REUE | Original article

Trends in sex differences in out-of-hospital cardiac arrest: an equity analysis in 2 cohorts (2012–2024)

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OBJECTIVE. To analyze temporal trends in sex differences in non-traumatic out-of-hospital cardiac arrest (OHCA) and to assess whether improvements in the chain of survival have benefited women and men equitably.

MATERIALS AND METHODS. We conducted a retrospective observational study of two 36-month cohorts (2012–2014 and 2021–2024) including adult patients (≥ 18 years) with non-traumatic OHCA attended by an urban emergency medical service. Cases with attempted cardiopulmonary resuscitation were included, with recorded sex, age, initial shockable rhythm (ISR), return of spontaneous circulation (ROSC), in-hospital survival, and neurological status at discharge according to the Cerebral Performance Category (CPC) scale. Logistic regression models adjusted for age and ISR were used, incorporating sex×cohort interaction terms.

RESULTS. A total of 1,750 episodes were analyzed (cohort 1, 806; cohort 2, 944). In both periods, women were older and had a lower frequency of ISR, which was the main predictor of favorable outcomes, showing a strong association with ROSC (OR, 2.79; 95 % CI, 2.26–3.45) and favorable neurological recovery (OR, 6.39; 95 % CI, 4.91–8.31). Age was inversely associated with ROSC. After adjustment, female sex was independently associated with a higher probability of ROSC (adjusted OR, 1.47; 95 % CI, 1.15–1.87; *P* = .002), with no significant differences in survival or neurological outcome. No statistically significant sex×cohort interactions were observed.

CONCLUSIONS. Crude sex differences in OHCA are largely explained by age and ISR. Although female sex was associated with a higher probability of ROSC after adjustment, this advantage did not translate into better subsequent outcomes. No significant changes in the sex gap over time were observed. Monitoring equity indicators and further exploration of process-related variables in future studies are recommended.

Keywords: Cardiac arrest. Health equity. Sex factors. Temporal factors. Emergency medical services.

Evolución temporal de las diferencias por sexo en la parada cardiaca extrahospitalaria: análisis de equidad en dos cohortes (2012-2024)

OBJETIVO. Analizar la evolución temporal de las diferencias por sexo en la parada cardiaca extrahospitalaria (PCEH) no traumática y evaluar si las mejoras en la cadena de supervivencia han beneficiado de forma equitativa a mujeres y hombres.

MATERIAL Y MÉTODOS. Estudio observacional retrospectivo de dos cohortes de 36 meses (2012-2014 y 2021-2024) de pacientes adultos (≥ 18 años) con PCEH no traumática atendidos por un servicio de emergencias urbanas. Se incluyeron los casos con intento de reanimación cardiopulmonar, analizando sexo, edad, ritmo inicial desfibrilable (RID), retorno de la circulación espontánea (RCE), supervivencia hospitalaria y estado neurológico al alta según la escala Cerebral Performance Category (CPC). Se emplearon modelos de regresión logística ajustados por edad y RID, incorporando términos de interacción sexo×cohorte.

RESULTADOS. Se analizaron 1.750 episodios (cohorte 1: 806, cohorte 2: 944). En ambos periodos, las mujeres presentaron mayor edad y menor frecuencia de RID, siendo éste el principal predictor de desenlaces favorables, con una asociación robusta con RCE (OR 2,79; IC 95 %: 2,26-3,45) y con la recuperación neurológica favorable (OR 6,39; IC 95 %: 4,91-8,31). La edad se asoció de forma inversa con RCE. Tras el ajuste, el sexo femenino se asoció de forma independiente con una mayor probabilidad de RCE (OR ajustado 1,47; IC 95 %: 1,15-1,87; p = 0,002), sin diferencias significativas en supervivencia ni en resultado neurológico. No se observaron interacciones sexo×cohorte estadísticamente significativas.

CONCLUSIONES. Las diferencias crudas por sexo en la PCEH se explican fundamentalmente por edad y RID. Aunque el sexo femenino se asoció con una mayor probabilidad de RCE tras el ajuste, esta ventaja no se tradujo en mejores desenlaces posteriores. No se evidenciaron cambios significativos en la brecha por sexo a lo largo del tiempo. Deben monitorizarse indicadores de equidad y profundizar en variables de proceso en estudios futuros.

Palabras clave: Parada cardiaca. Equidad en salud. Factores sexuales. Factores temporales. Servicios médicos de emergencia.

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Introduction

Out-of-hospital cardiac arrest (OHCA) is one of the main challenges in emergency medical systems due to its low survival rates and marked variability between regions and emergency systems.[1] In Europe, an annual incidence of 55 cases per 100,000 inhabitants is estimated.[2] Despite improvements implemented over the last decade, such as increased bystander cardiopulmonary resuscitation (CPR) and access to early defibrillation, survival to hospital discharge remains limited.[3] Additionally, women are known to present at older ages and less frequently with an initial shockable rhythm (ISR), which affects prognosis.[4,5] Furthermore, they receive fewer recommended interventions, such as bystander CPR, defibrillation with an automated external defibrillator (AED), coronary angiography, and targeted temperature management.[3,6-8] Sex is also closely related to other key prognostic factors, such as age and the initial presentation of OHCA.

The temporal evolution of these sex-related differences has not been sufficiently explored. Some international registries have suggested that improvements in survival have benefited men more than women.[5,9] The aim of this study was to analyze sex differences in clinical characteristics and outcomes of non-traumatic OHCA, as well as to evaluate the temporal evolution of these differences between 2 periods.

Material and methods

We conducted a retrospective observational study of 2 temporal cohorts of OHCA attended by an urban emergency medical service was conducted, following STROBE and Utstein 2024 recommendations.[10,11]

Study population

The study was conducted within the emergency medical service SAMUR-Protección Civil (Madrid, Spain), which operates mainly in public spaces and buildings.

All non-traumatic OHCA episodes attended during January 2012–December 2014 (cohort #1) and September 2021–August 2024 (cohort #2) were included. Inclusion criteria were patients ≥ 18 years, non-traumatic OHCA, attempted CPR, and availability of information on sex, age, ISR, and return of spontaneous circulation (ROSC).

Variables

The main exposure variable was sex (female/male). Age (in years) and care period (cohort 1/2) were recorded. ISR was classified as shockable (ventricular fibrillation or pulseless ventricular tachycardia) or non-shockable (asystole or pulseless electrical activity).[10,12]

Outcomes included: ROSC, survival to hospital admission, at 24 hours, at 7 days, and neurological status at discharge [Cerebral Performance Category (CPC), categorized as favorable (CPC 1–2) or unfavorable (CPC 3–5)].[10] Age was dichotomized into 2 groups: < 65 years and ≥ 65 years.

Age and ISR were selected as adjustment covariates because they are the main prognostic factors[5,13-16] and were fully available in both cohorts.

Statistical analysis

Categorical variables were compared using chi-square or Fisher's exact tests, and age using Welch's t test, since strict normality assumptions were not met. First, bivariate analyses stratified by cohort were performed. Subsequently, logistic regression models were fitted estimating OR, with 95 % CI. Crude and adjusted models were constructed including age and ISR.[13,15] To assess whether the association between sex and outcomes varied across periods, a difference-in-differences approach was applied using sex×cohort interaction terms.[4,13] Statistical significance of the interaction term was interpreted as evidence of modification of the effect of sex over time. Analyses were conducted on complete cases.[17] For CPC, a descriptive analysis comparing patients with and without available data was performed to assess potential selection bias.[10] Statistical significance was set at $\alpha = 0.05$. All analyses were performed using IBM SPSS Statistics (version 25).

Ethical considerations

The study was conducted in full compliance with current data protection regulations and approved by the Ethics Committee of Hospital Clínico San Carlos de Madrid (Act 7.2/25; code 25/536-E).

Results

In cohort #1, 853 episodes were recorded. After excluding patients < 18 years (n = 13) and traumatic OHCA (n = 35), the final cohort included 806 episodes. In cohort #2, a total of 1,137 episodes were recorded. After excluding patients < 18 years (n = 19) and traumatic OHCA (n = 174), 944 episodes were included.

The case selection process is shown in Figure 1. The overall sample included 1,750 non-traumatic OHCA cases (Table 1). In both periods, a predominance of men was observed, with no significant differences in the proportion of women between cohorts ($P = .097$).

Women were older (cohort #1: 71.55 ± 16.02 vs 62.92 ± 15.60 years; cohort #2: 70.50 ± 17.19 vs 64.75 ± 15.02; both $P < .001$), with differences of 8.7 and 5.7 years, respectively. Age group distribution (< 65 vs ≥ 65 years) was similar between cohorts ($P = .66$).

ISR by cohort and sex

ISR was more frequent in men in both periods (cohort #1: 43.5 % vs 20.9 % in women, $P < .001$; cohort #2: 36.7 % vs 22.5 % in women, $P < .001$), with a lower overall proportion in cohort #2 (31.8 % vs 37.8 %; difference of –6.0 percentage points; $P = .015$). When analyzed by sex, ISR frequency remained stable in women across periods (20.9 % vs 22.5 %; $P = .696$). In contrast, men showed a significant decrease (43.5 % vs 36.7 %; $P = .010$), resulting in a reduction of the sex gap in ISR from 22.6 to 14.2 percentage points (Table 2).

Bivariate analysis of outcomes by sex and cohort

As shown in Table 3, in cohort #1, no significant differences were found in ROSC or survival at 6 or 24 hours.

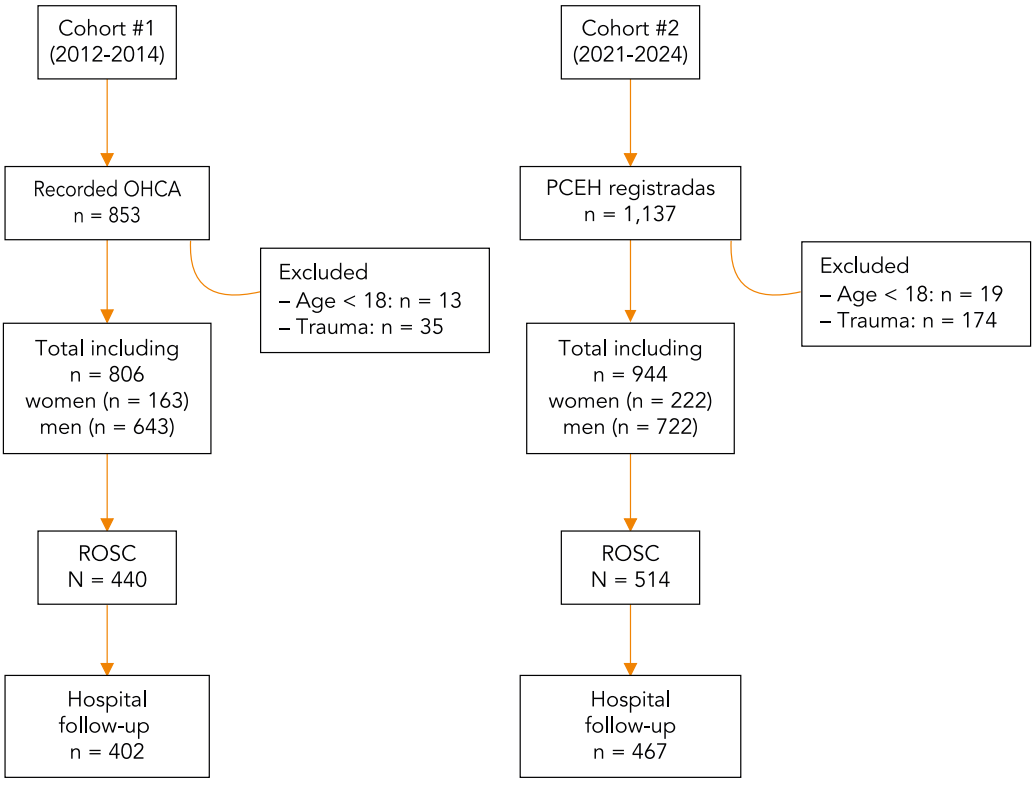

Figure 1. Flow diagram of study sample selection.
OHCA: out-of-hospital cardiac arrest; ROSC: return of spontaneous circulation.

However, men showed higher rates of survival at 7 days and favorable neurological recovery. In cohort #2, differences were attenuated: no significant differences were observed in ROSC or 6-hour survival. However, men showed higher survival rates at 24 hours, 7 days, and favorable neurological recovery.

Figure 2 shows Kaplan–Meier survival curves stratified by sex in both cohorts, presented descriptively and unadjusted.

Multivariable models: main effects

In models adjusted for age and ISR (Table 4), female sex was associated with a higher probability of ROSC, with no other statistically significant associations observed. ISR emerged as the main prognostic predictor for ROSC, survival at 24 hours and 7 days, and favorable CPC. Age was inversely associated with ROSC and favorable CPC; however, it did not reach statistical significance for survival at 24 hours or 7 days.[16]

Sex×cohort interaction analysis: temporal evolution of the sex gap

Sex×cohort interaction terms did not reach statistical significance (Figure 3). However, in the ROSC model, a trend toward significance of the interaction term was observed, consistent with a possible attenuation of the sex gap in the most recent period.

To evaluate the discriminative capacity of different prognostic models for ROSC, progressively more complex ROC curves were constructed (Figure 4). The model based on sex showed no discrimination (AUC = 0.506), whereas

Table 1. Baseline characteristics of non-traumatic out-of-hospital cardiac arrests, by sex and cohort

Variable	Cohort #1			Cohort #2		
	Women n (%)	Men n (%)	*P*	Women n (%)	Men n (%)	*P*
	163 (20.22)	643 (79.78)	–	222 (23.52)	722 (76.48)	–
Age, years [mean (SD)]	71.55 ± 16.02	62.92 ± 15.60	< .001	70.50 ± 17.19	64.75 ± 15.02	< .001
Age ≥ 65 years	418 (51.86)	–	480 (50.85)	–		
ISR	34 (20.9)	280 (43.5)	< .001	50 (22.5)	265 (36.7)	.010
ROSC	99 (60.7)	341 (53.0)	.078	120 (54.1)	394 (54.6)	.892
Survival at 6 hours	70 (42.96)	273 (42.46)	.91	89 (40.10)	313 (43.36)	.36
Survival at 24 hours	50 (30.68)	228 (35.46)	.25	68 (30.63)	276 (38.23)	.036
Survival at 7 days	26 (15.95)	169 (26.28)	.006	42 (18.92)	190 (26.32)	.023
Favorable CPC	19 (11.66)	134 (20.84)	.08	36 (16.22)	169 (23.41)	.023

ROSC: return of spontaneous circulation; CPC: Cerebral Performance Category; ISR: initial shockable rhythm.

Table 2. Initial shockable rhythm by sex and cohort

Cohort	Sex	N total	ISR, n (%)	*P*
1	Women	163	34 (20.9)	
	Men	643	280 (43.5)	< .001
	Total	806	314 (37.8)	–
2	Women	222	50 (22.5)	
	Men	722	265 (36.7)	< .001
	Total	944	315 (31.8)	–

ISR: initial shockable rhythm.

the inclusion of age and ISR improved predictive capacity (AUC = 0.618), with only a marginal gain when adding sex (AU = 0.618). The full model, additionally incorporating the care period, achieved the highest discriminative capacity (AUC = 0.717). This indicates that ROSC prognosis depends mainly on pathophysiological factors and care context, with limited independent contribution of sex.

Follow-up data availability and selection bias analysis

Among patients with ROSC, CPC information was available in 91.37 % in cohort #1 and 90.86 % in cohort #2 (*P* = .78).[10] Patients with available CPC data did not differ significantly from those without data in terms of age, sex, or ISR, suggesting no substantial selection bias (Table 5).[10,17,18]

Discussion

The main findings of this study are the persistence of a less favorable baseline profile in women, the independent association of female sex with a higher probability of ROSC—although without association with survival or neurological recovery after adjustment—a differential pattern in the temporal evolution of ISR, and finally, a possible recent attenuation of the sex gap in ROSC.[19-22]

Women were older and had a lower frequency of ISR in both periods, findings repeatedly described in European, North American, and Asian studies.[13,19,20,23] The lower proportion of ISR in women is a key element, as it is one of the most robust prognostic determinants of OHCA.[19,21] Recent studies indicate that these differences are not fully explained by age or CPR conditions, and that sex-specific pathophysiological mechanisms may exist, including differences in OHCA etiology, cardiovascular comorbidities, and hormonal and electrophysiological factors.[8,19,22]

In bivariate analyses, male sex was associated with better survival outcomes and neurological recovery. However, after adjustment for age and ISR, female sex was independently associated with a higher probability of ROSC, but not with 24-hour or 7-day survival, nor with favorable neurological recovery. This differential pattern suggests that the effect of sex on OHCA outcomes is phase-specific, limited to initial circulatory recovery, without translating into sustained benefit in survival or neurological function.

However, the absence of an independent association between sex and survival or neurological recovery after adjustment suggests that process-related and post-resuscitation care factors may be attenuating the initial ROSC benefit. International studies have documented that women have less access to evidence-based interventions during the hospital phase, including lower use of cardiac catheterization, percutaneous coronary intervention, and targeted temperature management, as well as a higher frequency of therapeutic effort limitation.[7,8,23] These findings reinforce the hypothesis that sex differences in OHCA reflect a complex interaction between biological factors, initial presentation, and care processes, rather than an effect of sex *per se*.[4,20,23] ISR was identified as the main prognostic predictor, consistent with international literature.[19,21] Age showed an inverse association with outcomes, consistent with greater comorbidity and frailty in older populations.[18,19]

A novel finding of this study is the differential temporal evolution of ISR by sex. The overall reduction in ISR was explained by a significant decrease in men, while in women the proportion remained stable, resulting in a reduction of the sex gap. This finding suggests temporal changes in presentation profile, related to shifts in cardiovascular epidemiology.[19,24] Studies in Sweden and other European countries have documented a global decrease in ISR attributed to changes in etiology and improvements in primary and secondary prevention of coronary disease.[24] However, this is the first study documenting a sex-specific pattern in this temporal trend. Possible explanations include women starting from a lower ISR proportion with less room for re-

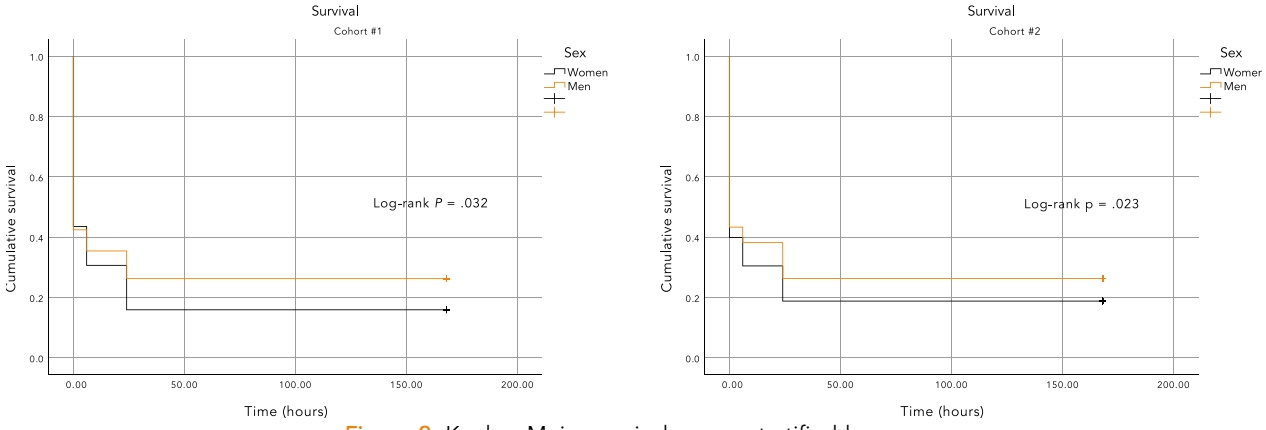

Figure 2. Kaplan–Meier survival curves stratified by sex.

Table 3. Bivariate analysis: outcomes by sex and cohort

Outcome	Cohort #1 (n = 806)			Cohort #2 (n = 944)		
	Women N = 163 n (%)	Men N = 643 n (%)	*P*	Women N = 222 n (%)	Men N = 722 n (%)	*P*
ROSC	99 (60.74)	341 (53.03)	.078	120 (54.1)	394 (54.6)	.89
Survival at 6 hours	70 (44.30)	273 (46.60)	.91	88 (55.7)	313 (53.4)	.33
Survival at 24 hours	50 (30.68)	228 (35.46)	.25	48 (30.18)	276 (38.23)	.03
Survival at 7 days	26 (15.95)	169 (26.28)	.006	42 (18.92)	190 (26.32)	.025
Favorable CPC	19 (11.66)	135 (21.00)	.008	36 (16.22)	170 (23.55)	.023

ROSC: return of spontaneous circulation; CPC: Cerebral Performance Category; OR: odds ratio; CI: confidence interval.

Table 4. Multivariable models: main effects on outcomes

Variable	ROSC		Survival at 24 hours		Survival at 7 days		Favorable CPC	
	OR (95 % CI)	*P*	OR (95 % CI)	*P*	OR (95 % CI)	*P*	OR (95%CI)	*P*
Sex (female vs male)	1.47 (1.15-1.87)	.002	1.54 (0.98-2.41)	.06	1.35 (0.85-2.16)	.20	1.15 (0.75-1.78)	.52
Age (per year)	0.991 (0.985-0.997)	.004	0.995 (0.988-1.002)	.17	0.996 (0.989-1.003)	.25	0.98 (0.97-0.99)	< .001
ISR	2.79 (2.26-3.45)	< .001	3.16 (2.33-4.16)	< .001	4.98 (3.76-6.60)	< .001	6.39 (4.91-8.31)	< .001

ROSC: return of spontaneous circulation; ISR: initial shockable rhythm; CPC: Cerebral Performance Category; OR:odds ratio; CI: confidence interval.

duction; differential impact of cardiovascular prevention strategies by sex; or changes in OHCA presentation context (e.g., more arrests at home vs public settings) affecting men and women differently.[8,19]

Although sex×cohort interaction terms did not reach statistical significance, a trend toward reduced sex gap in ROSC was observed. This finding, although to be interpreted cautiously, contrasts with studies reporting increasing disparities. A Dutch study documented greater improvements in 30-day survival in men between 2005 and 2017.[13] In contrast, our findings suggest a trend toward convergence in ROSC, reflecting improved equity in prehospital care. The lack of statistical significance may be related to limited statistical power or the influence of unavailable process-related variables.[9,20,25]

Clinical implications

This study shows that female sex confers a biological advantage in the initial phase of circulatory recovery, but this advantage does not translate into improved survival or neurological outcomes. This raises the hypothesis that barriers in post-resuscitation care may prevent the initial ROSC benefit from translating into better final outcomes for women.[7,8]

The 2025 American Heart Association guidelines emphasize the need to address disparities at every link in the chain of survival.[26,27] Recent studies have documented that women are less likely to receive evidence-based interventions, including lower rates of bystander CPR, public AED use, cardiac catheterization, and higher likelihood of therapeutic effort limitation.[9,20,25,28,29] Therefore, future research should specifically explore why the observed advantage in

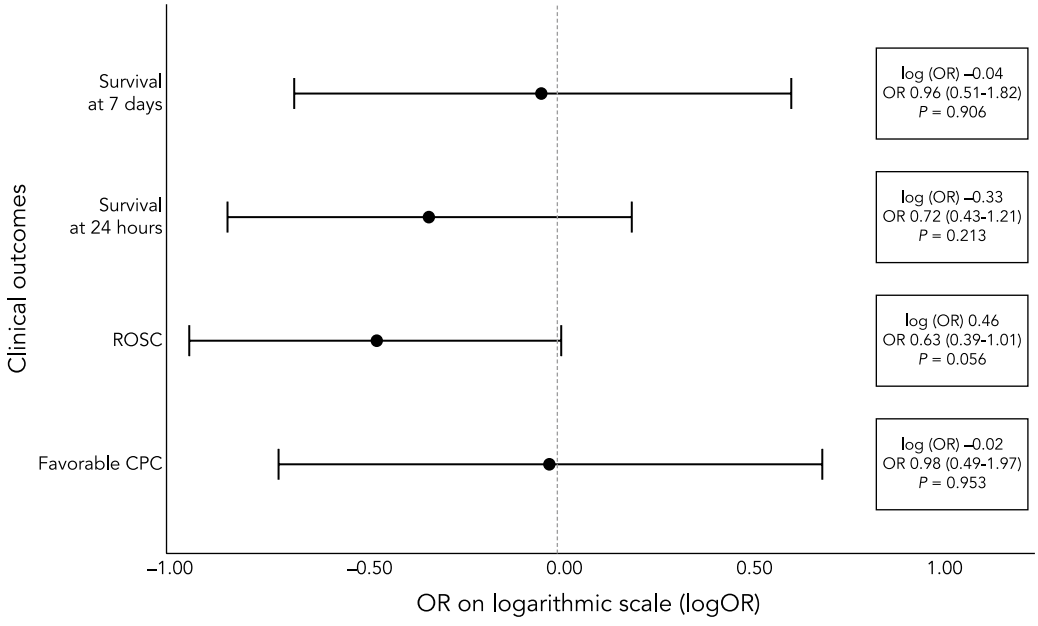

Figure 3. Sex × cohort interaction adjusted for age and initial shockable rhythm.
CPC: Cerebral Performance Category; OR: odds ratio;CI: confidence interval; ROSC: return of spontaneous circulation.

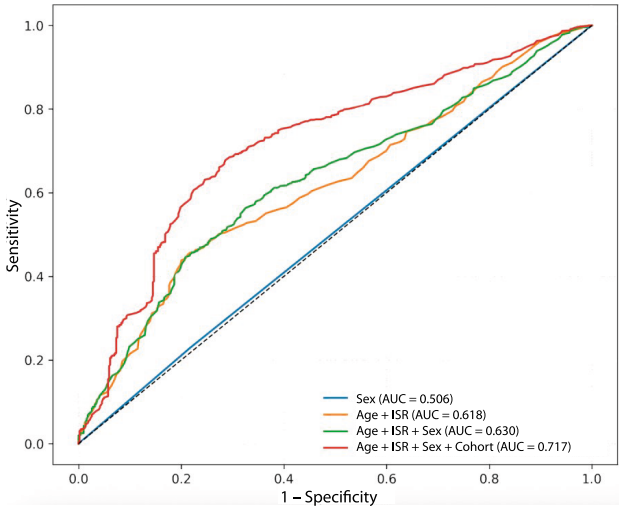

Figure 4. ROC curves for prediction of return of spontaneous circulation.
ISR: initial shockable rhythm.

ROSC among women does not persist in survival and neurological recovery, incorporating hospital process variables, decisions regarding therapeutic limitation, and access to advanced interventions stratified by sex.[7,8]

Study limitations include its retrospective design, limiting causal inference, and analysis restricted to a single urban emergency service, reducing generalizability.[10,11] Additionally, lack of information on relevant process variables (bystander CPR, public defibrillation, response time, hospital interventions, specific comorbidities) and sociodemographic factors beyond sex and age may influence observed differences.[7,19]

Conclusions

Women with non-traumatic OHCA consistently present a less favorable baseline profile, characterized by older age and lower ISR frequency. After adjustment for age and ISR, female sex was independently associated with higher ROSC probability, but not with early survival or favorable neurological outcome. This pattern indicates that the effect of sex on OHCA outcomes is phase-specific, limited to initial ROSC without sustained benefit.

ISR was identified as the main prognostic determinant across all outcomes, while age showed an inverse association with ROSC probability and favorable neurological recovery. A differential temporal pattern in ISR by sex was observed, with a significant decrease in men and stability in women, resulting in reduced sex gap. This novel finding suggests sex-specific epidemiological changes requiring further investigation.

Although sex×cohort interaction terms were not statistically significant, a trend toward attenuation of the sex gap in ROSC was observed, contrasting with international studies reporting increasing disparities.

Finally, the independent association of female sex with higher ROSC, without translation into improved survival or neurological outcomes, suggests the existence of barriers in post-resuscitation care that prevent sustained benefit. Emergency systems should systematically monitor sex equity indicators across all links in the chain of survival, particularly in the hospital phase.

Multicenter studies with greater statistical power and detailed process variables are needed to confirm the observed trend toward attenuation of the sex gap and to identify specific barriers perpetuating disparities in care.

Table 5. Availability of follow-up data

Variable	Cohort #1 n (%)	Cohort #2 n (%)	*P*
Patients with ROSC, n	440	514	–
CPC available	402 (91.37)	467 (90.86)	.78
Mean age with CPC (years)	64.09	63.92	.15
Mean age without CPC (years)	68.03	64.21	.91
Women with CPC	90 (22.38)	110 (23.60)	.83
Women without CPC	9 (23.68)	10 (21.28)	.65
ISR with CPC	188 (46.8)	209 (44.8)	.703
ISR without CPC	19 (50.0)	23 (48.9)	.58

ROSC: return of spontaneous circulation; ISR: initial shockable rhythm; CPC: Cerebral Performance Category.

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