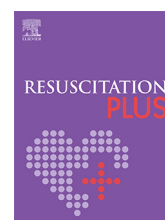


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Short paper

Morning peak and high prevalence of pulmonary embolism and psychiatric disorders in women with sudden cardiac arrest: results from the ReCaPTa study



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Abstract

Background: Sudden cardiac arrest (SCA) in women remains understudied, often leading to generalised approaches. We aimed to identify sex-specific differences in the clinical profile, risk factors, and causes of SCA to guide targeted interventions.

Methods: This prospective population-based study (ReCaPTa) analysed out-of-hospital cardiac arrests in a region of Spain (2014–2017). Data were triangulated from Emergency Medical Services, hospital records, and forensic autopsies. SCA was defined as an unexpected cardiac arrest, with a presumed cardiac cause, occurring within 1 h of symptom onset or seen to be alive and well within the last 24 h.

Results: Of 639 SCA cases, 191 (29.9%) were women. Compared with men, women were older (74 vs 66 years, $p < 0.001$), had more morning SCA and had a higher prevalence of previous psychiatric disorders (15.6% vs 9.0%, $p = 0.03$) and alcohol abuse (25.4% vs 16.1%, $p = 0.01$). Toxicological analysis showed significantly higher antidepressant positivity in women (11.3% vs 1.8%, $p = 0.004$). Women had fewer shockable rhythms (21% vs 36%, $p = 0.01$), fewer resuscitation attempts, and lower survival rates (4.2% vs 9.9%, $p = 0.01$). While acute coronary disease was the leading cause in women (20.0%), they exhibited a distinct non-ischaemic profile: pulmonary embolism (PE) was more frequent than in men (13.3% vs 3.0%, $p < 0.001$) and was universally fatal (0% survival).

Conclusion: Compared with men, women with SCA exhibited a disproportionately higher burden of PE and a greater involvement of psychotropic drugs and toxic substances.

Keywords: Sudden cardiac arrest, Sudden cardiac death, Women, Epidemiology

Introduction

Sudden cardiac death (SCD) is among the leading causes of death in developed countries.¹ Its incidence has recently been estimated at 37.1 per 100,000 person-years in the western Mediterranean area

and was 2.3-fold lower in women than in men, at 20.7 per 100,000 person-years.²

Sudden cardiac arrest (SCA) in women has been associated with fewer shockable rhythms, lower survival rates, and an increase in non-cardiac cardiovascular causes.^{3,4} The distinctive characteristics of risk factors, preventive strategies for SCA/SCD, and treatments

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<https://doi.org/10.1016/j.resplu.2026.101416>

Received 10 February 2026; Received in revised form 8 June 2026; Accepted 12 July 2026

during resuscitation attempts have not been fully studied in women because of the lack of comprehensive registries.⁵ The aim of this study is to determine sex-related differences in the clinical profile and risk factors of SCA/SCD using a population-based registry with multiple data sources.

Methods

Design and setting

This study was based on a population registry of SCA/SCD, drawing on multiple sources of information (ReCaPTa study). ReCaPTa contains data on all out-of-hospital cardiac arrest (OHCA) cases attended by Emergency Medical Services (EMS) and all autopsies performed by the reference pathology centre between April 2014 and April 2017. The study protocol was approved by the Clinical Research Ethics Committee of Hospital Universitari Joan XXIII in Tarragona (C.I.65/2014). Reporting of this study was guided by the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) statement.⁶ This study was conducted in a region located in the western Mediterranean (Spain) with a population of 610,865 inhabitants.

Definitions and inclusion and exclusion criteria

SCA is defined as an unexpected natural OHCA with a presumed cardiac cause, occurring within 1 h of symptom onset if witnessed, or within 24 h of last being seen in the usual state of health if unwitnessed.

SCD is defined as a sudden natural death presumed to be of cardiac cause, which occurs within 1 h of onset of symptoms when witnessed and within 24 h of last being seen alive and in the usual state of health when unwitnessed. As previously published, the term SCA covers both SCD and survivors of SCA.⁵

Cases were included if they met the definition of SCA/SCD based on the pre-hospital assessment made by the clinician (EMS or the forensic physician) who attended the case on site.

Cases with an obvious extracardiac cause, such as trauma, intoxication, suicide, or drowning, were excluded from the initial assessment. In addition, all non-unexpected deaths, such as cases with terminal illness, dementia, or cognitive impairment, and cases involving non-residents of the study area were excluded.

Assessment, registration procedure, and variables

All OHCA cases attended or treated by EMS and all patients submitted to an autopsy at the forensic service during the 3-year study period were assessed. Within EMS, the clinical assessment and treatment of patients are performed by emergency physicians. Pre-hospital variables were collected in accordance with the Utstein style. Shockable rhythm was defined as ventricular fibrillation or pulseless ventricular tachycardia. In addition, the type of symptoms prior to collapse and their duration (<1 h, >1 h, or undetermined) were recorded.

At the forensic service, the circumstances of each death, including symptoms prior to collapse and their duration, are documented at the scene by the forensic pathologist. In Spain, the Penal Code and the Criminal Procedure Law require a forensic autopsy for all violent deaths and for deaths of unknown cause, which includes sudden and unexpected natural deaths in non-hospitalised individuals. Autopsy examinations were performed at a single pathology centre by a specialised forensic team, following the protocol of the Institute of Legal

Medicine and Forensic Science of Catalonia (IMLCFC) for sudden death. This protocol included a complete toxicological analysis and histopathological study, as well as genetic analysis to assess suspected heritable causes of SCD or unascertained causes.

Causes of death were assigned in accordance with international guidelines and previous similar studies.^{7,8} Details of the study design, registration procedures, and the flow chart of registered cases have been reported in previous publications.^{2,9}

Patients were considered to have a history of alcohol abuse if an alcohol-related diagnosis was documented in the primary care electronic health record. Psychiatric disorders were defined based on previously recorded diagnoses (e.g. anxiety, bipolar disorder, schizophrenia, or depression).

Statistical analysis

Quantitative variables are expressed as mean $\pm$ standard deviation or median and interquartile range (IQR). Categorical or binary variables are presented as the number of cases and percentages. Comparisons of quantitative variables were performed using Student's *t*-test for normally distributed data or the Mann-Whitney *U* test for non-normally distributed data. Categorical or binary variables were compared using the chi-squared test or Fisher's exact test. The occurrence of SCA/SCD was categorised according to time of day as morning, afternoon, or night. The association between time-of-day category and sex was evaluated using Pearson's chi-square test of independence, based on a 3×2 contingency table of observed frequencies. All tests were two-tailed, and $p < 0.05$ was considered statistically significant. All analyses were performed using R software version 4.4.2.

Results

During the study period, a total of 191 women (29.9%) were included among 639 SCA/SCD cases. Among all included SCA cases, overall survival was lower in women than in men [8 (4.2%) vs 44 (9.9%), $p = 0.01$]. Fig. 1 shows the hourly distribution of SCA/SCD by sex. There was a peak in incidence among women at 09:00 and 10:00 in the morning. More cases occurred in women during the morning (07:00–14:59) than in the afternoon (15:00–22:59) and at night (23:00–06:59) [79 (53%) vs 166 (45.3%), 35 (23.5%) vs 127 (34.7%), and 35 (23.5%) vs 73 (19.9%), respectively; $p = 0.046$]. Fig. 1S showing the hourly distribution by tertiles is provided in the supplementary data.

The comparison of clinical characteristics and risk factors between women and men is shown in Table 1. The median (IQR) age at the time of SCA/SCD was higher in women. Women received fewer resuscitation attempts by EMS than did men [141 (73.8%) vs 367 (81.2%), $p = 0.03$], and SCA/SCD occurred more frequently at home [112 (79.4%) vs 242 (65.7%), $p = 0.003$]. Among resuscitation attempts, cases with an initial shockable rhythm and survival were fewer in women.

Regarding risk factors, women had a higher prevalence of hypertension, alcohol abuse, and previous psychiatric disorders than did men.

Of the 639 SCA/SCD cases, 238 (36.4%) were studied by autopsy, and hospital data were obtained for 130 cases (20.3%). The cause was established in 355 cases (55.5%). The cause of SCA/SCD was established in 47.1% of women compared with 59.2% of men. Fig. 2 and Table 1S in the supplementary data show

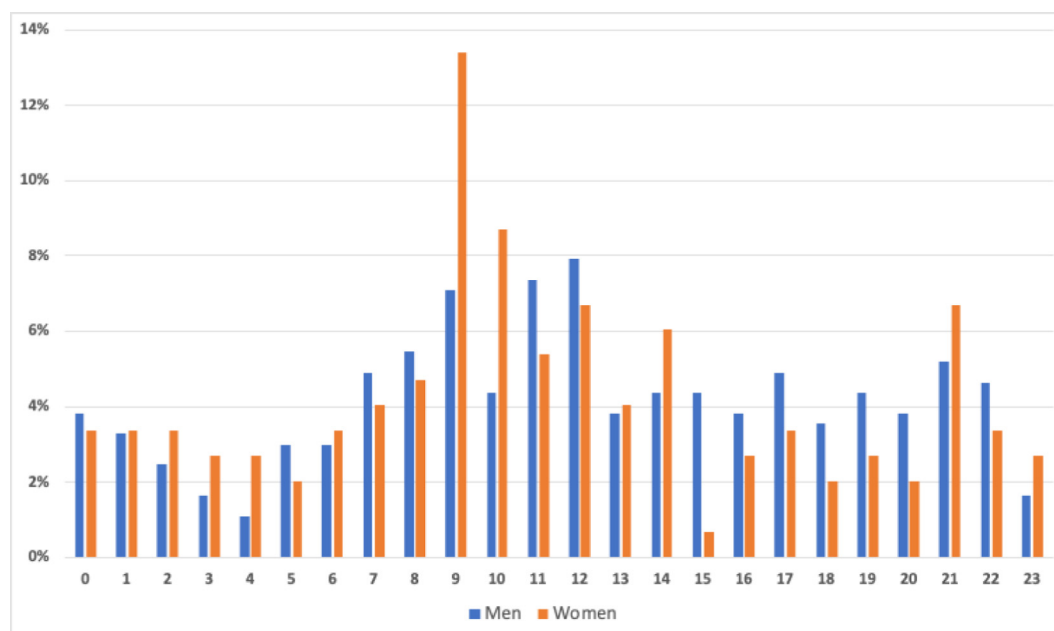


Fig. 1 – Distribution of SCA cases by time of day and sex.

The x-axis indicates the hour of the day, and the y-axis indicates the percentage of cases.

the distribution of causes by sex and survival by cause. Acute coronary disease remained the leading cause of SCA/SCD in women, and its prevalence was similar to that in men [18 (20.0%) vs 57 (21.5%), $p = 0.88$]. The primary sex divergence was observed in the burden of chronic pathology: women had a significantly lower prevalence of chronic coronary disease compared with men [14 (15.6%) vs 73 (27.6%), $p = 0.03$]. Conversely, women were significantly more likely to present with non-cardiac cardiovascular causes [23 (25.6%) vs 32 (12.1%), $p = 0.003$], driven largely by pulmonary embolism (PE) [12 (13.3%) vs 8 (3.0%), $p < 0.001$].

Among the 12 women with PE, the median age was 60.5 years (IQR 54.5–68.2). SCA/SCD occurred at home in all cases; among the eight cases that received cardiopulmonary resuscitation (CPR), the initial rhythm was asystole in 87.5%, and 25% presented with prior dyspnoea. None of these cases received thrombolytic agents during resuscitation. Notable medical histories included hypertension (33%), obesity (33%), alcohol abuse (40%), and a history of psychiatric disorder (50%). Two cases were admitted to the hospital alive, but none survived to discharge. Furthermore, 50% had positive toxicology results (psychotropic drugs in five cases and alcohol in two cases).

Among the 45 women with a history of alcohol abuse, the median age was 77 years (IQR 66–82); 84.5% had at least one cardiovascular risk factor, 66.6% had hypertension, and 20% had a history of psychiatric disorders. The most frequent cause of SCA/SCD was acute and chronic coronary heart disease (45.4%), followed by cardiomyopathy (18.2%) and PE (18.2%) among the 22 cases studied.

Fig. 3 shows the toxicology results of the autopsy cases studied. More positive results for antidepressants were found in women [7 (11.3%) vs 3 (1.8%), $p = 0.004$].

Discussion

This study found a distinct profile among women who presented with SCA/SCD, highlighting risk factors related to psychiatric disorders and causes such as PE.

In our series, the survival rate among women who received a CPR attempt was lower than that of men, as previously described.³ Furthermore, this series of SCA/SCD includes patients treated by EMS as well as patients found dead and attended by the forensic service, with fewer CPR attempts by EMS among women and, consequently, lower overall survival.²

As a novel finding, we observed that SCA/SCD occurs more frequently during the morning in women, with a peak in the early morning hours. This pattern may be associated with increased sympathetic activity, elevated blood pressure, or the influence of older age, as observed in the female cohort.¹⁰ By contrast, another study focusing exclusively on cardiac causes of sudden death reported a higher incidence during nighttime hours.¹¹

The cause of SCA/SCD was identified in 55.5% of cases, representing, to our knowledge, the highest rate reported in a population-based registry with multiple data sources.² A striking finding of our study is the role of PE as the third leading cause of SCA/SCD in women, with a prevalence significantly higher than in men. Among the eight women with cardiac arrest due to PE and attempted CPR, none survived to hospital discharge. This highlights a potential blind spot in current pre-hospital management, as PE was not suspected or treated with thrombolytics, likely because the presentation differed from the typical pattern (prior dyspnoea and PEA as the initial rhythm) described in series of OHCA survivors or in-hospital cardiac arrest cases.^{12,13} The marked sex disparity in PE prevalence

Table 1 – Comparison of the clinical profile and risk factors according to sex.

	Women	Men	p-value
<i>n</i> (%)	191 (29.9)	448 (70.1)	
Demographic data			
Age (years)	74 (63–82)	66 (56–76)	<0.001
Resuscitation variables			
Resuscitation attempt	141 (73.8)	367 (81.2)	0.03
Witnessed cardiac arrest ^a	119 (85.0)	280 (77.6)	0.08
Location^a			
Home	112 (79.4)	242 (65.7)	0.003
Public place	16 (11.3)	104 (28.3)	<0.001
Ambulance	2 (1.4)	6 (1.6)	1.0
Primary care health centre	11 (7.8)	16 (4.3)	0.18
Bystander CPR ^a	54 (38.9)	140 (38.8)	1.0
Initial shockable rhythm ^a	29 (21.0)	123 (33.6)	0.01
Initial rhythm ^a			0.01
Ventricular fibrillation	25 (18.1)	104 (28.4)	
Ventricular tachycardia	4 (2.9)	19 (5.2)	
Pulseless electrical activity	4 (2.9)	22 (6.0)	
Asystole	105 (76.1)	221 (60.4)	
Survival at hospital discharge ^a	8 (5.7)	44 (12.2)	0.05
Symptoms prior to collapse			
Syncope	79 (48.2)	232 (57.9)	0.04
Dyspnoea	35 (21.3)	58 (14.5)	0.06
Chest pain or anginal equivalent	23 (14.0)	42 (10.4)	0.29
Previous medical history			
Cardiovascular risk factors			
Hypertension	119 (66.1)	207 (48.8)	<0.001
Diabetes mellitus	54 (30.0)	115 (27.2)	0.55
Dyslipidaemia	66 (36.9)	156 (36.9)	1.0
Obesity	45 (25.3)	78 (18.7)	0.09
Body mass index (kg/m ²) ^b	31.5 (4.9)	30.0 (5.9)	0.14
Toxicology			
Active smokers	23 (12.9)	89 (21.3)	0.02
Former smokers	8 (4.6)	79 (19.7)	<0.001
Alcohol abuse	45 (25.4)	65 (16.1)	0.01
Cardiac history			
Any cardiac history ^c	66 (36.9)	153 (36.2)	0.94
Myocardial infarction	13 (7.2)	51 (12.1)	0.10
Coronary heart disease	17 (9.4)	75 (17.7)	0.01
Congestive heart failure	35 (19.4)	59 (14.0)	0.12
Atrial fibrillation/atrial flutter	30 (16.8)	53 (12.6)	0.22
Ventricular fibrillation/ventricular tachycardia	0 (0.0)	8 (1.9)	0.14
Implantable cardioverter defibrillator	0 (0.0)	3 (0.7)	0.62
Permanent pacemaker	2 (1.1)	16 (3.8)	0.13
Other medical history			
Chronic kidney disease	19 (10.6)	41 (9.7)	0.84
Seizure disorder	1 (0.6)	13 (3.1)	0.76
Stroke	6 (3.3)	20 (4.7)	0.59
Asthma	6 (3.3)	10 (2.4)	0.68
Chronic obstructive pulmonary disease	15 (8.4)	73 (17.3)	0.01
Obstructive sleep apnoea syndrome	4 (2.2)	13 (3.1)	0.76
Pulmonary embolism	0 (0.0)	2 (0.5)	0.88
Chronic hepatopathy	2 (1.1)	5 (1.2)	1.0
Psychiatric disease ^d	28 (15.6)	38 (9.0)	0.03
Active malignant neoplastic disease	0 (0.0)	4 (0.9)	0.45

The data are presented as numbers and percentages for categorical variables and as means and standard deviations, or medians and interquartile ranges, for continuous variables.

^a Calculated with respect to the 508 resuscitation attempts.

^b Cases >18 years of age with an autopsy.

^c Previous diagnosis of coronary heart disease, angina, myocardial infarction, congestive heart failure, cardiomyopathy, atrial fibrillation/flutter, ventricular tachycardia, permanent pacemaker, implantable automatic defibrillator, severe and moderate valvular disease, and congenital cardiac disease.

^d Previous diagnosis of anxiety, bipolar disease, schizophrenia, or depression.

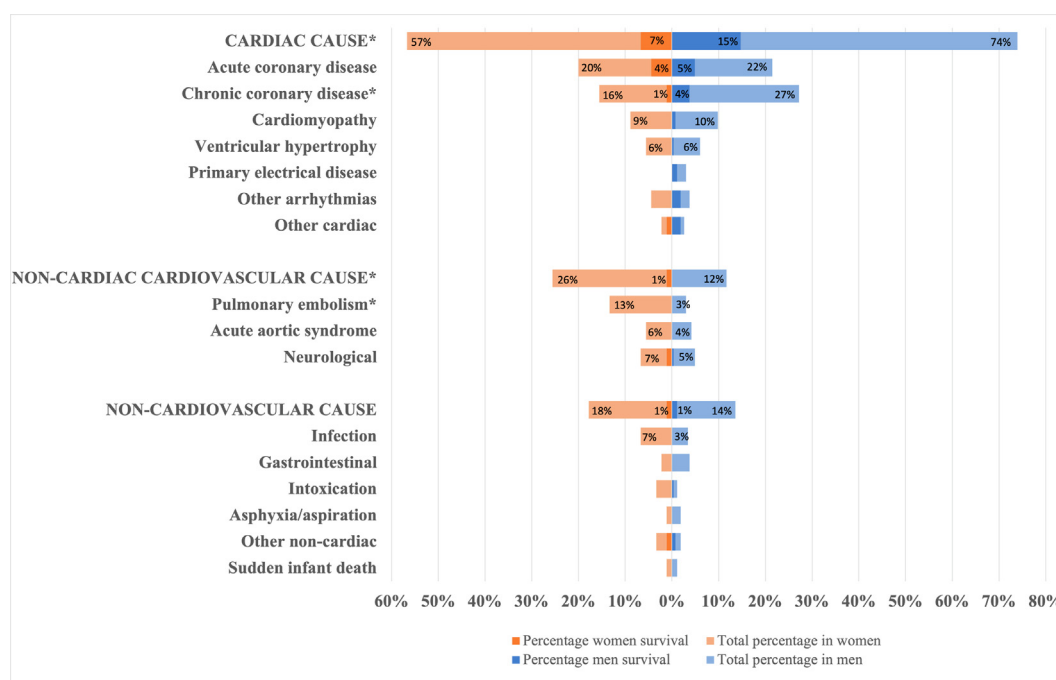


Fig. 2 – Sex-related differences in causes and survival of SCA.

The data on causes of SCA and survival for each cause are presented as percentages.

*Statistically significant difference in the percentage of the cause of SCA.

warrants a lower threshold for suspecting thromboembolic events in women collapsing at home, as well as the development of predictive models for detecting PE during resuscitation, potentially guiding earlier use of thrombolytics.^{14–16}

Our triangulation of forensic data revealed a unique ‘toxicological fingerprint’ in women. We observed a significant association between female SCA/SCD and the use of antidepressants and a history of psychiatric disorders.^{4,17} This interaction is likely multifactorial. First, the combination of psychotropic drugs and alcohol—found in a quarter of female cases—can synergistically prolong the QT interval, increasing the risk of torsade de pointes.¹⁸ Second, we found that women had a higher prevalence of hypertension, implying a greater probability, with increasing age, of a structural substrate (left ventricular hypertrophy) that makes the myocardium more vulnerable to drug-induced arrhythmias. This highlights the need for closer cardiovascular assessment and specific prevention strategies, such as QT interval monitoring, in women prescribed psychotropic medication, particularly those with co-occurring alcohol use.^{11,19}

As a limitation, the proportion of known causes of SCA/SCD was higher in men than in women because women were older and had lower survival; therefore, differences in aetiology should be interpreted with caution.

Conclusion

Women with SCA/SCD have a distinct risk profile, with a morning peak in occurrence and a high burden of PE, as well as involvement

of psychotropic drugs and toxic substances, highlighting the need for further research in this area.

Funding sources

The ReCaPTa study received a grant from the Catalan Resuscitation Council.

CRediT authorship contribution statement

Youcef Azeli: Writing – review & editing, Writing – original draft, Methodology, Investigation, Funding acquisition, Formal analysis, Data curation, Conceptualization. **Eneko Barbería:** Writing – review & editing, Investigation, Conceptualization. **Alberto Fernández:** Writing – review & editing, Investigation, Formal analysis, Data curation. **Inés Landín:** Writing – review & editing, Investigation, Data curation. **Cristina Rey-Reñones:** Writing – review & editing, Investigation, Data curation. **Silvia García-Vilana:** Writing – review & editing, Investigation, Formal analysis, Data curation. **Nina Vidal-González:** Writing – review & editing, Investigation, Data curation. **Gil Bonet:** Writing – review & editing, Investigation, Data curation. **Xavier Jiménez-Fàbrega:** Writing – review & editing, Investigation, Data curation. **Alfredo Bardají:** Writing – review & editing, Writing – original draft, Supervision, Investigation, Formal analysis, Conceptualization.

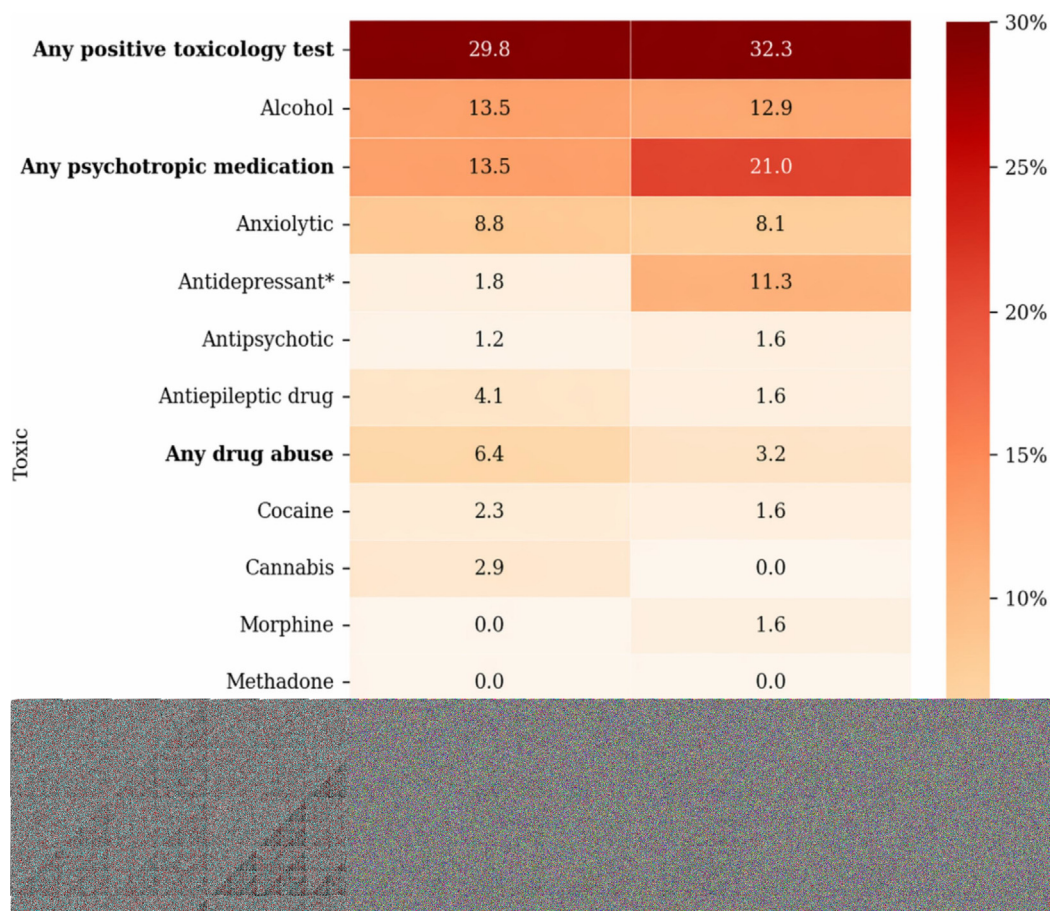


Fig. 3 – Sex-specific toxicological profile in SCA victims.

The heatmap displays the percentage of positive findings for each substance among autopsied cases. Women exhibited a distinct profile characterised by a significantly higher prevalence of antidepressants compared with men.

*Statistically significant difference ($p < 0.05$) in the positive toxicological result.

Declaration of competing interest

The authors have no conflicts of interest to declare.

Acknowledgements

We would like to thank the Swedish national registry of OHCA for their collaboration on the mobile application used for data collection and hosting. In addition, we thank Maria Jiménez-Herrera, Christer Axelsson, Eva Valero-Mora, Xavier Escalada, Isaac Lucas Guarque, Angels Mora, Monica Valero, Adnan Basic, Eva Hernando Gimeno, and Phil Hoddy for their support and contributions in different areas of the work; the staff of the Sistema d'Emergències Mèdiques de Catalunya for their assistance in data collection; and the research team of the Institute of Legal Medicine and Forensic Science of Catalonia for their collaboration, namely Pilar Torralba, Cristina Amaya, Carlos Laguna, and Ruth Alvarez.

Appendix A. Supplementary material

Supplementary material to this article can be found online at <https://doi.org/10.1016/j.resplu.2026.101416>.

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