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# The influence of age and gender on delay to treatment and its association with survival after out of hospital cardiac arrest

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## 1. Introduction

The total number of cardiac arrest cases have been reported to be 350,000 cases/year in the US[1], and 275,000 cases/year in Europe[2]. In Sweden, with about 10 million inhabitants, about 6000 out of hospital cardiac arrests (OHCA) with attempted resuscitation are reported to the Swedish Registry of Cardiopulmonary Resuscitation (SRCR) annually, with a 10% survival rate at 30 days[3]. Factors involved in improving survival after OHCA include earlier recognition and shorter response times, improved cardiopulmonary resuscitation (CPR) techniques and post-resuscitation care [4–10].

Age and gender have been implicated as factors affecting survival. Most previous reports have shown that advanced age is associated with a poorer survival after OHCA [11–15]. Women suffering from OHCA are usually older and present less frequently with a shockable rhythm (ventricular fibrillation [VF] or ventricular tachycardia [VT])[16,17].

The delay time from collapse until start of various interventions is critical. The influence of age and gender on the delay to treatment, and on the association between delay to treatment and outcome after OHCA is not well addressed in the literature.

### 1.1. Aims

In this study, we aimed to address the following questions:

- 1- Does age or gender influence the delay to treatment among patients who suffer from OHCA? Our focus was on the delay from collapse to call for the EMS; delay from collapse to start of CPR, and delay from collapse to defibrillation.
- 2- Does either age or gender interact with the association between delay to treatment and 30 -day survival after OHCA?

## 2. Methods

This is a retrospective study from The Swedish Registry of Cardiopulmonary Resuscitation. Within the time period 2011–2019, we included

21,799 OHCA patients aged >18 years where CPR had been attempted, and which were witnessed by a bystander. Patients were divided into two age groups, and higher age was defined as being older than 70 years. Delay times were divided into four increasing time intervals (0–2 min, 3–7 min, 8–12 min, and longer than 12 min, except for delay time to start of defibrillation, which were divided into time intervals 0–4, 5–14, 15–24 and > 24 min). These time intervals were chosen based on consensus opinions, and not on prior intervals that may have appeared in the literature. Patients with OHCA in whom CPR was not initiated, neither before nor after the arrival of the EMS, were excluded. Patients in whom the collapse was witnessed by EMS were excluded. Furthermore, cases which were witnessed but unknown by whom, and cases which were not witnessed at all, as well as cases with unknown 30-day survival status, were excluded. There were no exclusions made based on the etiology of OHCA. Thus, all cases with OHCA in whom CPR was started, and in whom the collapse was witnessed by a bystander, were included in the analyses.

## 3. The Swedish Registry of Cardiopulmonary Resuscitation

The Registry was initiated in 1990 as a national quality registry. Since 2011, all EMS systems in Sweden report OHCA, where resuscitation was attempted, to the Registry. The reporting of a treated OHCA is performed using a form of two parts. The EMS crew fills out the first part. The second part requires in-hospital medical records to address the questions and is completed by a local CPR coordinator (mostly an experienced nurse).

In the first part are the following reported: Age, sex, place of OHCA, assumed etiology, time of collapse, call for EMS, start of CPR, defibrillation and arrival of EMS, use of drugs (adrenaline and amiodarone) number of defibrillations, and the use of mechanical chest compression.

The second part includes the following information: Treatment with Percutaneous Coronary Intervention (PCI), Coronary Artery Bypass Grafting (CABG) Therapeutic Hypothermia (TH), discharged alive from hospital, Cerebral Performance Categories (CPC) score at hospital discharge among survivors at 30 days.

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### 3.1. Definitions of variables

The five key variables that were examined were:

- 1- Time of collapse: Estimated by the witness and recorded by the EMS clinician.
- 2- Time to call for EMS: Automatically recorded at the dispatch center.
- 3- Time to start of CPR: Estimated by the witness, the first responder, or by the EMS clinician, depending on who started CPR.
- 4- Time to defibrillation: Estimated by the person who performed the first defibrillation (first responder or EMS clinician).
- 5- Survival to 30 days: Confirmed by the Swedish Population Registry, to which all deaths are reported within one month after the date of death.

### 3.2. Statistical analysis

For patients with multiple OHCA during the study period, only the first was included in the study. Difference in delay times between patients younger and older than 70 years of age, and between men and women were tested using Mann-Whitney *U* test. The associations between delay times and survival in the age and gender groups were estimated using logistic regression, both with delay times divided into ordered interval groups (1–4) and with actual delay time in minutes. Interactions between gender and delay times and between age groups and delay times were tested by calculating the difference in  $-2 \log$  likelihood of a logistic regression model without the interaction term of interest and the model with the interaction term included. All tests are two-sided and *p*-values below 0.05 were regarded statistically significant. All analysis was performed using SAS 9.4 for Windows.

## 4. Results

In total, there were 46,060 individuals reported to the registry during the time of the survey, out of which 34% were not witnessed. Information on witnessed status was missing in 2.6%. Among the remaining 29,095 cases, 21.4% were crew-witnessed, and in 1.4% there was missing information on whether the case was crew- or bystander-witnessed. Thus, 22,445 cases were identified as bystander-witnessed. Among these cases 1.2% were below the age of 18, and information on 30-day survival was missing in 1.7%. These cases were therefore excluded from the analysis. Out of the remaining 21,799 (97.1% of all bystander-witnessed cases), 15,163 had information on delay to call for EMS and 18,559 had information on delay to CPR.

### 4.1. The association between age and gender and treatment times (Table 1)

Although we noted a statistically significant difference in the delay to calling the EMS in relation to age, with the delay being longer among the elderly, the clinical relevance of this difference could be questioned (the median delay was 2 min for both age groups and the absolute standardized difference was 0.11). However, we also noted a significantly longer time to start of CPR in patients over 70 years of age, compared to those under 70 years, with a more pronounced

difference (median 4 min vs 2 min,  $p < 0.0001$ , standardized difference 0.17). The median delay from collapse to first defibrillation was 13 min for both age groups ( $p = 0.04$ ).

There was also a significantly longer delay to start CPR in female patients ( $p = 0.0002$ ), with a standardized difference of 0.06.

### 4.2. The influence of age and gender on the association between the treatment times and 30-day survival

#### 1. The influence of age and gender on the association between the time to call for the EMS and survival (Table 2):

Survival decreased significantly with increased delay to call for the EMS in all age and gender groups. For each additional 5-min delay, the odds for survival dropped by 41%. There was no statistically significant interaction between neither age nor gender and delay from collapse to call for EMS regarding 30-day survival.

#### 2. The influence of age and gender on the association between the time to CPR and survival (Table 3):

Survival decreased significantly with increased delay to start of CPR in all subgroups. There was no significant interaction between age and delay to CPR regarding survival. However, there was a significant interaction between gender and the delay from collapse to start of CPR regarding survival, such that the decline in survival with increasing delay was steeper in men than in women. For each 5 min delay the odds for survival declined by 48% for men, as compared with 37% for women.

#### 3. The influence of age and gender on the association between the time to first defibrillation and survival (Table 4):

Survival decreased significantly with increased delay to defibrillation in all subgroups. There was no statistically significant interaction between neither age nor gender and the delay to defibrillation regarding survival.

## 5. Discussion

In this study, we examined whether age or gender has an association with the delay time to delivery of treatment among patients who suffer from OHCA. Although we found a statistically significant longer delay to call the EMS in patients over 70 years of age, the difference in medians was close to being negligible (2 min for both age groups). This can be viewed as positive news, since the interval between time of OHCA and call for EMS has been shown to be an independent predictor of survival [18]. However, we also noted a significantly longer delay to start CPR in patients >70 years of age, which is in line with previous reports [4,6,10]. The mechanisms behind the above findings can only be speculated upon. It is likely that older patients more frequently suffer from OHCA at home. Here, the activation of the chain of care may be slower due to a number of reasons. Fewer persons may be on the scene, and those who are on scene (the witnesses) may act slower simply due to their older age and their increased comorbidity.

**Table 1**

Delay times in relation to age and gender (median [10<sup>th</sup>–90<sup>th</sup> percentile]).

	All ( <i>n</i> = 21,799)	Age ≤ 70 ( <i>n</i> = 9326)	Age > 70 ( <i>n</i> = 12,473)	<i>p</i>	Stdzd diff.	Men ( <i>n</i> = 14,755)	Women ( <i>n</i> = 7024)	<i>p</i>	Stdzd diff.
CA to call for EMS (6636)*	2 (0–9)	2 (0–8)	2 (0–10)	<0.0001	0.11	2 (0–9)	2 (0–9)	0.81	0.00
CA to start of CPR (3240)*	3 (0–15)	2 (0–15)	4 (0–15)	<0.0001	0.17	3 (0–15)	3 (0–15)	0.0002**	0.06
CA to 1st defibrillation# (723)*	13 (6–24)	13 (6–23)	13 (6–24)	0.04	0.06	13 (6–24)	13 (6–24)	0.68	0.02

CA = Cardiac arrest, Stdzd diff. = (absolute) standardized difference.

\* Number of missing; \*\* Longer for men; # Defibrillated VF/VT patients (*n* = 5764).

**Table 2**

30-Day survival in relation to delay from OHCA to call for EMS.

		DELAY IN MINUTES				OR (95% C.I.)	p
		0–2	3–7	8–12	>12		
All patients		n = 8492 1447–17.0%	n = 4713 559–11.9%	n = 1252 93–7.4%	n = 706 31–4.4%	0.63 (0.59,0.68) [1] 0.59 (0.55,0.64) [2]	<0.0001 <0.0001
Age ≤ 70 years		n = 3868 983–25.4%	n = 1963 382–19.5%	n = 484 63–13.0%	n = 251 20–8.0%	0.67 (0.61,0.73) [1] 0.64 (0.58,0.70) [2]	<0.0001 <0.0001
Age > 70 years		n = 4624 464–10.0%	n = 2750 177–6.4%	n = 768 30–3.9%	n = 455 11–2.4%	0.61 (0.54,0.68) [1] 0.57 (0.49,0.65) [2]	<0.0001 <0.0001
p = 0.20 for interaction between age group and ordered delay group regarding 30-day survival.							
p = 0.19 for interaction between age group and actual delay [2] regarding 30-day survival.							
Men	n = 5907	n = 3311	n = 848	n = 464	0.63 (0.58,0.68) <sup>1</sup>		<0.0001
	1139–19.3%	448–13.5%	71–8.4%	24–5.2%	0.59 (0.54,0.64) <sup>2</sup>		<0.0001
Women	n = 2585	n = 1402	n = 404	n = 242	0.63 (0.55,0.73) <sup>1</sup>		<0.0001
	308–11.9%	111–7.9%	22–5.4%	7–2.9%	0.61 (0.52,0.72) <sup>2</sup>		0.0001
p = 0.96 for interaction between gender and ordered delay group regarding 30-day survival.							
p = 0.64 for interaction between gender and actual delay <sup>2</sup> regarding 30-day survival.							

<sup>1</sup> Refers to ordered delay groups.<sup>2</sup> Refers to per 5 min of actual delay value.

Regarding time to defibrillation, there was no difference between men and women. In contrast, there was a statistically significant longer delay to defibrillation in older patients ( $p = 0.04$ ). The clinical implication of this is questionable, and the observation that the difference was not even more pronounced, can most likely be attributed to the fact that defibrillation is mainly performed by healthcare professionals who are trained to perform rapid defibrillation regardless of age and gender.

Previous reports have shown that women with various manifestations of cardiovascular disease are not treated as effectively as men [19–21]. Women have also been reported to less often undergo bystander CPR than men [22]. In our report, the time to CPR in women was longer ( $p = 0.0002$ ). However, with a standardized difference of only 0.06, rendering the practical implications questionable.

We have also examined if age and gender interact with treatment times in regards to survival. Neither gender nor age interacted significantly with the delay from collapse until call for EMS and until defibrillation, respectively. The lack of interaction with age was surprising. One may assume that an aging heart is more vulnerable to a prolonged lack of coronary perfusion.

Our hypothesis was that the association between delay to start of CPR and to defibrillation and 30-day survival should be stronger, with a more rapid decline in survival, with increasing delay among elderly patients than among younger patients. Such a hypothesis is based on the reasonable assumption that with increasing age and comorbidity

(especially cardiovascular), the delay to treatment of for instance, ventricular fibrillation, would have a bigger effect in an older and likely more disease-burdened heart, than in a younger, and likely healthier heart. However, such an interaction with age could not be confirmed.

In contrast, we did find a significant interaction between gender and the delay to CPR regarding survival. This finding indicates that a longer delay to start CPR on men has a larger detrimental effect on survival compared to women. This could be due to the fact that men who suffer from OHCA tend to already have higher rates of cardiovascular disease [16,17,23], which would then increase the risk that a longer delay to CPR may have a greater net effect on survival. It is also worth noting that a contributing factor to this finding may have been a different etiology behind the cardiac arrest when women are compared with men [16,24]. Indeed, the actual survival rate at all intervals in our cohort is higher for males, which could be explained by the observation that women with OHCA are generally older than men, are less likely to have underlying coronary artery disease, and by extension, cardiac etiology. In addition, women are found in ventricular fibrillation less frequently [16,17].

### 5.1. Clinical implications

- 1) There appears to be a particular potential for shortening the delay from collapse to the start of CPR among elderly victims of OHCA.

**Table 3**

30-Day survival in relation to delay from OHCA to start of CPR.

		DELAY IN MINUTES				OR (95% C.I.)	p
		0–2	3–7	6–12	>12		
All patients		n = 8528 1621–19.0%	n = 4424 533–12.0%	n = 2849 192–6.7%	n = 2758 85–3.1%	0.54 (0.51,0.57) [1] 0.55 (0.52,0.58) [2]	<0.0001 <0.0001
Age ≤ 70 years		n = 3987 1126–28.2%	n = 1923 357–18.6%	n = 1039 124–11.9%	n = 1006 51–5.1%	0.55 (0.52,0.59) [1] 0.56 (0.53,0.60) [2]	<0.0001 <0.0001
Age > 70 years		n = 4541 495–10.9%	n = 2501 176–7.0%	n = 1810 68–3.8%	n = 1752 34–1.9%	0.56 (0.52,0.61) [1] 0.57 (0.52,0.62) [2]	<0.0001 <0.0001
p = 0.71 for interaction between age group and ordered delay group regarding 30-day survival.							
p = 0.78 for interaction between age group and actual delay [2] regarding 30-day survival.							
Men	n = 5677	n = 3040	n = 1960	n = 1899	0.51 (0.48,0.54) <sup>1</sup>		<0.0001
	1270–22.4%	436–14.3%	140–7.1%	60–3.2%	0.52 (0.49,0.55) <sup>2</sup>		<0.0001
Women	n = 2851	n = 1384	n = 889	n = 859	0.61 (0.55,0.68) <sup>1</sup>		<0.0001
	351–12.3%	97–7.0%	52–5.8%	25–2.9%	0.63 (0.57,0.70) <sup>2</sup>		<0.0001
p = 0.003 for interaction between gender and ordered delay group regarding 30-day survival.							
p = 0.002 for interaction between gender and actual delay <sup>2</sup> regarding 30-day survival.							

<sup>1</sup> refers to ordered delay groups.<sup>2</sup> refers to per 5 min of actual delay value.

**Table 4**

30-Day survival in relation to delay from OHCA to first defibrillation (only patients in VT/VF).

	DELAY IN MINUTES				OR (95% C.I.)	p
	0–4	5–14	15–24	>24		
All patients	n = 266 133–50.0%	n = 2752 1032–37.5%	n = 1570 330–21.0%	n = 453 53–11.7%	0.48 (0.44,0.53) [1] 0.66 (0.62,0.69) [2]	<0.0001 <0.0001
Age ≤ 70 years	n = 151 86–57.0%	n = 1478 729–49.3%	n = 849 235–27.7%	n = 226 42–18.6%	0.48 (0.42,0.54) [1] 0.66 (0.62,0.70) [2]	<0.0001 <0.0001
Age > 70 years	n = 115 47–40.9%	n = 1274 303–23.8%	n = 721 95–13.2%	n = 227 11–4.8%	0.45 (0.38,0.53) [1] 0.63 (0.58,0.69) [2]	<0.0001 <0.0001
p = 0.60 for interaction between age group and ordered delay group regarding 30-day survival.						
p = 0.44 for interaction between age group and actual delay [2] regarding 30-day survival.						
Men	n = 211 106–50.2%	n = 2249 845–37.6%	n = 1277 263–20.6%	n = 366 40–10.9%	0.47 (0.42,0.52) <sup>1</sup> 0.65 (0.61,0.69) <sup>2</sup>	<0.0001 <0.0001
Women	n = 55 27–49.1%	n = 503 187–37.2%	n = 293 67–22.9%	n = 87 13–14.9%	0.54 (0.44,0.66) <sup>1</sup> 0.70 (0.62,0.78) <sup>2</sup>	<0.0001 <0.0001
p = 0.24 for interaction between gender and ordered delay group regarding 30-day survival.						
p = 0.24 for interaction between gender and actual delay <sup>2</sup> regarding 30-day survival.						

<sup>1</sup> Refers to ordered delay groups.<sup>2</sup> Refers to per 5 min of actual delay value.

- Even with a prolonged delay to start of treatment of OHCA among the elderly there might still be some chance of survival.
- Delay to start of CPR appears to be particularly disadvantageous in men. However, this finding needs to be further explored.

## 5.2. Strengths and limitations

As with all register studies, the amount of missing data could affect the final outcome of the analyses. The time of collapse, start of CPR, and first defibrillation, are based on estimations only. Isaacs et al. have reported that 75% of the bystander estimates of such delay times erred by 20% or more[25]. Thus, these estimations may have affected the results, but most likely only in a limited way, that would not go as far to cause a directional change in the overall results. The strength of this study lies in its large sample size and the long data collection timespan.

## 6. Conclusion

Unsurprisingly, increased delay from collapse to call for the EMS; start of CPR, and defibrillation significantly decreases the odds for 30-day survival in OHCA. Older age was associated with an increased delay to start of CPR after a bystander witnessed OHCA. With increasing delay from collapse until start of CPR, the odds of surviving an OHCA declined more rapidly in men than in women. The decline in survival with increasing delay to CPR and to defibrillation was similar in the elderly as compared with younger patients. Thus, the potential for a further reduction in delay to the start of CPR is particularly marked among the elderly. Furthermore, the delay to defibrillation is still too long and needs to be shortened to a similar extent regardless of age and sex.

## Ethics

This study is approved by The Regional Ethics Committee in Gothenburg, Sweden (DNR 233–18). Survivors of OHCA are informed about their inclusion in the registry and are given the possibility to withdraw.

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## CRedit authorship contribution statement

**Nooraldeen Al-Dury:** Conceptualization, Investigation, Funding acquisition, Writing - original draft. **Araz Rawshani:** Investigation, Funding acquisition, Writing - original draft. **Thomas Karlsson:** Methodology, Formal analysis, Writing - original draft. **Johan Herlitz:** Conceptualization, Data curation, Funding acquisition, Writing - original draft. **Annica Ravn-Fischer:** Supervision, Project administration, Writing - original draft.

## Declaration of Competing Interest

The authors have conflicts of interest to declare.

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