Resuscitation 102 (2016) 116–121

Contents lists available at ScienceDirect

Resuscitation

journal homepage: www.elsevier.com/locate/resuscitation

Clinical paper

# Associations between gender and cardiac arrest outcomes in Pan-Asian out-of-hospital cardiac arrest patients☆

Yih Yng Ng[a,c,1], Win Wah[b,1], Nan Liu[c,d,*,1], Sheng Ang Zhou[e], Andrew Fu Wah Ho[f], Pin Pin Pek[c], Sang Do Shin[g], Hideharu Tanaka[h], Nalinas Khunkhlai[i], Chih-Hao Lin[j], Kwanhathai Darin Wong[k], Wen Wei Cai[e], Marcus Eng Hock Ong[c,l], for the PAROS Clinical Research Network[2]

[a] Medical Department, Singapore Civil Defence Force, Singapore
[b] Centre for Infectious Disease Epidemiology and Research, Saw Swee Hock School of Public Health, National University of Singapore, Singapore
[c] Department of Emergency Medicine, Singapore General Hospital, Singapore
[d] Centre for Quantitative Medicine, Duke-NUS Medical School, Singapore
[e] Department of Emergency Medicine, Zhejiang Provincial People's Hospital, Hangzhou, Zhejiang, China
[f] SingHealth Emergency Medicine Residency Program, Singapore
[g] Department of Emergency Medicine, College of Medicine, Seoul National University, Seoul, Republic of Korea
[h] Department of EMS System, Graduate School, Kokushikan University, Tokyo, Japan
[i] Department of Emergency Medicine, Rajavithi Hospital, Bangkok, Thailand
[j] Department of Emergency Medicine, National Cheng Kung University Hospital, College of Medicine, National Cheng Kung University, Tainan, Taiwan
[k] Emergency Department, Hospital Pulau Pinang, Penang, Malaysia
[l] Health Services and Systems Research, Duke-NUS Medical School, Singapore

ARTICLE INFO

*Article history:*
Received 21 December 2015
Received in revised form 6 February 2016
Accepted 4 March 2016

*Keywords:*
Out-of-hospital cardiac arrest
Gender
Registry

ABSTRACT

*Background:* The incidence of out-of-hospital cardiac arrest (OHCA) in women is thought to be lower than that of men, with better outcomes in some Western studies.
*Objectives:* This study aimed to investigate the effect of gender on OHCA outcomes in the Pan-Asian population.
*Methodology:* This was a retrospective, secondary analysis of the Pan Asian Resuscitation Outcomes Study (PAROS) data between 2009 and 2012. We included OHCA cases which were presumed cardiac etiology, aged 18 years and above and resuscitation attempted by emergency medical services (EMS) systems. We used multi-level mixed-effects logistic regression models to account for the clustering effect of individuals within the country. Primary outcome was survival to hospital discharge.
*Results:* We included a total of 40,159 OHCA cases, 40% of which were women. We found that women were more likely to be older and have an initial non-shockable arrest rhythm; they were more likely to receive bystander cardio-pulmonary resuscitation (CPR). The univariate analysis showed that women were significantly less likely to have return of spontaneous circulation (ROSC) at scene or in the emergency department (ED), and had lower rates of survival-to-admission and discharge, and poorer overall and cerebral performance outcomes. There was however, no significant gender difference on outcomes after adjustment of other confounders. Women in the reproductive age group (age 18–44 years) were significantly more likely to have ROSC at scene or in the ED, higher rates of survival-to-admission and discharge, and have better overall and cerebral performance outcomes after adjustment for differences in baseline and pre-hospital factors. Menopausal women (age 55 years and above) were less likely to survive to admission after adjusting for other pre-hospital characteristics but not after age adjustment.
*Conclusion:* Differences in survival outcomes between reproductive and menopausal women highlight a need for further investigations into the plausible social, pathologic or hormonal basis.


☆ A Spanish translated version of the abstract of this article appears as Appendix in the final online version at http://dx.doi.org/10.1016/j.resuscitation.2016.03.002.
* Corresponding author at: Department of Emergency Medicine, Singapore General Hospital, Outram Road, Singapore 169608, Singapore.
*E-mail address:* liu.nan@sgh.com.sg (N. Liu).
[1] These authors contributed equally to this work.
[2] Investigators listed in Appendix A.

http://dx.doi.org/10.1016/j.resuscitation.2016.03.002
0300-9572/

## Introduction

Out-of-hospital cardiac arrest (OHCA) is a major cause of mortality around the world. Approximately around 359,400 Americans suffered OHCA every year with an overall survival rate of 9.5% in the United States in 2013.[1] Overall survival-to-hospital-discharge rates were lower in the Pan-Asian population with rates ranging from 0.5% to 8.5%.[2]

The incidence of OHCA in women is thought to be lower than that of men. [3] Several published studies have suggested the favorable effect of female gender on chances of survival to hospital admission, one month survival and good neurological outcomes, due to the possible neuro-protective effect of female endogenous estrogen and progesterone hormones.[3,4] Most studies have been conducted in the US and Europe with a few studies done in Japan and Korea.[3,4] Although a larger number of these studies have shown the positive impact of female gender on OHCA outcomes, a few of these studies contradicted the finding.[3,4] This calls for further studies to elucidate the conflicting results found. To date, no study has been conducted in a multi-ethnic Asian population on the effects of gender on survival and neurological outcomes after OHCA.

This study aimed to investigate the effect of gender on OHCA outcomes in a Pan-Asian population. The study findings will give insight into the effect of gender and its possible underlying mechanisms.

## Methodology

### *Study design*

The Pan-Asian Resuscitation Outcomes Study (PAROS) registry, established as a resuscitation clinical research network, is a prospectively collected Asia-Pacific, multinational registry to provide baseline information about OHCA prevalence, management and outcomes, describe variations among emergency medical systems (EMS) in region and compare systemic and structural interventions to address OHCA.[5] The network aims to improve survival from sudden cardiac arrest and other prehospital emergency conditions by supporting research on cost-effective strategies to improve outcomes.[5]

This study involved 12 sites in seven countries – Singapore, Japan, South Korea, Malaysia, Thailand, Taiwan and United Arab Emirates.[5] The demographic, socioeconomic characteristics and EMS systems of PAROS countries vary across the region.[6] Each participating country is responsible for its own data collection through a standardized process. All data are inputted through a secured shared internet electronic data capture system hosted by the Study Coordination Centre (SCC) in Singapore.[5] Institutional review board approval was granted to each center and country according to the regulations of each participating country.

The PAROS registry includes OHCA of both presumed cardiac and non-cardiac etiology brought in by EMS or presenting at emergency departments (EDs), as confirmed by the absence of pulse, unresponsiveness and apnea. The registry excludes patients who were immediately pronounced dead and for whom resuscitation was not attempted, including those with decapitation, rigor mortis, and dependent lividity and "do not attempt resuscitation" orders.

### *Data collection and outcomes*

This retrospective observational study included OHCA collected by the PAROS registry from seven countries in Asia between 2009 and 2012. For this analysis, we included OHCA cases which were presumed cardiac etiology, aged 18 years and above and had resuscitation attempted by EMS.

Survival-to-hospital discharge (discharged alive/remained in hospital at 30th day post-arrest) was the primary outcome. Secondary outcomes were return of spontaneous circulation (ROSC) at scene or in the ED, survival-to-hospital admission and survival with good neurological status with post-arrest overall and cerebral performance scales of 1 or 2. Variables included in this study were age, gender, location type, medical comorbidity, arrest witnessed status, bystander cardio-pulmonary resuscitation (CPR), initial arrest rhythm, prehospital defibrillation, prehospital airway, prehospital drug administration and EMS response time.

### *Data analysis*

The analyses were conducted using STATA software (College Station, Texas, StataCorp LP). The association between gender and outcomes were assessed using chi-squared tests and independent samples *t*-test or Mann–Whitney-*U* test as appropriate. We used multi-level mixed-effects logistic regression models to account for the clustering effect of individuals within the country. Univariate analyses were done to select variables for an adjusted multivariate analysis. Statistical significance was set at $p < 0.05$ criteria. In Asia (Singapore as the reference), the mean age for natural menopause in women is around 49 years.[7] Though there are other age group definitions defined for reproductive age, studies have consistently used the age range of 18–44 years as measurements for reproductive age.[8] Subgroup analyses were done in younger and older OHCA cases aged 18–44 years and ≥55 years (excluding the perimenopausal groups age 45–54) to assess the association between estrogen exposure and survival.[9,10]

## Results

The selection process for the included cases is shown in Fig. 1. Of 66,780 OHCA cases collected between 2009 and 2012, we included 40,159 OHCA cases aged 18 years old and above, of presumed cardiac etiology and with resuscitation attempted by EMS/private ambulance. Of the 40,159 cases, 24,267 cases were men (60%) and 15,892 cases were women (40%). We found women were older and more likely to have an initial non-shockable arrest rhythm; they were more likely to receive bystander CPR (Table 1). Men were younger, more likely to have witnessed arrests in public areas, have medical comorbidities and receive prehospital defibrillation, airway and drug administration.

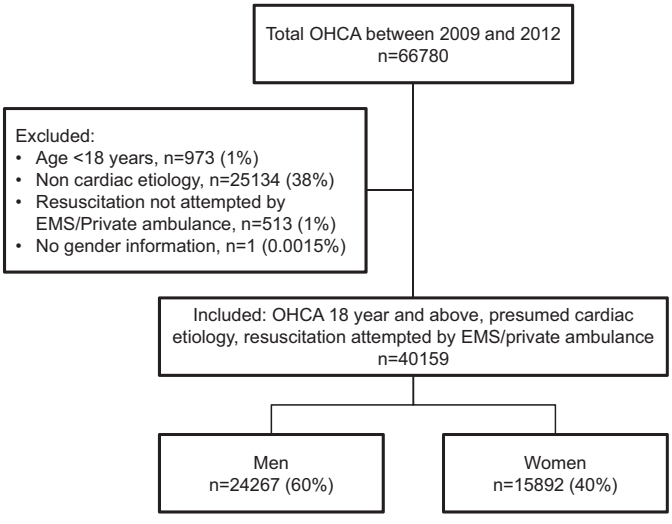


**Fig. 1.** Flow diagram of included cases.

**Table 1**
Characteristics of out-of-hospital cardiac arrest (OHCA) by gender.

| | Total | Male($n$ = 24,267) | Female($n$ = 15,892) | $p$ value[a] |
|---|---|---|---|---|
| Age, median (interquartile range) | 40,159 | 72 (60–81) | 82 (72–88) | <0.001 |
| **Patient brought in by** | | | | 0.547 |
| Non-EMS[b] | 32 | 21 (0.1) | 11 (0.1) | |
| EMS | 40,127 | 24,246 (99.9) | 15,881 (99.9) | |
| **Place of occurrence** | | | | <0.001 |
| Home residence | 12,974 | 7895 (32.5) | 5079 (32) | |
| Outside of home | 6176 | 4173 (17.2) | 2003 (12.6) | |
| **Medical history** | | | | <0.001 |
| No medical history | 1370 | 999 (4.1) | 371 (2.3) | |
| Presence of medical history | 9953 | 6313 (26) | 3640 (22.9) | |
| **Arrest witnessed** | 16,847 | 10,812 (44.6) | 6035 (38) | <0.001 |
| **Bystander CPR**[c] | 15,428 | 8885 (36.6) | 6543 (41.2) | <0.001 |
| **Initial arrest rhythm** | | | | <0.001 |
| Initial shockable rhythm | 5356 | 4296 (17.7) | 1060 (6.7) | |
| Initial non-shockable rhythm | 33,973 | 19,440 (80.1) | 14,533 (91.4) | |
| Prehospital defibrillation | 7121 | 5572 (23) | 1549 (9.7) | <0.001 |
| Prehospital airway | 16,265 | 10,014 (41.3) | 6251 (39.3) | <0.001 |
| Prehospital drug administration (epinephrine/atropine/amiodarone/bicarbonate/lidocaine/dextrose/other) | 4940 | 3451 (14.2) | 1489 (9.4) | <0.001 |
| Response time <8 min | 28,899 | 17,355 (71.5) | 11,544 (72.6) | 0.014 |
| ROSC[d] at scene or ED[e] | 3396 | 2429 (10) | 967 (6.1) | <0.001 |
| Survival-to-admission | 24,938 | 14,846 (61.2) | 10,092 (63.5) | <0.001 |
| Survival-to-discharge | 2567 | 1936 (8) | 631 (4) | <0.001 |
| Good post arrest cerebral performance[f] | 1490 | 1172 (4.8) | 318 (2) | <0.001 |
| Good post arrest overall performance[g] | 1174 | 912 (3.8) | 262 (1.6) | <0.001 |

[a] Statistical significance ($p < 0.05$).
[b] Emergency medical services.
[c] Cardiopulmonary resuscitation.
[d] Return of spontaneous circulation.
[e] Emergency department.
[f] Cerebral performance = 1 or 2.
[g] Overall performance = 1 or 2.

Among arrests aged 18–44 years, women were younger, less likely to be witnessed and more likely to happen at home and have an initial non-shockable rhythm and less likely to receive pre-hospital defibrillation or drug administration (Table 2). In the age group of 55 years and above, women were older, more likely to receive bystander CPR and have an initial non-shockable rhythm and receive bystander CPR but less likely to receive pre-hospital defibrillation, airway and or drug administration (Table 2).

The univariate analysis showed women were significantly less likely to have ROSC at scene or in the ED and had lower rates of survival-to-admission and discharge, and good overall and cerebral performance outcomes (Table 3). The multivariate analyses reported no significant gender difference on outcomes.

In sub-group analyses, we found women in the reproductive age group (age 18–44 years) were significantly more likely to have ROSC at scene or in the ED and had higher rates of survival-to-admission and discharge, and good overall performance outcomes after adjustment for differences in baseline and prehospital factors (Table 3). Menopausal women (age 55 years and above) were less likely to have ROSC at scene and had lower rates of survival-to-admission and discharge and good post-arrest overall and cerebral outcomes before adjustment for baseline and prehospital characteristics (Table 3). After adjustment of other confounders, the menopausal age group was significantly less likely to survive to hospital admission but not after the adjustment for age. In the subgroup analysis of initial rhythm, women showed lower rates of ROSC, survival-to-admission and discharge, and good post-arrest neurological outcomes in the univariate analysis but not after adjustment for other confounders.

## Discussion

In this multi-ethnic Asian population, we found that women in the reproductive age group had better survival and neurological outcomes after OHCA, menopausal women (age 55 years and above) were less likely to survive to admission after adjusting for baseline and other pre-hospital characteristics but not after age adjustment.

In this study, the incidence of OHCA in men was higher than women, consistent with other national registries.[3] This could be explained by higher prevalence of cardiovascular and life-style risk factors in men and possible cardio-protective effect of female estrogen and progesterone hormones on reduction of cardiac arrest risk in women.[11–13] In the analysis of overall arrests, women were more likely to have unfavorable pre-hospital factors and poorer survival and neurological outcomes after OHCA but there was no independent effect of gender on OHCA outcomes. This is consistent with previous studies showing lower overall survival rates among women[14] and in contrast with these studies by Adielsson et al. and Arrich et al.,[15,16] This could possibly be explained by poorer prognostic arrest characteristics among women such as older age, unwitnessed arrest, higher occurrence of arrests at home, and lower incidence of initial shockable rhythm despite higher rates of bystander CPR and shorter EMS response time consistent with previous studies.[4,17] A previous study suggested that female OHCA victims tended to have lower survival rates due to lesser pre-hospital resuscitative efforts and the social norms of a community in attempting chest compressions or administering defibrillation on females.[18] Consistent with previous findings, arrests with initial shockable rhythm were significantly higher in men, whereas women were more commonly found in initial

**Table 2**
Characteristics of out-of-hospital cardiac arrest (OHCA) by different age and gender groups.

| | Total | 18–44 years | | | Total | ≥55 years | | |
|---|---|---|---|---|---|---|---|---|
| | 2212 | Men *n* = 1640 | Women *n* = 572 | *p* value | 35,099 | Men *n* = 20,347 | Women *n* = 14,752 | *p* value[a] |
| Age, median (IQR) | 2212 | 38 (31–41) | 36 (30–41) | 0.002* | 35,099 | 75 (66–82) | 83 (75–89) | <0.001 |
| **Patient brought in by** | | | | 0.484 | | | | 0.674 |
| EMS[b] | 2205 | 1634 (99.6) | 571 (99.8) | | 35,082 | 20,338 (99.96) | 14,744 (99.9) | |
| Non-EMS | 7 | 6 (0.4) | 1 (0.2) | | 17 | 9 (0.04) | 8 (0.1) | |
| **Place of occurrence** | | | | <0.001* | | | | <0.001 |
| Home residence | 773 | 551 (33.6) | 222 (38.8) | | 11,111 | 6534 (32.1) | 4577 (31) | |
| Outside of home | 549 | 464 (28.3) | 85 (14.9) | | 4856 | 3024 (14.9) | 1832 (12.4) | |
| **Medical history** | | | | 0.715 | | | | 0.003 |
| No medical history | 319 | 253 (15.4) | 66 (11.5) | | 751 | 498 (2.4) | 253 (1.7) | |
| Presence of medical history | 487 | 381 (23.2) | 106 (18.5) | | 8528 | 5180 (25.5) | 3348 (22.7) | |
| **Arrest witnessed** | 1073 | 826 (50.4) | 247 (43.2) | | 14,382 | 8826 (43.4) | 5556 (37.7) | <0.001 |
| **Bystander CPR**[c] | 862 | 656 (40) | 206 (36) | | 13,516 | 7387 (36.3) | 6129 (41.5) | <0.001 |
| **Initial arrest rhythm** | | | | <0.001* | | | | <0.001 |
| Initial non-shockable rhythm | 1533 | 1081 (65.9) | 452 (79) | | 30,517 | 16,884 (83) | 13,633 (92.4) | |
| Initial shockable rhythm | 616 | 510 (31.1) | 106 (18.5) | | 3917 | 3056 (15) | 861 (5.8) | |
| **Prehospital defibrillation** | 763 | 625 (38.1) | 138 (24.1) | <0.001* | 5320 | 4027 (19.8) | 1293 (8.8) | <0.001 |
| Prehospital airway | 842 | 637 (38.8) | 205 (35.8) | 0.206 | 14,301 | 8475 (41.7) | 5826 (39.5) | <0.001 |
| Prehospital drug administration | 423 | 345 (21) | 78 (13.6) | <0.001* | 4006 | 2669 (13.1) | 1337 (9.1) | <0.001 |
| Response time <8 min | 1504 | 1100 (67.1) | 404 (70.6) | 0.116 | 25,464 | 14,705 (72.3) | 10,759 (72.9) | 0.171 |
| ROSC[d] at scene or ED[e] | 285 | 202 (12.3) | 83 (14.5) | 0.174 | 2752 | 1921 (9.4) | 831 (5.6) | <0.001 |
| Survival-to-admission | 1211 | 857 (52.3) | 354 (61.9) | <0.001* | 22,276 | 12,826 (63) | 9450 (64.1) | 0.061 |
| Survival-to-discharge | 317 | 231 (14.1) | 86 (15) | 0.555 | 1857 | 1371 (6.7) | 486 (3.3) | <0.001 |
| Good post arrest cerebral performance[f] | 219 | 164 (10) | 55 (9.6) | 0.197 | 1017 | 786 (3.9) | 231 (1.6) | <0.001 |
| Good post arrest overall performance[g] | 163 | 120 (7.3) | 43 (7.5) | 0.367 | 842 | 645 (3.2) | 197 (1.3) | <0.001 |

[a] Statistical significance ($p < 0.05$).
[b] Emergency medical services.
[c] Cardiopulmonary resuscitation.
[d] Return of spontaneous circulation.
[e] Emergency department.
[f] Cerebral performance = 1 or 2.
[g] Overall performance = 1 or 2.

non-shockable rhythm.[3,19–21] However, this study did not find any independent effect of gender on survival and neurological outcomes when stratified by initial rhythm.

A meta-analysis of 13 studies by Bougouin et al. highlighted that men were more likely to have witnessed arrests with initial shockable rhythm in public areas than women but bystander CPR rates were higher in females.[4] A closer examination of the paper showed that 11 of the 13 papers showed higher bystander CPR rates in males, but the two largest studies that were authored in Japan, had higher bystander CPR rates amongst women despite lower bystander witnessed rates. This is similar to what was found in the PAROS dataset. It is likely that there are cultural differences between an Asian and Caucasian population that led to the significantly different ratios of bystander CPR between genders which may warrant further investigation.

Women in the child-bearing age group of 18–44 years old showed higher rates of ROSC, survival-to-admission and discharge, and good overall performance outcomes after adjusting for prehospital differences; menopausal women (≥55 years old) had poorer survival-to-admission outcomes. Analysis of the interaction between age and gender in several studies also showed that females in child bearing ages had higher odds of survival-to-admission,[22–25] survival-to-discharge,[17] long-term survival,[20] and good neurological outcomes[22,19] after accounting for differences in the rates of witnessed status, bystander CPR and cardiac rhythm.[9,21,25] This could be explained by possible post-ischemic cardiac and neuro-protective mechanism of female endogenous estrogen and progesterone hormones after cardiac arrest and CPR.[11,12] Another postulation regarding better survival is the fact that women have smaller chests and hearts and more delicate chest walls, allowing greater compression force or depth to be achieved, which leads to more efficacious CPR and defibrillation.[26] This study highlights that the survival differences between male and females in the age group of 18–44 years could be explained more by other pre-hospital characteristics than age. For the menopausal age group, age is the main confounder influencing gender variation in survival outcomes.

Differences in survival outcomes between reproductive and menopausal women highlight a need for further investigations into the plausible social, pathologic or hormonal basis for the relationship found. Future prospective studies are needed to ascertain the protective effects of estrogen and progesterone on OHCA outcomes among different age groups. There are also suggestions that testosterone may play a part in OHCA survival. Further investigations are warranted to measure gonadal hormones and isolate the effect of individual gonadal hormones on OHCA survival.

The strength of this study lies in its large sample size and involvement of several countries in the Asia Pacific. However, there are also several limitations to this study. The registry does not collect detailed etiology data; pre-menopausal females may arrest more often from causes (e.g. thromboembolic diseases, attempted suicide or gender related diseases, such as ectopic pregnancy) that may have higher chances of survival as compared to cardiac causes. There is also a difference in proportion of females in the premenopausal age versus the menopausal age (26% versus 42%), which suggest a form of selection bias or perhaps reflect the effect of differences in gender physiology and their effect on death rates. Due to the retrospective nature of the study, we were unable to draw causal conclusions of the associations observed in this study. Another limitation is that there might be unmeasured confounders which could have affected the association between gender and outcomes. Additionally, estrogen and progesterone levels were not measured in this study and age groups were used as surrogates for hormonal levels in women. Lastly, this study was unable to identify the underlying socio-economic implications of gender on OHCA

**Table 3**
Overall and sub-group multivariate analysis on survival outcome of out-of-hospital cardiac arrest (OHCA) by gender.

| | Unadjusted OR | Adjusted OR[a] |
|---|---|---|
| **Female versus male (overall)** | | |
| ROSC[b] at scene or ED | 0.56 (0.52–0.61)[f] | 1.01 (0.88–1.16) |
| Survival-to-admission | 0.86 (0.82–0.91)[f] | 1 (0.92–1.09) |
| Survival-to-discharge | 0.48 (0.43–0.52)[f] | 0.94 (0.77–1.15) |
| Good cerebral performance | 0.41 (0.36–0.46)[f] | 0.88 (0.62–1.25) |
| Good overall performance | 0.39 (0.33–0.46)[f] | 1.04 (0.76–1.42) |
| **Female versus male (18–44 years)** | | |
| ROSC at scene or ED[c] | 1.09 (0.83–1.44) | 2.11 (1.27–3.52)[f] |
| Survival-to-admission | 1.16 (0.91–1.48) | 1.74 (1.19–2.54)[f] |
| Survival-to-discharge | 1.01 (0.77–1.32) | 1.82 (1.11–2.97)[f] |
| Good cerebral performance[d] | 0.85 (0.6–1.19) | 1.82 (0.93–3.57) |
| Good overall performance[e] | 0.89 (0.61–1.3) | 3.32 (1.27–8.66)[f] |
| **Female versus male (≥55 years)** | | |
| ROSC at scene or ED | 0.56 (0.52–0.61)[f] | 1.01 (0.87–1.17) |
| Survival-to-admission | 0.86 (0.82–0.91)[f] | 0.94 (0.83–1.08) |
| Survival-to-discharge | 0.47 (0.42–0.52)[f] | 1.04 (0.87–1.23) |
| Good cerebral performance | 0.4 (0.34–0.46)[f] | 0.95 (0.73–1.24) |
| Good overall performance | 0.39 (0.33–0.46)[f] | 1.04 (0.76–1.42) |
| **Initial shockable rhythm** | | |
| ROSC at scene or ED | 0.94 (0.8–1.09) | 1.09 (0.86–1.39) |
| Survival-to-admission | 0.93 (0.78–1.1) | 1.22 (0.99–1.52) |
| Survival-to-discharge | 0.8 (0.68–0.94)[f] | 0.88 (0.65–1.19) |
| Good cerebral performance | 0.85 (0.7–1.03) | 0.99 (0.71–1.38) |
| Good overall performance | 0.91 (0.74–1.12) | 1.12 (0.74–1.71) |
| **Initial non-shockable rhythm** | | |
| ROSC at scene or ED | 0.68 (0.64–0.72)[f] | 1 (0.85–1.18) |
| Survival-to-admission | 0.91 (0.87–0.95)[f] | 0.96 (0.87–1.06) |
| Survival-to-discharge | 0.57 (0.52–0.61)[f] | 1.01 (0.77–1.32) |
| Good cerebral performance | 0.5 (0.41–0.61)[f] | 0.87 (0.64–1.19) |
| Good overall performance | 0.48 (0.39–0.58)[f] | 0.88 (0.61–1.27) |

[a] Adjusted for significant covariates in univariate analysis (age, gender, location type, medical history, arrest witnessed status, bystander CPR, initial arrest rhythm, prehospital defibrillation, prehospital airway, prehospital drug administration, response time).
[b] Return of spontaneous circulation.
[c] Emergency department.
[d] Cerebral performance = or 2.
[e] Overall performance = 1 or 2.
[f] Statistical significance ($p < 0.05$).

outcomes since the focus of this study was on pre-hospital factors and socio-economic data were unavailable.

## Conclusion

This multi-ethnic Asian population study showed that women in the reproductive age group had better survival and neurological outcomes after OHCA; menopausal women had poor survival-to-admission outcomes. Differences in survival outcomes between reproductive and menopausal women highlight a need for further investigations into the plausible social, pathologic or hormonal basis for the relationship found.

## Conflict of interest statement

The authors declare that they have no conflict of interest.

## Funding sources

This study is supported by grants from the National Medical Research Council (Singapore), Ministry of Health, Singapore, and Korea Centers for Disease Control and Prevention.

## Acknowledgements

We would like to acknowledge the contributions of Ms Susan Yap and Ms Shahidah Ahmad from the Department of Emergency Medicine, Singapore General Hospital and the Singapore Clinical Research Institute for coordination of the study.

## Appendix A. PAROS Clinical Research Network

Participating site investigators: M.H.M. Ma (National Taiwan University, Taipei, Taiwan), P.C.I. Koh (National Taiwan University, Taipei, Taiwan), T. Nishiuchi (Kindai University, Osaka, Japan), T. Nakagawa (Aichi Medical University Hospital, Aichi, Japan), E.J. Lee (Seoul National University, Seoul, Korea), H.W. Ryoo (Kyungpook National Unversity Hospital, Daegu, Korea), K.J. Song (College of Medicine, Seoul National University, Seoul, Korea), N.A.R. Hisamuddin (School of Medical Sciences, Universiti Sains Malaysia, Kelantan, Malaysia), S.A. Karim (Hospital Sungai Buloh, Selangor, Malaysia), G.Y. Naroo (Rashid Hospital, Dubai, United Arab Emirates), A.S. Omer (Dubai Corporation for Ambulance Services, Dubai, United Arab Emirates), T. Yagdir (Dubai Corporation for Ambulance Services, Dubai, United Arab Emirates), P. Khruekarnchana (Rajavithi Hospital, Bangkok, Thailand), A. Monsomboon (Siriraj Hospital, Bangkok, Thailand), T. Piyasuwankul (Prince of Songkla University, Hatyai, Thailand), E.S. Goh (Khoo Teck Puat Hospital, Singapore), D.R.H. Mao (Khoo Teck Puat Hospital, Singapore), N.E. Doctor (Singapore General Hospital, Singapore), L.P. Tham (KK Women's & Children's Hospital, Singapore), K. Kajino (Osaka National Hospital, Osaka, Japan), R.A. Charles (Alexandra Hospital, Singapore), S.O. Cheah (Ng Teng Fong General Hospital), D.C.G. Foo (Tan Tock Seng Hospital, Singapore), M.Y.C. Chia (Tan Tock Seng Hospital, Singapore), H.N. Gan (Changi General Hospital, Singapore).

## References

1. *Cardiac Arrest Statistics*. Available from: http://www.heart.org/HEARTORG/General/Cardiac-Arrest-Statistics_UCM_448311_Article.jsp [accessed 10.12.15].
2. Ong ME, Shin SD, De Souza NN, et al. Outcomes for out-of-hospital cardiac arrests across 7 countries in Asia: the Pan Asian Resuscitation Outcomes Study (PAROS). Resuscitation 2015;96:100–8.
3. Hasan OF, Al Suwaidi J, Omer AA, et al. The influence of female gender on cardiac arrest outcomes: a systematic review of the literature. Curr Med Res Opin 2014;30:2169–78.
4. Bougouin W, Mustafic H, Marijon E, et al. Gender and survival after sudden cardiac arrest: a systematic review and meta-analysis. Resuscitation 2015;94:55–60.
5. Ong ME, Shin SD, Tanaka H, et al. Pan-Asian Resuscitation Outcomes Study (PAROS): rationale, methodology, and implementation. Acad Emerg Med 2011;18:890–7.
6. Ong ME, Cho J, Ma MHM, et al. Comparison of emergency medical services systems in the Pan-Asian Resuscitation Outcomes Study countries: report from a literature review and survey. Emerg Med Australas 2013;25:55–63.
7. *Managing menopause – the role of the GP*. Available from: https://www.kkh.com.sg/AboutUs/Publications/Documents/Managing%20menopause%20-%20the%20role%20of%20the%20GP_SD%20Jan-Feb14_V62_I1.pdf [accessed 30.11.15].
8. *Centers for Disease Control and Prevention. Chronic disease indicators; Indicator definitions – reproductive health*. Available from: http://www.cdc.gov/cdi/definitions/reproductive-health.html [accessed 30.11.15].
9. Bray JE, Stub D, Bernard S, Smith K. Exploring gender differences and the "oestrogen effect" in an Australian out-of-hospital cardiac arrest population. Resuscitation 2013;84:957–63.
10. Topjian AA, Localio AR, Berg RA, et al. Women of child-bearing age have better in-hospital cardiac arrest survival outcomes than equal aged men. Crit Care Med 2010;38:1254.
11. Noppens RR, Kofler J, Hurn PD, Traystman RJ. Dose-dependent neuroprotection by 17β-estradiol after cardiac arrest and cardiopulmonary resuscitation. Crit Care Med 2005;33:1595–602.
12. McCullough LD, Hurn PD. Estrogen and ischemic neuroprotection: an integrated view. Trends Endocrinol Metab 2003;14:228–35.
13. Jousilahti P, Vartiainen E, Tuomilehto J, Puska P. Sex, age, cardiovascular risk factors, and coronary heart disease: a prospective follow-up study of 14 786 middle-aged men and women in Finland. Circulation 1999;99:1165–72.

14. Safdar B, Stolz U, Stiell IG, et al. Differential survival for men and women from out-of-hospital cardiac arrest varies by age: results from the OPALS study. Acad Emerg Med 2014;21:1503–11.
15. Adielsson A, Hollenberg J, Karlsson T, et al. Increase in survival and bystander CPR in out-of-hospital shockable arrhythmia: bystander CPR and female gender are predictors of improved outcome. Experiences from Sweden in an 18-year perspective. Heart 2011;97:1391–6.
16. Arrich J, Sterz F, Fleischhackl R, et al. Gender modifies the influence of age on outcome after successfully resuscitated cardiac arrest: a retrospective cohort study. Medicine (Baltimore) 2006;85:288–94.
17. Johnson MA, Haukoos JS, Larabee TM, et al. Females of childbearing age have a survival benefit after out-of-hospital cardiac arrest. Resuscitation 2013;84:639–44.
18. Ahn KO, Shin SD, Hwang SS. Sex disparity in resuscitation efforts and outcomes in out-of-hospital cardiac arrest. Am J Emerg Med 2012;30:1810–6.
19. Akahane M, Ogawa T, Koike S, et al. The effects of sex on out-of-hospital cardiac arrest outcomes. Am J Med 2011;124:325–33.
20. Iwami T, Hiraide A, Nakanishi N, et al. Age and sex analyses of out-of-hospital cardiac arrest in Osaka, Japan. Resuscitation 2003;57:145–52.
21. Kim C, Fahrenbruch CE, Cobb LA, Eisenberg MS. Out-of-hospital cardiac arrest in men and women. Circulation 2001;104:2699–703.
22. Kitamura T, Iwami T, Nichol G, et al. Reduction in incidence and fatality of out-of-hospital cardiac arrest in females of the reproductive age. Eur Heart J 2010;31:1365–72.
23. Topjian AA, Localio AR, Berg RA, et al. Women of child-bearing age have better inhospital cardiac arrest survival outcomes than do equal-aged men. Crit Care Med 2010;38:1254–60.
24. Merchant RM. Race and gender disparities in survival to hospital discharge after cardiac arrest. Am Heart J 2011;16:705–11.
25. Pell J, Sirel J, Marsden A, Cobbe S. Sex differences in outcome following community-based cardiopulmonary arrest. Eur Heart J 2000;21:239–44.
26. Tomlinson A, Nysaether J, Kramer-Johansen J, Steen P, Dorph E. Compression force–depth relationship during out-of-hospital cardiopulmonary resuscitation. Resuscitation 2007;72:364–70.