



Comorbidity and favorable neurologic outcome after out-of-hospital cardiac arrest in patients of 70 years and older[☆]



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ABSTRACT

Introduction: Advanced age is reported to be associated with lower survival after out-of-hospital cardiac arrest (OHCA). We aimed to establish survival rate and neurological outcome at hospital discharge after OHCA in older patients and evaluated whether pre-OHCA comorbidity was associated with favorable neurologic outcome.

Methods: From a prospective registry of all cardiopulmonary resuscitation (CPR) attempts after OHCA, we established survival in 1332 patients aged ≥ 70 years in whom resuscitation with non-traumatic etiology was attempted in 2009–2011. Pre-OHCA factors (age, gender, residing in long-term care institution, Charlson Comorbidity Index [CCI] score) and resuscitation parameters (initial rhythm, bystander witnessed, bystander CPR and time to defibrillator connection) with survival at hospital discharge with favorable neurologic outcome were regressed in the 851 patients of whom CCI was known.

Results: We found a 12% survival to discharge rate in patients aged ≥ 70 years (70–79 years: 16%; ≥ 80 years: 8%, $p = 0.001$). Among surviving patients, 90% survived with favorable neurologic outcome. In a model with only pre-OHCA factors age was significantly associated with outcome (age OR 0.94, 95%CI 0.91–0.98), $p = 0.003$). High CCI score (≥ 4) was not statistically significant when associated with survival (7% vs. 12%, OR 0.53, 95%CI (0.25–1.13), $p = 0.10$). When adjusted for resuscitation parameters, OR for high CCI was 0.71 (95% CI 0.28–1.80, $p = 0.47$), also none of the other pre-OHCA factors remained statistically significant.

Conclusion: In the Netherlands, the survival rate in older patients was 12%; the great majority survived with favorable neurologic outcome. Resuscitation-related factors and not comorbidity determine outcome after OHCA in older patients.

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1. Introduction

Advanced age is reported to be associated with reduced survival rates after out-of-hospital cardiac arrest (OHCA).^{1–3} There is a general belief that (neurologic) outcome after cardiopulmonary

resuscitation (CPR) for OHCA may be poor in older patients, especially patients with multiple comorbidities. Since perceived health status and physical well-being generally decrease with increasing age,^{4–6} the desirability of CPR after OHCA in older persons is often discussed, especially in the context of advance care planning. Advance care planning is a process in which patients are informed and empowered to express their wishes and goals for their current and future treatment.^{7,8}

Previous studies on survival and neurologic outcome of CPR attempts after OHCA show varying results, differing per country, region and study period.^{9–17} Also, most studies on outcome have been performed in the general population, of which older patients

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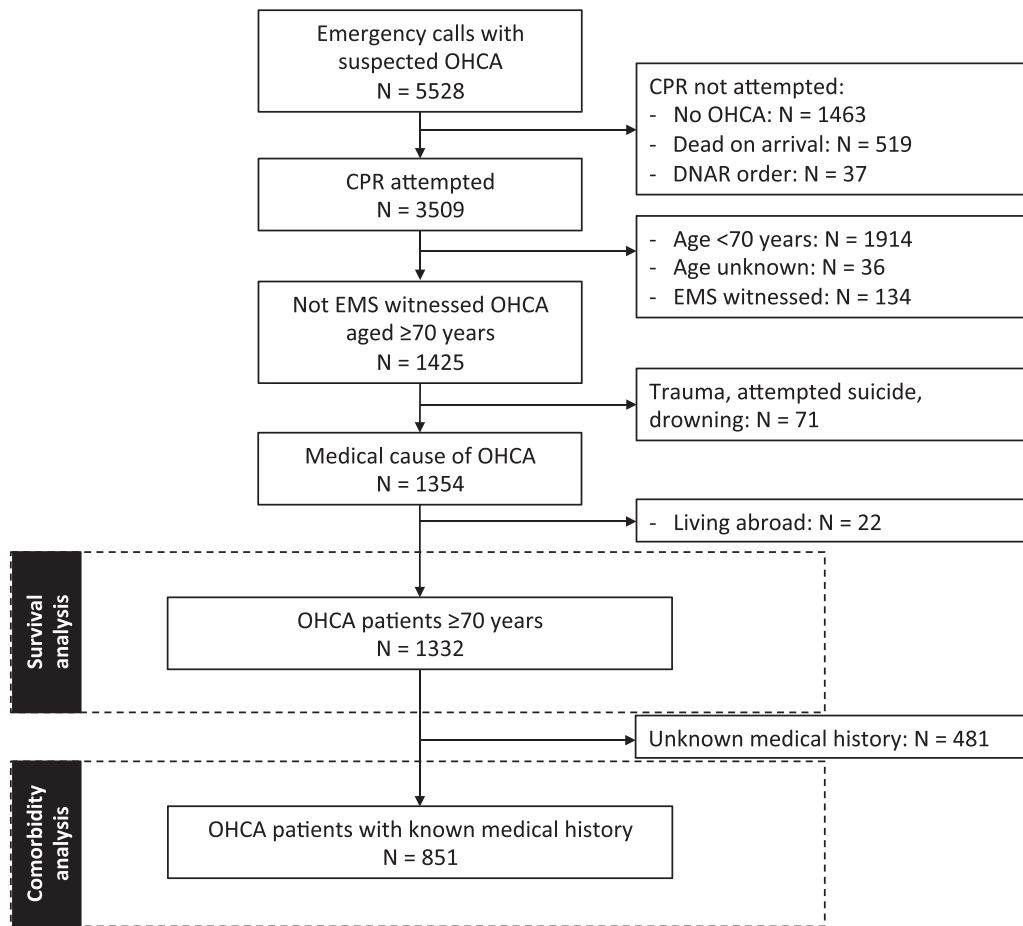


Fig. 1. Flowchart of patient inclusion. In 3509 cases, EMS personnel attempted to resuscitate, including 1332 patients aged ≥ 70 years (aged 70–79 years: $n = 699$, aged ≥ 80 years: $n = 633$) and living in the Netherlands. A complete medical history was obtained in 851 (64%) of these patients.

are a subset and rarely reported separately. A better knowledge of the impact of pre-OHCA comorbidities, (neurologic) outcome and long-term prognosis in the region concerned is important to assist older patients in informed decision-making concerning the desirability of a CPR attempt.

The aims of the present study are therefore (1) to establish the current survival rate and neurological status at hospital discharge and 1-year survival rate after an OHCA in older patients (≥ 70 years) in the Netherlands; and (2) to evaluate whether pre-OHCA comorbidity was associated with favorable neurologic outcome in these patients.

2. Methods

2.1. Setting

The Amsterdam Resuscitation Study (ARREST) is an ongoing, prospective registry of all-cause OHCA in the North-Holland province of the Netherlands. The registry cooperates with all emergency medical services (EMS) in the study region. The study region covers 2404 km² (urban and rural communities) and has a population of 2.4 million people. Details of the design of the data collection in the ARREST study are described elsewhere.¹⁸ All patients were treated according to the ERC Guidelines for resuscitation, including therapeutic hypothermia when indicated.¹⁹ The present investigation covered the study period January 1, 2009–December 31, 2011. The Medical Ethics Review Board of the Academic Medical Center, Amsterdam approved the study and considered the study exempt

for informed consent prior to study inclusion. Written informed consent was requested from all surviving patients.

2.2. Study design and data collection

We performed a prospective community-based cohort study with retrospective collection of comorbidity information. All non-traumatic OHCA patients of ≥ 70 years in whom CPR was attempted by EMS personnel were included in the survival analysis. We excluded aborted resuscitation efforts in individuals with a do-not-attempt resuscitation (DNAR) order, patients with signs of prolonged death, patients who live outside the Netherlands, and EMS witnessed cases. All EMS and hospital case files were reviewed to verify the presence of a non-traumatic etiology of the arrest and determine survival status. When analyzing comorbidity and outcome, only those patients whose medical history could be retrieved were included (Fig. 1).

Survival was assessed at three time points: survival to transfer of EMS care at the emergency room (hereafter called “survival to ER”), survival to hospital admission and survival to hospital discharge. Furthermore, survival at one year after OHCA or date of death was assessed through the civic registry. To categorize neurological functioning at discharge, the Cerebral Performance Category (CPC) scale was used. Category 1 represents good cerebral performance; category 2, conscious patients with moderate cerebral disability; category 3, conscious patients with severe cerebral disability; category 4, coma or vegetative state; and category 5, (brain) death. CPC class was decided after review of hospital records at

Table 1

Baseline characteristics of patients with a known medical history and patients with a missing medical history.

	All N = 1332	Complete medical history N = 851	Missing medical history N = 481	P-value	Missing N (%)
Patient-related factors					
Age, mean (SD)	79(6)	79(6)	79(6)	0.41	0(0)
Gender, n (%)				0.09	0(0)
Male	864(65)	566(67)	298(62)		
Female	468(35)	285(33)	183(38)		
Resuscitation parameters					
Initial rhythm, n (%)				<0.001	16(1.2)
Shockable	479(36)	343(41)	136(29)		
Not shockable	837(64)	501(59)	336(71)		
Witnessed arrest, n (%)				0.19	28(2.1)
Witnessed	957(73)	601(72)	356(76)		
Not witnessed	347(27)	232(28)	115(24)		
Bystander CPR, n (%)				0.42	28(2.1)
Bystander CPR	891(68)	564(68)	327(70)		
No bystander CPR	413(32)	271(32)	142(30)		
AED use, n (%)				0.71	0(0)
AED connected	534(40)	338(40)	196(41)		
No AED connected	798(60)	513(60)	285(59)		
Time to defibrillator connection, (minutes), median (25th–75th percentile)	9.1 (6.8–11.9)	9.1 (6.8–12.1)	8.9 (6.7–11.6)	0.23	96(7)

AED = Automated external defibrillator, CPR = Cardiopulmonary resuscitation. Percentages shown are column percentages.

discharge. Patients with a CPC of 1 or 2 at discharge were considered as survivors with a favorable neurologic outcome.²⁰

Patient-related factors were age, gender, pre-OHCA morbidity and place of residence (home or long-term care facility). Information about the patients' pre-OHCA morbidity was obtained from the patient's general practitioner (GP), who, in the Netherlands, has a complete overview of all diagnoses made by medical specialists of the patients under his care. This information was used to calculate the Charlson Comorbidity Index (CCI).²¹ The CCI takes into account the presence of diseases weighted on the basis of their association with mortality.

Resuscitation parameters that were taken into account were initial recorded rhythm, categorized as being shockable (ventricular fibrillation or pulseless ventricular tachycardia) or non-shockable (asystole or pulseless electric activity), bystander witnessed arrest, bystander CPR performed and time to defibrillator connection. Continuous ECGs from automated external defibrillators (AED) or ambulance manual defibrillators were analyzed to determine the first recorded rhythm. Time to defibrillator connection was defined as the time interval between start of EMS-call and connection of AED or ambulance manual defibrillator, whichever was connected first.

2.3. Statistical analysis

We evaluated differences in patient-related factors and resuscitation parameters between survivors and non-survivors in the group with a known medical history, using chi-square statistics, student *t*-test or Mann–Whitney *U* test where appropriate. The Mantel–Haenszel chi-square statistics was used for stratified data. We also regressed survival with favorable neurologic outcome, employing two multivariable logistic regression models: (1) including the CCI score (binary, <4 or ≥4) and all other patient-related factors that were univariable significantly associated with outcome, and (2) including the CCI score (binary) and all other patient-related factors and resuscitation parameters that were univariable significantly associated with outcome. Of both models, we plotted the Receiver–Operator Characteristic (ROC)-curve and calculated the area under the curve (AUC), to evaluate to what extent these models could account for outcome.

Continuous variables were described as means and standard deviations (SD), or medians and 25th–75th percentile where appropriate, and categorical variables as percentages. *P*-values <0.05 were considered statistically significant. All data were analyzed using the statistical software package of SPSS (SPSS for Mac, version 20, IBM SPSS Inc.).

3. Results

3.1. Study population

During the 36-month study period, 5528 EMS-calls with suspected OHCA were identified. In 3509 cases, EMS personnel attempted to resuscitate, including 1332 patients aged ≥70 years (70–79 years: *n* = 699, ≥80 years: *n* = 633). A complete medical history was retrievable in 851 (64%) of these patients (70–79 years: *n* = 453, ≥80 years: *n* = 398) (Fig. 1). Apart from a difference in the presence of shockable initial rhythm (*p* < 0.001), there were no significant differences in baseline characteristics between the 851 patients with a known medical history and the 481 patients without (Table 1). Supplemental Table 1 shows the prevalence of the comorbidities that constitute the CCI in the patients with known medical history.

3.2. Survival

Of the 1332 patients ≥70 years, 156 patients (12%) survived to hospital discharge. Most non-survivors had an unsuccessful CPR attempt and died onsite or in the emergency room (*n* = 868, 65%), or during admission within 7 days after the OHCA (*n* = 242, 18%; Supplemental Fig. 1). The chance of survival to hospital discharge decreased with advancing age (70–79 years: 16%; ≥80 years: 8%, *p* = 0.001; Table 2). Survivors to hospital discharge had a favorable neurologic outcome (CPC 1–2) in the vast majority (overall: 90%, 70–79 years: 92%, ≥80 years: 88%; Table 2).

The 1-year survival rate was 10% in the whole study cohort, and 88% (137 out of 156) among the patients who were discharged alive; in the latter group, death within 1 year occurred in 9 of the 100 patients (9%) with a CPC score of 1, in 6 of the 41 patients (15%)

Table 2
Survival per stage and neurologic outcome at hospital discharge.

Survival per stage	All patients ≥70 years N = 1332	70–79 years N = 699	≥80 years N = 633
To ER, n (%)	736 (55)	410 (59)	326 (52)
Admission to hospital, n (%)	464 (35)	273 (39)	191 (30)
Survival to discharge, n (%)	156 (12)	108 (16)	48 (8)
CPC score of surviving patients to discharge, n (%)			
CPC 1	100 (64)	70 (65)	30 (63)
CPC 2	41 (26)	29 (27)	12 (25)
CPC 3	11 (7)	6 (5)	5 (10)
CPC 4	0 (0)	0 (0)	0 (0)
CPC unknown	4 (3)	3 (3)	1 (2)
1-year survival, n (%)	137 (10)	96 (14)	41 (6)

ER = Emergency room, CPC = Cerebral performance category. CPC 1: good cerebral performance, CPC 2: moderate cerebral disability, CPC 3: severe cerebral disability, CPC 4: coma or vegetative state.

Percentages shown are column percentages.

with a CPC score of 2, and in 4 of the 11 patients (36%) with a CPC score of 3.

3.3. Patient-related factors and resuscitation parameters

Table 3 shows the patient-related factors and resuscitation parameters of patients with known medical history who survived with a favorable neurologic outcome ($n=94$), and those who did not survive or survived without favorable neurologic outcome ($n=756$). Of the patient-related factors, both age and gender were significantly associated with outcome. When stratified according to age group, survival with favorable neurologic outcome was still higher in males, although no longer statistically significant (patients 70–79 years, male: 16%, female 12%; patients ≥80 years, male: 9%, female: 5%, Mantel–Haenszel $p=0.07$). Patients with a high CCI (≥4) had a lower survival rate than patients with a lower CCI (0–3), but this difference was not statistically significant (7%

vs. 12%, $p=0.10$). From the individual illnesses that constitute the CCI, most had no separate univariable association with survival with favorable neurologic outcome. Only patients with a previous acute myocardial infarction (AMI) had a higher rate of favorable neurologic outcome than those without (15% vs. 9%, $p=0.009$). A shockable initial rhythm was seen in 55% of the patients with a previous AMI and in 34% of the patients without ($p<0.001$). Furthermore, only dementia was statistically significant negatively associated with survival: none of the 45 patients with this diagnosis survived to discharge.

All resuscitation parameters were significantly associated with outcome (Table 3).

3.4. Multivariable analysis

Table 4 shows the univariable and multivariable odds ratios (OR) of both patient-related factors and resuscitation parameters for

Table 3
Patient-related factors and resuscitation parameters for patients with CPC 1–2 and patients with a CPC 3–5.

	Survival with favorable outcome ^a		P-value	Missing
	Yes N = 94	No N = 756		N (%)
Patient-related factors				
Age, mean (SD)	77 (5)	79 (6)	0.001	0 (0)
Gender, n (%)			0.03	0 (0)
Male	72 (13)	493 (87)		
Female	22 (8)	263 (92)		
Usual residency, n (%)			0.82	4 (0.5)
Long term care facility	4 (10)	36 (90)		
Home	90 (11)	716 (89)		
Charlson Comorbidity Index, n (%)			0.22	0 (0)
0–1 score	47 (12)	352 (88)		
2–3 score	39 (12)	292 (88)		
≥4 score	8 (7)	112 (93)		
Resuscitation parameters				
Initial rhythm, n (%)			<0.001	7 (0.8)
Shockable	84 (25)	258 (75)		
Not shockable	9 (2)	492 (98)		
Witnessed arrest, n (%)			<0.001	18 (2.1)
Witnessed	88 (15)	512 (85)		
Not witnessed	4 (2)	228 (98)		
Bystander CPR, n (%)			<0.001	16 (1.9)
Bystander CPR	79 (14)	485 (86)		
No bystander CPR	15 (6)	255 (94)		
AED use, n (%)			<0.001	0 (0)
AED connected	56 (17)	282 (83)		
No AED connected	38 (7)	474 (93)		
Time to defibrillator connection, (min), median (25th–75th percentile)	5.9 (3.9–9.1)	9.4 (7.2–12.3)	<0.001	61 (7)

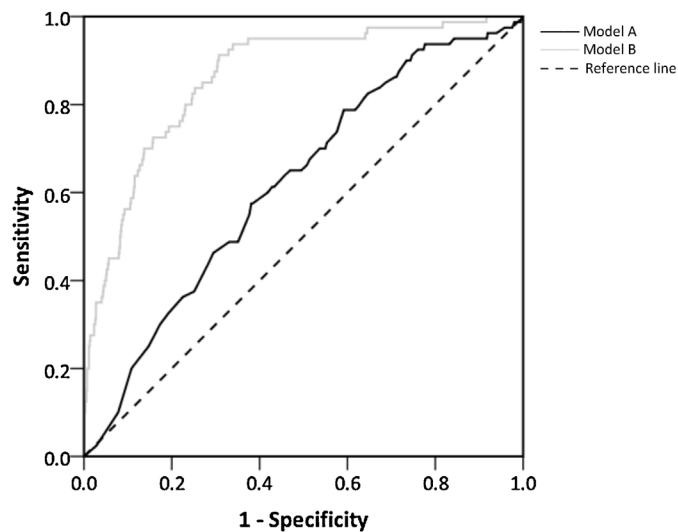
Percentages shown are row percentages. AED = Automated external defibrillator, CPR = Cardiopulmonary resuscitation. Survival with favorable outcome: CPC 1–2.

^a 1 unknown CPC score.

Table 4

Regression model with survival with favorable neurologic outcome.

	Crude OR		Adjusted OR ^a		Adjusted OR ^b	
	OR (95% CI)	P-value	OR (95% CI)	P-value	OR (95% CI)	P-value
Patient-related factors						
Charlson Comorbidity Index ≥ 4 score	0.54 (0.25–1.13)	0.10	0.53 (0.25–1.13)	0.10	0.71 (0.28–1.80)	0.47
Age per year	0.94 (0.90–0.97)	0.001	0.94 (0.91–0.98)	0.003	0.96 (0.92–1.01)	0.10
Male	1.75 (1.06–2.88)	0.03	1.60 (0.97–2.66)	0.07	0.93 (0.51–1.68)	0.80
Long-term care institution ^c	0.88 (0.31–2.54)	0.82	–	–	–	–
Resuscitation parameters						
Shockable initial rhythm	17.8 (8.81–36.0)	<0.001	–	–	10.0 (4.63–21.7)	<0.001
Witnessed arrest	9.80 (3.55–27.0)	<0.001	–	–	7.45 (2.26–24.5)	0.001
Bystander CPR	2.77 (1.56–4.91)	<0.001	–	–	1.26 (0.62–2.57)	0.53
Time to defibrillator connection per minute	0.81 (0.76–0.87)	<0.001	–	–	0.86 (0.80–0.93)	<0.001

CPR = Cardiopulmonary resuscitation, OR = Odds ratio. There was no interaction between age and gender ($p = 0.73$).^a Adjusted for the Charlson Comorbidity Index and all patient-related factors that were univariably associated with outcome.^b Adjusted for the Charlson Comorbidity Index, all patient-related factors and arrest variables that were univariably associated with outcome.^c Reference category is 'living at home'.**Fig. 2.** The ROC curve of (A) patient-related factors AUC: 0.621 ($p < 0.001$) and (B) patient-related factors and resuscitation parameters AUC: 0.863 ($p < 0.001$). Model A that only includes patient-related factors, explains a small part of outcome, while model B that also includes resuscitation factors explains a larger part of survival.

survival with favorable neurologic outcome. Of the patient-related factors only age remained significantly associated with outcome in a multivariable model, while CCI score was not ($p = 0.10$). When adding the resuscitation parameters to the model, none of the patient-related factors remained statistically significantly associated with outcome.

Fig. 2 further illustrates these observations, and shows the ROC of (A) a model including patient-related factors alone (AUC: 0.621 [$p < 0.001$]) and (B) a model including the patient-related factors and resuscitation parameters (AUC: 0.863 [$p < 0.001$]). Model A explains a small part of outcome, while model B explains a large part of survival.

4. Discussion

We found a 12% overall survival to discharge rate after OHCA in patients ≥ 70 years of age. Among survivors to hospital discharge, 90% had favorable neurologic outcome, while 88% were alive at one year. Of the patient-related factors only age was significantly associated with outcome in a multivariable model. We found no significant association of outcome with comorbidity as measured by the CCI score. When adjusted for resuscitation parameters, none of the studied patient-related factors had a statistically significant

relation with survival. It thus appears that resuscitation-related factors, rather than patient-related factors, are decisive determinants of outcome.

4.1. Survival

While the survival rate in this older cohort (aged ≥ 70 years) was lower than in the general population in the Netherlands (12% vs. 20%), favorable neurologic outcome occurred in a similarly high proportion among survivors in both groups (90% and 94%).¹⁷ These results are in concordance with a recent study among comatose patients admitted to intensive care units after OHCA.²² In that study, increasing age was associated with increased mortality, while patients who survived to hospital discharge had a favorable neurologic outcome in the great majority of cases. Furthermore, recent studies show a good perceived quality of life of older patients, comparable to a reference population.^{23,24} Notably, no surviving patients in our study cohort survived the OHCA in vegetative condition.

Importantly, survival rates vary widely per country and region,⁹ and have increased substantially in the north-western regions of Europe over the last 10–15 years, possibly due to increased lay-rescuer resuscitation after intense population training with chest compressions and ventilations²⁵ and wide-scale implementation of AEDs.¹⁷ Also the proportions of favorable neurologic outcome among survivors differ between countries, ranging from 31% in Korea¹⁴ to 69% in the Czech Republic¹³ and $\geq 85\%$ in Arizona, USA^{15,16}. In the Netherlands the proportion of favorable neurologic outcome have been consistently high since 1995.^{17,26} A possible explanation for the high proportion of favorable neurologic outcome observed in the current study is that in the Netherlands prognostication is indicated in patients with prolonged coma after resuscitation; in those with a very poor prognosis the treating physician can refrain from further treatment. Recent international recommendations²⁷ emphasize the need for protocol led prognostication after the first 72 h after return of organized rhythm after a cardiac arrest, including it as an important element of post-resuscitation care. Adherence to these recommendations prevents prolonged treatment of comatose patients without chance of good neurologic recovery.

These considerations are important in the context of advance care planning, for patients, their family members, GPs and treating physicians, and especially for individuals who consider issuing a DNAR order. Decisions regarding DNAR orders should be based on current information that reflects the present treatment practices and outcomes in the region of residence. Patients' informed choice should be leading when making end-of-life decisions.

4.2. Pre-OHCA comorbidity and resuscitation parameters

Consistent with existing literature^{17,25}, we found that resuscitation parameters (notably presence of shockable initial rhythm and time to connection of defibrillator device) were strong predictors of outcome. Adding resuscitation parameters to our multivariable model explained a much larger part of outcome than patient-related factors alone. Resuscitation parameters are, however, unknown in advance, and hence cannot be taken into account when discussing advance care planning.

In contrast to a previous study in patients with a shockable initial rhythm²⁸ we found no association between the pre-OHCA comorbidity and neurologic outcome. This contrasting outcome may be explained by a different study population (exclusion of patients with a not-shockable initial rhythm), and a different method of assessing patients' pre-OHCA comorbidity. The CCI score used in the present study takes into account the presence of diseases weighted on the basis of their association with mortality.²¹ Two recent studies^{29,30} that also used the CCI score showed similar associations in the general population: age, but not CCI, was associated with outcome. Although important, our study suggests that treatment decisions should be influenced by pre-OHCA comorbidity only as far as it causes a current poor quality of life and/or a short expected lifespan. Still, we found two comorbidity exceptions: previous AMI and dementia were both strongly associated with outcome, albeit in opposite directions. Patients with previous AMI had a higher chance of survival with favorable neurologic outcome than those without. This is in agreement with a recent study showing that a history of AMI independently predicted an increased survival rate in case of an OHCA.³¹ In our study, patients with a previous AMI had a significantly higher proportion of shockable initial rhythm, probably explaining the positive association with outcome. None of the 45 patients with dementia survived to discharge, although in this group survival to ER (57%) and admission to hospital (36%) is similar to patients without dementia. Though speculative, a possible explanation might be that in view of the mental condition of the patient family and resuscitation team might have considered advanced resuscitation efforts to be inappropriate.

4.3. Strengths and limitations

The strength of this study is that, we had not only information on resuscitation parameters and medical history data from the GP of patients who were transported to hospital, but also of those who died on scene, thereby avoiding selection bias. Accordingly, survival did not significantly differ between the 851 patients with a retrievable medical history and the 481 patients without.

A possible limitation of our study is the retrospective collection of data on patients' pre-OHCA comorbidities from their GP, though their records should be complete. A second limitation of our study is the possibility that CPR was not initiated in patients with the highest number of comorbidities, highest CCI score and perhaps the worst prognosis, because a DNAR order was in place. In that case, the survival rates reported in our study are higher than they otherwise would have been, while the proportion of survival with favorable neurologic outcome may be lower. Moreover, a negative influence of severe comorbidity could have remained undetected.

4.4. Conclusion

While overall survival rates after OHCA are lower in older patients, the vast majority of older patients who did survive had favorable neurologic outcome, comparable with younger patients. Resuscitation-related factors and not comorbidity are important determinants of outcome in older patients. In the Netherlands,

survivors can expect an acceptable quality of life when surviving OHCA.

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Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at <http://dx.doi.org/10.1016/j.resuscitation.2015.06.017>

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