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Survival rates in out-of-hospital cardiac arrest patients transported without prehospital return of spontaneous circulation: An observational cohort study☆

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ABSTRACT

Background: Some Emergency Medical Services currently use just one component of the Universal Termination of Resuscitation (TOR) Guideline, the absence of prehospital return of spontaneous circulation (ROSC), as the single criteria to terminate resuscitation, which may deny transport to potential survivors.
Objective: This study aimed to report the survival to hospital discharge rate in non-traumatic, adult out-of-hospital cardiac arrest (OHCA) patients transported to hospital without a prehospital ROSC.
Methods: An observational study of OHCA patients without a prehospital ROSC who met the Universal TOR Guideline for transport to hospital with ongoing resuscitation. Multivariable logistic regression was used to determine the association of each variable with survival to hospital discharge.
Results: Of 20,207 OHCA treated by EMS, 3374 (16.4%) did not have a prehospital ROSC but met the Universal TOR guideline for transport to hospital with ongoing resuscitation. Of these patients, 122 (3.6%) survived to hospital discharge. Survival to discharge was associated with initial shockable VF/VT rhythms (OR 5.07; 95% CI 2.77–9.30), EMS-witnessed arrests (OR 3.51; 95% CI 1.73–7.15), bystander-witnessed arrests (OR 2.11; 95% CI 1.18–3.77), and public locations (OR 1.57; 95% CI 1.02–2.40).
Conclusion: In OHCA patients without a prehospital ROSC who met the Universal TOR Guideline for transport with ongoing resuscitation survival rates were above the 1% futility rate. Employing only the lack of ROSC as criteria for termination of resuscitation may miss survivors after OHCA.

1. Background

With over 400,000 occurrences every year, out-of-hospital cardiac arrests (OHCA) represent a significant public health burden across North America.[1,2] Survival from OHCA varies, with most regions reporting rates of survival to hospital discharge of less than 10%.[1,2]

Historically, following full resuscitative effort by emergency medical services (EMS), OHCA patients were transported to hospital for continued resuscitation efforts in the emergency department. Most of these patients, however, did not survive to hospital discharge. Previous literature has identified medical futility as a probability of survival of less than 1%,[3,4] for which continued advanced cardiac life support in hospital fails to result in improved patient survival. This has led to a large body of literature indicating that termination of resuscitation in the field by EMS personnel may be appropriate under specific clinical conditions.[5–13]

Both national and international organizations support the use of termination of resuscitation protocols by EMS, indicating that prehospital termination of resuscitation is appropriate under specific circumstances and has a significant impact on transport rates of medically futile patients.[14,15] The adoption of termination of resuscitation protocols have decreased the costs associated with further attempted resuscitation (which includes EMS resources, bed/equipment availability, health care professional availability), decreased the number of emergency transport accidents, decreased variability in EMS resuscitation practices, and decreased distress for family members of cardiac arrest patients.[14,16] Despite widespread

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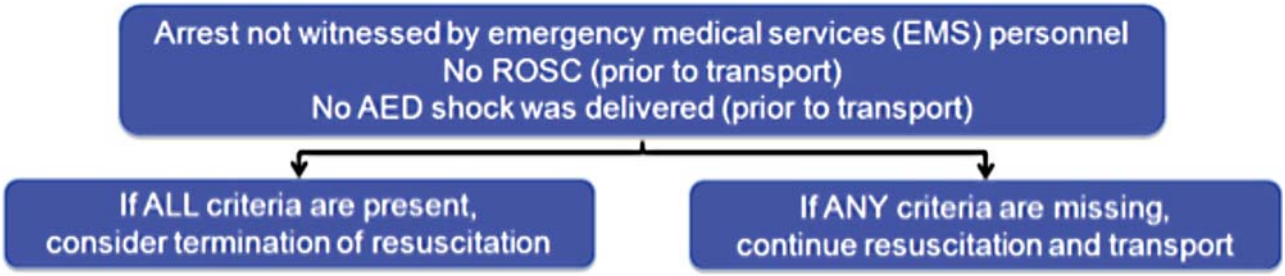

Fig. 1. Universal TOR guideline.[15]

support for field termination of resuscitation and recognition of its many benefits to cardiac arrest care, the local application of termination of resuscitation protocols are inconsistent across EMS services.

In 2009, Morrison et al.[17] derived and validated the Universal Termination of Resuscitation (TOR) Guideline as a tool to guide prehospital termination of resuscitation efforts by both basic life support (BLS) and advanced life support (ALS) providers. The Universal TOR Guideline recommended that resuscitation of OHCA patients be terminated in the prehospital setting, prior to transport, if there was a) no prehospital return of spontaneous circulation (ROSC), b) no shock delivered to the patient, and c) the arrest was not witnessed by EMS personnel (Fig. 1). These criteria must all be met for termination of resuscitation to occur.[17] The Universal TOR Guideline was found to yield a specificity of 100% for recommending transport of potential survivors, and a positive predictive value of 100% for death, while at the same time reducing the transport rate to 37% without missing any potential survivors.[17–21]

Despite the high positive predictive value of the Universal TOR Guideline, implementation of termination of resuscitation protocols within EMS have been inconsistent.[2,22] Previous literature has indicated that a prehospital ROSC is the largest determinant of patient survival to hospital discharge, with a 99.6% negative predictive value.[10,23] Despite this high value the validated Universal Termination of Resuscitation Guideline does not suggest termination based on the lack of ROSC alone. Regardless, there are a number of EMS services that have implemented a no ROSC no transport policy.

The primary objective of this study was to report survival rates of patients without a prehospital ROSC comparing those eligible for termination versus transport based on the Universal Termination of Resuscitation Guideline. The secondary objective was to examine patient and prehospital factors associated with survival to hospital discharge in patients without a prehospital ROSC, who meet the Universal TOR Guideline for transport to hospital.

2. Methods

2.1. Study design and setting

This study was a retrospective analysis of the Toronto site of the Resuscitation Outcomes Consortium (ROC) Epistry-Cardiac Arrest database.[24] This database is a population-based registry of consecutive EMS attended OHCA from 7 municipalities in southern Ontario (Toronto, Peel, York, Halton, Durham, Muskoka, and Simcoe), a population of 6.6 million people. Data collected for each OHCA patient included details regarding the 911 call, pick-up location, bystander CPR, EMS response and treatment, patient characteristics, cardiac arrest characteristics, destination hospital, and in-hospital clinical outcomes. Data was abstracted from available paramedic care records, fire department records and police department forms, and in-hospital charts by trained data abstractors at each regional site. More detailed methods for data collection within the ROC Epistry–Cardiac Arrest database have been described elsewhere.[24,25] The Research ethics boards of each of the 32 destination hospitals have reviewed and approved the ROC Epistry study protocol.

2.2. Emergency medical services

The EMS involved in this study included both advanced life support (ALS) and basic life support (BLS) paramedics. Basic Life Support paramedics were certified to perform semi-automated external defibrillation (S-AED), CPR and supraglottic airway (King-LT®) insertion. Advanced Life Support paramedics, in addition to the skills mentioned above, were certified in manual defibrillation, endotracheal intubation, intravenous and intraosseous catheter insertions, and medication administration (e.g. epinephrine, amiodarone, lidocaine, etc.) as per AHA cardiac arrest guidelines. All paramedics were certified under the medical delegation of base hospital physicians.

Emergency medical services response to 911 calls employed a 'closest ambulance' model whereby the ambulance closest to the call was dispatched regardless of whether they were BLS or ALS, followed by the closest available ALS vehicle for cardiac arrests. If the ALS ambulance was the closest, then they may have been the only ambulance that attended the cardiac arrest. All 911 calls for cardiac arrests also received a tiered response from the local fire department, who were trained in basic life support CPR. Therefore, a typical 911 response to a cardiac arrest included two to four paramedics as well as the fire department. No mechanical CPR devices were used by paramedics during this study period.

2.3. Study population

The study population included consecutive adult (≥18 years) OHCA patients of presumed cardiac etiology from April 1, 2007 and March 31, 2013. Cardiac arrests were presumed to be of cardiac etiology when no other obvious cause was identified (i.e. trauma, drowning, asphyxia, overdose, etc.). All eligible patients were transported to hospital without a prehospital ROSC in the field, and received EMS resuscitation from either ALS or BLS paramedics. Patients whose cardiac arrest was of non-cardiac etiology, who did not receive CPR by EMS personnel, who met legislative criteria for obvious death at the scene (decapitation, decomposition, rigor mortis, lividity, or hemisection), or who had written dated and signed "Do Not Resuscitate" (DNR) advanced directives were excluded.

All 32 destination hospitals were all involved in the Strategies for Post-Arrest Care (SPARC) Network trial (NCT00683683), which implemented a knowledge translation program to improve the delivery of care to post-cardiac arrest patients.[26,27] The use of targeted temperature management (TTM) for all patients was recommended and encouraged as well compliance was reported by

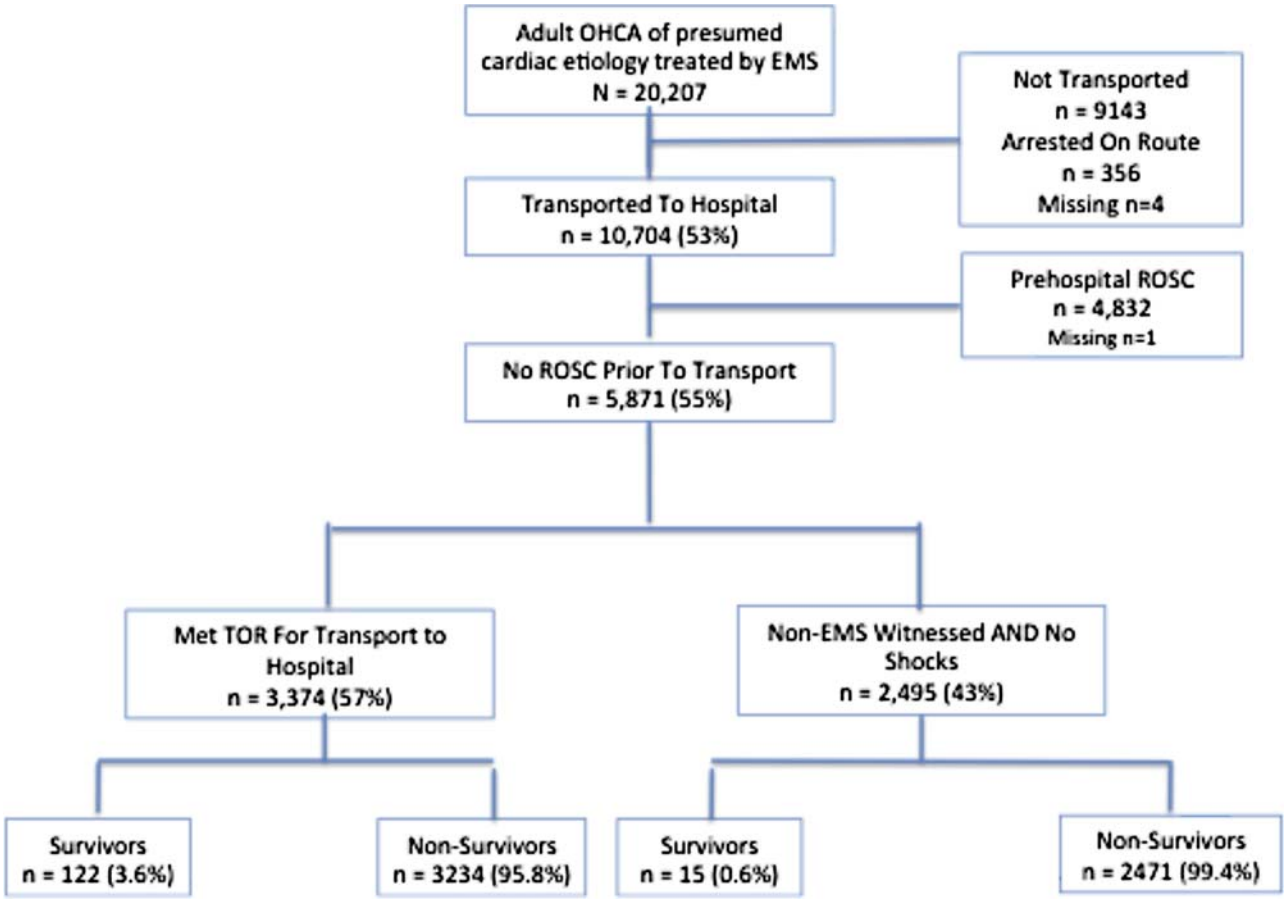

Fig. 2. Flow diagram of patient selection.

each institution. Percutaneous coronary intervention (PCI) was recommended for all patients post-cardiac arrest with ST-Elevation Myocardial Infarction (STEMI) on their first electrocardiogram (ECG). Implantable cardioverter-defibrillator was recommended for patients alive at 48 h who presented with VF but did not have STEMI on their ECG. Neuroprognostication was recommended after 72 h and the use of two neuroprognostic tests were recommended at this time.

2.4. Outcome measure

The outcome of interest was survival to hospital discharge.

2.5. Statistical analysis

Baseline descriptive statistics were calculated for all variables of interest. Continuous measures (e.g. age) were summarized using medians and interquartile range (IQR), while categorical measures (e.g. gender) were measured using counts and percentages. A Chi-square test was used to compare the survival rates between patients transported to hospital without a prehospital ROSC who met the Universal TOR Guideline for transport and those who met the Universal TOR Guideline for termination in the field with a two-tailed p-value of 0.05 (95% confidence interval) representing statistical significance.

Bivariate analyses were performed to assess the association between each covariate and the outcome of interest. If the covariate values were normally distributed, a t-test was used. Otherwise, a non-parametric Wilcoxon rank-sum test was used. Chi-square analyses were used to assess the association between categorical variables (e.g. initial arrest rhythm) and patient outcome. If the number of patients in any group were small (expected counts $\leq$5), the Fisher's exact test was used.

Multivariable logistic regression was used to determine the predictors of survival to hospital discharge in patients who met the Universal TOR Guideline for transport to hospital. In order to avoid biases generated from using stepwise variable reduction, we included core Utstein variables (age, EMS response time, gender, location, witness status, initial rhythm and bystander CPR), as well as other pre-determined variables of clinical interest such as use of advanced airway, defined as endotracheal intubation or supraglottic airway (King-LT®), insertion versus the use of bag-valve-mask ventilation, level of paramedic (ALS vs. BLS) and destination hospital characteristics in the model. Multicollinearity was assessed by calculating variance inflation factors, with a value greater than 4 indicating significant collinearity between variables.[28] The model was tested for goodness of fit using the Hosmer and Lemeshow test.

Statistical analyses were performed by SAS software version 8.0 (SAS Institute, Cary, NC, USA).

3. Results

During the study period, there were a total of 20,207 adult OHCA of presumed cardiac etiology treated by EMS; 10,704 (52.9%) were transported to the hospital and 9152 (45.3%) had resuscitation discontinued on scene due to presumed futility after conversation with medical physician oversight. Of the transported patients, 5871 (54.8%) did not have a prehospital ROSC and met the inclusion criteria of our study (Fig. 2). Patient characteristics are listed in Table 1. Of these eligible patients, 3374 (57.4%) met the Universal

Table 1
Study patient demographics.

Characteristics	Patients transported $n = 10{,}704$	No. prehospital ROSC $n = 5871$
Age (yr), median (IQR)	69 (56–80)	67 (54–79)
EMS response (min), median (IQR)	6.0 (4.9–7.5)	6.0 (5.0–7.9)
Male gender, *n* (%)	7190 (67.2)	4124 (70.3)
Public location, *n* (%)	2489 (23.3)	1553 (26.5)
Witness status, *n* (%)		
EMS witnessed	1653 (15.4)	962 (16.4)
Bystander witnessed	5070 (47.7)	2494 (42.8)
Bystander CPR, *n* (%)		
EMS witnessed	1653 (15.4)	962 (16.4)
Bystander CPR	3750 (35.0)	1851 (31.5)
VF/VT initial rhythm, *n* (%)	3639 (34.7)	1808 (30.9)
Advanced EMS provider, *n* (%)	9492 (88.7)	4829 (82.3)
Advanced airway, *n* (%)	8563 (81.1)	4667 (80.7)
Academic destination hospital, *n* (%)	1950 (18.2)	1039 (17.9)

TOR Guideline for continued resuscitation and transport to the hospital because their cardiac arrests were witnessed by EMS or they were defibrillated. Of these patients, 551 (16.3%) obtained a ROSC in-hospital and 122 (3.6%) survived to hospital discharge. Of the 2495 (42.6%) cases that met the Universal TOR Guideline for termination of resuscitation, 295 (11.8%) obtained a ROSC and 15 (0.6%) of the patients survived to hospital discharge; 3.6% survival to discharge using ROSC only versus 0.6% using Universal TOR Guideline, $p < 0.001$.

The clinical characteristics of survivors versus non-survivors are shown in Table 2. In the unadjusted analysis, patients who survived to hospital discharge were younger (60 vs. 66 years of age, $p < 0.01$), had a higher proportion of initial shockable (VF/VT) rhythms (82.6% vs. 52.6%, $p < 0.01$), EMS witnessed arrests (24.8% vs. 28.8%, $p < 0.01$), bystander witnessed arrests (60.3% vs. 43.0%, $p < 0.01$), and arrests that occurred in public locations (46.3% vs. 28.9%, $p < 0.01$). They also had a lower proportion of advanced airways (73.2% vs. 83.1%, $p = 0.01$) and advanced level providers (76.2% vs. 84.4%, $p = 0.02$).

In the adjusted analyses, survival to discharge was associated with younger age (OR 0.98; 95% CI 0.97–0.99; $p < 0.01$), initial shockable VF/VT rhythms (OR 5.07; 95% CI 2.77–9.30; $p < 0.01$), EMS-witnessed arrests (OR 3.51; 95% CI 1.73–7.15; $p < 0.01$), bystander-witnessed arrests (OR 2.11; 95% CI 1.18–3.77; $p = 0.01$), and public locations (OR 1.57; 95% CI 1.02–2.40; $p = 0.04$) (Table 3).

Table 2
Demographics of patients without a prehospital ROSC who met the TOR guideline for transport.

Characteristics	Survivors $n = 122$	Non-survivors $n = 3234$	*P*-value
Age (yr), median (IQR)	60.0 (51.0–70.0)	66.0 (55.0–78.0)	<0.01
EMS response (min), median (IQR)	5.6 (4.8–7.0)	6.0 (5.0–7.7)	0.19
Male gender, *n* (%)	96 (78.7)	2374 (73.4)	0.23
Public location, *n* (%)	56 (46.3)	932 (28.9)	
Witness status, *n* (%)			
EMS witnessed	30 (24.8)	927 (28.8)	
Bystander witnessed	73 (60.3)	1425 (43.0)	<0.01
Bystander CPR, *n* (%)			
EMS CPR	30 (24.8)	927 (28.8)	<0.01
Bystander CPR	43 (35.2)	1025 (31.7)	0.56
VF/VT initial rhythm, *n* (%)	100 (82.6)	1656 (52.6)	<0.01
Advanced EMS provider, *n* (%)	93 (76.2)	2731 (84.4)	0.02
Advanced airway, *n* (%)	87 (73.2)	2668 (83.1)	0.01
Academic destination hospital, *n* (%)	26 (21.3)	515 (16.0)	0.15

Table 3
Adjusted odds ratio.

Variable	OR (95%(CI)	*P*-value
Age (yr)	0.98 (0.97–0.99)	<0.01
EMS response (min)	0.97 (0.89–1.04)	0.37
Male gender	1.04 (0.62–1.74)	0.88
Public location	1.57 (1.02–2.40)	0.04
EMS witnessed	3.51 (1.73–7.15)	<0.01
Bystander witnessed	2.11 (1.18–3.77)	0.01
Bystander CPR	0.83 (0.52–1.34)	0.45
VF/VT initial rhythm	5.07 (2.77–9.30)	<0.01
Advanced EMS provider	0.69 (0.40–1.21)	0.20
Advanced airway	0.60 (0.37–1.00)	0.05
Academic destination hospital	1.42 (0.86–2.35)	0.17

4. Discussion

The results of our study indicate that using the absence of a prehospital ROSC as the sole criterion to terminate resuscitation in the field misses an unacceptably high number of potential survivors from OHCA, above the 1% defined as the threshold for medical futility.[3,4] Due to the increased rate of survival, it is important to consider the other contributory predictors of survival in the published Universal TOR Guideline. Sudden cardiac arrest is complex and dynamic process and it is unlikely that one variable could be used with high enough predictive value to terminate resuscitation efforts.

A previous study found a survival rate of 0.69% in patients that did not obtain a prehospital ROSC,[23] which is inconsistent with our study results. There are, however, important differences between these studies that must be addressed. Wampler et al. combined data from two fire department agencies from two cities.[23] Patients from one city contributed the majority of cases in the study and had a 0% overall survival rate, which may be due to a relatively low proportion of initial VF/VT shockable rhythms at 14.7%.[23] Patients from the other city had a similar proportion of initial VF/VT rhythms to our study (25%) and had 11 (2.6%) patients survive to hospital discharge that did not obtain a prehospital ROSC, which is above the 1% threshold for futility. Both studies suggest that initial shockable rhythms are associated with improved survival in non-prehospital ROSC patients. Furthermore, the authors acknowledge that if the Universal TOR Guideline had been applied, it would have recommended transportation to hospital for all 11 survivors.[23]

The results of our study showed that OHCAs without ROSC that were witnessed by EMS, and had an initial shockable (VF/VT) rhythm were significantly associated with survival, and had the largest effect size on patient survival at hospital discharge. These findings are consistent with the Universal TOR Guideline.[11,17,18] Correct application of the Universal TOR Guideline resulted in survival rates below the threshold of medical futility (1%) in our study. However, without the inclusion of all three criteria, and exclusive reliance on the lack of a ROSC to terminate resuscitation, survival was found to be much higher than the acceptable medical futility rate of 1%. Therefore, adherence to the Universal TOR Guideline is recommended, which results in a more conservative rate of termination of resuscitation, missing fewer potential survivors while maintaining a high positive predictive value for death.[15,17–21,29]

Another important clinical aspect to consider for termination of resuscitation based on the absence of ROSC alone is the duration of resuscitation. There is insufficient research to recommend a specific duration of resuscitation without ROSC that predicts futility, and current guidelines do not support the use of a predetermined time point to stop resuscitation.[15,30] There is limited research that has examined the effect of prolonged resuscitative efforts on patient outcome. A recent paper by Reynolds et al.[31] concluded that with current resuscitation strategies CPR

duration greater than 16.1 min resulted in less than 1% probability of survival with good functional outcome. The authors suggested that the use of novel resuscitation strategies such as PCI or extracorporeal membrane oxygenation (ECMO) may improve patient outcome, however due to the increased costs and resources required it needs to be applied to patients who have the most potential to benefit. Although the authors did not specifically look at the use of the Universal TOR Guideline in this study, they did find that witnessed arrests and initial shockable rhythms were associated with improved outcomes. Furthermore the absence of an AED shock delivered perfectly predicted a poor outcome. This is consistent with resuscitation strategies employed at other institutions that have successfully introduced ECMO for the treatment of OHCA refractory to standard resuscitation measures in patients carefully selected due to their increased chance of meaningful recovery (e.g. younger age, shockable rhythms, witnessed arrests).[32] These novel strategies may prove beneficial for cardiac arrest patients that have an increased likelihood of a positive outcome, however do not respond to traditional resuscitation efforts such as those who are identified by the TOR Guideline for transport even though they do not have ROSC. Strict adherence to the absence of ROSC to terminate resuscitation may fail to recognize patients with an increased probability of survival that may theoretically benefit from these novel strategies.

It is challenging to continue to resuscitate patients who meet the criteria for transport and require prolonged and high-quality CPR on route to hospital. It may by that mechanical CPR devices further increase the feasibility of evaluating novel resuscitation strategies by providing high-quality CPR during EMS transport, something that is challenging to achieve with a moving ambulance and manual CPR.

The findings of our study have many important implications for prehospital care involving both EMS providers and emergency physicians. Ongoing effort should focus on encouraging EMS services and medical oversight to adopt and adhere to the Universal TOR Guideline, while discouraging the use of prehospital ROSC alone as an indicator of futility or allowing termination of resuscitative efforts to be at the discretion of the online medical control physician. Adherence to the Universal TOR Guideline is needed to reduce variability and minimize the number of potential survivors that have their resuscitation terminated in the field.

5. Limitations

Although the data presented was derived from a large population-based registry, there were several limitations in our study. First, like other observational studies, there was a risk of measurement bias in data collection. However, this risk was minimized with the use of trained data guardians, computerized error checks, and random re-abstraction. Second, confounding by indication may have resulted in certain patients who may have not been transported to the hospital. Confounding by indication describes differences in treatment that may occur as a result of a perceived difference in patient prognosis. In our study, it may have been possible that physicians pronounced patients in the field due to a perceived poor prognosis and as a result, patients who may have contributed meaningful data to our study may have been excluded. Lastly, our study could not evaluate the relative effectiveness of in-hospital treatments, such as TTM and PCI. While all survivors obtained a ROSC and were potentially eligible for post-arrest treatment, the majority of non-survivors (84%) did not obtain a ROSC and were deemed ineligible for TTM and/or PCI. This would have led to an incorrect over-estimation of the effect size of these interventions

6. Conclusion

Employing the lack of prehospital ROSC as the sole criterion to terminate resuscitation in the prehospital setting is not recommended as this may lead to the termination of resuscitation in patients who may potentially survive. The validated Universal TOR Guideline, which is based on three criteria (shock delivered, EMS witnessed arrest and ROSC), misses <1% of patients who survive and it remains the best available tool to predict OHCA survival in the prehospital setting.

Conflict of interest statement

The authors report no conflicts of interest. The authors alone are responsible for the content and writing of the paper.

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