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Published in:
Resuscitation

DOI:
10.1016/j.resuscitation.2020.10.026

Publication date:
2021

Available online at www.sciencedirect.com

Resuscitation

journal homepage: www.elsevier.com/locate/resuscitation

Sex differences in patients with out-of-hospital cardiac arrest without ST-segment elevation: A COACT trial substudy

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Abbreviations: OHCA, Out-of-hospital cardiac arrest; STEMI, ST-segment elevation myocardial infarction; CAD, Coronary artery disease; ECG, Electrocardiogram; PCI, Percutaneous coronary intervention; CABG, Coronary artery bypass grafting; COACT, Coronary Angiography after Cardiac Arrest; MINOCA, Myocardial infarction with non-obstructive coronary arteries; CMD, Coronary microvascular disease; SCAD, Spontaneous coronary artery dissection.

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https://doi.org/10.1016/j.resuscitation.2020.10.026
Received 24 August 2020; Received in revised form 9 October 2020; Accepted 16 October 2020

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Abstract

Background: Whether sex is associated with outcomes of out-of-hospital cardiac arrest (OHCA) is unclear.

Objectives: This study examined sex differences in survival in patients with OHCA without ST-segment elevation myocardial infarction (STEMI).

Methods: Using data from the randomized controlled Coronary Angiography after Cardiac Arrest (COACT) trial, the primary point of interest was sex differences in OHCA-related one-year survival. Secondary points of interest included the benefit of immediate coronary angiography compared to delayed angiography until after neurologic recovery, angiographic and clinical outcomes.

Results: In total, 522 patients (79.1% men) were included. Overall one-year survival was 59.6% in women and 63.4% in men (HR 1.18; 95% CI: 0.76-1.81;p = 0.47). No cardiovascular risk factors were found that modified survival. Women less often had significant coronary artery disease (CAD) (37.0% vs. 71.3%;p < 0.001), but when present, they had a worse prognosis than women without CAD (HR 3.06; 95% CI 1.31−7.19;p = 0.01). This was not the case for men (HR 1.05; 95% CI 0.67−1.65;p = 0.83). In both sexes, immediate coronary angiography did not improve one-year survival compared to delayed angiography (women, odds ratio (OR) 0.87; 95% CI 0.58−1.30;p = 0.49; vs. men, OR 0.97; 95% CI 0.45−2.09;p = 0.93).

Conclusion: In OHCA patients without STEMI, we found no sex differences in overall one-year survival. Women less often had significant CAD, but when CAD was present they had worse survival than women without CAD. This was not the case for men. Both sexes did not benefit from a strategy of immediate coronary angiography as compared to delayed strategy with respect to one-year survival.

Clinical trial registration number: Netherlands trial register (NTR) 4973.

Keywords: out-of-hospital cardiac arrest, sex, differences, coronary angiography

Introduction

Out-of-hospital cardiac arrest (OHCA) is a major public health problem with high mortality rates.[1,2] In patients suffering from OHCA with initial shockable rhythm, coronary artery disease (CAD) is the most common underlying cause of the arrest and is reported in up to 70% of patients[3,4,5] and invasive coronary angiography is one of the key components in post-arrest care.[6] In patients who present with cardiac arrest due to ST-segment elevation myocardial infarction (STEMI), an acute thrombotic occlusion is often the cause of the arrest.[5,7] American and European guidelines recommend immediate coronary angiography and percutaneous coronary intervention (PCI) if indicated in these STEMI patients.[5,8,9,10] Current guidelines also encourage immediate coronary angiography in patients with cardiac arrest and shockable rhythm in the absence of STEMI but with high suspicion of myocardial ischaemia.[9,10] Until recently, no randomized data on the benefit of early coronary angiography in these patients has been available. The Coronary Angiography after Cardiac Arrest without ST-segment Elevation (COACT) trial, the first multicentre randomized controlled trial to investigate this[3,11], found no benefit of early coronary angiography compared to delayed coronary angiography strategy with respect to 90-days survival in these patients.[3,11]

In recent years, sex differences in patients with OHCA are being increasingly recognized in both pathophysiology and treatment of CAD.[12,13,14,15] Studies including cardiac arrest patients with all initial rhythms and presumed cardiac aetiology have shown that almost 80% of patients are male[12,14,16,17,18] and that cardiac arrest due to an initial shockable rhythm is more common in men than women.[12,15,17,18,19] If women suffer from OHCA, they are often older[15,17,19,20], and have a higher cardiovascular risk profile than men.[12,19] Present data on the association between sex and OHCA-related survival is mainly based on national registries containing a heterogeneous patient population. While some studies reported that female sex is associated with worse survival[15,16,19], others found no association[12,14,21] and one study even reported increased odds of survival for women.[22] The contradictory findings represent the current knowledge gaps regarding sex differences in OHCA patients. Using the randomized-controlled COACT database, we examined sex differences in patients who were successfully resuscitated after OHCA with initial shockable rhythm in the absence of STEMI on one-year survival. We also

examined sex differences and the effect of immediate coronary angiography on one-year survival, baseline characteristics and in-hospital treatment.

Methods

Study population

This study is a secondary analysis of the COACT trial[3,11], an investigator-initiated, randomized open-label multicentre trial, which was performed in 19 hospitals in the Netherlands. Patients were included if they were 18 years or older and successfully resuscitated after OHCA with initial shockable rhythm and absence of STEMI on the post-resuscitation electrocardiogram (ECG).[3] Important exclusion criteria were signs of STEMI, shock or an obvious or suspected non-coronary cause of the arrest.[3] Further in- and exclusion criteria were reported previously.[23] Eligible patients were randomized in a 1:1 ratio to an immediate strategy (i.e. as soon as possible, initiated within 2 hours after randomization) or a delayed strategy (i.e. after neurologic recovery) for coronary angiography. Post-resuscitation care was according to the international resuscitation guidelines.[6] Decisions on withdrawal or limit life-sustaining therapy was in accordance with Dutch and European guidelines. The COACT trial was approved by the ethical committee of Amsterdam UMC, location VUmc. Deferred written informed consent was obtained from all enrolled patients.

Study endpoints and definitions

In the present study, we examined sex differences in patients successfully resuscitated after OHCA with initial shockable rhythm and absence of STEMI. The primary point of interest was the overall survival at one year. The secondary points of interests were the benefit of immediate coronary angiography compared to a delayed strategy on one year survival, the presence of cardiovascular risk factors, angiographic characteristics and outcomes, and clinical outcomes (i.e. mechanical and catecholamine or inotropic support). Death was defined as death of all cause. Unstable coronary lesions were defined as a stenosis severity of >70% and the presence of characteristics of plaque disruption including irregularity, dissection, haziness or thrombus defined by coronary angiography.[3] Significant coronary artery disease was defined as coronary lesions with >70% stenosis severity without signs of plaque disruptions.

Table 1 – Baseline characteristics.

	Men (N = 413)	Women (N = 109)	P value
Age — years*	66.1 ± 11.7	63.0 ± 14.1	0.04
18-39	8 (1.9)	7 (6.4)	
40-60	114 (27.6)	38 (34.9)	
>61	291 (70.5)	64 (58.7)	
Hypertension — no. /total no. %	198/409 (48.4)	54/109 (49.5)	0.83
Previous myocardial infarction—no. /total no. %	125/413 (30.3)	19/109 (17.4)	0.008
Previous CABG — no./total no. %	58/412 (14.1)	7/109 (6.4)	0.03
Previous PCI — no./total no. %	89/411 (21.7)	14/109 (12.8)	0.04
Previous coronary artery disease – no. %	162/413 (39.2)	26/109 (23.9)	0.003
Previous cerebrovascular accident — no./ total no. %	25/412 (6.1)	9/109 (8.3)	0.41
Diabetes mellitus — no./total no. %	76/412 (18.4)	20/109 (18.3)	0.98
Current smoker — no./total no. %	93/383 (24.3)	18/99 (18.2)	0.20
Hypercholesterolemia — no./total no. %	125/408 (30.6)	20/109 (18.3)	0.01
Peripheral artery disease — no./total no. %	29/412 (7.0)	9/109 (8.3)	0.66
Arrest witnessed — no. %	329 (79.7)	79 (72.5)	0.11
Median time from arrest to basic life support [IQR] — min.	2 [1-5]	2 [0-5]	0.76
Median time from arrest to return of spontaneous circulation [IQR] — min.	15	15	0.85
Signs of ischaemia on ECG † — no./total no. %	265/388 (68.3)	64/106 (60.4)	0.13
Median GCS score at admission [IQR]	3 (3-3)	3 (3-3)	0.79
APACHE IV score	106.3 ± 30.4	104.4 ± 29.5	0.56
Baseline laboratory values			
pH	7.2 ± 0.1	7.2 ± 0.1	0.76
Median lactic acid [IQR]	5.0(2.9-8.6)	5.1(2.9-9.1)	0.78
Bicarbonate — mmol/liter	19.2 ± 4.4	19.1 ± 4.4	0.84
Base excess	−7.7 ± 6.0	−7.2 ± 6.9	0.47
Median partial pressure of oxygen [IQR] — kPa	14.5 [9.5-26.3]	16.8 [9.2-33.0]	0.23
Median Creatinine [IQR] — µmol/liter	105 [92-120]	86 [71-99]	<0.001
Median Creatinine Kinase [IQR] — U/liter	174 [125-263)	145 [100-211]	0.003
Median Creatinine Kinase MB [IQR] — µg/liter	6.5 [4.0-17.5)	4.5 [2.8-12.0]	0.02
Median Troponin T [IQR] — µg/liter	0.050 [0.028-0.104)	0.048 [0.028-0.085]	0.40

* Plus-minus values represents means and standard deviations±. †Signs of ischaemia on ECG meaning ST-segment depression of 1 mm or more in two contiguous leads and/or T-wave inversion in two contiguous leads. IQR denotes interquartile range, CABG coronary artery bypass graft, PCI percutaneous coronary intervention, ECG electrocardiogram, GCS Glasgow Coma Scale (scoring system ranging from 3-15, low score indicates reduced level of consciousness), APACHE IV Acute physiology and chronic health evaluation IV (scoring system assessing severity of illness and prognosis of intensive care unit patients, ranging from 0 to 286, with higher scores indicating a higher risk of death).

Statistical analysis

For descriptive analysis, continuous measurements were presented as means ± standard deviation or medians and interquartile ranges (IQR). Categorical variables were presented as number of observations and percentages. Baseline characteristics and angiographic outcomes were analysed using the independent samples t-test for continuous variables or Mann-Whitney U for variables that were not normally distributed. The chi-square or Fisher's exact test was used to compare binary and categorical outcomes. Survival outcomes were assessed using the Kaplan Meier method and compared between sexes using the log-rank test. Effect modification of associations between treatment or risk-factors and one-year survival by sex were assessed by logistic regression where the interaction between sex and treatment or risk factors was tested. A two-tailed p-value of 0.05 was regarded as statistically significant. All statistical analyses were conducted using IBM SPSS Statistics, version 26 (IBM, Armonk, New York).

Results

Patients baseline characteristics

In the randomized COACT trial, 552 patients were enrolled at 19 participating centres in the Netherlands during the time-period from January 2015 to July 2018.[3] Fourteen patients retroactively withdrew informed consent. In addition, 13 patients refused consent for the one-year follow-up and 3 patients were lost to follow-up. In total, 522 patients had data available for assessment at one year (n = 413 men, 79.1%) (Table 1). The proportions of witnessed arrest did not differ between the sexes (women 72.5% vs. men 79.7%; p = 0.11), nor did median time from arrest to basic life support (BLS) or return of spontaneous circulation (ROSC). Also, signs of ischaemia on ECG did not differ between men and women (women 60.4% vs. men 68.3%; p = 0.13). Women were younger than men, with a mean age of 63.0 ± 14.1 years compared to 66.1 ± 11.7 years in men (p = 0.04). Women had a lower cardiovascular risk profile as hypercholesterolemia (women 18.3% vs. men 30.6%; p = 0.01), a history of myocardial infarction (women 17.4% vs. men 30.3%; p < 0.01), previous coronary interventions such as percutaneous coronary intervention (PCI) (women 12.8% vs. men 21.7%; p = 0.04) and previous coronary artery bypass grafting (CABG) (women 6.4% vs. men 14.1%; p = 0.03). Except for higher creatinine levels in men, laboratory findings at baseline were not found to differ between the two sexes.

Angiographic findings and subsequent treatment

During hospitalization, coronary angiography was performed in 81.0% of the patients. Women were less likely to undergo coronary angiography than men (women 74.3% vs. men 82.8%; p = 0.04). The main reason for not performing coronary angiography was that the patient died before the procedure could take place, which was comparable in both sexes (women 19.3% vs. men 13.1%; p = 0.10) (Table 2). Women less often had significant CAD (women 37.0% vs. men 71.3%; p < 0.001), and were less likely to have severe CAD (one-vessel disease 18.5% vs. 29.8%; two-vessel disease 9.9% vs. 23.1%; three-vessel disease 8.6% vs. 18.4%; p < 0.001) and (consequently) less often underwent revascularization (women PCI 12.8% vs. men 30.0%; p < 0.001, CABG 1.8% vs. 8.0%; p = 0.02) as compared to their male counterparts (Fig. 1).

Table 2 – Reasons for not undergoing coronary angiography*.

	Men (N = 71)	Women (N = 28)
Death — no. of patients. (%)	54 (76.1%)	21 (75.0%)
Poor neurologic condition — no. of patients. (%)	5 (7.0%)	2 (7.1%)
Multiple co-morbidities — no. of patients. (%)	3 (4.2%)	1 (3.6%)
Cardiac imaging performed instead — no. of patients. (%)	3 (4.2%)	2 (7.1%)
Patient refused — no. of patients. (%)	0 (0.0%)	2 (7.1%)
Other — no. of patients. (%)	6 (8.5%)	0 (0.0%)

* Almost all patients (22/24) who survived hospitalization but did not undergo coronary angiography, were enrolled in the delayed arm.

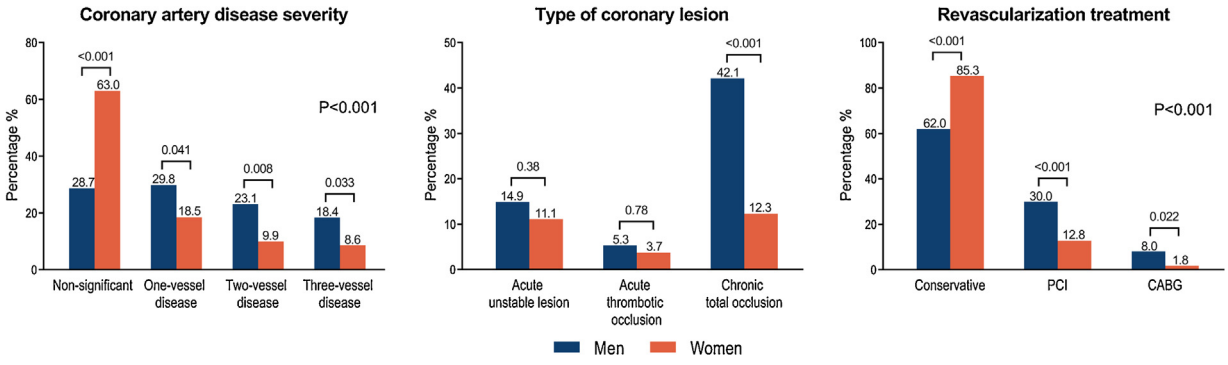

Fig. 1 – Angiographic outcomes and revascularization method*. *Significant coronary artery disease was defined coronary lesions with >70% stenosis severity without signs of plaque disruptions. Unstable coronary lesions coronary

In-hospital treatments and outcomes

Intensive care support, such as duration of mechanical ventilation (women 2 [1−3] days vs. men 2 [1−4] days; p = 0.09) or duration of inotropic support (women 1 [0.5−1.5] days vs. men 1 [0.5−2.0] days; p = 0.11) was not found to differ between sexes (Table 3). Similarly, there was no difference in need for renal replacement therapy (women 0.9% vs. men 4.4%; p = 0.15). Cardiac biomarkers such as troponin T and CK-MB were significantly lower in women compared to men. Women were discharged faster from the intensive care unit days (3 [2−6] days vs. 4 [2−6] days; p = 0.02).

Treatment strategies and survival

In total, at one-year follow-up 59.6% of women and 63.4% of men were alive (HR 1.18; 95% confidence interval [CI]: 0.76−1.81; p = 0.47) (Fig. 2). In patients who underwent immediate coronary angiography, 29 (59.2%) women and 133 (61.9%) men were alive at one year (p = 0.73). In the delayed group, 36 (60.0%) women and 129 (65.2%) men were alive at one year (p = 0.47). Causes of death were similar for the two sexes (Table S1). The presence of significant CAD in women was strongly associated with worse survival (HR 3.06; 95% CI 1.31−7.19; p = 0.01) among patients that underwent coronary angiography, with a one year survival rate of 56.7% in women with CAD compared to 82.4% in women without CAD. This difference was not found in men, with survival rates of 73.5% in men with CAD and 73.0% in men without CAD (HR 1.05; 95% CI 0.67−1.65; p = 0.83). In a post-hoc analysis performed separately in both sexes, we were not able to identify differences in baseline that clarified the lower survival in women with CAD. In both men and women, immediate coronary angiography did not improve one-year survival when compared to delayed angiography strategy and the effect was not found to be significantly modified by sex (OR 0.87; 95% CI 0.58−1.30; p = 0.49; vs. OR 0.97; 95% CI 0.45−2.09; p = 0.93; p-value for interaction = 0.81) (Fig. 3). At one-year follow-up, there was no difference between coronary interventions or hospitalizations between the sexes (Table S2).

Discussion

This is the first study to investigate sex differences in survival and the effect of immediate coronary angiography in successfully resuscitated cardiac arrest patients with initial shockable rhythm and absence of

Table 3 – In-hospital treatment and interventions.

	Men (N = 413)	Women (N = 109)	P value
Intensive care support			
Noradrenaline (epinephrine) administration — no. of patients (%)	363 (87.9)	93 (85.3)	0.47
Dobutamine administration — no. of patients (%)	112 (27.1)	29 (26.6)	0.92
Dopamine administration — no. of patients (%)	21 (5.1)	7 (6.4)	0.58
Phosphodiesterase administration — no. of patients (%)	31 (7.5)	13 (11.9)	0.14
Median duration of catecholamine or inotropic support [IQR] — days	1 [0.5-2.0]	1 [0.5-1.5]	0.11
Targeted temperature management — no. (%) of patients	387 (93.7)	102 (93.6)	0.96
Median time to targeted temperature management [IQR] — hours	5 [2−8]	4 [2−6]	0.05
Markers of shock			
Lowest MAP on day 1	61.4 ± 11.8	60.5 ± 13.6	0.48
Lowest MAP on day 2	61.9 ± 11.0	62.6 ± 13.7	0.68
Lowest MAP on day 3	67.6 ± 15.0	67.7 ± 15.9	0.97
Median maximal lactic acid [IQR]	4.7 [2.7-8.3]	4.8 [2.9-8.9]	0.62
Assist device used — no. of patients (%)	14 (3.4)	1 (0.9)	0.33
Median duration mechanical ventilation [IQR] — days	2[1−4]	2[1−3]	0.09
Need for renal replacement therapy — no. of patients (%)	18 (4.4)	1 (0.9)	0.15
Laboratory values			
Median peak value Troponin T [IQR] — μg/liter	0.677 [0.267-2.052]	0.462 [0.171-1.303]	0.009
Median peak value Creatinine Kinase [IQR] — U/liter	913 [390-2329]	658 [314-1327]	0.005
Median peak value Creatinine Kinase MB [IQR] — μg/liter	36.9 [16.3-95.1]	27.4 [12.5-58.0]	0.04
Complications			
Major bleeding — no. of patients (%)	15 (3.6)	5 (4.6)	0.58
Recurrence of VT needing defibrillation — no. of patients (%)	32 (7.7)	4 (3.7)	0.14
Medical treatment and interventions			
Salicylates — no. of patients (%)	345 (83.5)	81 (74.3)	0.03
P2Y12-inhibitor — no. of patients (%)	274 (66.3)	62 (56.9)	0.07
Unfractionated heparin/ LMWH — no. of patients (%)	373 (90.3)	94 (86.2)	0.22
Glycoprotein IIb/ IIIa inhibitor — no. of patients (%)	20 (4.8)	4 (3.7)	0.60
Statins — no. of patients (%)	284 (68.8)	61 (56.0)	0.01
Beta blocker — no./total no. of patients (%)	295/412 (71.6)	66/108 (61.1)	0.04
ACE-inhibitor/ ARB — no./total no. of patients (%)	261/412 (63.3)	61/108 (56.6)	0.19
ICD implantation — no. of patients (%)	164 (39.7)	45 (41.3)	0.77
Median GCS score at 72 hr [IQR]	13 [6−15]	14 [5−15]	0.41
Median duration at Intensive Care Unit [IQR] — days	4 [2−6]	3 [2−6]	0.02

*Plus-minus values represents means and standard deviations±. MAP denotes mean arterial pressure, VT ventricular tachycardia, LMWH low molecular weight heparin, ACE angiotensin converting enzyme, ARB angiotensin II receptor blocker, ICD implantable cardioverter-defibrillator, GCS Glasgow Coma Scale.

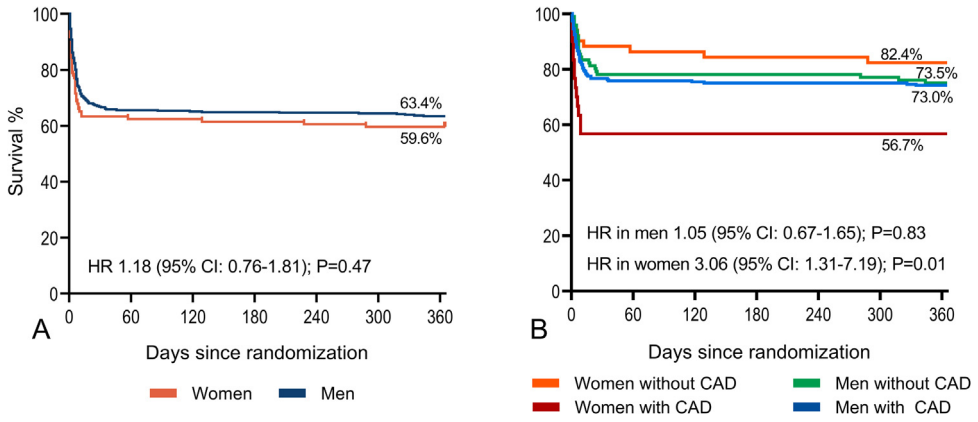

Fig. 2 – Kaplan Meier estimates of survival for men and women. Kaplan-Meier estimates on one-year survival between men and women. A: overall survival between men and women. B: survival in men and women with and without coronary artery disease (CAD).

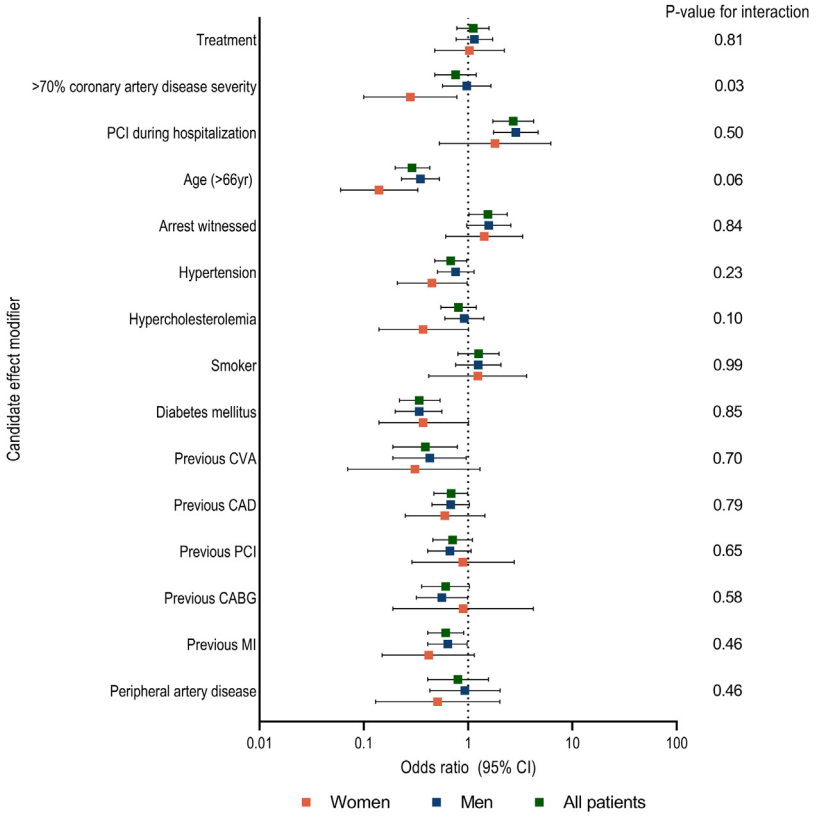

Fig. 3 – Assessment of effect modification of associations between treatment and risk factors and one-year survival by sex. Fig. 3 shows the assessment of associations between treatment and risk factors on one-year survival by sex. Coronary angiography treatment strategy denotes immediate invasive coronary angiography (i.e. 2 hours after randomization) or delayed coronary angiography (i.e. after neurological recovery).

STEMI. In this post-hoc study from the COACT trial, we found no difference in overall one-year survival between men and women. Although women had less significant CAD, they had significantly worse survival when CAD was present. Nevertheless, both men and women did not benefit from a strategy of immediate coronary angiography compared to a delayed strategy with respect to one-year survival.

Although patients did not differ in ECG findings indicating myocardial ischaemia, men had almost twice as frequent significant coronary artery lesions as compared to women. Several studies have demonstrated differences in angiographic outcomes between men and women in OHCA.[14,18] As men have a significantly higher prevalence of obstructive CAD, one would expect that in men, ischemic heart disease is more frequently the cause of the arrest, and

that early coronary angiography with PCI, if indicated, might benefit men more than women. However, we did not see this in our study. There are several possible explanations for this finding. As described in the COACT trial, the vast majority of men and women with obstructive CAD had stable coronary artery lesions.[3] Acute unstable coronary artery lesions were reported in approximately 15% of the patients, whereas acute thrombotic occlusions were reported in only 5%, without any differences between men and women.[3] PCI is associated with improved survival in patients with acute thrombotic occlusions[5,8], but not in patients with stable CAD, which may explain our results.[3,24] Also, in both men and women who did not survive hospitalization, neurologic complications subsequent to the arrest were the main cause of death, in line with previous studies.[25] Other causes of death, such as arrhythmias or cardiogenic shock, were responsible for approximately 15% of deaths during hospitalization and did not differ between the sexes.

In women with CAD, survival was substantially lower compared to men. In a post-hoc analysis, we were not able to identify differences in baseline, such as age, that clarified the lower survival rate in women. Since coronary angiography in the delayed strategy was postponed until after neurological recovery, one could argue that this could have affected our results. We therefore performed the same survival analysis in patients that underwent immediate coronary angiography (i.e. initiated within two hours after randomization). This showed similar survival outcomes in men and women with CAD. Therefore, selection bias for patients that survived until angiography does not seem to affect our results. Despite the lower survival rates in women with CAD, immediate coronary angiography did not improve survival compared to a delayed coronary angiography strategy. Further studies are needed to investigate the comparable outcome in survival with and without obstructive CAD in both sexes.

Several observational studies have described that women are less likely to undergo coronary angiography than men, especially when ST-segment elevation is absent.[26,27,28] The reduced utilization of coronary angiography in women has been suggested to arise from under-treatment or under-recognition.[12,29] In fact, a cardiac origin of the arrest is reported less often suspected in women.[14,15,16] In the COACT trial, all patients were randomized either to immediate or delayed coronary angiography strategy.[3] Interestingly, we also found that coronary angiography was significantly more often performed in men than in women in the delayed arm. The main reason for not undergoing coronary angiography was that the patient died before the procedure could take place. This was the case in 19% of women, and 13% of men but did not reach statistical significance. In patients who survived until hospital discharge but did not undergo coronary angiography, the most common reasons for not performing angiography were poor neurologic condition, co-morbidities making coronary angiography less of a priority and utilization of other imaging strategies. These reasons did not differ between men and women and concerned almost all patients enrolled in the delayed arm. Consequently, we were not able to determine which factors led to the lower use of coronary angiography in women.

Nearly 80% of the patients were men. Previous studies on out-of-hospital cardiac arrest patients found similar proportions between men and women[12,14,15] and appear to represent the population that survives until hospital admission. We observed a few significant differences in patient characteristics at baseline. In contrast to previous studies[14,15], we found no difference in the rate of witnessed arrest in men and women, neither in time from arrest to basic life support or time from arrest to return of spontaneous circulation. In addition, women in our study were significantly younger and had a lower prevalence of traditional cardiovascular risk factors compared to their male counterparts. Previously, an increase has been reported of young women who are not resuscitated who present with acute myocardial infarction.[30] As a result of a significantly lower burden of significant CAD, the pathogenesis of OHCA in the absence of ST-segment elevation is less clear in women. Since ECG findings indicating myocardial ischaemia were comparable in both sexes, ischaemia in women might be the result of coronary vasomotor dysfunction [epicardial vasospasm and/or microvascular dysfunction]. Few studies have investigated sex differences in the aetiology of cardiac arrest.[13,31] A large autopsy study including all sudden cardiac deaths without an obvious non-cardiac cause, found that women are more likely to have a non-atherosclerotic cause of cardiac death, such as primary myocardial fibrosis and myocarditis.[13,31] In addition, MINOCA (myocardial infarction with non-obstructive CAD) and spontaneous coronary artery dissection (SCAD) are two entities that are increasingly recognized among younger, non-resuscitated women presenting with acute myocardial infarction, and both are associated with sudden cardiac death.[32,33] In our study, we were not able to determine the exact aetiology of the arrest in women without significant CAD. Although the role of MINOCA and SCAD in cardiac arrest is currently unclear, additional diagnostic testing is worth considering in all patients with non-significant CAD after excluding other (non)cardiac causes. Further studies regarding the pathogenesis of cardiac arrest in patients without significant artery disease are required.

Limitations

This was a post-hoc study from the COACT trial and was not randomized or stratified for sex. Sex-specific risk factors such as pre-eclampsia, gestational diabetes, pre-term delivery or early menopause were not included in this study so we were unable to conclude whether this could have affected the results. Angiographic data was not available in patients that died before the procedure could take place and therefore, we do not know whether this was related to CAD severity. Data on the presence of SCAD on coronary angiography was not available. Lastly, the community response and efficiency of the system care in the Netherlands may not be the same around the world.

Conclusion

In patients with OHCA and shockable rhythm in the absence of STEMI, we found no difference in overall one-year survival between men and women. Women less often had significant CAD, but when CAD was present, they had significantly worse survival compared to women without CAD. This was not the case for men. Nevertheless, both men and women did not benefit from a strategy of immediate coronary angiography strategy as compared to a delayed angiography with respect to one-year survival. Further studies are needed to investigate the comparable outcome in survival with and without obstructive CAD in both sexes.

Credit author statement

Author contributions are as follows: Primary author Eva M. Spoormans was involved in analysis and interpretation of the data, and drafting of the manuscript; Niels van Royen (senior author) and Jorrit S. Lemkes were involved in the study design of the COACT

mainpaper, and were involved in the conception, interpretation of the data, drafting of the manuscript and provided critical revisions of this substudy; Gladys N. Janssens, Nina W. van der Hoeven, Lucia S.D. Jewbali, Eric A. Dubois, Peter M. van de Ven, Martijn Meuwissen, Tom A. Rijpstra, Hans A. Bosker, Michiel J. Blans, Gabe B. Bleeker, Remon Baak, Georgios J. Vlachojannis, Bob J.W. Eikemans, Pim van der Harst, Iwan C.C. van der Horst, Michiel Voskuil, Joris J. van der Heijden, Albertus Beishuizen, Martin Stoel, Cyril Camaro, Hans van der Hoeven, José P. Henriques, Alexander P.J.Vlaar, Maarten A. Vink, Bas van den Bogaard, Ton A.C.M. Heestermans, Wouter de Ruijter, Thijs S.R. Delnoij, Harry J.G.M. Crijns, Gillian A.J. Jessurun, Pranobe V. Oemrawsingh, Marcel T.M. Gosselink, Koos Plomp, Michael Magro, Paul W.G. Elbers, Yolande Appelman, Niels van Royen provided critical revisions.

Funding

Supported by unrestricted research grants from the Netherlands Heart Institute, Biotronik, and AstraZeneca.

Disclosures

Dr. Vlachojannis reports receiving grant support from MicroPort Orthopedics and Daiichi Sankyo; and Dr. van Royen, receiving grant support from Philips, Biotronik, and Abbott and honoraria from Medtronic. No other potential conflict of interest relevant to this article was reported.

Acknowledgements

None.

Appendix A. Supplementary data

Supplementary material related to this article can be found, in the online version, at doi:https://doi.org/10.1016/j.resuscitation.2020.10.026.

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