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Clinical paper

Characteristics, survival and neurological outcome in out-of-hospital cardiac arrest: A nationwide study of 56,203 cases with emphasis on cardiovascular comorbidities

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Abstract

Background: We studied clinical characteristics, survival and neurological outcomes in patients with pre-existing cardiovascular (CV) conditions who experienced an out-of-hospital cardiac arrest (OHCA).

Methods: We studied all cases of OHCA in the Swedish Registry for Cardiopulmonary Resuscitation (2010–2020). Patients were grouped according to the following pre-existing CV conditions prior: hypertension (HT), heart failure (HF) with HT, HF with ischemic heart disease (IHD), HF without HT or IHD, IHD, myocardial infarction (MI) and diabetes mellitus (DM), with groups being mutually exclusive. We studied 30-day survival and neurological outcomes using logistic and Cox regression.

Results: A total of 56,203 patients were included. The lowest rates of shockable rhythm occurred in cases with HT (19%), HF and HT (18%) and DM (18%). Median time to OHCA from diagnosis of HT was 2.0 years in cases aged 0–40 years at diagnosis of HT, 4.4 years in those aged 41–60 at diagnosis, 5.0 years in those aged 61–70 years, 5.6 years in those aged 71–80 years and 6.0 years in those aged 81 years or older. The lowest survival was noted for patients with HF and HT. Age and sex adjusted OR for CPC score 1 did not differ in any group.

Conclusion: The combination of HT and HF has the lowest survival of all cardiovascular comorbidities. Early onset of hypertension is a predictor for early cardiac arrest.

Keywords: Cardiac arrest, Hypertension, Cardiovascular disease

Introduction

Arterial hypertension (HT) is the leading contributor to premature death worldwide, accounting for about 10 million deaths yearly.[1,2] Blood pressure exhibits a causal and continuous relationship with the incidence of cardiovascular (CV) events (haemorrhagic stroke, ischaemic stroke, myocardial infarction, sudden cardiac arrest and heart failure).[3] The positive relationship between blood pressure and the risk of cardiovascular events is ubiquitous across the age span in adults.[4] Long-term HT causes anatomical and functional alterations of the cardiovascular system such as atherosclerosis,[5] left ventricular hypertrophy (LVH), left ventricular diastolic dysfunction, neurohormonal changes, all of which may cause or contribute to sudden cardiac arrest (SCA).[6,7]

The extent to which arterial HT and other cardiovascular comorbidities is associated with clinical characteristics in out-of-hospital cardiac arrest (OHCA) remains sparsely studied. Adjustment for comorbidity is sometimes neglected in OHCA,[8] and previous studies have shown conflicting results.[9,10] For example, diabetes (with and without complications) has been shown to be associated with a lower chance of 30-day survival.[11] However, no single study has elucidated clinical features and outcomes across the broader spectrum of cardiovascular comorbidities.

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We studied clinical characteristics, short- and long-term survival, as well as neurological function among survivors in individuals with a history of HT, contrasting them to cases with a history of heart failure (with or without HT, ischemic heart disease (with or without HT), myocardial infarction (MI) or diabetes mellitus (DM).

Methods

Study population

We used the Swedish Registry for Cardiopulmonary Resuscitation (SRCR), a nationwide quality registry launched in 1990. This study was approved by Swedish Ethical Review Authority (2019–01094). The funders had no role in the study. All ambulance organizations in Sweden participate in the registry and the level of ascertainment has been >90% since 2010. The registry and its variables have been described previously.[12,13] Reporting is done by trained nurses and physicians and follows the Utstein style of reporting. We included all cases of OHCA (where resuscitation was attempted) during Jan 1st 2010 to Dec 31st 2020.

Data linkage

In order to obtain data on coexisting conditions, medications, socioeconomic status and causes of death, we merged the SRCR with databases held by the Swedish government. Data linkage is seamless since every Swedish citizens has a unique 12-digit personal identification number that is used in all these sources.

The Swedish Inpatient Registry and Outpatient Registry include the primary and all secondary discharge diagnoses in inpatient and outpatient care throughout Sweden. The Inpatient Registry includes hospitalizations since 1987 and has been validated. The Outpatient Registry contains all outpatient visits since 2002. Both registries employed the 10th revision of the International Classification of Disease (ICD) during the study period. Prescribed drugs are recorded in the Swedish Prescribed Drug Registry, which collects/contains comprehensive information on all drug prescriptions since 2005. We retrieved all prescriptions in ATC (Anatomical Therapeutic Chemical) classes A, B and C (with 3 characters detail) since 1st Jan 2008. Socioeconomic data was retrieved from the LISA database (longitudinal integrated database for health insurance and labor market studies).

Definition of cardiovascular conditions

Patients were classified from diagnosed cardiovascular conditions before OHCA. For all diagnoses, the first date of diagnosis (in primary or secondary position) was retrieved from the Inpatient Registry or the Outpatient Registry (whichever came first). HT was defined by ICD-code I10, heart failure (HF) by ICD-code I50, diabetes by ICD codes E10 and E11 (ignoring the subtype), ischemic heart disease by ICD-code I20, I21 and I25, acute coronary syndromes by ICD-code I20 and I21. The group with HT only included cases in whom a diagnosis of I10 existed before cardiac arrest, but none of the other ICD codes listed above. An individual could only belong to one group. The definition of ischemic heart disease and myocardial infarction required that the case did not have a diagnosis of heart failure before cardiac arrest. The group with DM had no other ICD codes beyond those defining DM. Atrial fibrillation and renal failure did not constitute an exclusion criteria in any group (hence these diagnoses occur in all groups). OHCA patients without these pre-existing cardiovascular conditions were categorized as all other.

Outcomes

The primary outcome measure was 30-day survival. The secondary outcome measure was neurological function measured by cerebral performance category (CPC) score. The CPC score was assessed at discharge and ranged from 1 to 5 (1, no sequelae; 2, mild sequelae; 3, severe sequelae; 4, vegetative state; 5, brain dead).

Statistical analysis

Baseline characteristics are described using means and medians along with standard deviations and interquartile ranges, respectively. The study population includes virtually the whole population with OHCA in Sweden during the study period, and formal hypothesis testing is therefore not performed.

For patients with previous HT, time from diagnosis of HT to cardiac arrest was evaluated using Kaplan-Meier estimators. For all cases, crude survival rates are presented as the proportion alive at 30-day. Short- and long-term survival were calculated using Cox adjusted survival curves; adjustment was made for age, sex and no-flow time. Long-term survival was defined as overall survival during the study period, i.e from date of OHCA to death or censoring (31st Dec 2020).

Logistic regression was used to model 30-day survival as a binary outcome, with sequential model adjustment; model 1 was adjusted for age and sex; model 2 was additionally adjusted for location and time to CPR, and model 3 was additionally adjusted for initial rhythm.

The association between the cardiovascular conditions and CPC score (among survivors) was also studied using logistic regression, with adjustments for age and sex.

Subgroup analyses with regards to age, sex, characteristics at the time of OHCA and coexisting conditions were also performed. We also used logistic regression to study predictors of 30-day survival in patients with and without previous HT. The association between the probability of presenting with a shockable rhythm and no-flow time was modeled using restricted cubic splines, using 3 knots, adjusting for age and sex. Throughout, time to CPR was defined as time to any CPR.

Results

Characteristics of the study population

A total of 56 203 patients were included, of whom 7925 (14%) had been previously diagnosed with only HT, 2188 with HF and HT, 1485 with HF and IHD, 1694 with HF without IHD and HT, 4959 with IHD, 952 with AMI, 1521 with diabetes and 35,479 classified as all other (Table 1). Overall, 58.8% had at least one of these cardiovascular conditions. The overall prevalence of any HT diagnosis was 45%. There were 43% women in the HT only group and 42% women among patients with HF and HT compared with 22%–37% women in all other groups (Table 1). Mean age among patients with only HT was 75 years and for patients with HF and HT 79 years. Heart disease was the presumed underlying cause in about 62% of patients with HT only, and 72% in patients with HF and HT.

Bystander CPR was performed in about 50–55% in all groups studied. The initial rhythm was VF/pVT in 19% of cases with HT and in 18% of cases with HF and HT. In comparison, the initial rhythm was VF/pVT in 23% of cases with HF without IHD and HT, 37% in cases with HF and IHD, 30% in cases with IHD, 28% in cases with myocardial infarction, 18% in cases with DM and 23% for all other. PEA was most common in those with HT only (20%), HF with

Table 1 – Baseline characteristics in 56,203 patients with out of hospital cardiac arrest in relation to cardiovascular conditions.

	Hypertension only	Heart failure with hypertension	Heart failure with IHD	Heart failure without IHD & HT	Ischemic heart disease (IHD)	Myoardial infarction (MI)	Diabetes	All other
n	7925	2188	1485	1694	4959	952	1521	35,479
Women	3425 (43.3)	911 (41.7)	330 (22.3)	601 (35.5)	1371 (27.7)	264 (27.8)	557 (36.7)	11,569 (32.7)
Age – mean (sd)	74.55 (12.04)	79.45 (11.22)	77.29 (11.40)	73.84 (15.35)	76.07 (11.53)	74.36 (10.39)	68.02 (14.50)	65.49 (19.08)
Cause of cardiac arrest								
Heart disease	4291 (61.6)	1394 (71.9)	1150 (84.2)	1087 (71.4)	3496 (78.5)	692 (82.4)	776 (58.0)	18,337 (58.5)
Overdose or intoxication	88 (1.3)	7 (0.4)	9 (0.7)	15 (1.0)	28 (0.6)	1 (0.1)	25 (1.9)	1308 (4.2)
Trauma or accident	129 (1.9)	20 (1.0)	12 (0.9)	16 (1.1)	60 (1.3)	10 (1.2)	25 (1.9)	870 (2.8)
Pulmonary disease	482 (6.9)	198 (10.2)	75 (5.5)	159 (10.4)	200 (4.5)	29 (3.5)	83 (6.2)	1574 (5.0)
Suffocation	213 (3.1)	34 (1.8)	20 (1.5)	30 (2.0)	82 (1.8)	7 (0.8)	58 (4.3)	849 (2.7)
Suicide	81 (1.2)	5 (0.3)	4 (0.3)	6 (0.4)	25 (0.6)	5 (0.6)	15 (1.1)	989 (3.2)
Drowning	33 (0.5)	3 (0.2)	1 (0.1)	1 (0.1)	19 (0.4)	2 (0.2)	8 (0.6)	402 (1.3)
Other	1645 (23.6)	278 (14.3)	94 (6.9)	208 (13.7)	542 (12.2)	94 (11.2)	347 (26.0)	7035 (22.4)
Location of cardiac arrest								
Home	5978 (75.8)	1689 (77.5)	1074 (72.6)	1319 (78.0)	3438 (69.6)	700 (73.6)	1073 (71.0)	24,724 (70.0)
Public place	993 (12.6)	210 (9.6)	246 (16.6)	197 (11.6)	861 (17.4)	125 (13.1)	250 (16.5)	6258 (17.7)
Other places	914 (11.6)	279 (12.8)	160 (10.8)	175 (10.3)	641 (13.0)	126 (13.2)	189 (12.5)	4344 (12.3)
Witnessed cardiac arrest	5075 (65.9)	1449 (68.2)	999 (68.4)	1087 (66.7)	3329 (69.0)	646 (69.8)	931 (62.9)	21,891 (63.6)
Bystander CPR	4082 (53.7)	1145 (54.7)	784 (54.2)	883 (54.1)	2524 (52.9)	484 (53.0)	751 (51.2)	19,138 (56.0)
Defibrillated any	2127 (28.0)	613 (29.6)	693 (48.2)	565 (35.1)	1931 (40.1)	359 (38.7)	414 (28.4)	11,407 (33.4)
Adrenaline administered	6245 (79.8)	1652 (76.6)	1146 (78.4)	1306 (78.2)	3825 (78.1)	755 (80.1)	1211 (80.7)	27,528 (78.5)
Amiodarone administered	696 (9.0)	206 (9.7)	279 (19.2)	222 (13.5)	734 (15.3)	130 (13.9)	144 (9.7)	4057 (11.7)
Initial rhythm								
VF/pVT	1338 (19.1)	343 (17.9)	489 (36.8)	342 (23.2)	1305 (29.6)	231 (27.8)	240 (18.1)	7311 (23.4)
PEA	1403 (20.0)	406 (21.2)	259 (19.5)	258 (17.5)	763 (17.3)	140 (16.8)	215 (16.2)	5057 (16.2)
Asystole	4272 (60.9)	1162 (60.8)	580 (43.7)	876 (59.3)	2347 (53.2)	461 (55.4)	871 (65.7)	18,823 (60.3)
Pulse on EMS arrival at scene	1053 (14.1)	258 (12.6)	182 (12.9)	172 (10.7)	766 (16.2)	154 (17.3)	211 (14.7)	4729 (14.0)
Outcomes								
ROSC, any	2582 (34.4)	734 (36.0)	532 (37.2)	533 (33.4)	1796 (37.5)	312 (34.2)	467 (32.4)	11,677 (34.5)
CPC score at discharge								
CPC score 1 no sequele	381 (72.6)	66 (63.5)	94 (72.9)	68 (67.3)	383 (75.7)	46 (78.0)	59 (69.4)	2495 (76.9)
Survival at 30 days	723 (9.1)	143 (6.5)	179 (12.1)	135 (8.0)	652 (13.1)	92 (9.7)	122 (8.0)	4433 (12.5)
Survival at 365 days	641 (8.1)	106 (4.8)	139 (9.4)	111 (6.6)	575 (11.6)	82 (8.6)	102 (6.7)	3968 (11.2)

Abbreviations: CPC = cerebral performance category, ROSC = return of spontaneous circulation, VF = ventricular fibrillation, pVT = pulseless ventricular tachycardia, EMS = emergency medical system (ambulance), PEA = pulseless electrical activity.

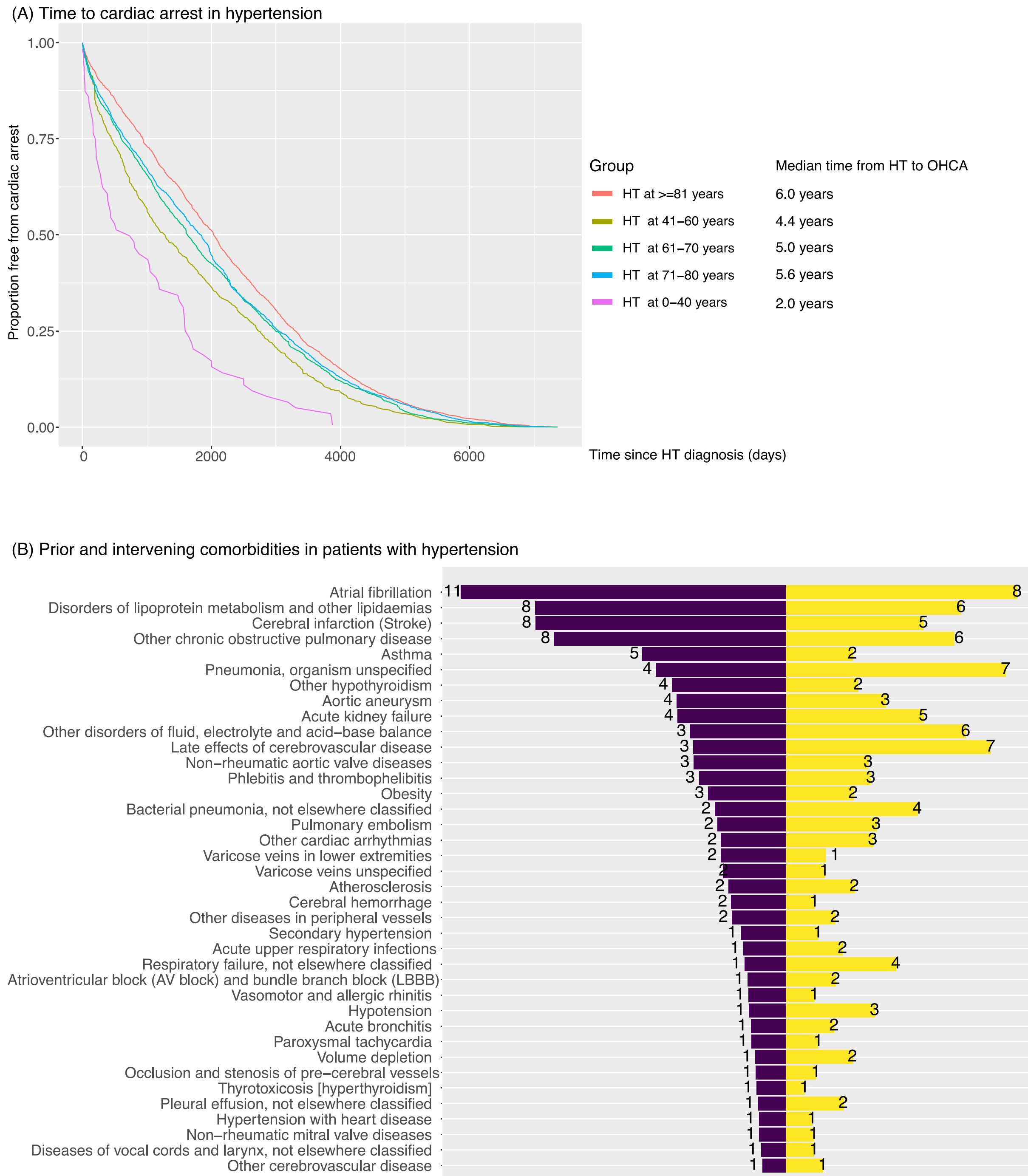


Fig. 1 – Time from diagnosis of hypertension to cardiac arrest and comorbidities prior to cardiac arrest. (A) Kaplan-Meier curves describing time from HT diagnosis to cardiac arrest in relation to age at HT diagnosis. Note that this analysis only includes patients with a history of HT diagnosis, all of whom did develop cardiac arrest and were thus included in the SRCR. (B) Panel B shows the prevalence of comorbidities before index HT diagnosis (purple bars) and after first HT diagnosis, but before cardiac arrest occurred (yellow bars).Figure 1B. **Time from diagnosis of hypertension to cardiac arrest and comorbidities prior to cardiac arrest (A) Kaplan-Meier curves describing time from HT diagnosis to cardiac arrest in relation to age at HT diagnosis. Note that this analysis only includes patients with a history of HT diagnosis, all of whom did develop cardiac arrest and were thus included in the SRCR. (B) Panel B shows the prevalence of comorbidities before index HT diagnosis (purple bars) and after first HT diagnosis, but before cardiac arrest occurred (yellow bars).**

HT (21%) and HF with IHD (19.5%), compared with 16.2–17.5% in the other groups. Asystole was more common in the two hypertensive groups, in HF without IHD and HT, in the DM group and among all others. Refer to Supplementary Table 1 for further details.

ROSC before hospital arrival varied from 32% to 37%. Survival at 30 days varied from 6.5% to 13%, where patients with HF and HT had the lowest survival rate, while the highest was observed in patients with IHD (Table 1).

Time to OHCA, prior and intervening comorbidities

Fig. 1A shows survival curves describing time from HT diagnosis to cardiac arrest in relation to age at diagnosis of HT. Time from HT diagnosis to cardiac arrest was shorter for younger patients. Median time to OHCA was 2.0 years in patients between 0–40 years of age at diagnosis of HT, 4.4 years in those aged 41–60 at diagnosis, 5.0 years in those aged 61–70 years, 5.6 years in those aged 71–80 years and 6.0 years in those aged 81 years or older.

Fig. 1B shows that that the most prevalent comorbidities prior to HT diagnosis were atrial fibrillation (11%), dyslipidemia (8%), stroke (8%) obstructive pulmonary disease (8%).

Survival

In cases with HT the crude overall rate of 30-day survival declined from 14.7% to 2.5% as no-flow time increased from <3 minutes to 11–15 minutes. Corresponding figures for patients with HF and HT were 11.2% to 2.9% (Supplementary Fig. 1). About half of cases in both groups reached ROSC when CPR was started <3 minutes. In cases with HT and a shockable initial rhythm 68% reached ROSC and 42% survived to 30-day when CPR was started within 3 minutes. Rates of ROSC were halved when presenting with PEA or asystole, while rates of 30-day survival were 0.4–4.8%. Considering all cardiovascular conditions, survival was similar when presenting with asystole or PEA. In cases presenting with VF/pVT, survival was lowest (23–27%) in those with HF.

Fig. 2 shows adjusted (for age, sex, no-flow time) survival curves during the entire follow-up. Short-term survival was highest in cases with IHD and those with HF with IHD. We observed a non-proportional hazard function for the latter group, which exhibited a more rapid decline over time; all other groups displayed proportional hazard over time. The lowest survival was noted for patients with HF with HT, and, secondly, those with HF without HT and IHD. Patients

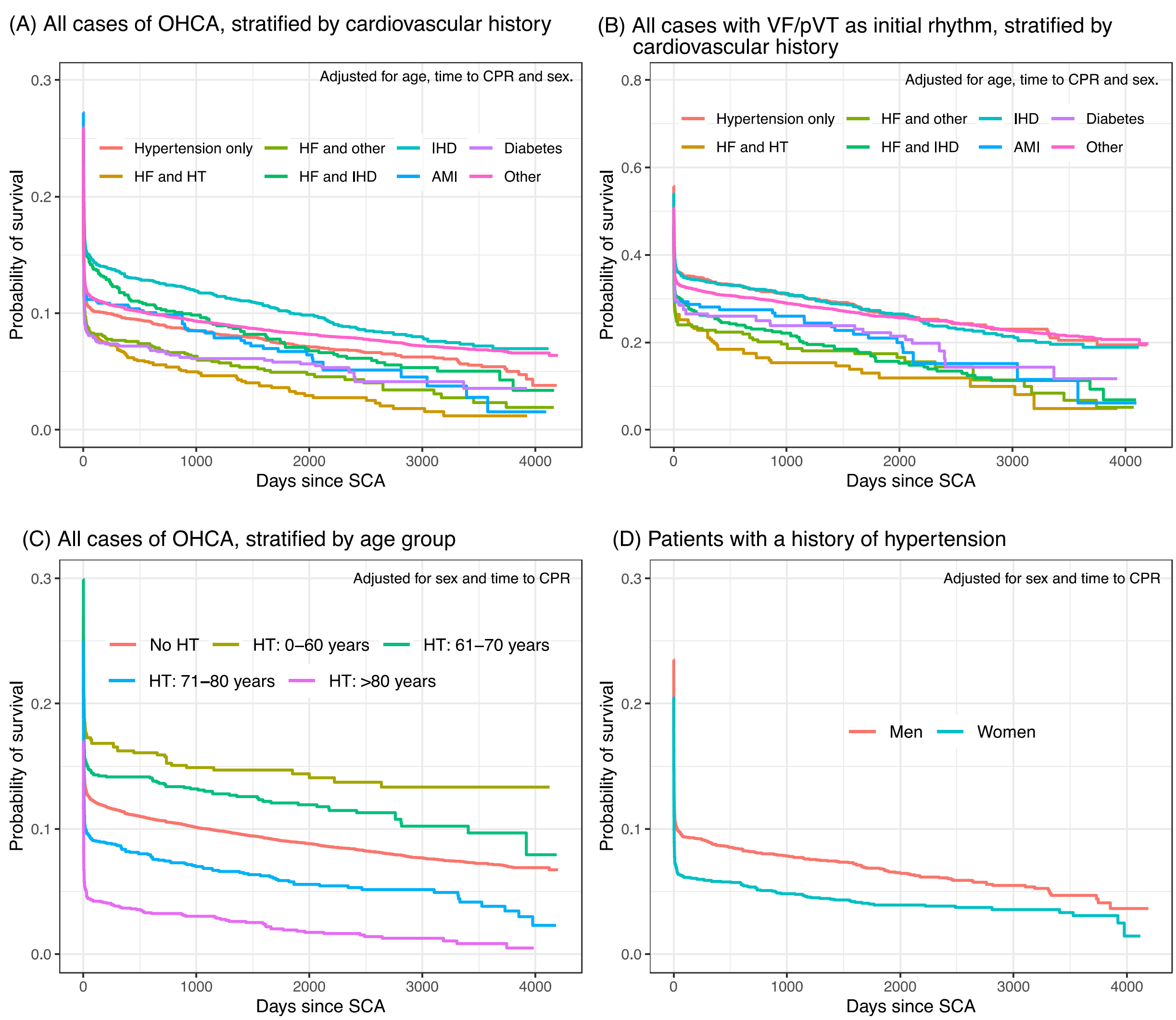
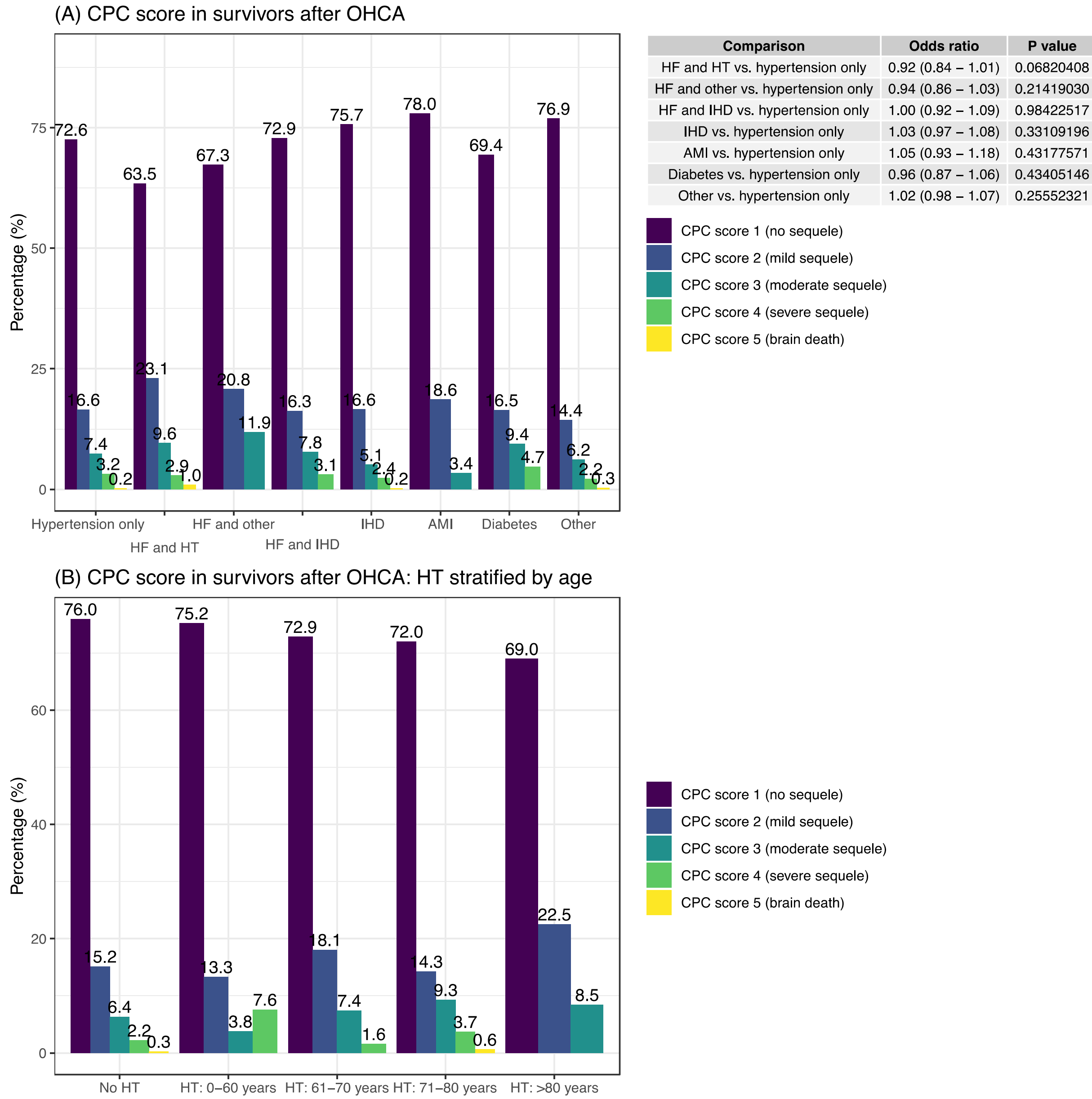


Fig. 2 – (A) Adjusted long-term survival in relation to diagnosis of hypertension and age. (B). Adjusted long-term survival in relation to diagnosis of hypertension and age. (C) Adjusted long-term survival in relation to diagnosis of hypertension and age. (D) Adjusted long-term survival in relation to diagnosis of hypertension and age.



Comparison	Odds ratio	P value
HF and HT vs. hypertension only	0.92 (0.84 – 1.01)	0.06820408
HF and other vs. hypertension only	0.94 (0.86 – 1.03)	0.21419030
HF and IHD vs. hypertension only	1.00 (0.92 – 1.09)	0.98422517
IHD vs. hypertension only	1.03 (0.97 – 1.08)	0.33109196
AMI vs. hypertension only	1.05 (0.93 – 1.18)	0.43177571
Diabetes vs. hypertension only	0.96 (0.87 – 1.06)	0.43405146
Other vs. hypertension only	1.02 (0.98 – 1.07)	0.25552321

Fig. 3 – (A) Cerebral performance category (neurological outcome) among discharged patientsCerebral performance category (CPC) score in patients discharged. CPC data was available in 97% of those who were alive at 30 days. (B) Cerebral performance category (neurological outcome) among discharged patientsCerebral performance category (CPC) score in patients discharged. CPC data was available in 97% of those who were alive at 30 days.

with HT only, HF or DM displayed comparable survival (Fig. 2A). In the subgroup presenting with a shockable rhythm, we did not observe the non-proportionality in hazard for cases with HF and IHD (Fig. 3B). Long-term survival in young patients with HT (0–60 years) was 15% (Fig. 2C). Among cases with HT only, women had worse survival than men (Fig. 2D).

Neurological outcome

The crude rate of CPC score 1 or 2 (no or mild sequelae) was 89% in patients with HT, as compared with 87% in patients with HF and HT, 88% in HF without IHD and HT, 89% in HF with IHD, 92% in IHD, 97% in patients with MI, 86% in patients with DM and 81% in all others (Fig. 3). Age and sex adjusted odds ratios (OR) for CPC score 1 did not differ in any group.

Adjusted 30-day survival

As compared with cases with HT only, OR for 30-day survival did not differ for those with previous IHD, HF and IHD, and those with previous AMI (Supplementary Fig. 2, model 3). Those with DM, however, displayed OR of 0.74 (95% CI 0.55–0.97) compared with HT only (Supplementary Fig. 2, model 3). Those with HF and HT displayed OR of 0.70 (95% CI 0.54–0.91), compared with HT only (Supplementary Fig. 2, model 3). Cases with HF without HT and IHD displayed an OR of 0.73 (95% CI 0.56–0.95). Subgroup analyses in relation to initial rhythm, sex, cardiac etiology and age-group are presented in Supplementary Fig. 2. In the subgroup with cardiac etiology, survival in those with HT did not differ from those with HF, unless HF was associated with IHD, in which survival was worse. In women, the only cardiovascular condition that differed was a history of acute MI, which displayed an OR of 0.25 (95% CI 0.08–0.58), compared with HT only.

Supplementary Fig. 3 shows predictors of 30-day survival in patients with and without prior HT. Survival decreased with age, with no difference in relation to HT. There were no sex differences, nor any other clinically relevant differences with regards to HT status.

Rates of non-shockable rhythms increased rapidly with increasing no-flow time in all groups (Supplementary Fig. 4).

No group displayed improvement in 30-day survival during 2010 to 2020 (Supplementary Fig. 5).

Discussion

In this nationwide study of 56,203 cases of OHCA, we studied how major cardiovascular conditions relate to characteristics and survival. These conditions, i.e HT, DM, HF, IHD, are strong predictors of cardiovascular morbidity and mortality. The overall prevalence of all these were 59% in our study population. We emphasized on HT, a leading contributor of death worldwide,[2] and demonstrated that early onset of HT is strongly associated with time to sudden cardiac arrest, the median time from diagnosis of HT to OHCA was only 2.0 years in patients between 0–40 years at diagnosis of HT, compared with 5.6 years in those aged 71–80 years at diagnosis.

The poorest overall short- and long-term outcomes were noted for cases with HF and HT in combination. Thus, this combination is a serious comorbidity in the setting of OHCA. Patients with HT displayed long-term survival comparable to patients with previous AMI, which further corroborates the significance of HT. Furthermore, subjects with HT with or without HF and subjects with DM displayed low rates of shockable rhythm. This could be an explanation to the poor outcome in patients with HT. The odds of 30-day survival was 26% lower in diabetics, 30% lower in HF and HT, and 27% lower in HF without IHD nor HT compared to HT only. This highlights that DM is also a substantial comorbidity in the setting of OHCA. It should also be viewed in light of recent reports that 30% of all deaths in people with diabetes are due to sudden cardiac arrest.[14]

All cardiovascular conditions were associated with high rates of ROSC when no-flow time was short. However, while rates of ROSC where relatively high across the range of no-flow times (irrespective of initial rhythm), survival dropped rapidly as no-flow time increased and there were virtually no survivors when no-flow exceeded 10 minutes when presenting with asystole or PEA. The dismal survival among those with long no-flow time suggests that in these cases the comorbidity has a limited effect on survival. In those with an initial shockable rhythm, however, we noted a significant number of survivors even when no-flow exceeded 10 minutes. These data suggest that resuscitation efforts may be warranted even at long no-flow times.

We also show that all seven cardiovascular comorbidities studied are associated with good neurological outcome (CPC 1–2) among survivors. We found no statistically significant difference in the probability of CPC 1 among survivors, it was clear that HT, HF and DM were associated with lowest crude rates of CPC 1 among survivors. While the rate of good neurological outcome was high in our study population, results are still in line with other European countries, as evident in the EuReCa reports.[15] Compared with other countries, Sweden has fewer OHCAs due to trauma,[16,17] and a very high degree of bystander CPR.[12]

The fact that early onset HT was strongly related to time to cardiac arrest is a phenomenon frequently seen in cardiovascular conditions, with early onset of risk factors and disease being strongly associated with poor outcome. While this analysis does not allow for assessing the relative risk of cardiac arrest caused by HT, it is very likely that early onset of risk factors and cardiovascular conditions predicts a more malign disease trajectory. Young individuals with manifestations of cardiovascular disease or risk factors should be treated aggressively to reduce their risk of complications and mortality.

Limitations

While our definitions of cardiovascular conditions include all diagnoses established in outpatient clinics and during hospitalization, we did not have access to primary care data. To some extent there may be misclassification of the exposure groups. Our group defined as HT only actually had cases with atrial fibrillation, renal failure, stroke and obstructive pulmonary disease. We decided to allow for this non-purity since the exposure groups would otherwise become too artificial. We did not have data on the exact cause of the cardiac arrest, which would be relevant for survival analysis. However, this is very difficult to determine and there are currently no reliable means of doing this with an acceptable level of ascertainment (only a fraction of all cases undergo autopsy).

In summary, we conclude that the combination of HT and HF has the lowest survival of all cardiovascular comorbidities and should be considered as serious comorbidity in the setting of OHCA. Furthermore, early onset of hypertension is a predictor for early cardiac arrest.

Author contribution statement

The authors confirm contribution to the paper as follows;

Study conception and design: Araz Rawshani, Anna Myredal
Data collection: Araz Rawshani
Analysis and interpretation of results: Araz Rawshani, Fredrik Hessulf, Sebastian Völz, Christian Dworeck, Jacob Odenstedt, Truls Råmunddal, Geir Hirlekar, Petur Petursson, Oskar Angerås, Truls Råmunddal, Dan Ioanes and Anna Myredal
Manuscript preparation: Araz Rawshani, Fredrik Hessulf, Sebastian Völz, Christian Dworeck, Jacob Odenstedt, Truls Råmunddal, Geir Hirlekar, Petur Petursson, Oskar Angerås, Truls Råmunddal, Dan Ioanes and Anna Myredal
All authors reviewed the results and approved the final version of the manuscript

Conflict of Interest Statement

The authors declare no conflicts of interest.

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Author contributions

AM wrote the first draft of the manuscript and conceived the study. AM and FH performed all statistical analyses. All authors reviewed, commented and revised all versions of the manuscript. All authors decided to submit the manuscript.

Appendix A. Supplementary material

Supplementary material to this article can be found online at https://doi.org/10.1016/j.resplu.2022.100294.

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