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Clinical paper

The interaction of sex and age on outcomes in emergency medical services-treated out-of-hospital cardiac arrest: A 5-year multicenter retrospective analysis

Ching-Yu Chen[a], *Cheng-Yi Fan*[b], *I-Chung Chen*[a], *Yun-Chang Chen*[a], *Ming-Tai Cheng*[a,c,d], *Wen-Chu Chiang*[a,c,d], *Chien-Hua Huang*[c,d], *Chih-Wei Sung*[b,c,1,*], *Edward Pei-Chuan Huang*[b,c,d,1,*]

Abstract

Background: Studies have established that sex and age influence outcomes following out-of-hospital cardiac arrest (OHCA). However, a knowledge gap exists regarding their interaction. This study aimed to investigate the interaction of age and sex and how they cooperatively influence OHCA outcomes.

Methods: This retrospective cohort study included adult, nontraumatic OHCA patients admitted to a university hospital and its affiliated hospitals in Taiwan from January 2017 to December 2021. Data including sex, age, body mass index, cardiac rhythm, and resuscitation information in the emergency department (ED) were collected from medical records. The study outcomes encompassed survival to intensive care unit (ICU) admission, survival to hospital discharge, and a favorable neurological outcome. Multivariable logistic regression was performed to estimate the influence of sex on study outcomes.

Results: We analyzed a total of 2,826 eligible subjects categorized into three groups: young (18–44 years, 149 males and 57 females), middle-aged (45–64 years, 524 males and 188 females), and old (≥65 years, 1,049 males and 859 females). Analysis of the effects of sex according to age stratification showed that old males had higher odds for survival to ICU admission (OR: 1.49, 95% CI: 1.21–1.83) and favorable neurological outcomes (OR: 2.74, 95% CI: 1.58–4.76) than did old females. Analysis of the effects of age according to sex stratification revealed that old males had lower odds for survival to hospital discharge (OR: 0.33, 95% CI: 0.21–0.51) and favorable neurological outcomes (OR: 0.26, 95% CI: 0.16–0.43) than did young males. Old females also showed the same trend as males, with lower odds for survival to hospital discharge (OR: 0.37, 95% CI: 0.17–0.78) and favorable neurological outcomes (OR: 0.11, 95% CI: 0.05–0.25) than did young females.

Conclusions: The interaction between sex and age in patients with OHCA results in diverse outcomes. Within the same sex, age demonstrated varying effects on distinct outcomes.

Keywords: Out-of-hospital cardiac arrest, Outcome, Age, Sex, Interaction

Introduction

Out-of-hospital cardiac arrests (OHCAs), which occur in approximately 100 cases per 100,000 people, is significant global public health concern. For decades, OHCA survival rates have remained poor.[1,2] To improve outcomes, efforts have been invested to identify and control risk factors, albeit with limited success.

While sex and age have been widely recognized as crucial factors associated with OHCA outcomes, the consistency of this association varies among different studies.[2–20] Regarding the effects of sex, some studies have indicated that female patients with OHCA

* Corresponding authors at: Department of Emergency Medicine, National Taiwan University Hospital Hsin-Chu Branch, No.25, Lane 442, Sec.1, Jingguo Rd, Hsinchu City 300, Taiwan.

E-mail addresses: chihweisung@ntu.edu.tw (C.-W. Sung), edward56026@gmail.com (E.P.-C. Huang).

[1] These authors contributed equally.

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had better survival outcomes[14,15,7] and neurological recovery[13,14,7,8] than did male patients, whereas others found that males had higher rates in return of spontaneous circulation (ROSC)[5] or survival to hospital discharge.[16–19] However, some cohort studies found no sex differences in outcomes.[6,10,13] Regarding the effects of age, Ishii et al. found that younger males had better outcomes than did older males,[3] whereas Funada et al. showed decreased frequency of favorable neurological outcomes with age.[12].

The interaction effects between sex and age on OHCA outcomes are quite complicated. Some reports indicate that their results were associated with sex and/or age. Johnson et al. found that young female OHCA patients had higher survival rates to hospital discharge than did their young male counterparts.[16] Another study found a positive correlation between increased age and hospital mortality among female but not male OHCA patients.[15] Given the interaction effects between sex and age on OHCA outcomes, treating both factors as independent may be inappropriate.

Interestingly, a study by Hagihara et al. found that Japanese female OHCA patients had higher survival rates than did their male counterparts across all age groups. However, no significant differences in neurological outcomes were observed. When considering age as a factor, the younger age group consistently exhibited better neurological recovery than did the older age group, regardless of sex.[11] Although Japan and Taiwan are both located in Asia, their demographic structure differs, with no recent studies on this topic having been published in both countries. This study specifically examines the effects of gender, age, and their interaction on the outcomes of OHCA within the Taiwanese population. It also tests the hypothesis that elderly males in this cohort experience poorer outcomes.

Methods

Study design and participants

This multicenter retrospective study enrolled OHCA patients admitted to the National Taiwan University Hospital (NTUH) and two of its affiliated hospitals from January 2017 to December 2021. NTUH is a third-level hospital located in Taipei City with approximately 200 intensive care unit (ICU) beds. Its affiliated hospitals consist of a second-level urban hospital in Hsinchu City (Hsin-Chu Branch) and a rural hospital in Yunlin County (Yun-Lin Branch). The study protocol was approved by the ethics committees of the NTUH (code: 202307016RINA). The approving bodies waived the need for informed consent from the subjects due to the retrospective nature of this study with minimal intervention. All patients included herein were adults (age $\geq$18 years) who experienced nontraumatic OHCA and were brought to the hospitals for resuscitation and critical care. We excluded patients who achieved ROSC but were transferred to other hospitals for admission. Next, we excluded the patients from the healthcare facilities such as nursing homes. Furthermore, those whose medical record entries were ambiguous or invalid were excluded.

The decision to screen patients was made during study meetings conducted each month. The medical records of eligible patients were reviewed by independent physicians, and data were collected using the Research Electronic Data Capture system, a web-based software platform designed to support research data collection.[21] The medical chart review process followed strict procedures to minimize information bias.

Definition of variables

A case was classified as OHCA if the individual has no palpable pulse or normal breathing at the scene. This confirmation was performed by the emergency medical technician. Our data was collected based on the Utstein-style template[22]. Demographic data included age, sex, and body mass index (BMI). Data from Emergency Medical Services (EMS) were gathered from reports of each medical service encounter. This data encompassed a range of variables including witnessed collapse, bystander CPR, EMS response time, and resuscitation management, among others. Covariates encompassed initial cardiac rhythm, medical events during ICU or ward stays, neurological outcome, prehospital ROSC, immediate "do not resuscitate" (DNR) status upon arrival at the ED, termination of resuscitation (TOR), and CPR duration. The EMS response time was defined as the time between notification of an occurrence and the ambulance arrival at the scene. A shockable rhythm was defined as the presence of pulseless ventricular tachycardia or ventricular fibrillation during resuscitation. Prehospital ROSC defined as any restoration of spontaneous circulation and breathing before hospital arrival. Immediate DNR was defined as failure of patients in the ED to receive any CPR after their family announced withdrawal of resuscitation upon hospital arrival. After the activation of the EMS system, it was a protocol that patients could not discontinue resuscitation efforts prior to hospital arrival. Hence, TOR referred to the cessation of ongoing CPR by family in the ED. These patients received CPR initially but was terminated for any reason within a short time. CPR duration was defined as the time from patient's ED arrival to CPR termination or ROSC.

Outcomes

The outcomes included survival to ICU admission, survival to hospital discharge, and favorable neurological outcome. Survival to ICU admission was defined as the admission of a living patients who achieved ROSC in the ED to the ICU, whereas survival to hospital discharge was defined as the discharged of a living patient. At the time of discharge, independent intensivists, who cared for the patients but did not participate in the study, documented the patient's neurological status, which was used to determine neurological outcome. Glasgow–Pittsburgh Cerebral Performance Category (CPC) scores were used to quantitatively assess neurological outcomes. CPC scores of 1 or 2 indicated favorable neurological outcomes.

Statistical analysis

Data collection, data cleaning, and statistical analysis were performed by a statistician. All analyses were performed using SPSS version 26 (International Business Machines Corporation, IBM), with a two-sided p value of <0.05 indicating statistical significance. Initially, the categorization of young, middle-aged, and elderly groups lacked a universally accepted definition. In this study, patients were segmented into three distinct age brackets: young adults (18–44 years), middle-aged individuals (45–64 years), and seniors (aged 65 and older). This tripartite age classification aligns with the demographic divisions outlined in the National Center for Health Statistics' annual mortality report and has been widely adopted in prior research[23]. Second, descriptive statistics were performed, stratifying the patients according to the sex and age groups. The normality of data distribution was determined using the Shapiro–Wilk test.[24] Continuous variables with a normal distribution were compared using Student's t-test or analysis of variance and presented as mean ± the standard deviation. Categorical variables were compared using the chi-square test and presented as number (percentage).

To evaluate the mean differences across three age groups, we conducted an Analysis of Variance (ANOVA) test. Upon finding a significant result, we proceeded with a correction for multiple comparisons. For this purpose, the Bonferroni correction method was employed in our post-hoc analysis. This step entailed adjusting our alpha significance level in proportion to the number of comparative analyses conducted. More precisely, the significance threshold was set at a p-value of less than 0.017. This figure was calculated by dividing our initial alpha level of 0.05 by the number of tested hypotheses, resulting in 0.05/3 = 0.017. Subsequently, we compared the p-values from each group comparison to this revised alpha level. Any p-value that was below this adjusted threshold was deemed to signify a statistically relevant difference.

To ascertain the presence of an age and sex interaction effect on OHCA outcomes, our initial step involved testing for this interaction. We employed a multivariable logistic regression analysis to explore the relationships between sex, age, and their interaction (sex*age) with the outcomes. This analysis yielded adjusted odds ratios (aORs) and their respective 95% confidence intervals (CIs). In cases where a significant interaction was identified, we further examined the interaction effects between sex and age on the outcomes. We amalgamated the age groups and sex, stratifying the OHCA patients into six groups: young females, young males, middle-aged females, middle-aged males, old females, and old males. We calculated the ORs and 95% CIs for each outcome in the five remaining groups, with the young female group as the reference group. To investigate the influence of sex within specific age groups, we estimated the ORs and 95% CIs according to age stratification. Additionally, to assess the impact of age on outcomes within each sex category, we calculated the ORs and 95% CIs according to sex stratification.

Results

A flowchart for patient enrollment is presented in Fig. 1. A total of 3,252 OHCA patients were identified during the recruitment period. Pediatric (n = 69) and traumatic OHCAs (n = 325) were excluded. Data from the remaining 2,858 patients were assessed and extracted. Among these patients, 29 were transferred to other hospitals, and 3 had missing medical records. Ultimately, 2,826 OHCA patients who satisfied the screening criteria were included and classified into three groups (young: 206, 7.3%; middle-aged: 712, 25.2%; and old: 1,908, 67.5%). In all age groups, males outnumbered females, with the percentage of males ranging from 55.0% to 73.6%.

Table 1 summarizes the baseline characteristics of OHCA patients stratified according to ages. The proportion of males was significantly lower in the old group (55.0%) than in the other two groups (p < 0.001). Patients in the old-age group had significantly lower BMI as compared with other two age groups (22.6 vs. 24.2 or 22.6 vs. 24.3, p < 0.001). Middle-age patients had significantly higher rate of witnessed collapse than old-aged patients (52.5 vs. 43.0, p < 0.001). Young-aged patients received significantly higher rate of bystander CPR than old-aged patients (44.7 vs. 35.7, p = 0.007). For cardiac rhythm, young-aged and middle-aged patients had a significantly higher rate of shockable rhythm than old-aged patients (17.5% and 18.7% vs. 10.1%). Old patients had a significantly higher rate of immediate DNR (15.7%) and TOR (25.2%) in the ED, significantly a lower rate of prehospital ROSC (5.6%), and significantly shorter CPR duration (19.1 min). Regarding outcomes, the old group had a significantly lower the rate of survival to ICU admission than did the other two groups (27.1% vs. 39.3% and 46.9%, respectively; p < 0.001). The rate of survival to hospital discharge was significantly lower in the old group (7.5%) than in both the young-aged (20.4%) and middle-aged (19.5%) groups. Additionally, old patients had the lowest rate of favorable neurological outcome (3.8%) among the three age groups (17.0% and 11.8% in the young and middle-aged groups, respectively; p < 0.001).

Fig. 2 further shows the differences in outcomes stratified according to sex in each age group. Accordingly, the rate of survival to ICU admission was significantly higher in the young-aged (p < 0.01) and middle-aged (p < 0.001) than in old males. Similarly, middle-aged females had significantly higher rate of rate of survival to ICU admission than did both young (p < 0.05) and old females (p < 0.001). Moreover, old males had a significantly lower rate of survival to hospital discharge than did both young (p < 0.001) and middle-aged males (p < 0.001). Similarly, old females had a significantly lower

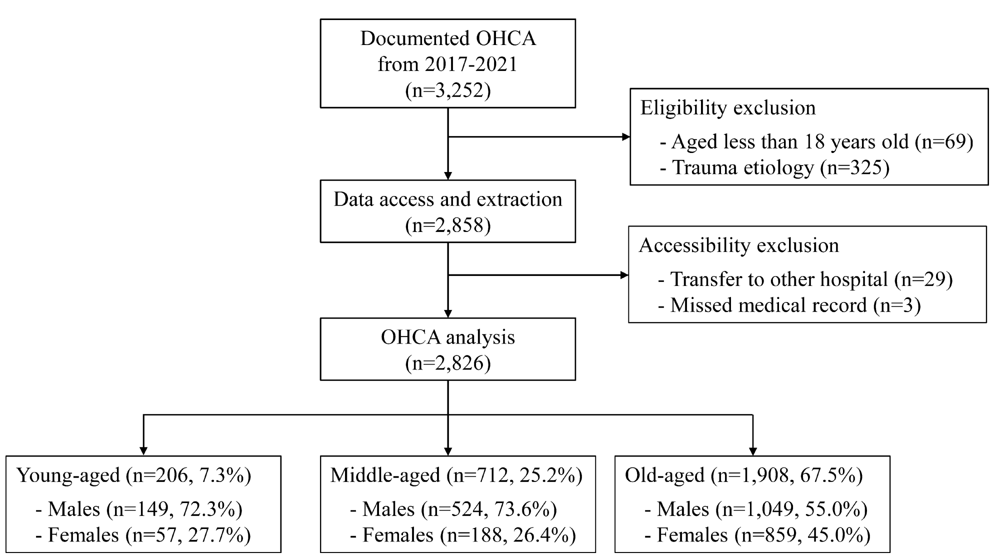

Fig. 1 – The flow of patients' enrollment.

Table 1 – Baseline characteristics for OHCA patients stratified by ages, from 2017 to 2021.

	Young-aged (18–44) (*n* = 206)	Middle-aged (45–64) (*n* = 712)	Old-aged (≥65) (*n* = 1,908)	*p*
Sex (males)	149 (72.3)	524 (73.6)	1049 (55.0) $^{\delta}$	<0.001
BMI	24.2 ± 6.1	24.3 ± 5.2	22.6 ± 4.7 $^{\delta}$	<0.001
Cases by years				0.822
2017	40 (19.4)	133 (18.7)	387 (20.3)	
2018	36 (17.5)	115 (16.2)	348 (18.2)	
2019	38 (18.4)	140 (19.7)	372 (19.5)	
2020	43 (20.9)	164 (23.0)	388 (20.3)	
2021	49 (23.8)	160 (22.5)	413 (21.6)	
Witnessed collapse	93 (45.1)	374 (52.5) $^{\eta}$	820 (43.0) $^{\theta}$	<0.001
Bystander CPR	92 (44.7) $^{\eta}$	289 (40.6)	681 (35.7) $^{\theta}$	0.007
EMS response time (in minutes)	5.6 ± 2.3	5.4 ± 3.5	5.3 ± 2.8	0.238
Shockable rhythm	36 (17.5)	133 (18.7)	192 (10.1) $^{\delta}$	<0.001
Survival to ICU admission	81 (39.3)	334 (46.9)	517 (27.1) $^{\delta}$	<0.001
Survival to hospital discharge	42 (20.4)	139 (19.5)	144 (7.5) $^{\delta}$	<0.001
Favorable neurological outcome	35 (17.0)	84 (11.8)	72 (3.8) $^{\delta}$	<0.001
Prehospital ROSC	33 (16.0)	84 (11.8)	107(5.6) $^{\delta}$	<0.001
Immediate DNR at ED	13 (6.3)	45 (6.3)	299 (15.7) $^{\delta}$	<0.001
TOR at ED	14 (6.8)	67 (9.4)	480 (25.2) $^{\delta}$	<0.001
CPR duration (in minutes)	25.8 ± 14.7	22.7 ± 15.6	19.1 ± 14.1$^{\delta}$	<0.001

post-hoc analysis: η,θ: these two groups are significantly different; δ: this group differs from the other two groups.

Data were presented as mean ± standard deviation, or number (percent).

BMI: body mass index; CPR: cardiopulmonary resuscitation; DNR: do not resuscitate; ED: emergency department; ROSC: return of spontaneous circulation; TOR: termination of resuscitation

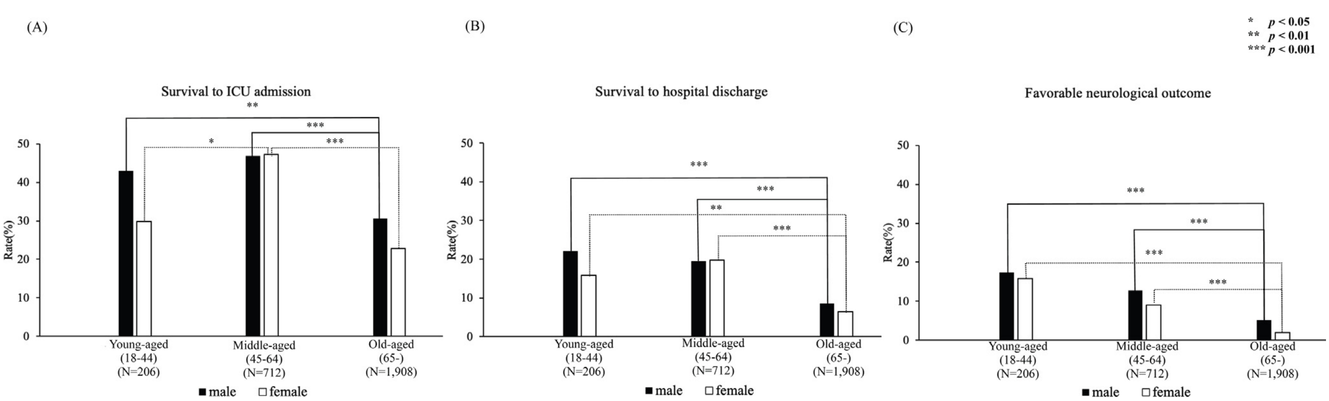

Fig. 2 – The comparisons of OHCA outcomes stratified by sex from in age groups: (a). survival to ICU admission; (b). survival to hospital discharge; (c). favorable neurological outcome.

rate of survival to hospital discharge than did young-aged (p < 0.01) and middle-aged females (p < 0.001). Furthermore, old males and females had a significantly lower rate of favorable neurological outcome than did both young (p < 0.001) and middle-aged males and females (p < 0.001).

Table 2 summarizes the baseline characteristics of OHCA patients stratified according to sex. Accordingly, female patients were older (74.9 vs. 68.3 years; p = 0.001) and had lower rates of shockable rhythm (10.3% vs. 14.3%, p = 0.002) and prehospital ROSC (5.6% vs. 9.4%, p < 0.001) but higher rates of immediate DNR (16.3% vs. 10.3%, p < 0.001) and TOR (22.2% vs. 18.4%, p = 0.012) than did male patients. Regarding outcomes, the rates of survival to ICU admission (27.4% vs. 36.6%, p < 0.001), survival to hospital discharge (9.1% vs. 13.0%, p = 0.002), and favorable neurological outcome (3.9% vs. 8.6%, p < 0.001) were significantly lower in female than male patients. No differences in BMI and recruitment years were observed between male and female patients.

The interaction of age and sex was included in the Table 3. We found that older ages were significantly associated with decreased odds ratio in survival to ICU admission (aOR: 0.97, 95% CI: 0.97–0.98, p < 0.001), Survival to hospital discharge (aOR: 0.96, 95% CI: 0.96–0.97, p < 0.001), and favorable neurological outcome (aOR: 0.95, 95% CI: 0.94–0.96, p < 0.001). Additionally, the interaction coefficient was significant in survival to ICU admission (aOR: 1.00, 95% CI: 1.00–1.01, p = 0.002), and favorable neurological outcome (aOR: 1.01, 95% CI: 1.00–1.02, p < 0.001).

Table 4 further outlines the interaction effects between sex and age on outcomes in OHCA patients. The young group was taken as the reference group for comparisons according to sex. Among females, middle-aged patients had higher odds for survival to ICU

Table 2 – Baseline characteristics for OHCA patients stratified by sex, from 2017 to 2021.

	Females (n = 1,104)	Males (n = 1,722)	p
Age	74.9 ± 15.2	68.3 ± 16.1	0.001
BMI	23.0 ± 5.2	23.2 ± 4.9	0.335
Cases by years			0.927
2017	220 (19.9)	340 (19.7)	
2018	198 (17.9)	301 (17.5)	
2019	218 (19.7)	332 (19.3)	
2020	235 (21.3)	360 (20.9)	
2021	233 (21.1)	389 (22.6)	
Witnessed collapse	455 (41.2)	832 (48.3)	<0.001
Bystander CPR	375 (34.0)	687 (39.9)	0.002
EMS response time (in minutes)	5.3 ± 3.6	5.3 ± 2.5	0.907
Shockable rhythm	114 (10.3)	247 (14.3)	0.002
Survival to ICU admission	302 (27.4)	630 (36.6)	<0.001
Survival to hospital discharge	101 (9.1)	224 (13.0)	0.002
Favorable neurological outcome	43 (3.9)	148 (8.6)	<0.001
Prehospital ROSC	62 (5.6)	162 (9.4)	<0.001
Immediate DNR at ED	180 (16.3)	177 (10.3)	<0.001
TOR at ED	245 (22.2)	316 (18.4)	0.012
CPR duration (in minutes)	19.3 ± 14.0	21.4 ± 15.1	0.122

Data were presented as mean ± standard deviation, or number (percent).

BMI: body mass index; CPR: cardiopulmonary resuscitation; DNR: do not resuscitate; ED: emergency department; ROSC: return of spontaneous circulation; TOR: termination of resuscitation

Table 3 – The association between age and sex and outcomes in the multivariable logistic regression mode.

	Survival to ICU admission		Survival to hospital discharge		Favorable neurological outcome	
Variables	aOR (95% CI)	p	aOR (95% CI)	p	aOR (95% CI)	p
Age	0.97 (0.97–0.98)	<0.001	0.96 (0.96–0.97)	<0.001	0.95 (0.94–0.96)	<0.001
Sex						
Age × Sex	1.00 (1.00–1.01)	0.002			1.01 (1.00–1.02)	<0.001

Data were presented as adjusted odds ratio (95% confidence interval).

aOR: adjusted odds ratio; ICU: intensive care unit;

admission (OR: 2.12, 95% CI: 1.12–4.00), whereas old patients had higher risk for in-hospital mortality (OR for survival to hospital discharge: 0.37, 95% CI: 0.17–0.78) and poor neurological outcome (OR for favorable neurological outcome: 0.11, 95% CI: 0.05–0.25). Among males, old patients had higher risk for in-hospital mortality (OR for survival to hospital discharge: 0.33, 95% CI: 0.21–0.51) and poor neurological outcome (OR for favorable neurological outcome: 0.26, 95% CI: 0.16–0.43).

For comparisons according to age, female sex was taken as the reference group. Among the old group, male patients had higher odds for survival to ICU admission (OR: 1.49, 95% CI: 1.21–1.83) and favorable neurological outcome (OR: 2.74, 95% CI: 1.58–4.76). No other interaction effects between sex and age on outcomes were found.

Discussion

The current study showed that older OHCA patients tended to have worse outcomes in terms of survival and neurological recovery than did middle-aged or young patients. Additionally, we observed that female OHCA patients might tend to have poorer survival and neurological recovery outcomes than did their male counterparts. Overall, our findings emphasize the inevitable presence of an interaction between sex and age. Therefore, when analyzing data for OHCA patients, physicians need to specifically focus on the individual effects of sex and age within the context of their corresponding sex and age groups. When examining the effects of sex within each age group, we observed that among older individuals, males might tend to have better survival rates upon ICU admission and neurological outcomes than did females. However, no significant sex differences were observed in the other two age groups. Furthermore, when considering the effects of age according to sex, we found that among females, those in the middle-aged group might have a higher rate of survival to ICU admission, whereas those in the old group might have a higher risk for in-hospital mortality and poor neurological outcomes. Among males, we discovered the same trend. Older individuals might experience poorer survival to hospital discharge and neurological recovery than did their younger counterparts. Overall, these findings emphasize the importance of analyzing the interaction between sex and age given that importance in understanding the mixed effects observed in our study.

Our primary findings differed from those of two other studies that also analyzed the interaction between sex and age. In Hahihara's

Table 4 – The interaction of sex and age on outcomes for OHCA patients, from 2017 to 2021.

Outcomes	Sex		OR (95% CI) for sex within strata of age (Reference: female)
	Female	Male	
Survival to ICU admission			
Age			
Young (18–44)	Reference	1.77 (0.92–3.41)	1.77 (0.92–3.41)
Middle (45–64)	2.12 (1.12–4.00)	2.07 (1.14–3.74)	0.98 (0.70–1.36)
Old (above 65)	0.70 (0.39–1.25)	1.04 (0.58–1.86)	1.49 (1.21–1.83)
OR (95% CI) for middle-aged within strata of sex (Reference: young-aged)	2.12 (1.12–4.00)	1.17 (0.81–1.68)	
OR (95% CI) for old-aged within strata of sex (Reference: young-aged)	0.70 (0.39–1.25)	0.59 (0.41–0.83)	
Survival to hospital discharge			
Age			
Young (18–44)	Reference	1.52 (0.68–3.41)	1.52 (0.68–3.41)
Middle (44–64)	1.31 (0.59–2.90)	1.29 (0.61–2.71)	0.99 (0.65–1.50)
Old (above 65)	0.37 (0.17–0.78)	0.49 (0.24–1.04)	1.36 (0.96–1.92)
OR (95% CI) for middle-aged within strata of sex (Reference: young-aged)	1.31 (0.59–2.90)	0.85 (0.55–1.32)	
OR (95% CI) for old-aged within strata of sex (Reference: young-aged)	0.37 (0.17–0.78)	0.33 (0.21–0.51)	
Favorable neurological outcome			
Age			
Young (18–44)	Reference	1.13 (0.49–2.58)	1.13 (0.49–2.58)
Middle (45–64)	0.53 (0.22–1.26)	0.78 (0.37–1.67)	1.48 (0.84–2.58)
Old (above 65)	0.11 (0.05–0.25)	0.30 (0.14–0.63)	2.74 (1.58–4.76)
OR (95% CI) for middle-aged within strata of sex (Reference: young-aged)	0.53 (0.22–1.26)	0.69 (0.42–1.14)	
OR (95% CI) for old-aged within strata of sex (Reference: young-aged)	0.11 (0.05–0.25)	0.26 (0.16–0.43)	

Data are presented as OR (95% CI).

CI: confidence interval; ICU: intensive care unit; OR: odds ratio.

study, female patients with OHCA of presumed cardiac origin had increased ROSC and 1-month survival rates, whereas older male patients with OHCA, whether of presumed cardiac or noncardiac origin, exhibited decreased 1-month survival and favorable neurological outcome rates. However, over 90% OHCA patients included in Hahihara's study were presumed to have a cardiac origin (24,216 vs. 1,215 presumed cardiac and noncardiac origin cases, respectively), which was significantly higher than that in other cohorts. Despite not conducting a subgroup analysis based on presumed cardiac origin, we note that the rate of shockable rhythms was higher in males than females (14.3% vs. 10.3%; $p = 0.002$). This observation may suggest that male OHCA patients had higher survival rates than did their female counterparts. Moreover, while Hahihara's study used an age cutoff of 56 and 52 years for presumed cardiac and noncardiac origin, respectively, which corresponded to the medians within those groups, our study categorized OHCA patients into three age groups using fixed cutoff points. This difference in classification method may have contributed to the disparity between our results.

Our results partially contradict those reported by Ishii, who indicated that reproductive-age females (between 15 and 49 years old) had more favorable neurological outcomes following OHCA than did similarly aged males.[3] In our study, however, we observed that older males exhibited better neurological outcomes than did older females. One of the most significant differences between our studies was the age groups used for classification. Our study did not include pediatric OHCA cases given the differences in etiology between pediatric and adult OHCA. Furthermore, we categorized our patients into young (20–44 years), middle-aged (45–64 years), and old (≥65 years), whereas Ishii's study used different age groups, namely reproductive (15–49 years), middle to young-old (50–74 years), and older (≥75 years). Another notable difference was the discrepancy in patient enrollment methods. Ishii's study was a population-based nationwide registry of all OHCA patients in Japan, whereas ours was a retrospective multicenter cohort study. Furthermore, Ishii's study incorporated variables related to prehospital management, which were not included in our in-hospital treatment-focused study. In contrast, our study examined ED-related variables, such as resuscitation duration, TOR criteria, and initial cardiac rhythm, which may significantly impact neurological recovery outcomes. Moreover, neither study included neuroprotective management as part of the analysis.

Our findings partially align with those presented in previous studies, particularly those confirming that increased age might be associated with poorer outcomes.[7,9,12,15] Older patients often presented with multiple pre-existing comorbidities, rendering them more susceptible to complicated complications and sudden physiological changes than younger patients. Bray's study indicated that reproductive-age females (between 18 and 44 years old) had no survival benefit compared to males of the same age. This finding was consistent with our research.[20] Our study also observed a higher incidence of immediate DNR and TOR decisions in the old group than in the other two age groups (Table 1). Families tended to withdraw resuscitative efforts rapidly in this age group, reflecting an "ED-hospice" concept, which contributed to the higher mortality rate. We note that the documentation of immediate DNR or TOR decisions had been infrequently reported in previous studies.

Several limitations constrain the generalizability of our results. First, OHCA patients in this study were recruited from various hospitals across different regions of Taiwan, which may minimize regional differences. However, these hospitals were associated with one university teaching hospital and its affiliated institutions, potentially leading to patient homogeneity and potential selection bias. Second, the retrospective nature of the cohort study introduced information bias given our failure to report certain critical details regarding procedures or interventions in the ICU, such as the rate of targeted temperature management and electroencephalography reports. These factors may confound the interaction between sex and age. Third, this study did not account for the potential impact of the COVID-19 pandemic, which may have affected the resuscitation capacity of different hospitals to varying degrees. Finally, and most crucially, it was imperative to recognize that this research, being a single-center study, may not fully represent wider populations. This limitation potentially restricted its generalizability and applicability to other contexts. Consequently, the findings presented should be interpreted with a degree of caution. Given this context, it became evident that additional, broader investigations were essential. Future studies, ideally encompassing multiple centers and a more diverse patient demographic, are required to ascertain if there has been a shift in outcome distributions during the pandemic years.

Conclusion

The interaction between sex and age played a significant role in determining outcomes among OHCA patients. Regardless of sex, older OHCA patients might exhibit lower rates of survival to hospital discharge and neurological recovery than did their middle-aged and young counterparts. Furthermore, within the old age group, male patients might have higher rates of survival and favorable neurological outcomes than did their female counterparts.

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CRediT authorship contribution statement

Ching-Yu Chen: Visualization, Software, Methodology, Formal analysis. **Cheng-Yi Fan:** Visualization, Software, Methodology, Formal analysis. **I-Chung Chen:** Validation, Supervision, Resources, Investigation. **Yun-Chang Chen:** Resources, Data curation. **Ming-Tai Cheng:** Supervision, Resources. **Wen Chu Chiang:** Writing – review & editing, Resources, Methodology. **Chien-Hua Huang:** Writing – review & editing, Supervision. **Chih-Wei Sung:** Writing – review & editing, Methodology, Investigation, Funding acquisition, Conceptualization. **Edward Pei-Chuan Huang:** Conceptualization, Methodology, Writing – review & editing.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Appendix A. Supplementary material

Supplementary data to this article can be found online at https://doi.org/10.1016/j.resplu.2024.100552.

Author details

[a]Department of Emergency Medicine, National Taiwan University Hospital Yun-Lin Branch, Douliu, Taiwan [b]Department of Emergency Medicine, National Taiwan University Hospital Hsin-Chu Branch, Hsinchu, Taiwan [c]Department of Emergency Medicine, College of Medicine, National Taiwan University, Taipei, Taiwan [d]Department of Emergency Medicine, National Taiwan University Hospital, Taipei, Taiwan

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