Duration of Prehospital Resuscitation Efforts After Out-of-Hospital Cardiac Arrest

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Background—During out-of-hospital cardiac arrest, it is unclear how long prehospital resuscitation efforts should be continued to maximize lives saved.

Methods and Results—Between 2005 and 2012, we enrolled 282 183 adult patients with bystander-witnessed out-of-hospital cardiac arrest from the All-Japan Utstein Registry. Prehospital resuscitation duration was calculated as the time interval from call receipt to return of spontaneous circulation in cases achieving prehospital return of spontaneous circulation or from call receipt to hospital arrival in cases not achieving prehospital return of spontaneous circulation. In each of 4 groups stratified by initial cardiac arrest rhythm (shockable versus nonshockable) and bystander resuscitation (presence versus absence), we calculated minimum prehospital resuscitation duration, defined as the length of resuscitation efforts in minutes required to achieve ≥99% sensitivity for the primary end point, favorable 30-day neurological outcome after out-of-hospital cardiac arrest. Prehospital resuscitation duration to achieve prehospital return of spontaneous circulation ranged from 1 to 60 minutes. Longer prehospital resuscitation duration reduced the likelihood of favorable neurological outcome (adjusted odds ratio, 0.84; 95% confidence interval, 0.838–0.844). Although the frequency of favorable neurological outcome was significantly different among the 4 groups, ranging from 20.0% (shockable/bystander resuscitation group) to 0.9% (nonshockable/bystander resuscitation group; $P<0.001$), minimum prehospital resuscitation duration did not differ widely among the 4 groups (40 minutes in the shockable/bystander resuscitation group and the shockable/no bystander resuscitation group, 44 minutes in the nonshockable/bystander resuscitation group, and 45 minutes in the nonshockable/no bystander resuscitation group).

Conclusions—On the basis of time intervals from the shockable arrest groups, prehospital resuscitation efforts should be continued for at least 40 minutes in all adults with bystander-witnessed out-of-hospital cardiac arrest.

Clinical Trial Registration—URL: http://www.umin.ac.jp/ctr/. Unique identifier: 000009918. **(*Circulation*. 2016;133:1386-1396. DOI: 10.1161/CIRCULATIONAHA.115.018788.)**

Key Words: cardiopulmonary resuscitation ■ heart arrest ■ out-of-hospital cardiac arrest ■ resuscitation

Out-of-hospital cardiac arrest (OHCA) is a major public health problem, affecting ≈420 000 individuals in the United States[1] and 110 000 individuals in Japan annually.[2] Despite decades of efforts to promote resuscitation, neurologically intact survival rates for OHCA remains low worldwide.[3–9] Frequently, resuscitation efforts are unsuccessful and death occurs.[4] Achievement of return of spontaneous circulation (ROSC) is a prerequisite for neurologically intact survival, and it may be appropriate to extend resuscitation efforts if ROSC might occur. Recent resuscitation guidelines state that end-of-life decision making is an important component of resuscitation[3–9] and recommend the following termination of resuscitation (TOR) rules for basic life support (BLS) in adult

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Received August 4, 2015; accepted January 29, 2016.

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The online-only Data Supplement is available with this article at http://circ.ahajournals.org/lookup/suppl/doi:10.1161/CIRCULATIONAHA.115.018788/-/DC1.

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OHCA patients: arrest not witnessed by emergency medical service (EMS) responders, no ROSC after 3 full rounds of BLS and automated external defibrillator (AED) analysis, and no AED shocks. The TOR rules for advanced life support (ALS) include the BLS criteria and 3 additional criteria: arrest not witnessed by bystander, no bystander resuscitation, and no ROSC after full ALS in the field. When all criteria are met before transport, resuscitation efforts can be terminated,[4] reducing BLS transport by 54% to 63%[10,11] and ALS transport by 31%.[11] However, these guidelines state only the mandatory elements of "adequate" resuscitation efforts and do not specify the minimum duration for resuscitation efforts.[3–9] Recent studies of in-hospital cardiac arrest demonstrate that increasing the duration of resuscitation efforts improves the likelihood of survival.[12,13] These findings suggest that clearly defining the length of prehospital resuscitation efforts is essential to optimal implementation of TOR rules.

The EMS system in Japan is ideal for evaluating this question: EMS responders must start resuscitation efforts immediately for all OHCA patients except when the victim is obviously moribund; EMS responders must continue resuscitation efforts until achievement of ROSC or until hospital arrival, whichever comes first; and EMS responders cannot make the decision to terminate resuscitation efforts.[2,5,14,15] We therefore assessed prehospital resuscitation duration for neurologically intact survival in all adult patients with bystander-witnessed OHCA. We expected that prehospital resuscitation duration for neurologically intact survival would differ in 4 groups stratified by initial cardiac arrest rhythm (shockable versus nonshockable) and bystander resuscitation status (presence versus absence), with longer prehospital resuscitation duration producing more survivors in the 2 groups with the presence of bystander resuscitation.

Methods

Data Source and EMS System

The All-Japan Utstein Registry, a prospective, nationwide, population-based registry of OHCA, was established January 1, 2005, by the Fire and Disaster Management Agency[4–16] following the ethics guidelines in Japan[17] and has been described in detail previously.[14–16,18] All fire stations with dispatch centers and all collaborating medical institutions participate in the registry. A subcommittee of resuscitation science in the Japanese Circulation Society was provided with registry data following the prescribed governmental legal procedures and conducted the study with approval from the ethics committee at Surugadai Nihon University Hospital.[18] Japan had a population of 127 million in 2011. There are 802 municipally governed fire stations with dispatch centers operating around the clock, following uniform guideline-based resuscitation protocols.[14] Each ambulance has 3 EMS responders, including at least 1 emergency lifesaving technician certified to insert intravenous lines and adjunct airways. Specially trained emergency lifesaving technicians are permitted to insert tracheal tubes and to administer intravenous epinephrine.[14] All OHCA patients receiving prehospital resuscitation efforts are transported to the nearest emergency hospital.[2,14–16,18]

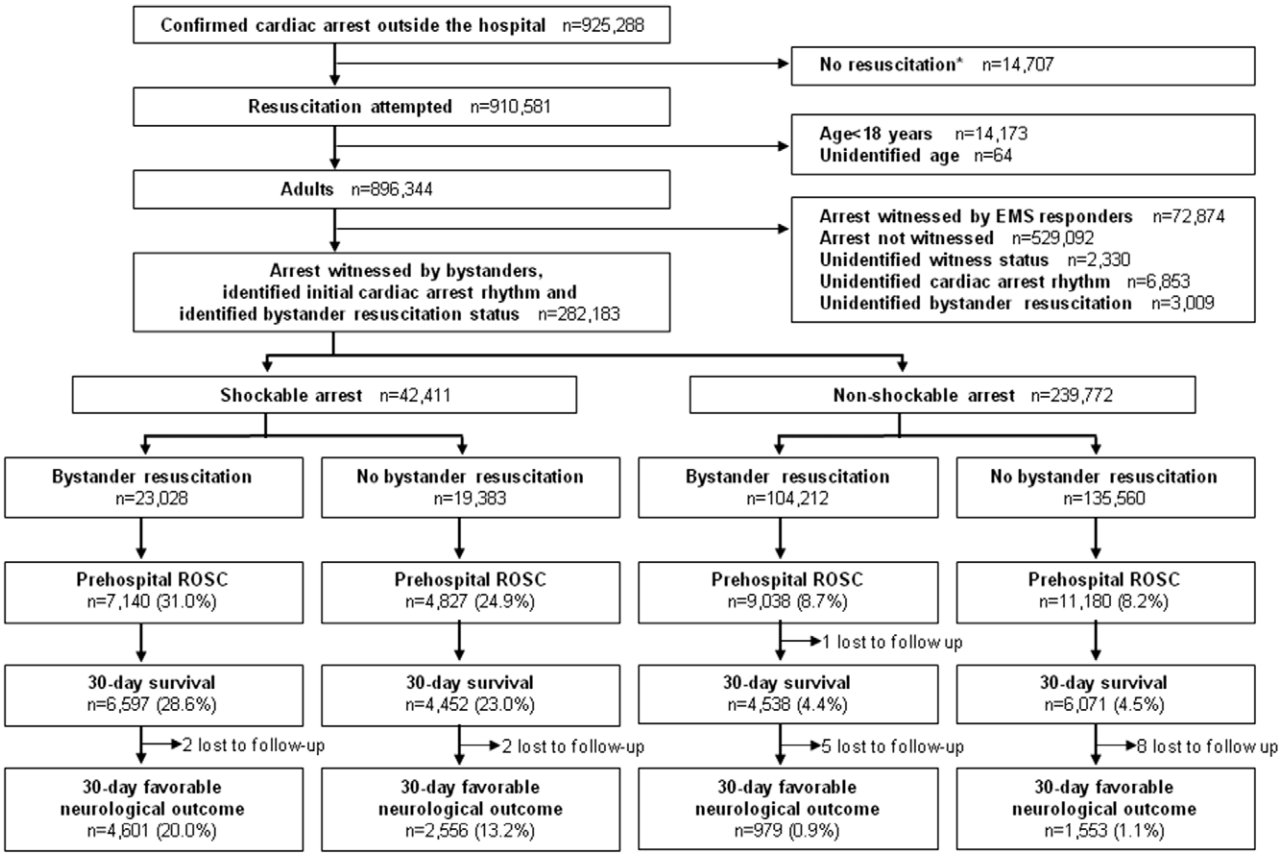

Figure 1. Study flow diagram and outcomes. Each percent represents the number of each study outcome divided by the total number of patients in each of the 4 subgroups stratified by initial cardiac arrest rhythm and bystander resuscitation status. EMS indicates emergency medical service; and ROSC, return of spontaneous circulation. *Includes patients with "do not resuscitate" order.

Study Population

Between January 1, 2005, and December 31, 2012, adult patients with bystander-witnessed OHCA in whom EMS responders performed prehospital resuscitation care and who were transported to the hospital were included. Exclusion criteria were age <18 years, cardiac arrest after EMS responder arrival, unwitnessed OHCA, unidentified witness status, unidentified initial cardiac arrest rhythm, unidentified bystander resuscitation status, and a "do not resuscitate" order.

Data Collection

Data elements were collected prospectively on the basis of the Utstein guidelines.[19] Estimated times of collapse and initiation of bystander resuscitation were obtained from bystanders. All event times were synchronized by the dispatch center clock.[2,14–16,18] EMS responders documented the presence or absence of bystander resuscitation efforts and noted bystander resuscitation technique, classified as documented chest compressions with or without rescue breathings or unidentified resuscitation technique (change of technique, resuscitation without documented chest compressions, etc).[2,14–16,18,20] The initial cardiac arrest rhythm was classified as shockable (ventricular fibrillation or pulseless ventricular tachycardia) or nonshockable (pulseless electric activity or asystole) on the basis of AED analysis.[2,14–16,18] Patients receiving bystander-delivered shocks with a public-access AED were classified as having a shockable arrest.[14–16] Prehospital ROSC was defined as any spontaneous palpable pulse confirmed by cardiac rhythm monitoring occurring before hospital arrival.[2,14–16,18,20] Causes of arrest were determined clinically by the physicians in charge after hospital arrival and defined as presumed cardiac cause unless an obvious noncardiac cause was elicited.[2,14–16,18–20] Resuscitation outcomes were collected by the receiving hospital physicians in collaboration with EMS responders.[2,14–16,18] For patients discharged from the hospital alive, neurological outcomes were determined during 30-day follow-up interviews[2,14–16,18] with the use of the Cerebral Performance Category scale.[19] The data form was filled out by the EMS personnel in cooperation with the physicians in charge of the patients, and the data were integrated into the registry system on the Fire and Disaster Management Agency database server and then logically checked by the computer system. If the data form was incomplete, the Fire and

Table 1. Baseline Characteristics of the Patients Stratified by Initial Cardiac Arrest Rhythm and Bystander Resuscitation Status*

	Shockable/Bystander Resuscitation Group (n=23 028)	Shockable/No Bystander Resuscitation Group (n=19 383)	Nonshockable/Bystander Resuscitation Group (n=104 212)	Nonshockable/No Bystander Resuscitation Group (n=135 560)
Age, y	66 (56–77)	67 (57–76)	81 (71–88)	77 (66–85)
Male sex, n (%)	17 792 (77.3)	15 285 (78.9)	55 400 (53.2)	82 725 (61.0)
Dispatcher resuscitation instruction, n (%)	13 399 (58.2)	4422 (22.8)	65 058 (62.4)	34 082 (25.1)
Bystander resuscitation, n (%)				
Chest compression only	14 963 (65.0)		71 320 (68.4)	
Chest compression with rescue breathing	8065 (35.0)		32 892 (31.6)	
Public-access defibrillation, n (%)	3437 (14.9)	27 (0.1)	0 (0.0)	0 (0.0)
Initial cardiac arrest rhythm, n (%)				
Pulseless ventricular tachycardia	43 (1.9)	505 (2.6)		
Ventricular fibrillation	22 594 (98.1)	18 878 (97.4)		
Pulseless electric activity			39 230 (37.6)	55 305 (40.8)
Asystole			64 982 (62.4)	80 255 (59.2)
Defibrillation by EMS responder, n (%)	20 282 (88.1)	18 481 (95.3)	5154 (4.9)	7085 (5.2)
Advanced airway management, n (%)	9945 (43.2)	9224 (47.6)	50 833 (48.8)	61 911 (45.7)
Intravenous fluid, n (%)	7409 (32.2)	6434 (33.2)	29 732 (28.5)	37 031 (27.3)
Prehospital epinephrine, n (%)	3795 (16.5)	3085 (15.9)	15 002 (14.4)	16 455 (12.1)
Cardiac cause, n (%)	20 179 (87.6)	16 992 (87.7)	53 797 (51.6)	67 583 (49.9)
Achievement of prehospital ROSC, n (%)	7140 (31.0)	4827 (24.9)	9038 (8.7)	11 180 (8.2)
Time interval, min				
From collapse to call receipt†	2 (0–4)	1 (0–3)	2 (0–5)	2 (0–5)
From call receipt to scene‡	7 (5–9)	6 (5–8)	7 (5–9)	7 (5–9)
From call receipt to hospital arrival§	30 (24–38)	30 (24–37)	31 (25–38)	31 (25–39)
Prehospital resuscitation duration,¶ min	27 (18–35)	27 (20–34)	30 (24–37)	30 (24–38)
EMS responder resuscitation duration‖, min	19 (12–27)	20 (14–27)	22 (17–29)	23 (17–30)

EMS indicates emergency medical service; and ROSC return of spontaneous circulation.

*Values are expressed as median (25th–75th percentile).

The time intervals from collapse to call receipt, scene, and hospital arrival were calculated in †97.6% (275 322 of 282 183), ‡99.9% (281 864 of 282 183), and §99.7% (281 436 of 282 183) of patients.

The durations of prehospital resuscitation and EMS responder resuscitation were calculated in ¶99.6% (281 005 of 282 183) and ‖99.5% (280 793 of 282 183) of patients. There were significant differences among the groups with respect to any of variables listed ($P<0.001$).

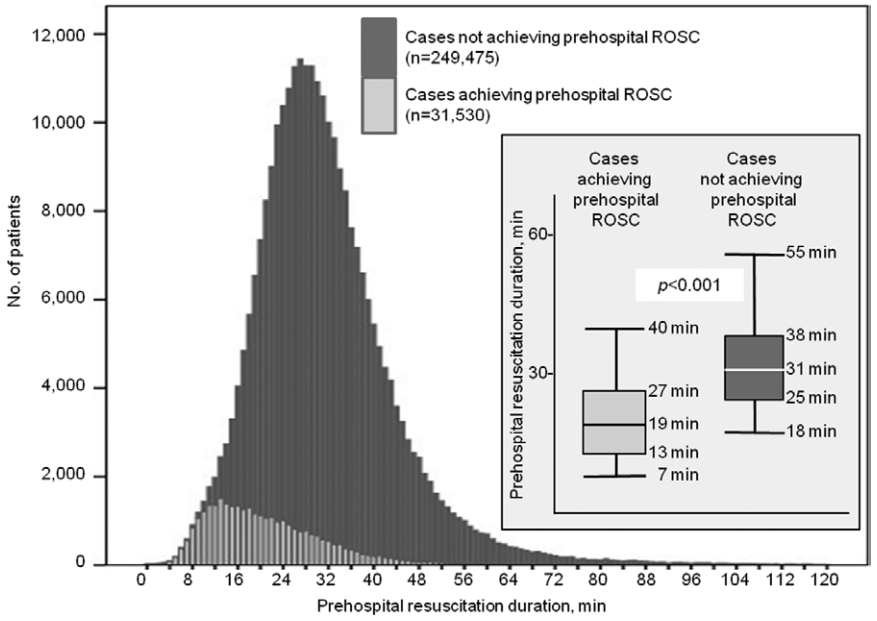

Figure 2. Distributions of prehospital resuscitation duration for the entire study population. Each stacked bar shows the number of cases stratified by prehospital return of spontaneous circulation (ROSC) status. Each box plot (5th, 25th, 50th, 75th, and 95th percentile values) represents the prehospital resuscitation duration stratified by prehospital ROSC status.

Disaster Management Agency returned it to the respective fire station for data completion.[2,14–16,18]

End Points

The primary end point was favorable 30-day neurological outcome, defined as a Cerebral Performance Category 1 (good performance) or 2 (moderate disability) on a 5-category scale.[19] Cerebral Performance Category 3 (severe disability), 4 (vegetative state), and 5 (death) were regarded as unfavorable neurological outcome. The secondary end points were prehospital ROSC and 30-day survival (Cerebral Performance Category 1–4).

Statistical Methods

The prehospital resuscitation duration, inclusive of EMS responder resuscitation efforts with or without bystander resuscitation efforts, was calculated as the call-receipt-to-ROSC interval in cases achieving prehospital ROSC or the call-receipt-to-hospital-arrival interval in cases not achieving prehospital ROSC. The resuscitation duration provided exclusively by EMS responders was calculated as the scene-arrival-to-ROSC interval in cases achieving prehospital ROSC or the scene-arrival-to-hospital-arrival interval in cases not achieving prehospital ROSC.

The study cohort was divided into 4 groups according to initial cardiac arrest rhythm (shockable versus nonshockable) and bystander resuscitation status (documented chest compressions with or without rescue breathings versus no bystander resuscitation). Baseline characteristics and study outcomes were compared by use of the χ^2 test for categorical variables and the Mann-Whitney *U* test or the Kruskal-Wallis rank test for continuous variables. We graphed the distributions of prehospital resuscitation duration using stacked bars in the entire study cohort stratified by prehospital ROSC status. On the basis of the distribution of prehospital resuscitation duration to achieve prehospital ROSC, the following analyses were done in the subset of patients with ≤60 minutes of prehospital resuscitation duration. We graphed the cumulative rates of 30-day neurological outcomes and favorable 30-day neurological outcome. A multiple logistic-regression analysis was performed for independent predictors of favorable 30-day neurological outcome, including prehospital resuscitation duration, age, study period (year the arrest occurred), sex, bystander resuscitation status, initial cardiac arrest rhythm, ALS, and cause of cardiac arrest. In each group stratified by initial cardiac arrest rhythm and bystander resuscitation status, curve estimation in a quadratic model was used to illustrate the relationship between the prehospital resuscitation duration and favorable 30-day neurological outcome. We calculated the sensitivity and negative predictive values of the prehospital and EMS responder resuscitation durations for having favorable 30-day neurological outcome in each group. Consistent with previous studies for the TOR rules,[10,11,21,22] a sensitivity of ≥99% for favorable 30-day neurological outcome was used to determine the minimum prehospital and EMS responder resuscitation durations; we also calculated the maximum prehospital and EMS responder resuscitation durations associated with a sensitivity of 100% and a negative predictive value of 100%. Compared with previous sample sizes (1240–13 684 patients[10,11,21,22]), our larger sample size (283 183 patients) provided >80% power (1-side α=0.05) with a misclassification rate <1%. All statistical analyses were performed with SPSS software (version 16.0J).

The authors had full access to and take full responsibility for the integrity of the data. All authors have read and agree to the manuscript as written.

Results

Patient Characteristics

Of the 925 288 OHCA victims between 2005 and 2012, 910 581 (98.4%) had prehospital resuscitation attempts and were transported to the hospital (Figure 1). Of these, 628 398 were excluded. This study included 282 183 adult patients with bystander-witnessed OHCA: 23 028 (8.2%) shockable/bystander resuscitation cases, 19 383 (6.9%) shockable/no bystander resuscitation cases, 104 212 (36.9%) nonshockable/bystander resuscitation cases, and 135 560 (48.0%) nonshockable/no bystander resuscitation cases. Baseline characteristics and arrest factors exhibited significant differences between groups, including age, sex, intravenous fluid administration, and cardiac cause of the arrest (Table 1).

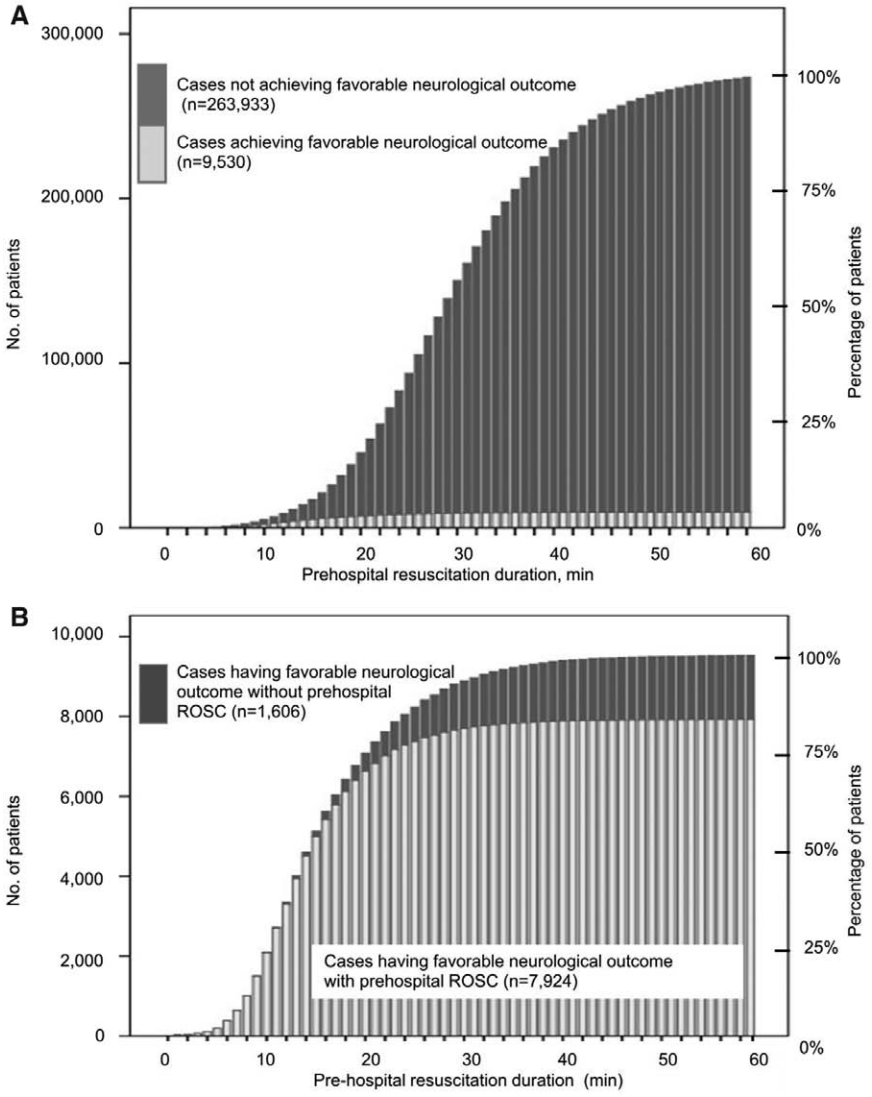

Figure 3. Cumulative rates of 30-day neurological outcomes (**A**) and favorable 30-day neurological outcome (**B**). ROSC indicates return of spontaneous circulation.

Outcomes

Frequencies of prehospital ROSC, 30-day survival, and favorable 30-day neurological outcome (Figure 1) were 31.0% (7140 of 23 028), 28.6% (6597 of 23 028), and 20.0% (4601 of 23 026) in the shockable/bystander resuscitation group; 24.9% (4827 of 19 383), 23.0% (4452 of 19 383), and 13.2% (2556 of 19 381) in the shockable/no bystander resuscitation group; 8.7% (9038 of 104 212), 4.4% (4538 of 104 211), and 0.9% (979 of 104 206) in the nonshockable/bystander resuscitation group; and 8.2% (11 180 of 135 560), 4.5% (6071 of 135 560), and 1.1% (1533 of 135 552) in the nonshockable/no bystander resuscitation group (P<0.001).

Prehospital and EMS Responder Resuscitation Durations

The prehospital resuscitation duration ranged from 1 to 60 minutes in cases achieving prehospital ROSC and from 1 to 120 minutes in cases not achieving prehospital ROSC (Figure 2). In the subset of patients with ≤60 minutes of prehospital resuscitation duration (Figure 3A), 3.5% (9530 of 273 463) had favorable 30-day neurological outcome. Of the 9530 patients having favorable neurological outcome, 7924 (83.1%) were in cases achieving prehospital ROSC (Figure 3B). We found that only 0.7% (1606 of 241 943) of the cases not achieving prehospital ROSC went on to have favorable neurological outcome. Figure 4 shows a multiple logistic regression analysis for favorable 30-day neurological outcome in the 273 463 patients with ≤60 minutes of prehospital duration. Longer prehospital resuscitation duration reduced the likelihood of favorable neurological outcome (adjusted odds ratio, 0.84; 95% confidence interval, 0.838–0.844; P<0.001). In curve estimation in a quadratic model of each group stratified by initial cardiac arrest rhythm and bystander resuscitation status (Figure 5), the likelihood of favorable 30-day neurological outcome decreased for every minute that prehospital resuscitation efforts continued (R^2=0.295–0.037; P<0.001). Table 2 shows the sensitivities and negative predictive values of the prehospital resuscitation duration and the EMS responder

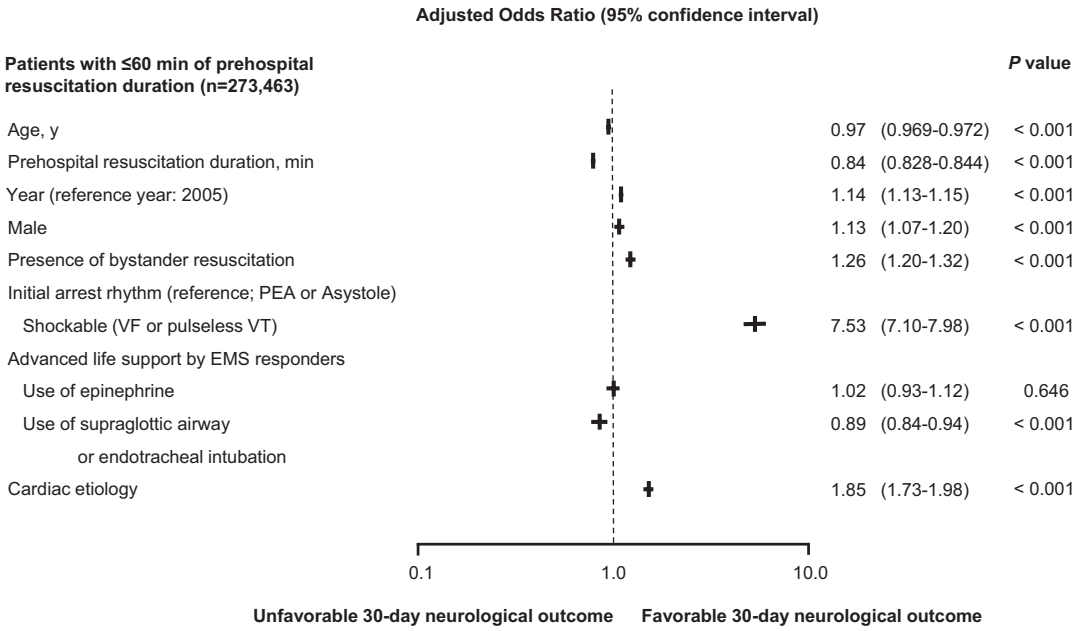

Figure 4. Adjusted odds ratios for favorable 30-day neurological outcome. EMS indicates emergency medical service; PEA, pulseless electric activity; ROSC, return of spontaneous circulation; VF, ventricular fibrillation; and VT, ventricular tachycardia.

resuscitation duration for favorable 30-day neurological outcome in each group stratified by initial cardiac arrest rhythm and bystander resuscitation status. Similar prehospital resuscitation durations were necessary to achieve a sensitivity of ≥99% for favorable 30-day neurological outcome (minimum) in each of the 4 groups (40 minutes in the shockable/bystander resuscitation and the shockable/no bystander resuscitation group, 44 minutes in the nonshockable/bystander resuscitation group, and 45 minutes in the nonshockable/no bystander resuscitation group). To achieve a sensitivity and negative predictive value of 100% (maximum), concordant prehospital resuscitation durations were needed in the 4 groups, ranging from 56 to 59 minutes. Moreover, similar results were found for the EMS responder resuscitation durations, with the minimum ranging from 33 to 39 minutes and the maximum ranging from 51 to 55 minutes.

Discussion

Since 1992, all resuscitation guidelines have stated that early access, early BLS, early defibrillation, and early ALS are essential components of a series of actions designed to reduce the mortality associated with cardiac arrest.[3–9,19] We analyzed the prehospital resuscitation duration from call receipt, inclusive of EMS responder resuscitation efforts with or without bystander resuscitation efforts, to determine the minimum period of prehospital resuscitation efforts to maximize good neurological outcomes. This nationwide, population-based study of prehospital resuscitation without implementation of TOR rules demonstrates that the prehospital resuscitation duration for favorable 30-day neurological outcome did not differ widely among 4 groups stratified by initial cardiac arrest rhythm and bystander resuscitation status, with the minimum, to achieve ≥99% sensitivity, ranging from 40 to 45 minutes and the maximum, to achieve 100% sensitivity and 100% negative predictive value, ranging from 56 to 58 minutes. Furthermore, similar results were found for the EMS responder resuscitation duration, with the minimum ranging from 33 to 39 minutes and the maximum ranging from 51 to 55 minutes. These findings suggest that prehospital resuscitation efforts should be continued for at least 40 minutes from call receipt, including at least 33 minutes of EMS responder resuscitation efforts from scene arrival, in all adult patients with bystander-witnessed OHCA.

In 2000, the national association of EMS physicians standards and clinical practice committee suggested that EMS responder resuscitation efforts could be terminated in patients who do not respond to 20 to 30 minutes of ALS.[23] However, our study suggests that prehospital resuscitation efforts, inclusive of EMS responder resuscitation efforts, can be continued for longer intervals with the possibility of success than previous thought. Several factors might account for longer durations of prehospital resuscitation efforts being associated with successful resuscitation in our study. Since 2000, the resuscitation protocols have been revised 4 times.[3–9] Our previous study revealed a significant increase in neurologically intact survival, from 2.1% in 2005 to 4.3% in 2009 for bystander-witnessed OHCA,[2] suggesting that the overall quality of resuscitation care, inclusive of the increment of bystander resuscitation with or without public-access AED[2,16,17,20] and post–cardiac arrest care,[24] has improved. Similar results were shown in this study. In 2012, Goldberger et al[12] demonstrated that patients with cardiac arrest occurring in hospitals where the median length of resuscitation efforts was longer were more likely to survive to discharge than those in hospitals where the median length of resuscitation efforts was shorter. In-hospital resuscitation duration ranged from 1 to 60 minutes for 31 198 patients achieving ROSC. In our study, the range of prehospital resuscitation duration to achieve prehospital ROSC was similar; however, frequencies of favorable 30-day neurological outcome were

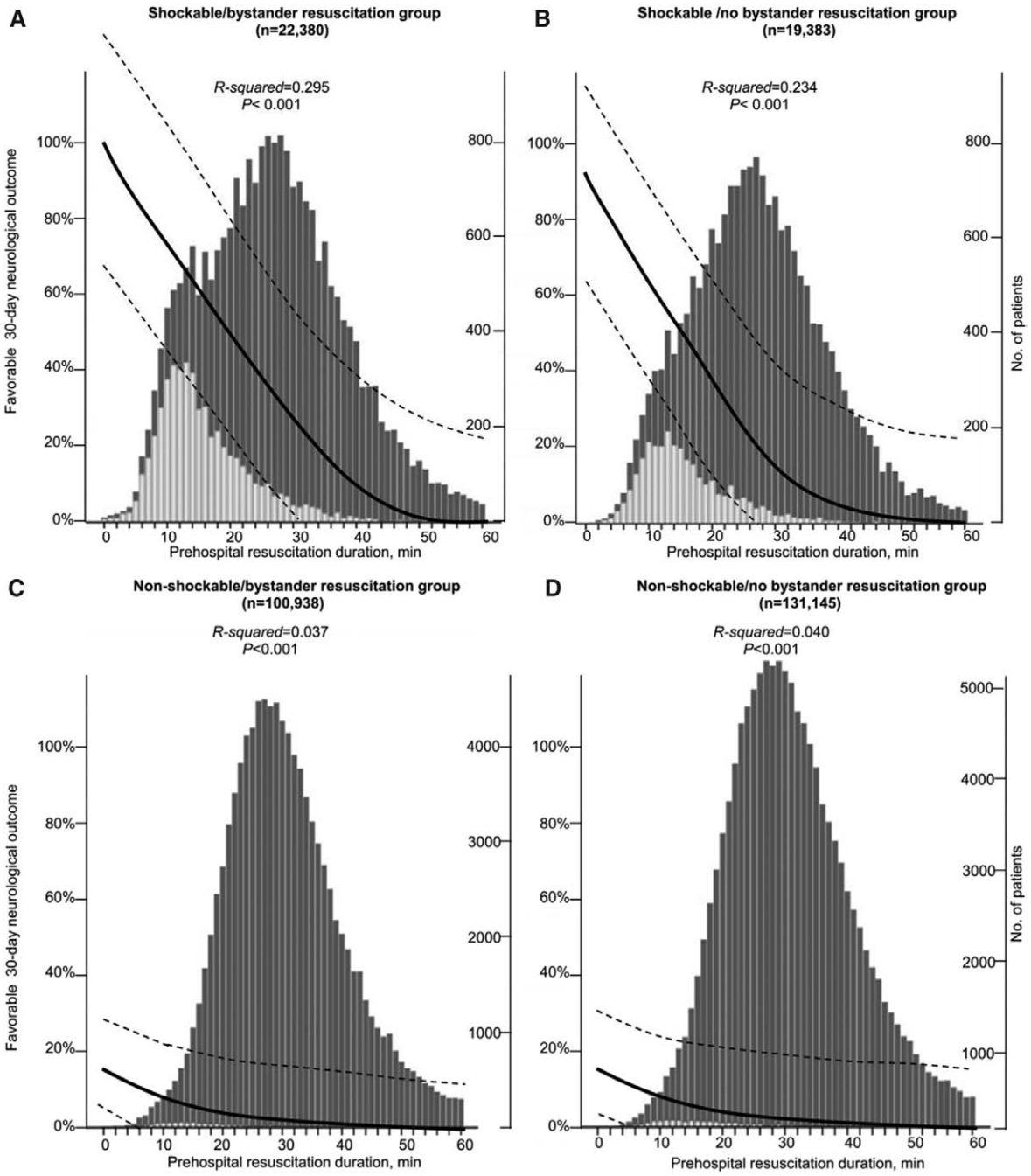

Figure 5. The relationship between prehospital resuscitation duration and favorable 30-day neurological outcome. The curve estimation in quadratic model of the shockable/bystander resuscitation group (**A**), the shockable/no bystander resuscitation group (**B**), the nonshockable/bystander resuscitation group (**C**), and the nonshockable/no bystander resuscitation group (**D**). Each solid curve with dotted lines shows predicted values with 95% confidence intervals for favorable 30-day neurological outcome. Each light gray box represents the actual number of cases achieving favorable 30-day neurological outcome, and each deep gray box represents the actual number of cases not achieving favorable 30-day neurological outcome.

lower. Possible explanations for these findings include differences in characteristics between the 2 study populations, more rapid deployment of high-quality resuscitation during in-hospital arrest, and improved access to high-quality post–cardiac arrest care in the in-hospital setting. Regardless, our findings suggest that high-quality resuscitation care expands the length of prehospital resuscitation efforts that produce favorable neurological outcomes, similar to the findings for in-hospital arrests.

In the 2010 resuscitation guidelines, the TOR rules included no ROSC after 3 full rounds of BLS or no ROSC after full ALS before transport.[4] In 2013, Reynolds et al[25] reported EMS responder resuscitation duration under the TOR rules. They showed that 90% of the neurologically intact survivors had achieved prehospital ROSC within 16.1 minutes of EMS responder resuscitation duration. However, 57.5% (3168 of 5517) of the OHCA patients met BLS TOR rules and did not receive EMS responder resuscitation

Table 2. Durations of Prehospital Resuscitation Efforts and EMS Responder Resuscitation Efforts for Favorable 30-Day Neurological Outcome

Shockable/bystander resuscitation group	
Prehospital resuscitation duration (n=22 380)	
Minimum duration, min	40
n/total, n (%)*	4490/4536 (99.0)
Sensitivity, % (95% CI)	99.0 (98.7–99.3)
n/total, n †	2594/2640
Negative predictive value, % (95% CI)	98.3 (97.8–98.8)
Maximum duration, min	58
n/total, n (%)*	4536/4536 (100)
n/total, n (%)†	79/79 (100)
EMS responder resuscitation duration (n=22 562)	
Minimum duration, min	33
n/total, n (%)*	4434/4479 (99.0)
Sensitivity, % (95% CI)	99.0 (98.7–99.3)
n/total, n †	2313/2358
Negative predictive value, % (95% CI)	98.1 (97.5–98.6)
Maximum duration, min	54
n/total, n (%)*	4479/4479 (100)
n/total, n (%)†	10/10 (100)
Shockable/no bystander resuscitation group	
Prehospital resuscitation duration (n=19 004)	
Minimum duration, min	40
n/total, n (%)*	2487/2513 (99.0)
Sensitivity, % (95% CI)	99.0 (98.6–99.4)
n/total, n †	2140/2166
Negative predictive value, % (95% CI)	98.8 (98.3–99.3)
Maximum duration, min	59
n/total, n (%)*	2513/2513 (100)
n/total, n (%)†	27/27 (100)
EMS responder resuscitation duration (n=19 113)	
Minimum duration, min	34
n/total, n (%)*	2491/2513 (99.0)
Sensitivity, % (95% CI)	99.1 (98.8–99.5)
n/total, n †	1886/1908
Negative predictive value, % (95% CI)	98.8 (98.4–99.3)
Maximum duration, min	54
n/total, n (%)*	2513/2513 (100)
n/total, n (%)†	70/70 (100)
Nonshockable/bystander resuscitation group	
Prehospital resuscitation duration (n=100 934)	
Minimum duration, min	44
n/total, n (%)*	952/961 (99.1)
Sensitivity, % (95% CI)	99.1 (98.5–99.7)
n/total, n †	9650/9659
Negative predictive value, % (95% CI)	99.9 (99.8–100)
Maximum duration, min	56
n/total, n (%)*	961/961 (100)
n/total, n (%)†	1219/1219 (100)
EMS responder resuscitation duration (n=102 813)	
Minimum duration, min	37
n/total n (%)*	943/952 (99.1)
Sensitivity % (95% CI)	99.1 (98.4–99.7)
n/total n †	8289/8298
Negative predictive value % (95% CI)	99.9 (99.8–100)
Maximum duration, min	51
n/total n (%)*	952/952 (100)
n/total n (%)†	1104/1104 (100)
Nonshockable/no bystander resuscitation group	
Prehospital resuscitation duration (n=131 145)	
Minimum duration, min	45
n/total n (%)*	1505/1520 (99.0)
Sensitivity % (95% CI)	99.0 (98.5–99.5)
n/total n †	11 491/11 506
Negative predictive value % (95% CI)	99.9 (99.8–99.9)
Maximum duration, min	58
n/total n (%)*	1520/1520 (100)
n/total n (%)†	690/690 (100)
EMS responder resuscitation duration (n=133 375)	
Minimum duration, min	39
n/total n (%)*	1506/1521 (99.0)
Sensitivity % (95% CI)	99.0 (98.5–99.5)
n/total n †	9490/9505
Negative predictive value % (95% CI)	99.8 (99.8–99.9)
Maximum duration, min	55
n/total n (%)*	1521/1521 (100)
n/total n (%)†	696/696 (100)

CI indicates confidence interval; and EMS, emergency medical service.

*Number of patients with favorable 30-day neurological outcome.

†Number of patients with unfavorable 30-day neurological outcome. Sensitivity and negative predictive value for favorable 30-day neurological outcome were calculated in the study cohort with ≤60 minutes of prehospital resuscitation duration who were stratified by initial cardiac arrest rhythm and bystander resuscitation status.

attempts. In an analysis of data from the All-Japan Utstein Registry in which EMS responders do not implement TOR rules, Kajino et al[26] showed that standard TOR rules had high specificity and positive predictive value for predicting unfavorable neurological outcome, but the specificity did not reach 99%. These findings suggest that TOR rules affect the

length of prehospital resuscitation efforts and the number of neurologically intact survivors.

The central question raised by this study is how long EMS responders should continue resuscitation efforts. This is a difficult question to answer because community systems of emergency care vary around the world, and ethical and cultural norms must be considered. It is clear that field termination reduces transport to the hospital,[10,11,21–23,25,26] but the optimal prehospital resuscitation duration has not previously been established. Our results demonstrate that prehospital resuscitation efforts to achieve favorable neurological outcome should be continued for at least 40 minutes from call receipt, inclusive of bystander and EMS responder resuscitation efforts, and for at least 33 minutes from scene arrival for EMS responder resuscitation efforts exclusively. We believe that this study will help optimize treatment for OHCA patients to maximize the number of neurologically intact survivors of cardiac arrest and will inform the development of future TOR rules.

This study has several limitations. First, in all epidemiological studies, data integrity, validity, and ascertainment bias are potential limitations. However, uniform data collection, a large sample size, and a population-based design covering all known OHCA in Japan minimize these potential sources of bias.[2,16,18,26] Second, the time of call receipt was used as the time of first resuscitation care to calculate the prehospital resuscitation duration. Collapse or first bystander resuscitation attempts might be better time indicators, but both are difficult to record accurately.[3–5,19] If bystander resuscitation is not performed, the interval from call receipt to ROSC includes a period of no flow followed by a period of EMS responder resuscitation efforts. When bystander resuscitation is performed, we have no way of knowing the percentage of the time from call receipt to EMS arrival; the bystanders actually performed resuscitation. However, we found similar lengths of time in all 4 groups when we analyzed the length of EMS responder resuscitation efforts exclusive of bystander attempts, suggesting that the presence of absence of bystander efforts does not substantially alter the time frame needed to maximize neurologically intact survivors. Furthermore, the time interval from call receipt to scene arrival is critical for survival.[3–5] The time of scene arrival was used as the time of first EMS responder resuscitation care to calculate the EMS responder resuscitation duration. Arrival at patient's side or first EMS responder resuscitation attempts might be better time indicators, but the time interval rushing to the patient's side from scene arrival is an important part of EMS responder resuscitation efforts.[19] Third, although the quality of resuscitation affects neurological outcome,[3–9,27,28] data on resuscitation quality were lacking. Fourth, information on ongoing resuscitation efforts after hospital arrival was lacking. We provided data demonstrating that 16.9% of patients who had favorable neurological outcomes achieved ROSC after hospital arrival; however, <1% of all patients who did not achieve prehospital ROSC went on to have favorable neurological outcome. Our analysis of this subgroup is limited because we do not have information about whether these patients received epinephrine or further defibrillation or how long the resuscitation effort was continued after hospital arrival. Fifth, details on post–cardiac arrest care[3–9,24,29–33] and use of extracorporeal cardiopulmonary resuscitation[34–36] were lacking. With broader adoption of these treatments, optimum length of the prehospital recitation efforts may need to be extended. Finally, neurological outcomes were measured at 30 days after OHCA, but some patients might recover more gradually. A recent consensus statement acknowledged that optimal times for follow-up after OHCA have yet to be established. A 3-month postdischarge period would balance the opportunity for recovery with the number of patients lost to follow-up.[37]

Conclusions

On the basis of results from the 2 shockable arrest groups, prehospital resuscitation efforts should be continued for at least 40 minutes from call receipt, including at least 33 minutes of EMS responder resuscitation efforts from scene arrival, in all adult patients with bystander-witnessed OHCA to achieve a ≥99% sensitivity of favorable 30-day neurological outcome. The costs and benefits of prolonging prehospital resuscitation efforts must be taken into consideration when these results are translated into clinical practice, and further studies are needed.

Acknowledgments

We thank all the EMS personnel and concerned physicians in Japan, the staff of the Fire and Disaster Management Agency and Institute for Fire Safety and Disaster Preparedness of Japan for their generous cooperation in establishing and following the Utstein database, Hiroshi Maekawa and Makoto Kobayashi who did office work at the subcommittee of resuscitation science in the Japanese Circulation Society, and Gary Cooper who helped edit the English composition.

Disclosures

The authors have completed and submitted the International Committee of Medical Journal Editors form for disclosure of potential conflicts of interest. Dr Gaieski reported receiving research funding from Bard and consulting for Bard and Stryker. Dr Saku reported receiving Endowed Departments of Advanced Therapeutics for Cardiovascular Disease supported by Boston Scientific Japan Co Ltd, Japan Medtronic Co Ltd, Japan Lifeline Co Ltd, and St. Jude Medical Japan Co Ltd, and an Endowed Department of Molecular Cardiovascular Therapeutics, Fukuoka University, supported by MSD Co Ltd and Department of Community and Emergency Medicine (supported by Izumi General Medical Center), which relates emergency medicine supports by Kagoshima City. Dr Saku had a grant from the Public Interest Incorporated Foundation of Clinical Research Promotion Foundation in Fukuoka, Japan. The other authors report no conflicts.

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CLINICAL PERSPECTIVE

Since 1992, all cardiopulmonary resuscitation guidelines have stated that the chain of survival (early access, early basic life support, early defibrillation, and early advanced cardiovascular life support) is an essential series of actions designed to reduce the mortality associated with out-of-hospital cardiac arrest. Recent cardiopulmonary resuscitation guidelines state that termination of resuscitation (TOR) rules are an important component of cardiopulmonary resuscitation, but TOR rules have not specified the minimum duration for prehospital resuscitation efforts. Furthermore, TOR rules are difficult to define objectively because community systems of emergency care vary around the world and ethical and cultural norms must be considered. It is clear that field termination reduces transport to the hospital, but the optimal prehospital cardiopulmonary resuscitation duration to maximize the number of patients with good neurological outcome has not previously been established. From the All-Japan Utstein Registry, in which emergency medical service responders do not implement TOR rules, we demonstrate that prehospital resuscitation efforts to achieve favorable neurological outcome should be continued for at least 40 minutes from call receipt, inclusive of bystander and emergency medical service responder resuscitation efforts, and for at least 33 minutes from scene arrival for emergency medical service responder resuscitation efforts exclusively. We believe that this study will help optimize treatment for patients with out-of-hospital cardiac arrest to maximize the number of neurologically intact survivors of cardiac arrest and will inform the development of future TOR rules. The costs and benefits of prolonging prehospital resuscitation efforts must be taken into consideration when these results are translated into clinical practice, and further studies are needed.

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Duration of Prehospital Resuscitation Efforts After Out-of-Hospital Cardiac Arrest

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Circulation. 2016;133:1386-1396; originally published online February 26, 2016;
doi: 10.1161/CIRCULATIONAHA.115.018788
Circulation is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231

Print ISSN: 0009-7322. Online ISSN: 1524-4539

SUPPLMENTAL MATERIAL

Appendix

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