rhythm is VF in a few locales, many jurisdictions, including the nation's largest metropolitan areas, report dismal survival for such patients.[2 3 4]

Factors associated with survival after out-of-hospital cardiac arrest have been described in the decades since Pantridge and Geddes[5] first reported the successful resuscitation of out-of-hospital victims of VF in Belfast, Northern Ireland. Initial cardiac rhythm, delay from collapse to initiation of manual CPR, and delay from collapse to electrical defibrillation have all been demonstrated to influence survival to hospital discharge in these patients.[6] Using data sets collected from two midsized urban areas located in the Pacific Northwest and southwestern US, we developed a simple, generalizable, predictive model of survival after out-of-hospital sudden cardiac arrest associated with VF. Use of this model allows the quantitative prediction of improved survival due to potential EMS interventions locally and nationally.

Methods

EMS Systems

The EMS systems of Tucson, Ariz (population, 415 000; area, 406 km^2) and King County, Washington (population, 1 038 000; area, 1399 km^2) are two-tiered. The first responding tier consists of firefighters trained to the basic EMT level. The second tier consists of paramedics.

Study Data

The Tucson data were collected from 1988 through 1993. An ongoing epidemiological survey of prehospital cardiac arrest undertaken jointly by the Tucson Fire Department and the University of Arizona College of Medicine identified 205 cases. The King County database was collected from 1976 through 1991. An ongoing epidemiological survey of prehospital cardiac arrest undertaken jointly by King County Department of Health and the University of Washington College of Medicine identified 1667 cases. At both sites, resuscitation was not attempted on patients found with rigor mortis, dependent lividity, decapitation, incineration, or other obvious evidence of irreversible death. Cases in which the cardiac arrest was the result of a suicide, drowning, electrocution, hanging, suffocation, known terminal illness, drug overdose, or sudden infant death syndrome were not considered. Details on the collection of data at each site have been reported.[7 8]

Time-of-Collapse and Collapse-to-Event Intervals

In Tucson, the time of patient collapse was determined by telephone interview of witnesses to the arrest. Collapse-to-event intervals were calculated through the use of paramedic monitor-defibrillator units (Lifepak 5, Physio-control Corp) equipped with event documentation units (ECG/voice recorder, model 8101595-00, Physio-control Corp). These units recorded in real time the cardiac rhythm and surrounding audible events during each arrest. Arrest recordings were reviewed with an automated playback/reporting system (ECG/voice translator, model 8904782-00, Physio-Control Corp). Software in the playback device, if programmed with the clock time of any event in the record, established the clock time of other events occurring on the taped record. Dispatcher time checks were audible on all tapes, allowing accurate timing of events during the arrest.

In King County, the time of collapse was extracted from dispatcher recordings and paramedic on-scene reports. Collapse-to-event intervals were established as follows: the time interval to bystander-initiated CPR was taken from interviews with the bystander or from the incident report prepared by EMS personnel; the time interval to EMS-initiated CPR was estimated from the EMS response interval plus 1 minute (the time needed for EMTs or paramedics to arrive at the scene, reach the patient's side, and position the patient). The time interval needed for EMTs or paramedics to attach the defibrillator and clear the patient for defibrillation once CPR was in progress was estimated to be 2 minutes past EMT arrival or 1 minute past time of initiation of CPR by EMTs. These intervals to interventions are the best estimates of EMTs, paramedics, and EMS medical directors in King County. The study was approved by the human subjects committee of the University of Arizona College of Medicine. In King County, the County Department of Health has statutory authority to collect and analyze cardiac arrest data as part of its public health quality assurance responsibilities.

Case and Survival Definitions

All subjects were at least 18 years of age. Collapse was witnessed, and the initial cardiac rhythm was VF. Survival in each population was defined as discharge alive from hospital and was determined by review of hospital medical records.

Statistical Methods

Descriptive statistics such as proportions, means, and SDs were used to summarize the results for Tucson and King County. Differences between the two sites were tested with a Wilcoxon rank-sum test (continuous variables) or a χ^2 test (categorical variables).

Models relating patient survival (yes/no) to the independent predictors were developed by logistic regression. Predictor variables included age, sex, bystander-initiated CPR (yes/no), I_{CPR}, and I_{defib}. A logistic regression model for the Tucson data was first developed. Variables in the final model were selected with a step-down procedure; the decision to remove terms was based on a likelihood-ratio test. All potential predictors were first included in the "full" model, then predictors were sequentially removed if their removal did not result in a significant change in the log-likelihood. After selection of the best intermediate model including main effects only, interaction terms were included in the full model; a step-down procedure was again used to determine whether sequential removal of the interaction terms resulted in a significant change in the log-likelihood.[9] The overall predictive ability of the final model was assessed by use of the area under the ROC curve. The sensitivity and specificity of this model in predicting survival were calculated. Next, the Tucson logistic regression model was used to predict the King County results. Finally, a model using data from both sites was developed by use of the logistic regression procedure outlined above, and its sensitivity and specificity were calculated. A graphical display of the observed versus expected probability of survival was computed on the basis of the Hosmer-Lemeshow Goodness-of-Fit Test.[9] All analyses were performed with STATA 5.0 (Stata Corp).

Results

Cardiac Arrest in the Study Communities

Characteristics of all adult cardiac arrests in the study communities are described in Table 1⇓. There were 665 cases of cardiac arrest from Tucson and 7635 from King County. Collapse was witnessed in 63% of Tucson cases and 55% of King County cases. The proportions of bystander CPR were 33% and 46%, respectively. In Tucson, VF was the initial detected cardiac rhythm in 348 of 665 patients (52%). Cases of initial VF accounted for 41 of 46 survivors to hospital discharge (89%). In King County, Washington, there were 7635 cardiac arrests in adults. Of these, VF was the initial detected cardiac rhythm in 3138 of 7565 patients (41%). Cases of initial VF accounted for 852 of 1086 survivors to hospital discharge (78%). The study data sets were derived from these two populations of adult cardiac arrest.

Table 1.

Characteristics of Cardiac Arrest in Study Communities

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Tucson

A summary of the demographic characteristics and collapse-to-event intervals is shown in Table 2⇓. Of the 205 patients, 36 (18%) survived to discharge. Patients were predominantly male (72%), with a mean age of 66 years. The mean I_{CPR} was 4.7 minutes, and the mean I_{defib} was 9.5 minutes. Bystander-initiated CPR was performed in 43% of the cases. When performed by bystanders, the mean I_{CPR} was 1.9 minutes (see Table 2⇓).

Table 2.

Demographics of Cardiac Arrest in Study Communities

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The logistic regression model included age, sex, bystander-initiated CPR, I_{CPR}, and I_{defib} as potential predictors. Stepping down from this full model resulted in the sequential removal of sex (P=.995) and age (P=.103). Inclusion of potential two-way interaction terms suggested that the interaction between I_{CPR} and I_{defib} was significant (P=.002) but that bystander-initiated CPR (P=.182) and all other interaction terms were not significant (P>.50). The final model therefore included I_{CPR}, I_{defib}, and their interaction. The coefficients of this final model are shown in Table 3⇓. The area under the ROC curve for the model was 0.783. The significant interaction between I_{CPR} and I_{defib} can best be illustrated by considering two categories of I_{CPR} (those with I_{CPR} <5 minutes versus those with I_{CPR} >5 minutes) and I_{defib} (those with I_{defib} <10 minutes versus those with I_{defib} >10 minutes);

these categories were chosen arbitrarily (see Table 4⇓). As shown in Table 4⇓, the presence of both a longer I_{CPR} and a longer I_{defib} results in significantly poorer survival.

Table 3.

Logistic Regression Coefficients for Tucson Data Set (n=205)

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Table 4.

Combined Effect of CPR Delay and Defibrillation Delay on Survival

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Although individual prediction of which patients would survive to discharge was not a primary goal of the study, we computed the sensitivity and specificity of the logistic regression model. To ensure at least 80% sensitivity, a predicted probability cutpoint of 0.24 was required (ie, if the predicted probability of survival was ≥0.24, the patient was classified as positive, but if the predicted probability of survival was <0.24, the patient was classified as negative). This cutpoint resulted in a sensitivity of 80.6% (29 of 36 survivors correctly classified), with a specificity of 63.9% (108 of 169 nonsurvivors correctly classified). It was not possible to define a cutpoint that would lead to >80% sensitivity and >80% specificity.

King County

A summary of the demographic characteristics and collapse-to-event intervals is contained in Table 2⇑. Of the 1667 patients, 542 (33%) survived to discharge. Again, they were predominantly male (80%), with a mean age of 64 years. The mean I_{CPR} was 3.4 minutes and the mean I_{defib} 5.1 minutes. Bystander-initiated CPR was performed in 57% of the patients; the mean collapse-to-initiation of bystander CPR interval in these cases was 2.1 minutes (see Table 2⇑).

Table 2⇑ also compares the Tucson and King County patients. Significantly more patients survived in King County than in Tucson (33% versus 18%; P=.0001). More of the King County patients were male (80% versus 72%; P=.0143), and they were slightly younger (mean age, 64 versus 66 years; P=.0408). A significantly greater proportion of the King County patients had bystander-initiated CPR (57% versus 43%; P<.0001). Although there were highly significant differences in the mean I_{CPR} (3.4 versus 4.7 minutes; P<.0001) and mean I_{defib} (5.1 versus 9.5 minutes; P<.0001), there was not a statistically significant difference in the mean collapse-to-bystander-initiated-CPR interval (2.1 versus 1.9 minutes; P=.74).

The logistic regression model developed from the Tucson database included I_{CPR}, I_{defib}, and their interaction (Table 3⇑). One method of validating this model is to determine its sensitivity and specificity for the King County patients. Using the same predicted probability cutpoint (0.24) resulted in a sensitivity of 63% (342 of 542 survivors), with a specificity of 40% (455 of 1125 nonsurvivors). As expected, due to the differences in the proportions surviving, I_{CPR}, and I_{defib}, both the sensitivity and specificity were lower than those observed for the Tucson patients (81% and 64%, respectively). The area under the ROC curve for application of the Tucson model to King County was 0.5410, again indicating poorer predictive ability.

Tucson and King County

A logistic regression model was fitted to the combined data (n=1872) to determine the factors that significantly predict survival. The logistic regression model included site (1=Tucson, 0=King County), age, sex, bystander-initiated CPR, I_{CPR}, and I_{defib} as potential predictors. Stepping down from this full model resulted in the sequential removal of sex (P=.850) and site (P=.456). The remaining main effects were all significantly related to survival (age, P=.0003; bystander-initiated CPR, P=.0236; I_{CPR}, P<.0001; I_{defib}, P<.0001). Thus, there was no significant difference between the Tucson and King County results after adjustment for differences in age, bystander-initiated CPR, I_{CPR}, and I_{defib}. After assessment of potential interaction terms, the final model included age, bystander-initiated CPR, I_{CPR}, I_{defib}, bystander CPR/I_{CPR} interaction (P=.0359), and I_{CPR}/I_{defib} interaction (P=.0013). The coefficients for this final model are shown in Table 5⇓. The area under the ROC curve was 0.664. The interaction between I_{CPR} and I_{defib} is again best illustrated by the categories defined previously as shown in Table 4⇑. Again, the presence of both a longer I_{CPR} and a longer I_{defib} led to significantly poorer survival. The interaction between bystander-initiated CPR and I_{CPR} was a result of much better survival in those patients receiving bystander-initiated CPR with a longer (>5 minutes) I_{CPR}. For these subjects, 25% of those with bystander-initiated CPR survived versus 15% in those without bystander-initiated CPR. For those who received CPR initiated in <5 minutes, there was little difference in survival between those with and without bystander-initiated CPR (36% survival in those with bystander-initiated CPR versus 35% in those without bystander-initiated CPR).

Table 5.

Simplified and Explanatory Logistic Regression Survival Models for Combined Tucson and King County Data Sets (n=1872)

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To ensure at least 80% sensitivity of the combined model, a predicted probability cutpoint of 0.27 was required. This cutpoint resulted in a sensitivity of 82% (476 of 578 survivors correctly classified), with a specificity of 41% (532 of 1294 nonsurvivors correctly classified).

In the final model, six factors were associated with survival: age, bystander-initiated CPR, I_{CPR}, I_{defib}, and the interaction terms $I_{CPR} \times I_{defib}$ and $I_{CPR} \times$bystander CPR. However, the inclusion of the terms age, bystander-initiated CPR, and the interaction terms $I_{CPR} \times I_{defib}$ and $I_{CPR} \times$bystander CPR, although statistically significant, yielded a more complicated model for prediction purposes. A simplified model that included only I_{CPR} and I_{defib} resulted in only a slight decrease in predictive ability, as measured by the area under the ROC curve (see Fig 1⇓). The area under the ROC curve was 0.650 for the simplified model versus 0.664 for the explanatory model. The coefficients of this simplified model are shown in Table 5⇑. A plot of the observed versus expected survival based on the simplified model is shown in Fig 2⇓. The model overestimates survival for the smallest category of predicted probability but performs reasonably well for other categories.

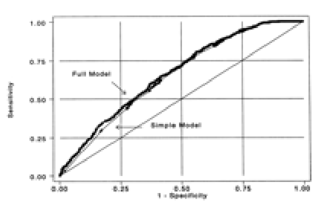

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Figure 1.

Cardiac arrest survival models: predictive performance. ROC curves are shown for full (includes all predictors and interactions significantly associated with survival) and simplified (contains only collapse to CPR and collapse to defibrillation) logistic regression survival models derived from combined King County, Washington, and Tucson, Ariz, cases of out-of-hospital, witnessed VF.

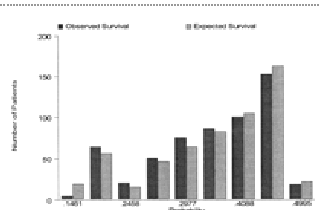

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Figure 2.

Graphical representation of observed vs expected survival based on the simplified predictive model (includes collapse to CPR and collapse to defibrillation intervals only).

Discussion

We chose to limit our model to cardiac arrests due to VF because these cases account for 40% to 50% of all out-of-hospital cardiac arrests and for the vast majority of cases in which the victim survives to hospital discharge.[10] The analysis was further limited to patients whose collapse was witnessed, because only in such cases is some estimate of the interval of brain and cardiac ischemia possible. The interventions that affect survival, manual external CPR and electrical defibrillation, are well described and have changed little since the 1970s. At present, attempts to improve survival rates of necessity focus on the availability and timing of these two interventions.

One of us (M.P.L.) previously reported a similar linear regression model[8] based on collapse-to-CPR interval and collapse-to-defibrillation interval. However, logistic regression, the technique used in the present study, is more appropriate for use in predictive models when the outcome is dichotomous. In particular, at extreme values, linear regression can predict probabilities of survival >1 or <0, predictions that are obviously impossible. This limitation does not occur in logistic regression, which therefore yields models with greater face validity.

An important and new finding of the present study is the demonstration that valid predictions are made by a single model for two distinct populations. After control for bystander CPR, age, delay to CPR, delay to defibrillation, and interactions, there was no difference in the survival modeling of the two populations. However, Tucson, Ariz, and King County, Washington, differ demographically (eg, the proportion of the general population of Hispanic background is 29% in Tucson versus 3% in King County[11]) as well as in climate and geography. The rejection of site as a predictor during regression analysis is strong evidence that the model may be generalized from Tucson and King County to other jurisdictions in the United States.

We propose that a simplified model derived from data combined from the two sites and containing only the predictors collapse to CPR and collapse to defibrillation is useful for projecting the magnitude of changes in survival resulting from potential interventions to improve the accessibility and promptness of CPR and electrical defibrillation in out-of-hospital cardiac arrest due to VF. Graphical representation of this model vividly demonstrates several important features of cardiac arrest due to VF (see Fig 3⇓). The delay to CPR and delay to defibrillation are both critical to patient survival. For every minute of delay from collapse to CPR or defibrillation, death is 1.1 times more likely. Moreover, there is a window of opportunity imposed by both interventions. Delay of CPR for >10 minutes renders defibrillation ineffectual; similarly, delay of defibrillation >10 minutes largely eliminates the benefit of prompt CPR. The shape of the curves corresponding to incremental delays from collapse to CPR illustrates that the rate of decline in probability of survival with time is not constant; rather, the rate of change is greatest early in the course of the arrest.

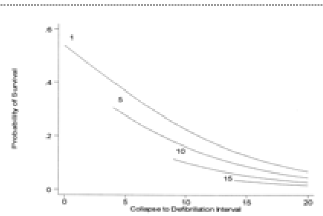

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Figure 3.

Relation of collapse to CPR and defibrillation to survival: simplified model. Graphical representation of simplified (includes collapse to CPR and collapse to defibrillation only) predictive model of survival after witnessed, out-of-hospital cardiac arrest due to VF. Each curve represents change in probability of survival as delay (minutes) to defibrillation increases for a given collapse-to-CPR interval (minutes).

The utility of the model may be limited by persistent variation in reporting of predictive time intervals in out-of-hospital cardiac arrest. The two time intervals modeled by us, collapse to CPR and collapse to defibrillation, were selected because they best represent the “ischemic interval,” the period during which blood flow and oxygen delivery to the heart are compromised.[12] The Utstein consensus conference, convened to promote standardization of reporting in cardiac arrest, defined time of collapse as a "core" time point; its collection is necessary for the approximation of the ischemic interval.[13] However, major case series[2 3 4 14] as well as smaller studies[15] reported since recommendation of the Utstein style have not attempted to establish time of collapse or use it for the calculation of the ischemic interval in cardiac arrest. Reports that do not estimate the time of collapse and, hence, the ischemic interval do not follow the Utstein consensus recommendations. Alternatives to collapse-to-event intervals have been proposed and used since the promulgation of the Utstein style, but these alternative reporting schemes complicate comparisons among EMS systems.

New initiatives are currently under consideration for improving survival after out-of-hospital cardiac arrest.[16] Among these is the training and equipping of nontraditional emergency responders with a new generation of simplified automatic external defibrillators. Any such public health effort must survive the intense scrutiny and economic analysis that is part of a medical care system perceived to be resource constrained.[17] Necessary to such analysis is the quantification of potential benefit, eg, additional lives saved or additional years of life saved, of any potential intervention. Use of this model allows policy makers to project the likely number of additional lives saved from out-of-hospital VF resulting from such interventions. In combination with EMS system-specific implementation cost data, the number of dollars necessary to save an additional life and additional year of life may be calculated. In this way, initiatives such as wider dissemination of automatic external defibrillation may be compared with alternative resource uses. Moreover, the predictions of the model, derived only from witnessed VF, will likely be underestimates, because some cases of unwitnessed VF as well as other dysrhythmias will respond to earlier cardioversion.

Our results reemphasize the importance of both early CPR and early defibrillation to improved survival after out-of-hospital cardiac arrest due to VF. Communities emphasizing either CPR or defibrillation to the exclusion of the other probably will be disappointed by the results of their attempts to improve survival.[18] The models presented use predictors that are physiologically appropriate, feasible to collect, and strongly correlated with survival rate. Use of this model in combination with survival analysis of patients discharged from hospital[19 20] permits robust economic analysis of alternatives to improve the chances of the cardiac arrest victim.

Selected Abbreviations and Acronyms

CPR	=cardiopulmonary resuscitation
EMS	=emergency medical services
EMT	=Emergency Medical Technician
I_{CPR}	=interval from collapse to manual CPR initiation, min
I_{defib}	=interval from collapse to electrical defibrillation initiation, min
ROC	=receiver-operating characteristic
VF	=ventricular fibrillation

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