PGY-1

Critical Review Form

Cohort

[Goto Y, Funada A, Goto Y. Relationship between the duration of cardiopulmonary resuscitation and favorable neurological outcomes after out-of-hospital cardiac arrest: a prospective, nationwide, population-based cohort study. J Am Heart Assoc, 2016 Mar 18;5(3):e002819.](http://pmid.us/26994129)

**Objectives: "1) to determine the relationship between duration of prehospital CPR conducted by EMS providers and survival with favorable neurological outcomes after OHCA, and (2) to determine, according to the initial rhythm in OHCA [out-of-hospital cardiac arrest), the critical prehospital CPR duration that would achieve prehospital ROSC [return of spontaneous circulation] and produce a cumulative proportion >99% of survivors and survivors with favorable neurological outcomes." (pp. 1-2)**

**Methods: This nationwide, observational study included all adult patients (18 year and older) who underwent resuscitation for OHCA and who achieved prehospital ROSC in Japan between January 1, 2011 and December 31, 2012. All patients in Japan with OHCA have been enrolled in a database controlled by the Fire and Disaster Management Agency (FDMA) since 2005 as part of an ongoing observational study, and this study was completed using data from this database. Patients were divided into 3 cohorts based on initial rhythm (ventricular fibrillation (VF)/pulseless ventricular tachycardia (VT), pulseless electrical activity (PEA), and asystole), and were classified as having cardiac or non-cardiac arrest based on physician and EMS personnel reporting.**

**The primary endpoint was favorable neurologic outcome, defined as a** [**Cerebral Performance Category score**](https://www.azdhs.gov/documents/preparedness/emergency-medical-services-trauma-system/save-hearts-az-registry-education/cerebral-performance-categories-scale.pdf) **of 1 or 2, one month following arrest. The secondary endpoint was survival at one month following arrest. Univariate and multivariate logistic regression were used to control for other variables and clarify the relationship between CPR duration and outcomes.**

**Out of 254,975 patients identified in the database over the 2-year study period, 17238 were eligible for enrollment. The median age was 74 years and 62.4% were male. Of the cohort, 28.2% had VF/pulseless VT, 43.1% had PEA, and 28.7% had asystole.**

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| **Critical Review Form: Cohort Study** |
| Guide | Comments |
| **Are the results valid?** |
| **Did experimental and control groups being the study with a similar prognosis?** |
| Did the study address a clearly focused issue?  | Yes. The authors specifically sought to understand the effect of CPR duration on outcomes in OHCA of various etiologies and to use this information to determine if there was a critical duration of CPR beyond which the survival rate and neurologic outcomes would support cessation of further resuscitative efforts. |
| Did the authors use an appropriate method to answer their question? - Is a cohort study a good way of answering the question under the circumstances?  | Yes. A cohort study including all patients with the exposure of interest (resuscitation with ROSC for OHCA) over a predetermined time period is optimal way to answer the questions being addressed. |
| Was the cohort recruited in an acceptable way? - Was the cohort representative of a defined population? - Was there something special about the cohort? - Was everybody included who should have been included?  | Yes. The authors identified patients from a nationwide database that included all patients undergoing resuscitation for OHCA. This represents a reliably representative sample that can be applied to patients in Japan. There was nothing special about the cohort and the authors included all relevant subjects. |
| Was the exposure accurately measured to minimize bias? - Did they use subjective or objective measurements? - Do the measures truly reflect what you want them to (have they been validated)? - Were all the subjects classified into exposure groups using the same procedure?  | Yes. The exposure was OHCA with ROSC, an objectively defined entity entered into a nationwide database. Patient classification based on initial rhythm was performed using [Utstein-style](https://www.ahajournals.org/doi/full/10.1161/HCQ.0000000000000024) reporting and was the same for all three groups. Initial rhythm is known to be a [significant determinant of outcomes](http://pmid.us/21796098) and hence represent a useful means of classifying patients. |
| Was the outcome accurately measured to minimize bias? - Did they use subjective or objective measurements? - Do the measures truly reflect what you want them to (have they been validated)? - Has a reliable system been established for detecting all the cases (for measuring disease occurrence)? - Were the measurement methods similar in the different groups? - Were the subjects and/or the outcome assessor blinded to exposure(does this matter)?  | Yes. The primary outcome of interest (survival with a neurologically favorable outcome at one month) is reasonably objective. The CPC score is a [well-validated tool](http://pmid.us/26744101) for assessing neurologic outcome following cardiac arrest, and was calculated and collected *a priori* as part of a larger database separate from this study. Use of neurologic outcome measures, rather than survival alone, has been recommended by the [Research Working Group of the American Heart Association Emergency Cardiovascular Care Committee](http://pmid.us/21969010). While blinding to exposure was not possible, the objective nature of the outcomes make this an unlikely source of bias.The use of a nationwide database, as detailed in the study, seems to be a reliable means of detecting all cases of OHCA in Japan over the specified time period. |
| Have the authors identified all important confounding factors and have they taken account of the confounding factors in the design (i.e. modelling, regression, propensity analysis, or sensitivity analysis to correct, control or adjust for confounding factors)? | Yes. The authors considered several key confounding factors: age, sex, bystander-witnessed arrest (yes or no), bystander CPR (yes or no), presumed cardiac cause (yes or no), initial cardiac rhythm (VF/pulseless VT, PEA, or asystole), automated external defibrillator administration (yes or no), use of advanced airway management (yes or no), epinephrine administration (yes or no), call-to-response time, and CPR duration. They used [logistic regression analysis](https://www.cdc.gov/nchs/tutorials/dietary/Advanced/EstimatePrevalence/Info3.htm) to control for the effects of the confounding factors on the outcomes of interest. |
| Was the follow up of subjects complete and was the follow up of subjects long enough?  | Yes and no. Follow-up was purportedly complete, again using the nationwide database previously mentioned. One-month follow-up is likely reasonable, although [90-day neurologic outcomes have been suggested as a more appropriate measure for studies of cardiac arrest](https://pubmed.ncbi.nlm.nih.gov/21969010/). |
| **What are the results?** |
| What are the results of this study?  |

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| Table. Outcomes by initial rhythm |
| Initial rhythm | 1-month survival | CPC 1-2 at 1 month |
| Overall | 36.6% | 21.8% |
| VF/pulseless VT | 68.0% | 52.1% |
| PEA | 30.5% | 13.7% |
| Asystole | 15.7% | 4.5% |

* The rate of overall 1-month survival was 36.8% and the rate of 1-month survival with a favorable neurologic outcome was 21.8%. See the table below for rates by rhythm
* CPR duration ≤ 30 minutes was independently associated with improved 1-month survival while duration ≤ 20 minutes was independently associated with improved 1-month neurologically favorable outcomes.
	+ For every 1-minute increase in CPR time, there was an adjusted unit odds ratio (OR) for 1-month survival of 0.95 (95% CI: 0.95–0.96) and an adjusted unit OR for a favorable 1-month neurological outcome of 0.95 (95% CI: 0.94–0.95).
	+ After 30 minutes of CPR, the 1-month survival rate decreased to 0.8% (95% CI: 0.7–1.0) and the rate of 1-month survival with a favorable neurological outcome decreased to 0.4% (95% CI: 0.3–0.5%).
	+ No patients who received CPR for more than 53 minutes survived at 1 month.
	+ For 1-month survival, a cumulative proportion >99% was reached after 35 minutes of CPR (95% CI: 34–38 minutes) among the total sample, 35 minutes (95% CI: 34–39 minutes) among VF/pulseless VT patients, 34 minutes (95% CI: 33–39 minutes) among PEA patients, and 39 minutes (95% CI: 36–46 minutes) among asystole patients.
	+ Moreover, for 1-month survival with favorable neurological outcomes, a cumulative proportion >99% was reached after CPR durations of 35 minutes (95% CI: 34–39 minutes) for all patients, 35 minutes (95% CI: 34– 40 minutes) for the VF/pulseless VT cohort, 35 minutes (95% CI 31–41 minutes) for the PEA cohort, and 42 minutes (95% CI: 31–49 minutes) for the asystole cohort.
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| How precise are the results? (i.e. what 95% CIs were associated with the results?) | See above. This was a large study with fairly narrow 95% confidence intervals. |
| Do you believe the results?  | Yes. That there is a relationship between duration of CPR and rates of survival and favorable neurologic outcome is not surprising. This studies merely provides some quantification of this relationship. |
| **Will the Results Help Me Locally?** |
| Were the study patients similar to my patient? | No. This study was conducted entirely in Japan, [where life expectancy is several years longer than in the US](https://www.worldlifeexpectancy.com/world-rankings-total-deaths) and where leading [causes of death](https://www.worldlifeexpectancy.com/usa-vs-japan-top-10-causes-of-death) are quite different. The prevalence of several key risk factors for cardiovascular disease are much higher in the US (including [diabetes mellitus](https://www.webmd.com/diabetes/news/20040426/diabetes-rates-worldwide#1) and [obesity](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2676846/)), and [death due to cardiovascular disease is more common among young people in the US when compared with a similar age group in Japan](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2676846/). The median age for OHCA [in the US was found to be 66](https://www.ahajournals.org/doi/full/10.1161/CIR.0000000000000152), while the median age in this study was 74. It is likely that these factors would affect outcomes following cardiac arrest and would affect survival rates at certain CPR duration cutoffs. |
| Do the results of this study fit with other available evidence?  | Yes. Prior evidence suggests that [survival rates are much higher for patients with shockable rhythms](http://pmid.us/21796098) than non-shockable rhythms, although the rates were much higher in this study (undoubtedly due to exclusion of patients who did not achieve ROSC in the prehospital setting). [Prior studies](https://emcrit.org/wp-content/uploads/2018/06/NF-and-LF-duration-for-arrest.pdf) have also demonstrated lower rates of survival with longer duration of CPR. |

**Limitations:**

1. **The authors chose to look at outcomes at one month, while** [**some experts**](http://pmid.us/21969010) **recommend looking at longer-term outcomes as far out as 90 days.**
2. **Nearly 80% of subjects in the database were excluded due to lack of ROSC in the field. Exclusion of this large cohort of patients likely had a significant impact on the results.**
3. **Difference in risk factors and age between this cohort and cardiac arrest victims in the US make it likely that different results would be found in a similar cohort in this country (**[**external validity**](http://www.epmonthly.com/archives/features/understanding-external-validity/)**).**

**Bottoms Line:**

**This large, prospective, observational study conducted in Japan found that longer duration of CPR was inversely correlated with rates of one-month survival and survival with a good neurologic outcome. Based on these data, the optimal cutoff for CPR to achieve a greater than 99% cumulative proportion of survivors was 35 minutes for VF/pulseless VT, 35 minutes for PEA, and 42 minutes for asystole. The primary limitation of this study was its external validity with regards to OHCA in the US.**