Gender differences and survival after out-of-hospital cardiac arrest

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Background

- Out-of-hospital cardiac arrest (OHCA) is one of the leading causes of death in Western countries.
- Gender differences exist in demographic **characteristics**, resuscitation, post-arrest **care** and **outcomes**.

CONSISTENT FINDINGS	INCONSISTENT FINDINGS
Women OHCA patients are older	Survival
Lower rates of initial shockable rhythm	Neurological outcome
Lower rates of bystander CPR	
Lower rates of witnessed arrest	

- Numerous studies report better survival for men others for women and some did not find gender-related difference in survival.

J.T. Gräsner, *et al.***European Resuscitation Council Guidelines 2021: epidemiology of cardiac arrest in Europe**. Resuscitation, 161 (2021.
M.T. Blom, *et al.* **Women have lower chances than men to be resuscitated and survive out-of-hospital cardiac arrest**. Eur Heart J, 40 (2019).
A.F. Jarman, *et al.* **When the female heart stops: sex and gender differences in out-of-hospital cardiac arrest epidemiology and resuscitation** Clin Ther, 41 (2019).

Background

- Some of the discrepancies can be explained by **different inclusion criteria** (e.g. inclusion of shockable rhythms only, presumed cardiac cause only…).
- Most of the currently published studies examined gender differences using **prehospital resuscitation** data.
- Majority of the studies published **presumed and not the real underlying** cause of OHCA which is a major determinant of the initial rhythm, treatment and outcomes.
- Numerous studies have therefore concluded that it is desirable to **determine gender differences in the underlying causes of OHCA.**

J.T. Gräsner, *et al.***European Resuscitation Council Guidelines 2021: epidemiology of cardiac arrest in Europe**. Resuscitation, 161 (2021.
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Aims

- To examine gender differences related to
  - resuscitation and treatment characteristics
  - underlying cause of cardiac arrest
  - outcomes

in patients admitted for OHCA to a cardiac arrest center

Methods - study design

- Single center registry study.
- All adult (≥18 years) patients admitted to the General University Hospital in Prague for OHCA from **Jan 2012 to Dec 2020**.
- Diagnostic and treatment procedures in the hospital are performed according to the current guidelines valid at the time.
- The Prague OHCA registry is offering a detailed description of the prehospital, hospital characteristics (including cause of arrest) and outcomes.
- Data are prospectively entered into the database from emergency service and hospital records and the outpatient database.
- Data are collected according to **Utstein** recommendations.

G.D. Perkins, *et al.* **Cardiac arrest and cardiopulmonary resuscitation outcome reports: update of the Utstein resuscitation registry templates for out-of-hospital cardiac arrest: a statement for healthcare professionals from a task force of the International liaison Committee on resuscitation (American heart association, European resuscitation Council, Australian and New Zealand Council on resuscitation, heart and stroke Foundation of Canada, InterAmerican heart Foundation, resuscitation Council of southern Africa)**. Circulation., 132 (2015), pp. 1286-1300

Outcomes

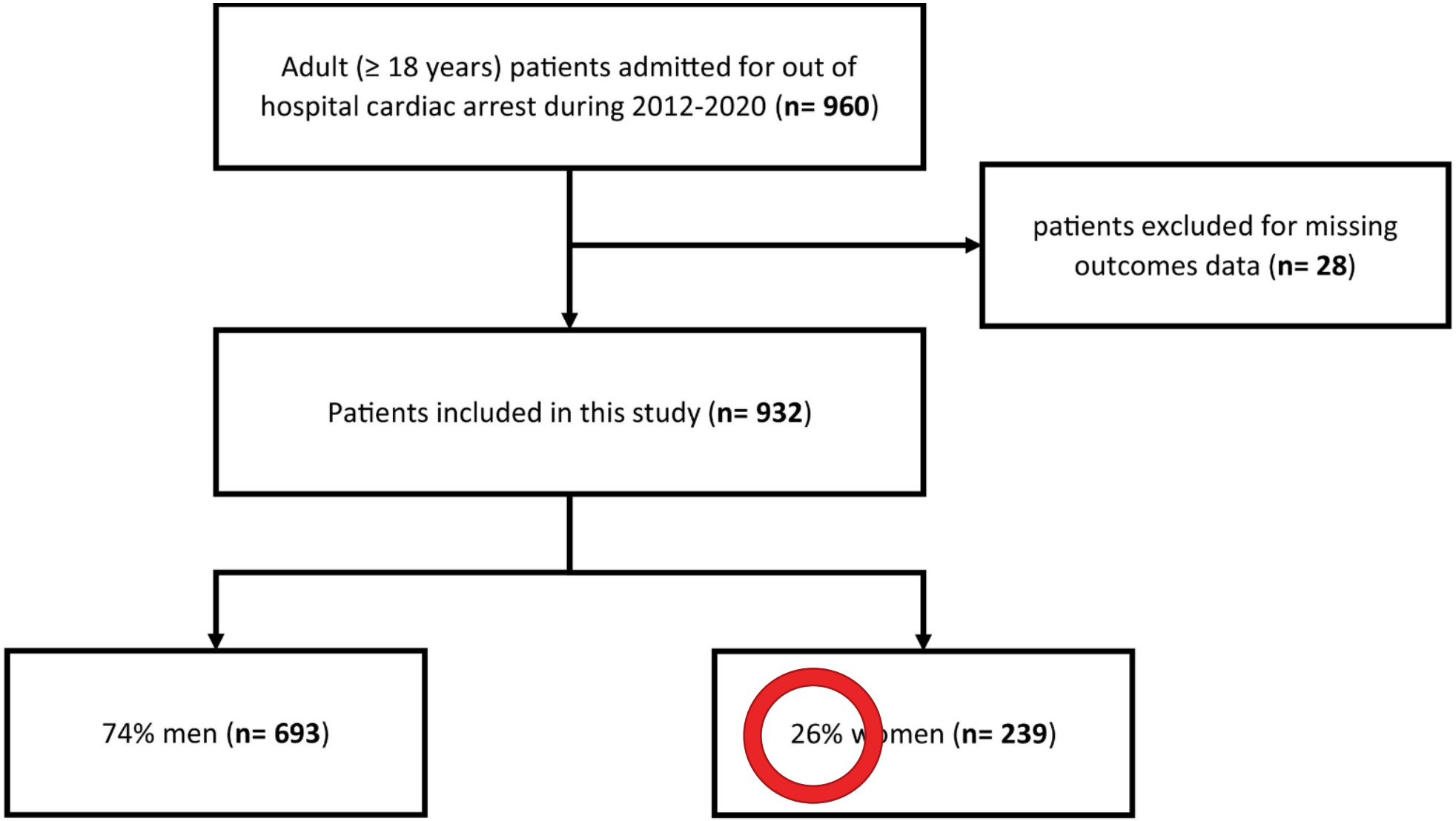
- Primary outcome of this analysis is **30-day mortality**.

- Secondary outcome is **good neurological outcome at hospital discharge**.
  - Cerebral performance category (CPC) 1–2 is considered a good outcome
  - CPC 3–5 is a poor neurological outcome.

Statistical analysis

- Standard descriptive statistics.
- The survival analysis was performed by Kaplan-Meier analysis and log-rank test.
- To establish the association of gender to 30-day survival, a multivariate analysis was performed by logistic regression with adjustment to evaluated factors: including **gender, age, witnessed arrest status, bystander CPR status, initial rhythm, time of resuscitation, sustained ROSC on admission, place of cardiac arrest, and cause of arrest**.
- The associated risk is expressed by the odds ratio (OR).
- All P values are two-tailed, $P < 0.05$ was considered statistically significant.
- Statistical analyses were performed with TIBCO Statistica Software version 14.0, and with the R (R Core Team, 2021) software, version 4.1.0 (2021-05-18).

Results


Adult (≥ 18 years) patients admitted for out of hospital cardiac arrest during 2012-2020 (**n= 960**)
patients excluded for missing outcomes data (**n= 28**)
Patients included in this study (**n= 932**)
74% men (**n= 693**)
26% women (**n= 239**)

Baseline characteristics

Variable	Women (n = 239)	Men (n = 693)	P value
Age, median (IQR), years	64.0 (54.0–75.0)	60 (50–68)	**<0.001**
Medical history			
Hypertension	141/228 (62%)	356/639 (56%)	0.11
Diabetes	55/228 (24%)	157/638 (25%)	0.88
Smoking history	86/223 (39%)	382/624 (61%)	**<0.001**
CAD	45/224 (20%)	175/635 (28%)	0.27
History of MI	22/223 (10%)	129/634 (20%)	**<0.001**
History of PCI	20/225 (9%)	97/634 (15%)	**0.016**
History of CABG	9/225 (4%)	40/636 (6%)	0.20
Dyslipidemia	74/228 (32%)	208/638 (33%)	0.97
Atrial fibrilation	37/224 (17%)	87/633 (14%)	0.31
Chronic heart failure	45/228 (20%)	108/640 (17%)	0.33
Chronic kidney disease	27/226 (12%)	73/638 (11%)	0.84

Resuscitation characteristics

Variable	Women (n = 239)	Men (n = 693)	P value
Location of cardiac arrest			
Home	88/239 (37%)	237/693 (34%)	
Public	146/239 (61%)	446/693 (64%)	0.57
Unknown	5/239 (2%)	10/693 (1%)	
Initial rhythm			
VF/VT	112/239 (47%)	448/693 (65%)	
Asystole	73/239 (30%)	135/693 (19%)	**<0.001**
PEA	52/239 (22%)	106/693 (15%)	
Unknown	2/239 (1%)	4/693 (1%)	
Witnessed arrest	198/237 (84%)	620/685 (91%)	**0.003**
Bystander CPR	195/237 (82%)	594/689 (86%)	0.14
Mechanical CPR	73/239 (31%)	270/693 (39%)	**0.02**
Time to ROSC, median (IQR)	20 (14–34)	23 (13–44)	0.21

In-hospital interventions

Hospitalization treatment	Women (*n* = 239)	Men (*n* = 693)	P value
TTM	170/231 (74%)	580/678 (86%)	**<0.001**
ECLS	26/239 (11%)	108/693 (16%)	0.07
CAG	150/239 (63%)	550/693 (79%)	**<0.001**
PCI	69/150 (46%)	301/550 (55%)	0.06

Cardiac arrest cause

Variable	Women (n = 239)	Men (n = 693)	P value
Cause of cardiac arrest			
Cardiac	129/239 (54%)	521/693 (75%)	
Non-cardiac	96/239 (40%)	141/693 (20%)	**<0.001**
Unknown	14/239 (6%)	31/693 (5%)	

Detailed cause of cardiac arrest

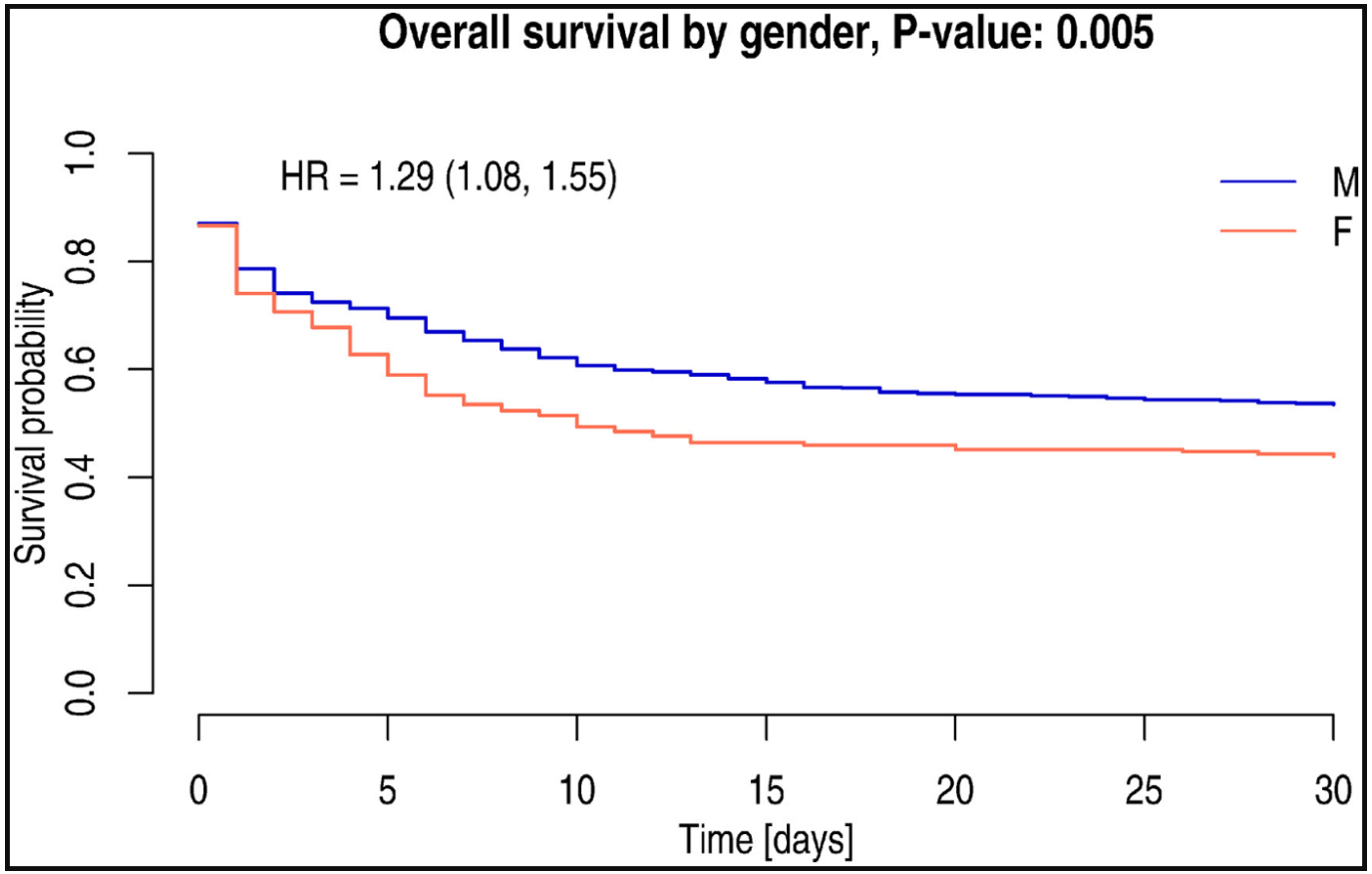
Variable	Women (n = 239)	Men (n = 693)	P value
Cardiac			
Acute coronary syndrome	71/129 (55%)	334/521 (64%)	
Coronary artery disease	15/129 (11%)	99/521 (19%)	
Arrhytmia	17/129 (13%)	27/521 (5%)	
Chronic heart failure	10/129 (8%)	13/521 (3%)	**<0.001**
Cardiomyopathy	9/129 (7%)	32/521 (6%)	
Valvular disease	5/129 (4%)	10/521 (2%)	
Myocarditis	2/129 (2%)	6/521 (1%)	

Detailed cause of cardiac arrest

Variable	Women (n = 239)	Men (n = 693)	P value
Non-cardiac			
Hypoxia	40/96 (42%)	56/141 (40%)	**0.45**
Pulmonary embolism	23/96 (24%)	25/141 (18%)	
Bleeding	11/96 (11%)	15/141 (11%)	
Other	10/96 (10%)	12/141 (8%)	
Aortic dissection type A	3/96 (3%)	13/141 (9%)	
Accidental hypothermia	4/96 (4%)	10/141 (7%)	
Intoxication	5/96 (5%)	10/141 (7%)	

Outcomes

- 30-day survival of women was **45%** compared to **53%** in men (log-rank p=0.005).
- CPC 1/2 was achieved in **37%** of women vs. **47%** of men (p=0.008).



Multivariate logistic regression analysis of 30-day survival

Factor	Odds Ratio	Confidence Interval	P value
Gender (female)	**0.98**	**0.65–1.50**	**0.94**
Age (years)	**0.97**	**0.95–0.98**	**<0.001**
Witnessed arrest (yes)	1.72	0.98–3.02	0.06
Bystander CPR (yes)	1.08	0.64–1.81	0.78
Time of resuscitation (min)	**0.96**	**0.95–0.97**	**<0.001**
Initial shockable rhythm (yes)	**7.86**	**4.93–12.54**	**<0.001**
Cause of arrest (cardiac)	1.52	0.92–2.52	0.10
Place of arrest (public)	**2.03**	**1.39–2.97**	**<0.001**
Sustained ROSC on admission (yes)	**1.84**	**1.02–3.32**	**0.04**

Limitations

- Observational study design - despite adjusting for covariates, other **unmeasured factors** may have influenced the association between gender and outcomes.
- A **single-center** study with a **limited sample size** from the in-hospital based registry reflecting results of a specialized tertiary cardiac arrest center which limits the generalizability of our results.
- There were **missing data** in the studied subset, nevertheless, the missing data were distributed proportionally between both sexes.

Conclusions

- **There are important gender differences** among OHCA patients admitted to the cardiac arrest center.
- Women OHCA patients were **older**, **lower rates** of initial **shockable** rhythm and **witnessed** arrest status.
- Women OHCA patients were **treated less agresivelly** (mechanical CPR, TTM, ECPR, CAG/PCI).
- **Survival and good neurological outcome was lower** in women, but after adjusting for the most important factors, **gender was not associated with survival** nor with good neurological outcome.
- The possible reason of OHCA gender disparity may be due to significant **differences in the OHCA underlying etiology** subsequently leading to differences in the initial rhythm, treatment and outcomes.

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