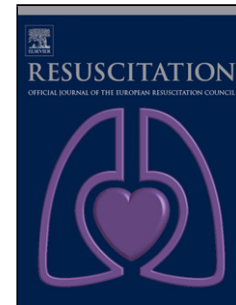


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**Title:** Out-of-hospital cardiac arrest survival in international airports

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## Abstract

### Background

The highest achievable survival rate following out-of-hospital cardiac arrest is unknown. Data from airports serving international destinations (international airports)

provide the opportunity to evaluate the success of pre-hospital resuscitation in a relatively controlled but real-life environment.

## Methods

This retrospective cohort study included all cases of out-of-hospital cardiac arrest at international airports with resuscitation attempted between January 1<sup>st</sup>, 2013 and December 31<sup>st</sup>, 2015. Crude incidence, patient, event characteristics and survival to hospital discharge/survival to 30 days (survival) were calculated. Mixed effect logistic regression analyses were performed to identify predictors of survival. Variability in survival between airports/countries was quantified using the median odds ratio.

## Results

There were 800 cases identified, with an average of 40 per airport. Incidence was 0.024/100,000 passengers per year. Percentage survival for all patients was 32%, and 58% for patients with an initial shockable heart rhythm.

In adjusted analyses, initial shockable heart rhythm was the strongest predictor of survival (odds ratio, 36.7; 95% confidence interval [CI], 15.5 to 87.0). In the bystander-witnessed subgroup, delivery of a defibrillation shock by a bystander was a strong predictor of survival (odds ratio 4.8; 95% CI, 3.0 to 7.8). Grouping of cases was significant at country level and survival varied between countries.

## Conclusions

In international airports, there was 32% of patients survived an out-of-hospital cardiac arrest, substantially more than in the general population. Our analysis suggested similarity between airports within countries, but differences between countries.

Systematic data collection and reporting is essential to ensure international airports continually maximise activities to increase survival.

**Keywords: out-of-hospital cardiac arrest resuscitation international epidemiology survival**

## **Introduction**

The purpose of pre-hospital resuscitation systems is to optimise survival from out-of-hospital cardiac arrest (OHCA) by implementing the Chain of Survival [1]. The first three links in the Chain – early recognition and call for help; immediate cardiopulmonary resuscitation (CPR); early defibrillation – must all be initiated immediately and effectively in the pre-hospital environment. Due to the variability in reported survival worldwide, a key question for policy makers and health care providers is, in an ‘ideal world’, what is the best survival from OHCA that can be achieved?

In 2015, the Cardiac Arrest Registry to Enhance Survival (CARES) in the United States collected data from 12 state-based registries and 50 community sites. It was estimated that the incidence of non-traumatic OHCA with resuscitation attempted was 57 per 100,000 population, with survival to discharge of 11% [2]. In a one-month survey during October 2014, OHCA incidence across 27 European countries with resuscitation attempted ranged from 19 to 104 cases per 100,000 population with an average survival of 10% for at least 30 days or to hospital discharge [3]. In airports serving international destinations (international airports) however, where the incidence of OHCA is low compared to passenger throughput, the proportion of survival is much higher than in the general OHCA population [4-6]. International airports are unique environments. They are constructed similarly, are geographically discrete from the surrounding environs, and have a high public footfall. Under international aviation law, international airports are required to have on-site police, fire and rescue services [7]. In an airport, it may be assumed that the majority of people who suffer OHCA believed themselves to be fit enough to go to work or to travel on that day. International airports therefore can be considered a natural laboratory to evaluate how successful pre-hospital resuscitation is in a relatively controlled real life situation.

The primary aim of this study was to determine survival from OHCA at international airports with resuscitation attempted. The study also aimed to estimate the incidence of OHCA at international airports and to identify the impact of known predictors of OHCA survival.

## Methods

This was a retrospective cohort study of all cases of OHCA at international airports with resuscitation attempted over a 3-year period from the 1st of January 2013 to the 31st of December 2015. Thirty-four countries were requested to provide data. In 32 countries, data was requested by contacting individuals who had previously published using OHCA registry data in that country. These individuals then advised on the appropriate contact for international airport data in their country, or personally assisted with the provision of data, in line with ethical and data protection requirements in their jurisdiction. In 2 countries, OHCA data collection from international airports was not established, and therefore direct contact with international airports in both countries was attempted. Between October 2016 and February 2017 attempts were made to engage non-responding countries, using either repeat emails or by pursuing alternative contacts.

Data requested included patient age and gender; witnessed status (not witnessed/ bystander/ emergency medical services (EMS)); initial arrest rhythm (asystole/pulseless electrical activity/shockable/ unspecified nonshockable); CPR before EMS arrival (bystander CPR) (yes/ no); shock delivered using an automated external defibrillator (AED) before EMS arrival (bystander AED defibrillation attempted) (yes/ no); interval in minutes from emergency call to emergency medical service arrival (EMS call-response interval); survival to hospital discharge (yes/no). Participating countries were also requested to provide data on the passenger throughput of each international airport for each year of data provided. Country data was obtained based on the agreement that no airport or individual country was identified during the analysis or in the study results.

Overall crude incidence of OHCA with resuscitation attempted per 100,000 passengers per year was calculated and descriptive analyses of patients, event characteristics and outcome were performed. Survival to hospital discharge or survival at 30 days (survival) was calculated for the study population and for subgroups of each categorical variable.

Mixed effect logistic regression analyses were performed to identify predictors of survival. Predictors of survival were estimated for the entire study population.

In order to assess whether there was grouping of variables at airport and/or country level, null/empty single (patient level only), 2-level (patient and airport level; patient and country level) and 3-level (patient, airport and country level) logistic regression models for survival were compared using the likelihood ratio test, plots of random effects and the effect on resulting odds ratios (ORs) [8]. Plots of random effects were used to allow interpretation of differences in the mean residual effect or area (airport or country) level variance in survival before any predictor variables are added to the model [9]. Due to multicollinearity, separate estimates of regression coefficients for survival were calculated for each known predictor of survival, with each model adjusted to account for patient age and gender, resulting in 6 final models. Coefficients were transformed into ORs to aid interpretation. To quantify the variability between airports/countries in survival after OHCA, a median odds ratio was calculated using Larsen's mOR [10]. A mOR equal to one signifies no differences between airports/countries in the probability of survival from OHCA. As mOR is a measure of random effects, a Bayesian credible interval (crI) was calculated based on the distribution of the mOR to distinguish it from a fixed effects OR confidence interval (MLWiN version 2.35). Model fit was assessed using the deviance information criterion (DIC). A lower DIC suggested a better model fit, and a difference of less than 5 in model DIC is not considered sufficient to distinguish between two models [11].

The study was approved by the Research Ethics Committee of the National University of Ireland Galway (Ref: 16-Sep-18). Informed consent was not required as non-identifiable data was used. The corresponding author had full access to all the data in the study and takes responsibility for its integrity and the data analysis.

## Results

Data on 800 OHCA cases with resuscitation attempted were received from 70 airports in 9 countries. Data were requested from 34 countries in all: 2 were unable to participate due to data protection restrictions; 9 did not participate because data were unavailable or insufficiently comprehensive; 14 countries did not respond. Data for the full study period (1<sup>st</sup> January 2013 and 31<sup>st</sup> December 2015) were available from 64 airport sites. Three sites provided data for 2013 and 2014, and the remaining 3 provided data for 2015 only.

A total of 32% of all patients survived to hospital discharge. The frequency of events across airports ranged from 1 to 72, with an average number of 41 cases per airport over the three year period (standard deviation, 19). The total denominator population was 3.3 billion passengers and the incidence of OHCA in airports with resuscitation attempted was 0.024/100,000 passengers per year.

Patients were predominantly male (Table 1). There was no difference in the average age of men and women (62.5 vs. 62.3 years respectively). Forty-two percent of patients had a shockable rhythm at the time of initial rhythm analysis. The majority of patients suffered a bystander-witnessed arrest (74%), and the majority of these patients had bystander CPR performed (77%). A significantly higher proportion of males had bystander AED defibrillation attempted compared to females (35% vs. 22%). Median EMS call-response interval was 8 minutes, and 34% of patients received an EMS response in 5 minutes or less. Proportionate survival was significantly higher for patients who had bystander AED defibrillation attempted. The proportion of survivors was greater for males than females and also for patients who received an EMS response in 5 minutes or less, but this difference was not significant. There was a high proportion of survival in the unspecified nonshockable subgroup (27%). Patients who had a witnessed and initially shockable event had the highest proportion of survival (58%). A similar proportion of patients survived in the bystander-witnessed and EMS-witnessed group. Percentage missing data was below 10% for all variables except bystander AED defibrillation attempted (20%) and EMS call-response interval (24%).

The likelihood ratio test suggested that there was variable grouping at both airport and country level. When compared to the 2-level patient and country-only model however, the use of the 3-level model (patient, airport and country) did not alter the mOR for country or the individual ORs for the predictor variables, suggesting that most of the group-level variability was at country level. Caterpillar plots of random effects at airport level and country level confirmed that most of the group-level variation observed was accounted for by country, with only one airport having a 95% confidence interval for residual effect that was significant (Figures 1a&b). For this reason the less complex 2-level model was used to account for country-level grouping.

Table 2 presents the mixed effect logistic regression models for each predictor variable. Male gender was a significant predictor of survival, while patient age showed no association (Model 1). All initial heart rhythms were strongly predictive of survival when compared to asystole, including the unspecified nonshockable category (Model 2). When compared to non-witnessed status, bystander witnessed and EMS witnessed status were similarly predictive of survival (Model 3). In the bystander-witnessed subgroup, bystander CPR did not influence patient survival however attempted bystander AED defibrillation was a strong predictor of survival (Models 4&5). In the subgroup of patients who did not have an EMS-witnessed collapse, EMS call-response interval was not associated with improved survival (Model 6). Addition of predictor variables significantly improved fit for all models.

The cluster effect or country level variance is presented as mOR and the higher the mOR the more pronounced the difference between countries. The lowest mOR for country level effect was 1.6 in the model with initial heart rhythm, and the highest mOR was 3.0 in the model with bystander AED defibrillation attempted.

## Discussion

To the best of our knowledge, the proportion of OHCA survival observed in our study is among the highest achieved for any location worldwide. Systematic OHCA data collection and reporting in international airports can identify strengths and weaknesses in pre-hospital resuscitation interventions. These could then be acted

upon as part of continual quality improvement in individual airports to sustain and maybe even increase overall airport OHCA survival rates.

In international airports, the incidence of OHCA in relation to the passenger throughput is low, but the frequency of events is relatively high. In a state-wide study in Arizona over a 3-year period, Moon et al identified the ‘top’ location types of OHCA incidents [12]. These included 65 events across all public business/office/workplaces; 43 events across all outdoor recreation facilities and 39 events across all Arizona’s stores and malls. This compares to an average of 41 cases per airport across a 3-year period in our study. The population in an international airport is mobile and relatively healthy compared to the general population and a collapse is more likely to be observed by staff or a member of the public. The majority of events had the characteristics that determine survival: predominantly witnessed; a high proportion of initial shockable rhythms; a high proportion of bystander CPR and attempted bystander AED defibrillation.

Registries with nationwide coverage have reported OHCA survival of 5% in Japan, 6% in Ireland and 7% in England. After decades of quality improvement initiatives, survival in Denmark and Sweden has reached 11% and 14% in Norway [13-18]. The large scale, collaborative databases of CARES, and the Resuscitation Outcomes Consortium of North America (ROC) reported overall survival to discharge of 11% for non-traumatic OHCA in 2015 and 10% for 2010 respectively [19, 20]. Almost one in three patients who had an OHCA in international airports survived to hospital discharge, which is substantially better than in the general population. Despite the advantages of the airport environment however, the survival observed in our study has been equalled and bettered. For example, in 2002, Caffrey et al observed an overall survival of 61% in the witnessed shockable subgroup, suggesting that there is potential for even higher survival in the airport environment [21]. In the city of Rotterdam in the Netherlands, survival of 31% was reported between 1988 and 1994 [22]. In a study where security officers in US casinos were trained in both CPR and AED use, overall OHCA survival of 38% was achieved [23]. In the casino study, 59% of patients who had a witnessed and initially shockable arrest survived. In our study, more than 20 years later, survival for the same subgroup was almost identical (59% vs. 58%).

As shown in Figures 1&2 and in the calculation of mORs, our analysis showed the importance of clustering of data at the country level over airport level. This suggests similarity between airports within countries, but differences between countries that can be considered substantial. To interpret the mORs it can be imagined that if a person having an OHCA in an airport in one country were to have had their OHCA at an airport in another country with higher probability of survival (independent of individual factors), their chance of survival will (in median) increase 1.6 to 3.0 times [9]. This finding invites further research and data collection on country/airport level characteristics to understand what explains this variance in survival after OHCA between countries.

Contrary to previous studies, we found little difference in the likelihood of survival between bystander-witnessed and EMS-witnessed patients [24, 25]. This finding, coupled with the lack of association between EMS call-response interval reinforces the value of rapid defibrillation, regardless of whether it is attempted by a bystander or EMS personnel. Similarly, the benefits of bystander CPR may also have been masked by availability of rapid defibrillation [26].

Our population had a higher proportion of shockable rhythms than is observed in the general OHCA population. Previous research has invariably shown that patients who are in a shockable rhythm have the best chance of survival and this conclusion is highlighted by our results. The high proportion of shockable rhythm is likely to be reflective of a short interval between collapse and attempted defibrillation. In our study, 59% of patients who had a bystander defibrillation attempt survived to hospital discharge. The ROC investigators recently reported percentage survival of 67% following a bystander defibrillation attempt for patients who had an observed, shockable OHCA [27]. Both studies add to the evidence that lay responders can successfully use AEDs, which can in turn result in higher percentages of shockable rhythms and consequently greater survival. The likelihood of a relatively healthier travelling/working population with fewer of the comorbidities that are more likely to result in pulseless electrical activity (PEA) and asystole arrests, should also be acknowledged [28, 29].

The frequency of OHCA in international airports is relatively high and the potential to save a life in an airport is greater than in the majority of locations where OHCA may

occur. The need to continuously strive to improve survival by ensuring a strong and rapid sequence of pre-hospital resuscitation is as critical in international airports as in any other community or location. In fact, the airport location has many advantages over other locations due to the constant high volume of passengers and workers, and the large proportion of public spaces. Systematic OHCA data collection and reporting in the 'Utstein style' is an essential step, without which it cannot be assumed that an airport is maximising their improvement activities to increase survival [30, 31].

Our study has a number of limitations. Firstly, only 9 of the countries surveyed provided data and we have no information on airport survival in non-participating countries. However, to the best of our knowledge, our study is the most comprehensive analysis of OHCA incidence and outcomes in international airports to date. Secondly, data on defibrillation and EMS call-response interval was missing for 23% of cases which may limit interpretability of our results, as may the proportion of cases categorised as 'unspecified, nonshockable'. In order to assess the impact of missing data, odds ratios for bystander AED defibrillation attempted and EMS call-response interval were generated using imputed data but did not differ significantly from ORs where original data was used. Thirdly, in 13% of cases, the initial cardiac rhythm was reported as unspecified nonshockable. This is likely to be a consequence of AED use by bystanders, where cases have been labelled as unspecified nonshockable because the AED code summary was not immediately available and/or not subsequently interpreted. Fourthly, we did not collect information on the advanced pre-hospital interventions and in-hospital treatment available to patients. Our study however accounts for the critical pre-hospital resuscitation interventions that largely determine survival, without which advanced care and hospital interventions would be futile [32]. Finally, airport or country level variables were not collected, which means that inter-airport and inter-country differences could not be further explored.

In conclusion, our study demonstrated that in a public location where availability of defibrillation was high, bystanders attempted defibrillation in 59% of cases, 42% of patients were in an initial shockable rhythm and almost one in three patients survived. Our findings suggest that, while public access defibrillation is not the panacea for improving OHCA survival, it has a vital role to play when strategically used in appropriate locations such as international airports.

### Conflicts of Interest

None to declare.

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## Legend to Tables and Figures

### Figures 1a&b Caterpillar plots of mean residual effects for (a) airports and (b)

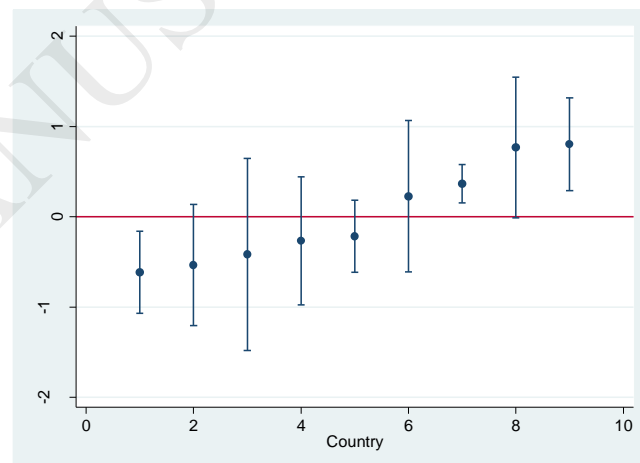
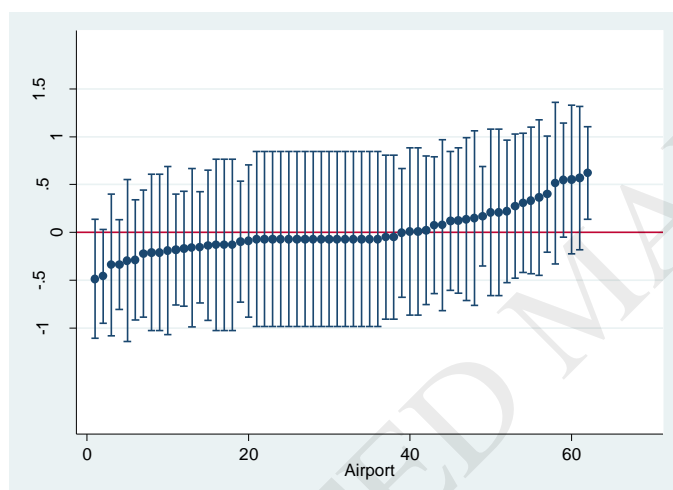
#### country

##### Legend

Y-axis – Mean residual effect is a measure of the area (airport or country) level variance in survival prior to the addition of predictor variables to the model . If the error bars for the mean residual effect do not cross 0, that airport or country is significantly different to the other airports or countries.

### Figures 1a&b Caterpillar plots of mean residual effects for (a) airports and (b)

#### country



##### Legend

Y-axis – Mean residual effect is a measure of the area (airport or country) level variance in survival prior to the addition of predictor variables to the model . If the error bars for the mean residual effect do not cross 0, that airport or country is significantly different to the other airports or countries.

**Table 1 Patient, event and survival characteristics**

	<b>n (%)</b>	<b>Percentage Crude survival (95% CI)</b>
<b>Sex</b>		
Male	580 (73)	34 (30-38)
Female	195 (27)	25 (20-32)
Age in years	64.2 (14.8) <sup>†</sup>	NA
<b>Initial heart rhythm</b>		
Shockable	325 (42)	55 (49-60)
Unspecified nonshockable	114 (15)	27 (19-36)
Pulseless Electrical Activity	107 (14)	12 (7-21)
Asystole	220 (29)	4 (2-7)
<b>Witness status</b>		
Bystander witnessed	581 (74)	36 (32-40)
EMS witnessed	77 (10)	28 (19-40)
Not witnessed	125 (16)	12 (7-19)
<b>Bystander CPR<sup>§</sup></b>		
Yes	439 (77)	37 (32-41)
No	131 (23)	33 (26-42)
<b>Bystander AED defibrillation attempted<sup>§</sup></b>		
Yes	147 (32)	59 (51-67)
No	319 (68)	25 (21-30)
<b>EMS call-response interval 5 minutes or less <sup>¶</sup></b>		
Yes	183 (34)	37 (30-45)
No	354 (66)	27 (22-32)
<b>Discharged alive or 30 day survival</b>		
Yes	231 (32)	NA
No	497 (68)	NA

<sup>†</sup> Mean (standard deviation); <sup>§</sup> Bystander witnessed cases only; <sup>¶</sup> Excludes EMS witnessed; CPR, cardiopulmonary resuscitation; EMS, Emergency Medical Services

**Table 2 Measures of association between individual and area characteristics and OHCA survival**

Measures of Association	Model 1	Model 2	Model 3	Model 4	Model 5	Model 6
Number of cases included	800			581		706
<i>Individual Level Variables (OR, 95% CI)</i>						
Male	<b>1.6 (1.1-2.4)</b>	0.9 (0.5-1.4)	<b>1.6 (1.1-2.5)</b>	<b>1.7 (1.1-2.8)</b>	1.1 (0.7-1.9)	1.3 (0.8-2.1)
Age centred on the mean (in years)	1.0 (1.0-1.0)	1.0 (1.0-1.0)	1.0 (1.0-1.0)	1.0 (1.0-1.0)	1.0 (1.0-1.0)	1.0 (1.0-1.0)
Initial heart rhythm (ref asystole)						
Shockable	<b>36.7 (15.5-87.0)</b>					
Unspecified nonshockable	<b>9.2 (3.6-23.5)</b>					
Pulseless Electrical Activity	<b>4.1 (1.5-11.8)</b>					
Witness status (ref not witnessed)						
Bystander witnessed			<b>4.3 (2.3-7.8)</b>			
EMS witnessed			<b>3.6 (1.6-8.2)</b>			
Bystander CPR†				1.5 (0.9-2.4)		
Bystander AED defibrillation attempted†				<b>4.8 (3.0-7.8)</b>		
EMS call-response interval 5mins or less‡						1.3 (0.8-2.1)
<i>Measure of Variation or Clustering</i>						
mOR for country (95% crI)	1.9 (1.3-4.4)	1.6 (1.1-3.7)	2.0 (1.4-4.8)	2.1 (1.4-5.2)	3.0 (1.6-14.3)	1.8 (1.3-5.1)
DIC	856.1	651.2	816.3	644.2	511.8	555.2
Difference between DIC and null model DIC§	27.0	231.9	66.8	29.0	161.4	231.5

†Bystander witnessed cases only

‡Excludes EMS witnessed cases

§DIC for null models. All cases = 883.1 (M1 – age and gender only; M2 – age, gender and initial heart rhythm; M3- age, gender and witness status). Bystander witnessed cases only = 673.2 (M4 – age, gender and bystander CPR; M5 – age, gender and bystander AED defibrillation attempted). Excluding EMS witnessed cases = 786.7 (M6 – age, gender and EMS call-response interval 5mins or less)

CI, confidence interval; crI, credible interval; DIC, deviance information criteria - a lower DIC suggests a better model fit, and a difference of less than 5 between the null model and model DIC is not considered sufficient to distinguish between two models; EMS, Emergency Medical Service; mOR, median odds ratio; OR, odds ratio