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Review

Association between bystander cardiopulmonary resuscitation initiation and patient's sex: a systematic review and meta-analysis

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Abstract

Background and aim: The chain of survival, including cardiopulmonary resuscitation (CPR) and automated external defibrillation (AED), improves patients' outcomes in case of cardiac arrest. Socioeconomic status, race, and gender appear to be associated with the likelihood of receiving resuscitation. The aim of this systematic review and meta-analysis was to evaluate the association between female sex and the odds of bystander CPR initiation and AED application in patients with cardiac arrest, compared with male individuals.

Methods: The protocol of this systematic review was prospectively registered in PROSPERO (CRD42024512024). PubMed, Scopus, and Cochrane were searched for studies describing the association between patient sex and the initiation of bystander CPR or the application of AED pads.

Results: Fifteen observational cohort studies were included, for a total of 499,854 patients. The analysis from adjusted estimates of the primary outcome showed substantial heterogeneity (I^2 = 89%, very low certainty evidence) and was narratively summarised. Female sex was associated with reduced odds of AED pad application compared with males (OR 0.79; 95% CI 0.66–0.94; P = 0.008; I^2 = 45%; moderate certainty evidence).

Conclusions: The evidence regarding the association between bystander CPR initiation and patient's sex is characterised by substantial heterogeneity. Female sex appears to be associated with a lower probability of AED pad application compared with males.

Keywords: Cardiac Arrest, Cardiopulmonary resuscitation (CPR), Automated external defibrillator (AED), Gender, Sex, Female

Introduction

Cardiac arrest and the associated morbidity and mortality have a significant impact on the public health burden worldwide. According to the data reported by the International Liaison Committee on Resuscitation (ILCOR), the estimated annual incidence of out-of-hospital cardiac arrests treated by emergency medical services (EMS) in the countries of North America, Europe, Asia and Oceania ranges from 28 to 244 cases per 100,000 inhabitants.[1] Survival following out-of-hospital cardiac arrest (OHCA) remains low and varies among different geographic regions: between 3.1% and 20.4% of EMS-treated patients survived to hospital discharge or for at least 30 days.[1,2] In Europe, cardiopulmonary resuscitation (CPR) is attempted or continued by EMS in approximately 50–60% of cases, and survival to hospital discharge ranges from 0% to 18%.[3]

The vast majority of OHCAs occur at home or in a residential setting, and individuals who receive witness CPR while waiting for EMS arrival are nearly twice as likely to survive the event.[4,5] Despite recent progress, only 39.2% of adults receive layperson CPR and,

Abbreviations: AED, automated external defibrillator, BLS, basic life support, CI, confidence interval, CPR, cardiopulmonary resuscitation, EMS, emergency medical service, ILCOR, International Liaison Committee on Resuscitation, OHCA, out of hospital cardiac arrest, OR, odd ratio, SE, standard error

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in the general population, an automated external defibrillator (AED) was used in only 11.9% of cases with large geographical variability.[6] In Europe, the rate of CPR by lay-rescuers varies across countries with an average of 58% of cases while AED use remains low with an average 28% of cases.[3] Several socioeconomic, racial, and gender variables have been examined and appear to be associated with the likelihood of receiving basic life support (BLS). Studies in the United States have shown that Black and Hispanic people receive CPR less frequently than White individuals, suggesting implicit and explicit biases that may impact the likelihood of lay rescuers initiating CPR.[7,8] Fear of infection or personal injury among lay rescuers is strongly linked to the presence of mouth-to-mouth ventilation in the CPR protocol, which increases reluctance to initiate CPR when the subject is a stranger.[9,10] Furthermore, this fear may have been exacerbated during the recent COVID-19 pandemic.[11–13]

Recently, the female sex of the patient has been identified as a potential barrier to the initiation of BLS maneuvers.[14–16] Some studies suggest that female patients are less likely to receive BLS compared with males, while other studies have shown no significant differences between sexes. These results also vary depending on the cardiac arrest setting and according to methodological quality.[17–36]

The aim of this systematic review and meta-analysis was to evaluate the association between female sex (I) and the odds of bystander CPR initiation and AED application (O) in patients with cardiac arrest (P), compared with male individuals (C) from the available body of evidence.

Methods

The protocol of this systematic review was prospectively registered in PROSPERO with the identifier CRD42024512024.

We performed a comprehensive search of PubMed, Scopus and Cochrane databases from inception until the 22nd of September 2024. We conducted a search for randomised controlled trials (RCTs) and non-randomised studies that described the association between the sex of the cardiac arrest patient and the initiation of CPR or the application of AED pads. Case reports and case series were excluded. No language restrictions were applied. The search strategy included keywords as exact phrases and subject headings, according to databases syntaxes. The full search strategy is described in **Supplementary Material 1**.

Studies were included if they provided data on at least one outcome of interest (initiation of CPR or AED application), had a control group (male sex), and applied statistical methods to adjust for potential confounders in case of non-randomised studies. Male and female sex or gender were defined according to authors' definitions adopted in the included studies. Studies involving the paediatric population were included as per protocol to analyse the highest number of cases possible, as done in previous literature.[23] The inclusion of paediatric population would favour the null hypothesis if considered that differences in treatment between sexes may arise from secondary sexual characteristics from puberty on. After protocol registration, at manuscript peer review step, we decided to include only studies that evaluated the initiation of CPR and AED application by bystander to reduce the possible heterogeneity of the included population.

The full results of the literature search were independently screened by two authors (GC, NS) to identify all relevant articles from titles and abstracts. The selected articles were then assessed by full text according to the inclusion criteria. Any disagreements on the inclusion of studies were resolved by consensus involving two other authors (AC, MI). The corresponding authors of the selected studies were contacted in case of doubts about eligibility or data interpretation. The references of the relevant articles were also subjected to a screening procedure (snowballing method). Data were extracted in duplicate by two authors (GC, NS) using a standardized data extraction form. Discrepancies in the extracted data were resolved by consensus with the assistance of two other authors (AC, MI). The final version of the database was validated by all researchers involved in data collection. When two or more studies were based on the same patient dataset, the one with the largest number of patients was included in the analysis. Data were presented according to the Preferred Reporting of Items for Systematic Reviews and Meta-Analyses (PRISMA) checklist (**Supplementary Material 2**).[37] No Ethics approval was required for the purpose of this research.

Outcomes

The primary outcome of the study was the odds of bystander CPR initiation in patients with cardiac arrest. The secondary outcome was the odds of bystander AED pads application in patients with cardiac arrest. The analyses were conducted on adjusted estimates. Due to substantial heterogeneity the evidence regarding the primary outcome was narratively summarised according to the Synthesis Without Meta-Analysis (SwiM) reporting guidelines.[38]

Risk of bias assessment

Two investigators (GC, NS) independently assessed the risk of bias of the included studies. Any disagreements on the risk of bias assessments were resolved by consensus with two authors (AC, MI). The Risk Of Bias in Non-randomised Studies of Interventions (ROBINS-I) tool was used for non-randomised studies with a control group.[39] The Risk-of-Bias VISualisation (robvis) tool was used to generate risk of bias assessment graphs (traffic light plots and weighted summary plots).[40] The degree of certainty of the evidence (i.e. overall effect estimates) was assessed for the primary and secondary outcomes using the Grading of Recommendations Assessment, Development and Evaluation (GRADE) method.[41]

Statistical analysis

We used the generic inverse variance method to pool adjusted estimates and standard errors (SEs) from included studies reporting odds ratios (ORs) and 95% confidence intervals (CI) from multivariable models. The ORs were transformed to natural logarithm, and SEs were calculated from the 95% CIs using standard formulas.[42,43] The results were reported as ORs with their 95% CIs. Male patients were considered as control group. In case the included studies presented female sex as the control group, the corresponding author of the study was contacted, and the OR and CI were calculated through the inversion of the reference group. [42] The meta-analysis was performed using adjusted estimates from multivariate models or propensity-matched cohorts for the primary and secondary outcomes. ORs and CIs were transformed into natural logarithms and SEs using standard formulas.[42] If included studies provided more than one adjusted analysis for the same cohort and outcome, the data resulting from the model adjusted for the largest number of relevant covariates were used. Random effects models were used for all analyses. We planned sensitivity analyses based on the risk of bias of the included studies. Pre-planned subgroup analyses were

performed to address possible heterogeneity arising from the geography of the studies, the age of the patients, and the location of cardiac arrest. We also performed an analysis based on the unadjusted data (events and totals) for the primary outcome. All P-values were two-sided. P-values inferior to 0.05 were considered statistically significant. Statistical heterogeneity (i.e., random variation between studies) was assessed using the non-parametric c^2 test (Cochran Q), the I^2 statistic, and by visual inspection of forest plots.[43] Heterogeneity was considered likely if Q > df (degrees of freedom) and confirmed if the P-value was 0.10 or less. Analyses were performed using RevMan version 5.4 (Review Manager (RevMan). Version 5.4. The Cochrane Collaboration, 2020).

Results

Search results and characteristics

Overall, the literature search identified 2210 studies, and after removing duplicates, 1665 articles were screened by titles and abstracts. Among them, 100 full-text articles were assessed for eligibility. Nineteen studies reported data of interest, three of which considered data from clinical registries investigated by other studies and were excluded in favour of studies that included a larger number of cases.[29,30,35] Two studies were excluded because they did not provide adjusted data for the outcome of interest[44,45] and one study was excluded because it provided only disaggregated data related to the study intervention for the outcome of interest.[36] Additionally, one study was excluded because it presented data on CPR initiation and AED application by EMS.[22] Thus, fifteen studies were included in the systematic review and meta-analysis for a total of 499,854 patients, of which 174,951 were female (35%).[17–21,23–28,31–34] **Supplementary Material 3** shows the inclusion and exclusion process according to the requirements of the Preferred Reporting of Items for Systematic Reviews and Meta-Analyses (PRISMA).[46]

All included studies are observational cohort studies. No RCTs, quasi-randomised, or cluster-randomised studies were identified. The included studies were conducted in the United States, Canada, South Korea, Qatar, Germany, Japan, Malaysia, Singapore, Taiwan, Thailand, United Arab Emirates, China, India, and Australia. All studies reported events of OHCA. Seven studies explicitly adopted the Utstein definition of cardiac arrest.[20,21,24,25,31,33,47] The remaining studies reported the definition of cardiac arrest in the methods section. All studies provided analyses adjusted for patient and event characteristics as potential confounders (e.g., age, location of cardiac arrest, presence of witnesses, response time of emergency services, year). The full list of covariates for each adjusted analysis included is shown in **Supplementary Material 4**. Detailed characteristics of the included studies are provided in Table 1.

Risk of bias

Twelve of fifteen studies were qualitatively assessed for the primary outcome (bystander CPR initiation) using the ROBINS-I tool. Eight of the twelve studies were assessed at moderate risk of bias, and four were assessed at serious risk of bias due to confounding. Six studies were qualitatively assessed for the secondary outcome (bystander AED application) using the ROBINS-I tool. All were assessed at moderate risk of bias due to confoundings. Fig. 1 shows the judgments for each domain per study as traffic light plots and the distribution of risk of bias judgments within each domain as weighted bar plots.

Primary outcome – Bystander CPR initiation

Twelve studies reported adjusted analysis on bystander CPR initiation and were included in the meta-analysis for the primary outcome. The result of the meta-analysis regarding the association between bystander CPR initiation and patient's sex was characterised by substantial heterogeneity (I^2 = 89%, very low certainty evidence), so we decided to summarise the evidence narratively. The Forrest Plot in Fig. 2 shows the adjusted estimate for the primary outcome of the included studies. The included studies evaluated a total of 430,974 cases. Most studies did not report significant differences in the adjusted odds ratios of bystander CPR initiation in female patients compared with males.[19–21,23,24,27,28,31,33] Liu et al found an advantage for female sex[34] in contrast with the more recent findings of Munot et al[25]. Matsuyama's et al. results were divided per location with a reduction of CPR initiation in female patients in case of cardiac arrest in public.[17] Reasons for heterogeneity may reside in population characteristics and residual confounding. Seven studies included only adult patients[17,20,21,27,28,31,34] according to study definition, Okubo et al. included paediatric patients[33], Matsui et al. included patient with scholar age (6–21 year-old)[19] and lastly the studies by Munot et al. Paratz et al. and Souers et al. did not apply any age restriction.[23–25] Three studies included only cases of witnessed OHCA[17,25,33] and five studies excluded OHCA occurring in healthcare facilities or nursing homes.[17,25,27,31,34]

Secondary outcome – Bystander AED application

Six studies reported adjusted analysis for the outcome of bystander AED application and were therefore included in the meta-analysis regarding the secondary outcome. Female sex was associated with reduced odds of receiving AED pads application compared with male patients in case of cardiac arrest (OR 0.79; 95% CI 0.66–0.94; P = 0.008; I^2 = 45%; moderate certainty evidence; Fig. 3). **Supplementary Material 5** summarises the degree of certainty of the evidence assessed using GRADE.

Sensitivity analysis

The pre-planned sensitivity analysis was performed as per protocol including studies at low and moderate risk of bias. The analysis did not produce a consistent reduction in heterogeneity. (I^2 = 64%); **Supplementary Material 6**).

Following the review process one further sensitivity analysis was performed regarding the secondary outcome. In this analysis the study by Chavez et al[31] was excluded as it might be interpreted that "bystander AED", as reported in the original study, might indicated bystander shock delivery instead of bystander AED application. The sensitivity analysis showed results comparable to the analysis of the secondary outcome (OR 0.81; 95% CI 0.67–0.97, P = 0.03, I^2 = 47%; **Supplementary Material 7**).

Subgroup analysis

As per protocol subgroup analyses studying the association between female sex and bystander CPR initiation were performed on location of cardiac arrest (public vs private), age (adults vs paediatric) and geographic regions (Asian vs non-Asian countries). Geographic subgroups were formed according to the distribution and the number of studies included. As shown in **Supplementary Material 8** studies on public location more often reported data on lower odds of bystander CPR initiation in female sex compared with male, while the trend was opposite in private location. Trends regarding age and geography

Table 1 – Summary of included studies. AED automated external defibrillator; CPR cardiopulmonary resuscitation; EMS emergency medical service; OHCA out of hospital cardiac arrest.

Study ID	Country	Study Type	Years of Interest	Patients, N°	Population Characteristics	Setting	Outcome of Interest
Awad et al. 2020	Canada	Observational analysis of the British Columbia Cardiac Arrest registry	2011–2016	8,115	Adult patients (≥18 years) with non-traumatic OHCA treated by EMS. Patients with "do not resuscitate" orders, those pronounced dead on EMS arrival were excluded.	OHCA in public and private locations attended by EMS	Bystander CPR initiation defined as CPR performed before the EMS arrival
Awad et al. 2023	Qatar	Retrospective analysis of Hamad Medical Corporation OHCA registry	2016–2022	4,283	Adult patients (≥18 years) or older with non-traumatic OHCA treated by EMS. Patients pronounced dead on EMS arrival were excluded.	OHCA in public and private location attended by EMS	Bystander CPR initiation defined as CPR performed by lay-person before the EMS arrival
Blewer et al. 2018	United States, Canada	Retrospective Cohort Study of the Resuscitation Outcomes Consortium registry	2011–2015	19,331	Adult patients (≥18 years) with non-traumatic OHCA attended by EMS. Arrest events that occurred in a residential institution or healthcare center and those that were witnessed by EMS were excluded.	OHCA in public and private locations attended by EMS	Bystander CPR initiation defined as BCPR from a layperson excluding those from police, healthcare workers, EMS, or other first responders
Bockler et al. 2023	Germany	Observational cohort study from the German Resuscitation registry	2006–2022	58,798	Adult patients (≥18 years) with all cause OHCA attended by EMS	OHCA in public and private locations attended by EMS	Bystander CPR initiation
Chavez et al.2022	United States	Retrospective registry-based study of Texas Cardiac Arrest Registry to Enhance Survival (CARES)	2019–2020	8,037	Adult patients (≥18 years) with all cause OHCA attended by EMS during two study periods: pre-COVID-19 and during COVID-19. Observations of cardiac arrest witnessed by EMS or occurring at a healthcare facility were excluded.	OHCA in public and private locations attended by EMS	Bystander CPR initiation and AED application
Grunau et al. 2020	United States, Canada	Observational cohort study based on the Resuscitation Outcomes Consortium (ROC) Epistry 3 cardiac arrest registry	2011–2015	61,473	Patients (≥10 years) with EMS-treated non-traumatic OHCA. Cases of cardiac arrest witnessed by EMS were excluded.	OHCA in public and private locations attended by EMS	Bystander AED application
Kiyohara et al. 2020	Japan	Retrospective population-based registry study based on the Osaka Municipal Fire Department register for OHCA	2011–2018	4,358	Patients (all ages) with all-cause OHCA treated by EMS personnel. Cases of cardiac arrest witnessed by EMS personnel or family members were excluded from the analyses.	OHCA in public location attended by EMS	Bystander AED application defined as application of public-access AED pads on a patient's chest by bystanders.

Table 1 (continued)

Study ID	Country	Study Type	Years of Interest	Patients, N°	Population Characteristics	Setting	Outcome of Interest
Liu et al. 2022	Japan, South Korea, Malaysia, Singapore, Taiwan, Thailand, UAE, China and India	Secondary analysis of the Pan-Asian Resuscitation Outcomes Study (PAROS)	2009–2018	56,192	Adult patients (≥18 years) with non-traumatic OHCA patients transported by EMS. Cases of cardiac arrest with CPR performed by healthcare providers in healthcare facilities, nursing homes, witnessed by EMS/ private ambulance crews, with no attempted resuscitation or pronounced dead on the scene were excluded.	OHCA in public and private locations attended by EMS	Bystander CPR initiation defined as layperson BCPR, which includes dispatcher-assisted performed by layperson bystanders in all sites
Matsui et al. 2019	Japan	Observational cohort study from the SPRITS database	2008–2015	232	Patients (from 6 to 21 years) with non-traumatic OHCA with resuscitation attempt performed by EMS personnel or bystanders. Cases in which OHCA occurred after EMS arrival were excluded	OHCA in school campus attended by EMS or bystander	Bystander CPR initiation and AED application
Matsuyama et al. 2019	Japan	Observational study based on the All-Japan Utstein registry	2013–2015	84,734	Adult patients (≥18 years) with OHCA of medical origin resuscitated by by-standers or EMS personnel and transported to medical institutions. OHCA not witnessed, with unknown documented or occurring in health care facility or unknown location were excluded.	OHCA in public and private location witnessed by bystanders	Bystander CPR initiation
Munot et al. 2024	Australia	Observational analysis of the NSW Public Health Risks and Outcome registry	2017–2019	4,491	Patients (all ages) with non-traumatic bystander-witnessed cases of OHCA attended by EMS. Cases EMS-witnessed, unwitnessed, with an advance care directive, occurring in nursing homes, medical centres, police stations, correctional facilities and ambulance stations were excluded.	OHCA in public and private locations attended by EMS and witnessed by bystanders	Bystander CPR initiation and AED application defined as CPR provided by any person who hap- pens to be nearby and is not part of the organised emergency response system and AED connected to the patient prior to ambulance arrival.
Okubo et al. 2018	Japan	Nationwide cohort study from the All-Japan Utstein registry	2005–2015	4,525	Pediatric patients (≤17 years) with layperson-witnessed all-cause OHCA and EMS attempted resuscitation. EMS-witnessed arrest, unwitnessed arrest, unknown age, unknown witness status, unknown first documented rhythm, and unknown layperson CPR were excluded.	OHCA in public and private locations attended by EMS witnessed by bystanders	Bystander CPR initiation

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Table 1 (continued)

Study ID	Country	Study Type	Years of Interest	Patients, N°	Population Characteristics	Setting	Outcome of Interest
Paratz et al. 2023	Australia	Retrospective study based on the Victorian Ambulance Cardiac Arrest registry	2002–2021	32,502	Patients (all ages) with OHCA of presumed cardiac cause EMS attended. Cardiac arrests witnessed by EMS personnel were excluded.	OHCA in public and private locations attended by EMS	Bystander CPR initiation
Souers et al. 2021	United States	Retrospective analysis of NEMSIS (National Emergency Medical Services Information System)	2019	149,734	Patients (all ages) with all cause OHCA attended by EMS	OHCA in public and private locations attended by EMS	Bystander CPR initiation
Thompson et al. 2024	United States	Secondary analysis of data prospectively collected as part of the Portland cardiac arrest epidemiology registry	2018–2021	3,049	Adult patients (≥18 years) with non-traumatic EMS treated OHCA. Cardiac arrests in patients with preexisting do not resuscitate orders, or EMS witnessed OHCA were excluded.	OHCA in public and private locations attended by EMS	Bystander (including law enforcement) AED application

were of unclear interpretation. **Supplementary Material 9, 10.** Heterogeneity remained substantial in all subgroup analyses, with a reduction in the subgroup analysis per age (I^2 = 54%).

Unadjusted analysis

The analysis of unadjusted data (events and totals) for the outcome of bystander CPR initiation showed substantial heterogeneity. **Supplementary Material 11.**

Discussion

To the best of our knowledge, this is the first systematic review and meta-analysis to assess the association between cardiac arrest patient's sex and the odds of bystander CPR initiation or AED pad application. Thresholds for the interpretation of the I^2 statistic can be misleading, since the importance of inconsistency depends on several factors.[48] As a consequence, the evidence regarding the association between patients' sex and bystander CPR initiation was presented narratively due to the substantial heterogeneity resulting from the meta-analysis. Notably, pre-planned and post-hoc subgroup and sensitivity analyses failed to reduce the heterogeneity significantly. We found a significant adjusted association between female sex and the lower probability of bystander AED pads application in the event of cardiac arrest (moderate certainty of evidence).

The importance of the chain of survival, prompt initiation of resuscitation manoeuvres and improved survival following early defibrillation are well documented in the literature.[49–54] Matsuyama et al. in a scoping review investigated the factors favouring and inhibiting the willingness of lay rescuers to perform CPR manoeuvres. Among the latter, the fear of causing harm to the subject, personal physical factors, physical characteristics of the subject such as the presence of vomit or blood, socioeconomic level, race and gender of the patient were identified.[16] The role of patient sex has been investigated in the literature and the results are heterogeneous. Several studies report lower rates of bystander CPR for women than men, even after adjusting for potential confounders.[20,27,55] This difference appears to be more evident in the context of cardiac arrest occurring in public locations, where the subject is less likely to be known by bystanders.[34] In contrast, other studies report comparable rates of CPR in both sexes. Large studies conducted in Japan and Korea have shown equivalent or even higher rates of bystander CPR in women.[34] Cultural factors and widespread CPR education may therefore have contributed to overcoming the hesitations found in more Westernized countries.[24,56,57]

Heterogeneity was not overcome by subgroup analyses of bystander CPR initiation in female patients experiencing cardiac arrest in a public or private location, in Asian or non-Asian countries and in adult or paediatric populations. The studies evaluating cardiac arrest in a public place trend toward a disadvantage for women in receiving CPR, except for the study by Awad et al.[21] The latter includes events of cardiocirculatory arrest occurred in Qatar. It is possible that the different trend of this study may be justified by sociocultural customs with an extremely low percentage of women who experience cardiac arrest in public locations. [21] Studies often report results separately for public and private locations, acknowledging the distinct contexts of cardiac arrests in these settings.[17] Moreover, some studies excluded events of cardiac arrest in nursing homes, healthcare facilities and those witnessed by EMS: these

peculiar situations may alter the rate of bystander CPR initiation. Interesting results may arise from the evaluation of the specific location of the cardiac arrest such as home, working places or rural contexts. Additional data on this variable might be useful to better explain hindering factors to the initiation of bystander CPR and AED application. The presence of substantial heterogeneity among the studies included in the synthesis without meta-analysis of the primary outcome results in a very low certainty of evidence. This could be partially explained by population factors such as different timing and organization of EMS, whether all cases were registered or only cases of cardiac arrest transported to hospital, time of the day of cardiac arrest and other confounding factors not evaluated by some studies such as telephone-assisted CPR by emergency services. Furthermore, the included studies reported data on cohorts of adult and paediatric patients. The subgroup analysis per age partially reduced heterogeneity. A possible explanation lies in the facts that adult patient cohorts also include elderly patients. In fact, as shown by Matsuyama et al. and Kiyohara et al., there is an association between the advanced age and paediatric age and a greater willingness to start bystander CPR or apply AED pads compared with younger women.[17,18]

The evidence regarding bystander AED pads application in women with cardiac arrest is scarcer but the results are consistent in observing a lower use of the AEDs, and a delay in shock delivery

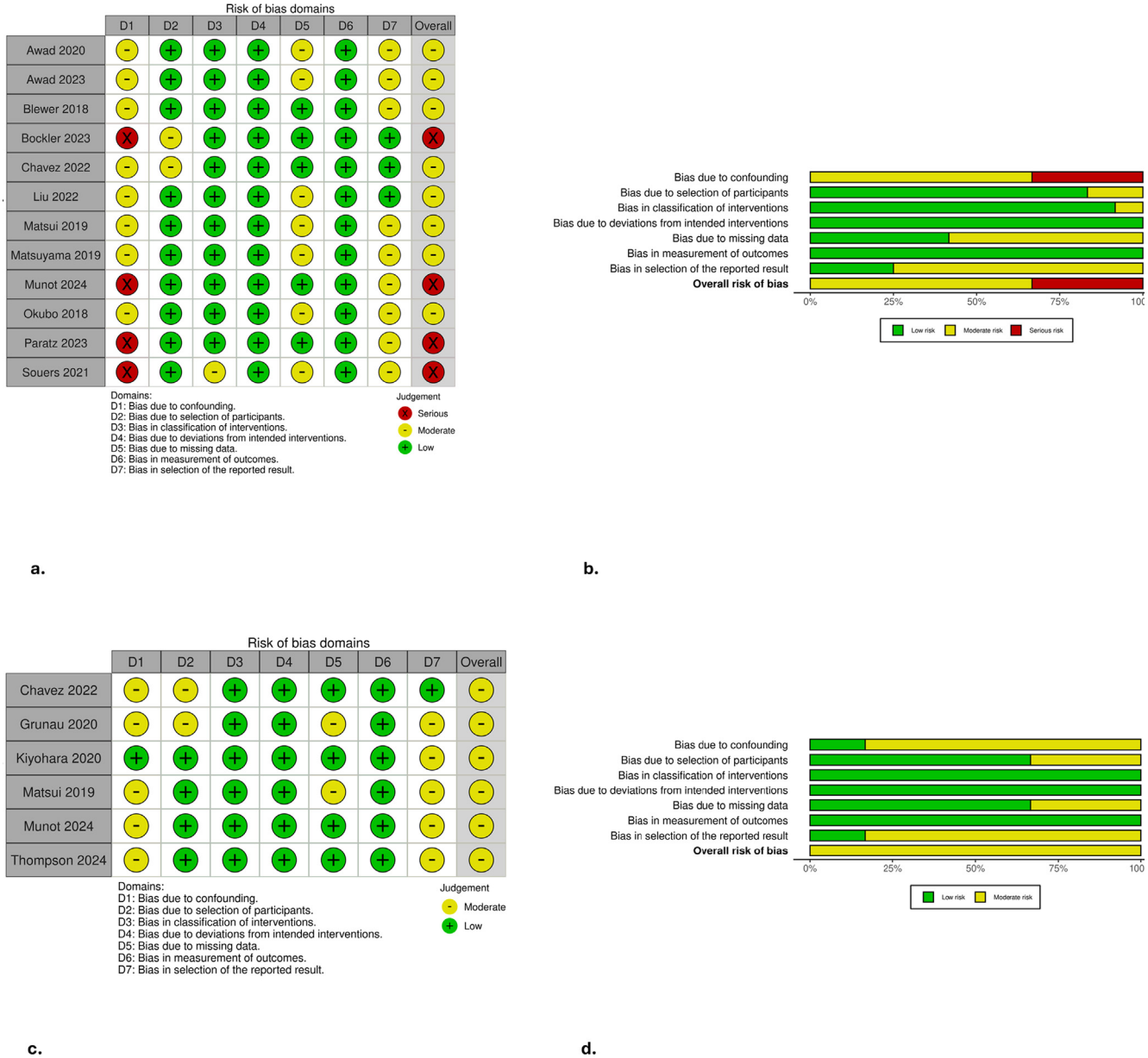

Fig. 1 – Risk of bias assessment of included studies. The figure shows the qualitative assessment of the included studies, performed using the ROBINS-I tool. The ratings of each domain per study are shown as "traffic light" plots (panels a. and c.). The distribution of risk of bias ratings within each bias domain is shown as weighted bar plots (panels b. and d.). Panels a. and b. show the evaluation for the outcome bystander CPR initiation. Panels b. and d. show the evaluation for the outcome bystander AED application.

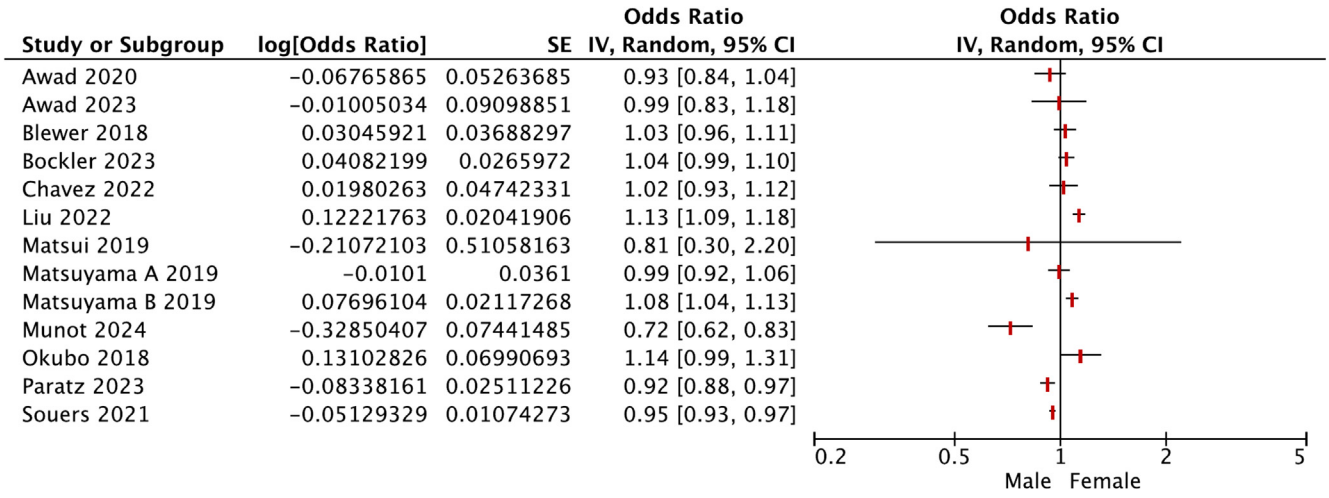

Fig. 2 – The figure shows the forest plot with the adjusted estimates regarding the studies included for the primary outcome "bystander CPR initiation". The study by Matsuyama et al. was included in two separate cohorts, as provided by the authors (cohort A patients with cardiac arrest in public location, B with cardiac arrest in private location).

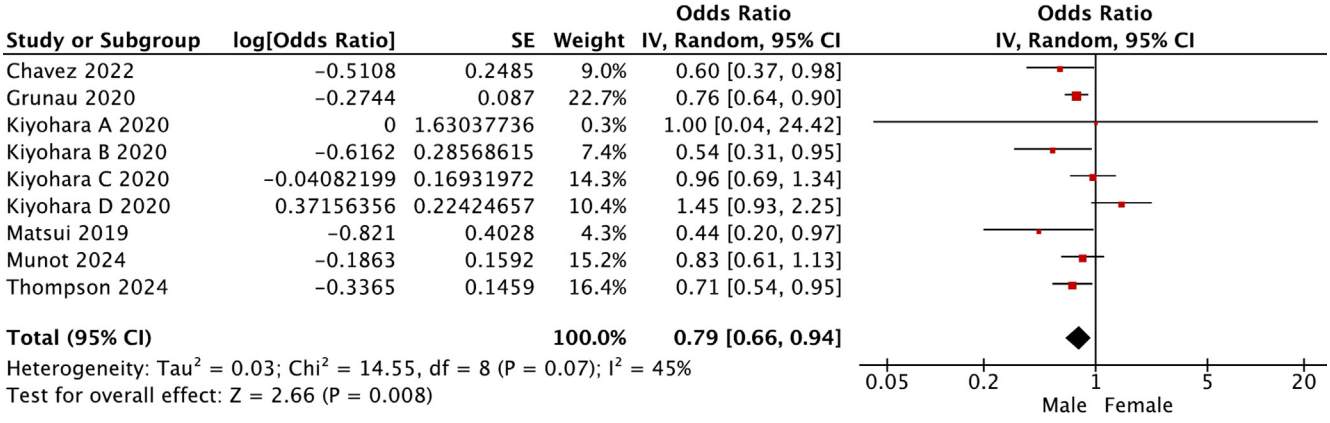

Fig. 3 – The figure shows the forest plot with the results of the meta-analysis on the adjusted estimates regarding the secondary outcome "bystander AED application". The study by Kiyohara et al. was included in the analysis with four separate cohorts, as provided by the authors (cohort A patient aged 0 to 14 years, B 15–49 years, C 50–74 years, D greater than 75 years).

in women in cardiac arrest.[19,24–26,32,45,58] The results from this meta-analysis reflect the data in the literature: female patients with cardiac arrest have a significantly reduced probability of having applied an AED with a moderate degree of evidence.

It has been hypothesized that the difference in the willingness of rescuers to perform CPR, compared with using the AEDs, may be explained by the need to fully expose the patient's chest for the execution of the second maneuver.[19,57] Perman et al. and Becker et al., through surveys, investigated the possible causes that may lead to a lower willingness to perform resuscitation manoeuvres both in subjects with and without BLS training. These studies raise concerns about the exposure of the women's breasts, the sexualization of the woman's body, the possibility that the breasts interfere with CPR manoeuvres, the possibility that resuscitation manoeuvres can cause damage, the altered perception of the severity of woman's clinical condition and the concern of being accused of sexual abuse.[59,60]

Throughout this paper we refer to the patient's sex as reported in the included studies. Future research should specifically investigate the role of patients' gender due to the possible role of socially constructed characters, behaviours and identities in the willingness of bystander CPR initiation and AED application as done in two of the included studies.[26,32,61]

Education and training to perform BLS manoeuvres in individuals with female secondary sexual characteristics may help reduce this important gender gap. In fact, according to Kramer et al, in a scenario in which female secondary characteristics were attributed to the simulation mannequin, rescuers removed less clothing from the female mannequin, compared with the male, with a difference between male and female rescuers.[62] Furthermore, apart from mannequins simulating pregnant women, simulation mannequins currently on the market do not have specifically feminine physical characteristics. They have a torso identical to a male, plastic hair styled differently and a typically female name.[23] The presence of

mannequins with female secondary sexual characteristics and the presence of a greater number of female volunteers in BLS courses and simulated scenarios involving female patients may be useful for students to familiarize with events of cardiac arrest in female patients.[63,66]

Another important aspect is the role of dispatcher assisted CPR and the characteristics and training of EMS in recognizing a possible cardiac arrest in female patients by phone.[64] The study by Ko et al. shows an increase in the rate of initiation of CPR in the group in which telephone-assisted resuscitation was performed with instructions and encouragement.[36] As underlined by Chen et al. these topics are rarely investigated in literature.[14]

Limitations

The first limitation of this study lies in the substantial heterogeneity of the primary outcome which led to the synthesis of the results without meta-analysis. Future research should investigate further variables possibly linked to this result. We were unable to evaluate the eventual role of the gender of first responders as effect modifier of the association between our outcomes and patient's gender due to the lack of reporting of the included studies. Similarly, we could not assess whether patients were known to the bystander rescuer or were strangers. Only one study reported data from Europe[28] and no study was carried out in countries with a high gender inequality index. [65] Thus, we cannot speculate on the impact of specific (granular) geographic locations and the review findings. Timely resuscitation is pivotal to improve clinical outcome.[49,52,53] Our study examines bystander CRP initiation and AED pads application, but we were unable to evaluate the promptness of the starting of resuscitation manoeuvres, which represents a variable of major clinical importance.

Conclusions

The evidence regarding the association between bystander CPR initiation and patient's sex is characterised by substantial heterogeneity. In cardiac arrest, female sex appears to be associated with lower probability of bystander AED pad application compared with males (moderate certainty evidence). Our findings should be cautiously interpreted due to the lack of granular geographic distribution of the included studies. Further research should evaluate this association in more detail in different clinical settings, geographic areas and age subgroups and by evaluating the role of telephone assisted CPR. Research and education initiatives should aim to identify the causes of this gap and solve it by educating rescuers to perform BLS manoeuvres in settings that include female patients.

Authors' contributions

GC, AC and MI conceived the content, drafted the manuscript, approved the final version to be submitted. NS helped in data examination. MI, NS, PI, ANG and AG helped in writing the manuscript and revised it critically for important intellectual content, approved the final version to be submitted. All authors have agreed on the journal to which the article will be submitted, gave final approval of the version to be published, and agree to be accountable for all aspects of the work.

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CRediT authorship contribution statement

Giulia Catalisano: Conceptualization, Data curation, Formal analysis, Investigation, Methodology, Project administration, Validation, Visualization, Writing – original draft, Writing – review & editing. **Mariachiara Ippolito:** Conceptualization, Investigation, Methodology, Supervision, Validation, Writing – original draft, Writing – review & editing. **Noemi Spina:** Data curation, Visualization, Writing – review & editing. **Pasquale Iozzo:** Validation, Visualization, Writing – review & editing. **Alberto Nicolò Galvano:** Validation, Visualization, Writing – review & editing. **Antonino Giarratano:** Validation, Visualization, Writing – review & editing. **Andrea Cortegiani:** Conceptualization, Data curation, Formal analysis, Investigation, Methodology, Project administration, Supervision, Validation, Writing – original draft, 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.

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Appendix A. Supplementary material

Supplementary data to this article can be found online at https://doi.org/10.1016/j.resplu.2025.100916.

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