Resuscitation 120 (2017) 71–76

Contents lists available at ScienceDirect

Resuscitation

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

Clinical paper

The relationship between chronic health conditions and outcome following out-of-hospital ventricular fibrillation cardiac arrest☆

Florence Dumas[a,b,*], Jennifer Blackwood[c], Lindsay White[c], Carol Fahrenbruch[c], Xavier Jouven[a], Alain Cariou[a], Thomas Rea[c]

[a] INSERM U970, Parisian Cardiovascular Research Center, Paris Descartes University, Paris, France
[b] Emergency Department, Cochin/Hotel-Dieu Hospital, APHP, Paris, France
[c] Emergency Medical Services, Division of Public Health for Seattle and King County, University of Washington, Seattle, WA, USA

ARTICLE INFO

Article history:
Received 10 June 2017
Received in revised form 24 August 2017
Accepted 25 August 2017

Keywords:
Cardiac arrest
Outcome
Comorbidities

ABSTRACT

Introduction: The cumulative burden of chronic health conditions could contribute to out-of-hospital cardiac arrest (OHCA) physiology and response to attempted resuscitation. Yet little is known about how chronic health conditions influence prognosis. We evaluated the relationship between cumulative comorbidity and outcome following ventricular fibrillation OHCA using 3 different scales.

Methods: We performed a cohort investigation of persons >= 18 years who suffered non-traumatic OHCA and presented with ventricular fibrillation between January 1, 2007 and December 31, 2013 in a metropolitan emergency medical service (EMS) system. Chronic conditions were ascertained from EMS reports. The primary relationship between cumulative comorbidity and outcome (survival to hospital discharge) used the Charlson Index and two other scales. Analyses used logistical regression (LR), multiple imputation and inverse probability weighting.

Results: During the study period 1166/1488 potential patients were included. The median Charlson Index was 1 (25th-75th%: 0–2). Overall survival was 43.9%. Comorbidity was associated with a dose-dependent decrease in the likelihood of survival. ompared to Charlson Score of 0, the odds ratio of survival was 0.68 (0.48–0.96) for Charslon of 1, 0.49 (0.35–0.69) for Charlson of 2, and 0.43 (0.30–0.61) for Charlson of >= 3 after adjustment for Utstein predictors using multivariable LR. This inverse comorbidity-survival association was similar for the other 2 scales and was observed for different clinical outcomes (admission to hospital, functional survival, 30-day survival, and 1-year survival).

Conclusion: Based on these results, cumulative comorbidity can help explain survival variability and improve prognostic accuracy. Whether information about cumulative comorbidity or specific health conditions can inform resuscitation care is unknown though the results suggest comorbidity may influence acute pathophysiology and treatment response.

Introduction

Out-of-hospital cardiac arrest (OHCA) is a leading cause of death worldwide [1]; The links in the chain of survival are important for successful resuscitation. However the Utstein data elements which include demographic, circumstance, and care characteristics only account for a modest portion of the variability in outcome [2]. Identifying other characteristics that influence prognosis can improve scientific understanding of resuscitation, help explain outcome differences across populations or geographies, and potentially provide the basis to improve care.

The pathophysiology of OHCA is dynamic, with evidence suggesting a time-dependent physiology that ideally could be matched with specific therapies to maximize the chances of survival [3]. Although the Utstein elements such as early CPR and interval to defibrillation can affect this physiology [4], patient-specific clinical characteristics could influence the acute pathophysiology and in turn patient outcome. For example, persons who suffer OHCA have a range of clinically-recognized chronic health conditions. For some, the OHCA event is the initial manifestation of clinical heart disease, while others may have clinically-established cardiac and non-cardiac health conditions. This cumulative burden of chronic health conditions could potentially contribute to arrest physiology at the outset and during the evolution of attempted resuscitation.

☆ A Spanish translated version of the abstract of this article appears as Appendix in the final online version at http://dx.doi.org/10.1016/j.resuscitation.2017.08.239.

* Corresponding author at: 27 rue du Faubourg Saint Jacques, 75014, Paris.
E-mail address: florence.dumas@aphp.fr (F. Dumas).

http://dx.doi.org/10.1016/j.resuscitation.2017.08.239
0300-9572/

Fig. 1. Cumulative comorbidity scales.

The few studies that have evaluated the relationship between chronic health conditions and OHCA outcome have provided inconsistent results – some reporting an inverse relationship between increasing chronic comorbidity and a lower likelihood of outcome and others observing a null relationship [5,6]. In this investigation, we evaluated the relationship between pre-existing, clinically-recognized, chronic health conditions using different scales to assess the relationship between cumulative comorbidity and resuscitation outcome following ventricular fibrillation cardiac arrest. We hypothesized that cumulative comorbidity would be independently associated with outcome even after accounting for traditional Utstein data elements.

Methods

Study population and setting

We performed a cohort investigation of all persons 18 years or older who suffered non-traumatic OHCA presenting with ventricular fibrillation between January 1, 2007 and December 31, 2013 in a large metropolitan emergency medical service (EMS) system. The EMS system serves a population of approximately 1.3 million persons residing in urban, suburban, and rural settings covering an area of about 2000 square miles. The EMS is a two-tiered system. Basic life support is provided by emergency medical technician-trained firefighters who are equipped with automated external defibrillators. Advanced life support is delivered by paramedics who are trained in rhythm recognition and provide intubation, manual defibrillation, and intravenous medications. Resuscitation care is based on the American Heart Association guidelines [7]. Patients who are resuscitated are transported to area hospitals, each equipped with coronary catheterization and intensive care services. Hospital-based care is at the discretion of the treating physician [8,9]. The institutional review boards at the University of Washington and Public Health – Seattle & King County approved the study.

Data collection and definitions

The EMS system maintains an ongoing registry of all EMS-treated cardiac arrests. Information about demographics, circumstances, care, and outcome is ascertained using emergency dispatch, EMS, defibrillator, hospital, and death records. The information is organized according to the Utstein Guidelines for reporting OHCA [10].

Chronic health conditions, symptoms, and cumulative comorbidity

We collected information about pre-existing, clinically-recognized, chronic health conditions and pre-arrest symptoms from the EMS reports. Ascertainment of health conditions and symptoms used a uniform abstraction form (Appendix). Abstraction was performed without knowledge of hospital survival status.

Chronic health conditions were characterized as present, absent, or unknown. We classified a condition as absent when the particular condition was not noted in the report but information was available about other chronic health conditions and/or chronic medication treatments. We classified chronic health conditions as missing when there was no information available about any chronic health conditions *and* when the record did not explicitly note the absence of prior clinical health history.

We modeled chronic health conditions and symptoms using different scales to assess the relationship between cumulative comorbidity and resuscitation outcome (Fig. 1). We considered a simple model of any pre-existing cardiac condition or non-cardiac condition. We subsequently evaluated the relationship using the Charlson Index given its common use in other conditions, and a previously-published comorbidity scale (Scale 2) used specific to resuscitation [5,11]. Finally we evaluated a new scale that incorporated information about comorbidity and symptoms to assign a condition/symptom specific score to assess whether this condition-specific scoring could improve prediction (Scale 3). In the new scale, we weighted individual conditions that achieved a p-value of <0.2 in the multivariable regression according to their beta coefficient.

Outcome

The primary outcome was vital status at hospital discharge. Secondary outcomes included Cerebral Performance Category at discharge, 30-day mortality, and 1-year mortality. Cerebral Performance Category (CPC) provides an assessment of functional status

Table 1
Distribution of Utstein characteristics according to Chalson Comorbidity Index.

	Overall N = 1164	CCI = 0 N = 439	CCI = 1 N = 224	CCI = 2 N = 250	CCI = 3 N = 251	p-value*	missing data N = 324
Age y.o., mean (SD)	63.6 (15.0)	58.7 (15.6)	64.6 (15.7)	65.5 (13.1)	69.3 (12.5)	<0.001	59.0
Male Gender	876 (75.3)	340 (77.5)	170 (75.9)	185 (74)	181 (72.1)	0.10	271 (83.6)
Public Location	287 (24.7)	127 (28.9)	54 (24)	63 (25.2)	43 (17.1)	0.001	226 (69.8)
Witnessed status	99 (77.3)	348 (79.3)	176 (78.6)	191 (76.4)	185 (73.7)	0.08	234 (72.2)
Bystander CPR	913 (78.4)	354 (80.6)	177 (79.0)	189 (75.6)	193 (76.9)	0.14	240 (74.1)
EMS response <5 min	743 (63.9)	265 (60.4)	145 (64.7)	161 (64.4)	172 (68.5)	0.04	218 (67.3)

EMS = Emergency Medical services; CCI = Charlson Comorbidity Index; SD = Standard Deviation; CPR = Cardio-pulmonary Ressuscitation; *p*-value for test for trend across Charlson Index.

and was determined from review of the full hospital record [12]. A CPC of 1 or 2 was defined as favorable neurological outcome [13]. Thirty-day survival and 1-year survival were determined through linking to state and national vital records.

Statistical analysis

We used descriptive statistics to summarize categorical variables as proportions, and continuous variables as mean with standard deviation or as median with interquartile range. For the purposes of presentation, we stratified Utstein elements according to cumulative comorbidity using the Charlson index divided into 4 categories. The distribution of Utstein elements according to the other two scales is presented in the supplemental online appendix.

We evaluated the relationship between individual chronic health conditions and outcome or individual symptoms and outcome using chi-square test or Fisher's exact test. We then undertook multivariable logistic regression to determine if cumulative comorbidity and symptoms were associated with outcome after adjustment for the Utstein data elements. We modeled discrete categories of comorbidity as well as performed test for trend across the categories. Sensitivity analyses assessed the potential influence of missing data. We performed multiple imputation using a sequence of conditional imputation model as well as analyses using inverse probability weighting [14,15]. We tested whether the association between cumulative comorbidity and outcome differed according to age or gender by including an interaction term between the comorbidity scale and the covariate of interest.

We also generated receiver operating curves to compare the extent of prediction of cumulative comorbidity in the context of the prediction characteristics of the basic Utstein circumstance elements (witness status and location) and Utstein care elements (bystander CPR and EMS response interval) when added to basic demographic information (age and gender). We calculated the amount of variability by determining the area under the curve (AUC). The area under the curve could vary from 0.5 (no prediction) to 1.0 (perfect prediction). The final quantitative measure of prediction associated with the collective data elements were calculated as ([the area under the curve– 0.5]/0.5) [2]. All tests were two-sided with a *p*-value considered significant if <0.05. Analyses were performed using STATA/SE 14.0 (Lakeway Drive, TX, USA).

Results

During the study period, 1488 patients experienced OHCA and presented with ventricular fibrillation. Of the 1488, a total of 1258 (85%) had some information about comorbidity though only 1166 (78%) had sufficient information to determine cumulative comorbidity scales. The n = 92 (1258–1166) without sufficient information to complete the scale had basic information to generically indicate the presence of some form of heart disease or non-cardiac health condition but did not include information about the specific conditions.

Table 1 presents the characteristics of the cohort overall, according to Charlson index, and among those with unknown chronic health condition status. Overall, patients were an average of 63 years of age and more commonly male. Three quarters of patients had a witnessed event and a similar proportion received bystander CPR. About a third of events occurred in the public setting.

Among the 1166 with information about chronic health conditions, the median (25th, 75th percentile) Charlson index wasied by cumulative comorbidity based on Charlson index, older age was more common with increasing Charlson index while public location decreased with increasing index (Table 1). Compared to those with information (definite absence or presence of chronic health conditions), those with unknown status were younger, more likely to experience the arrest in public, but experienced similar survival discharge to hospital discharge (44.8% versus 43.6%).

Among those with information about chronic health conditions, return of spontaneous circulation at the end of EMS care was 66.2%, survival to hospital discharge was 43.6% and survival with a favorable CPC of 1 or 2 was 40%. Thirty-day survival was 42.9% and 1 year survival was 41.2%.

Table 2 presents the relationship between the individual chronic health conditions and survival to hospital discharge. Multiple individual chronic health conditions were associated with the likelihood of survival to hospital discharge. Specifically, patients with congestive heart disease, coronary artery disease, diabetes mellitus, stroke or other neurological condition, respiratory disease, or cancer history were less likely to survive compared to patients without these individual chronic health conditions ($p < 0.05$). Conversely, symptoms of chest pain or seizure were associated significantly with higher survival ($p < 0.05$).

When cumulative chronic comorbidity was measured according to the Charslon index, the odds of survival to hospital discharge decreased in a graded fashion as Charlson index increased after adjustment for potential confounding Utstein characteristics (Table 3). Multiple imputation and inverse probability weighting to account for missing information about chronic health conditions produced similar results. This relationship of increasing cumulative comorbidity and lower odds of survival was also observed using the other two scales with each scale demonstrating a statistically-significant test for trend when comorbidity categories were modeled continuously (Table 3). The results were similar when evaluating secondary outcomes of favorable functional status (CPC 1 or 2), 30-day survival, and 1-year survival (Table 4). We did not observe an interaction between age and comorbidity scale ($P > 0.10$) or gender and comorbidity scale ($p > 0.10$ for interaction).

The AUC of the receiver operating curve was 0.64 with the base model that included only the demographic measures of age and gender. The addition of cumulative comorbidity scale significantly improved the fit of the model with AUC increasing from 0.64 to 0.67. This increase in AUC was similar to the increase with the addition circumstance characteristics (witness status and location) to demographics (AUC increase from 0.64 to 0.69) or the addition of prehospital treatment characteristics (bystander CPR

Table 2
Distribution of chronic conditions and symptoms according to survival status[a].

	Overall	Survivors	Non Survivors		Unadjusted OR
	N = 1488	N = 653 (44)	N = 835 (56)	p-value	
Any comorbidities n = 1258	**1143 (91)**	**461 (86)**	**682 (95)**	**<0.001**	**0.33 [0.22–0.50]**
Pre-existing Heart disease n = 1176	**645 (55)**	**248 (48)**	**397 (60)**	**<0.001**	**0.63 [0.50–0.79]**
Prior cardiac arrest	17 (1)	5 (1)	12 (2)	0.33	0.54 [0.19–1.53]
Myocardial infarction	168 (14)	62 (12)	106 (16)	0.06	0.73 [0.52–1.02]
Congestive heart failure	187 (16)	63 (12)	124 (19)	0.003	0.61 [0.44–0.85]
Coronary Artery Disease	177 (15)	62 (12)	114 (17)	0.02	0.68 [0.49–0.94]
Peripheric arterial disease	45 (4)	16 (3)	29 (4)	0.29	0.71 [0.38–1.32]
Atrial Fibrillation	117 (10)	51 (10)	66 (10)	0.99	1.0 [0.68–1.47]
Heart Procedure	287 (24)	117 (23)	170 (26)	0.28	0.86 [0.66–1.13]
Valvulopathy	31 (3)	11 (2)	20 (3)	0.46	0.71 [0.34–1.49]
Non-cardiac medical history n = 1201	**951 (79)**	**376 (73)**	**575 (84)**	**<0.001**	**0.51 [0.38–0.67]**
Hypertension	528 (44)	218 (42)	310 (45)	0.29	0.88 [0.70–1.11]
Hypercholesterolemia	96 (8)	46 (9)	50 (7)	0.33	1.24 [0.82–1.88]
Diabetes	295 (25)	103 (20)	192 (28)	0.001	0.64 [0.49–0.84]
Stroke	59 (5)	15 (3)	44 (6)	0.005	0.43 [0.24–0.79]
Liver history	13 (1)	4 (1)	9 (1)	0.41	0.58 [0.18–1.91]
Lung disease	126 (10)	37 (7)	89 (13)	0.001	0.52 [0.34–0.77]
Gastrointestinal disease	119 (10)	43 (8)	76 (11)	0.11	0.72 [0.49–1.07]
Kidney disease	87 (7)	32 (6)	55 (8)	0.22	0.75 [0.48–1.19]
Cancer history	82 (7)	15 (3)	67 (10)	<0.001	0.28 [0.16–0.49]
Mental health disease	124 (10)	45 (9)	79 (12)	0.13	0.73 [0.50–1.07]
Other neurological disease	56 (5)	13 (3)	43 (6)	0.002	0.34 [0.20–0.72]
HIV	3 (0.2)	0	3 (100)	***	***
Tissue/Inflammatory disease	29 (2)	12 (2)	17 (2)	1	0.93 [0.44–1.97]
Metabolic disease	47 (4)	14 (3)	33 (5)	0.07	0.55 [0.29–1.04]
Symptoms	**691 (46)**	**312 (48)**	**379 (45)**	**0.36**	**1.10 [0.90–1.35]**
Chest, arm, jaw, or back pain	275 (18)	149 (23)	126 (15)	<0.001	1.66 [1.28–2.16]
Dyspnea	176 (12)	76 (12)	100 (12)	0.84	0.97 [0.70–1.33]
Indigestion, abdominal pain, nausea	115 (8)	48 (7)	67 (8)	0.63	0.91 [0.62–1.34]
Malaise, Tiredness, Weakness	198 (13)	85 (13)	113 (14)	0.77	0.96 [0.71–1.29]
Syncope	78 (5)	41 (6)	37 (4)	0.13	1.44 [0.92–2.28]
Diaphoresis	60 (4)	28 (4)	32 (4)	0.69	1.12 [0.67–1.89]
Seizure	26 (2)	18 (3)	8 (1)	0.01	2.93 [1.26–6.78]

[a] Percentages are taking into account missing data (n = 230 (15%) had no information about comorbidity, n = 312 (21%) had no information regarding heart disease, n = 287 (19%) had no information on non cardiac medical history).

Table 3
Association between cumulative comorbidity and survival to hospital discharge.

		% survival	Univariate Odd Ratio	Adjusted Odds Ratio[a,#]	MultipleImputation[#]	IPW[#]
Charlson Index	CCI = 0	55.6	1	1	1	1
	CCI = 1	43.8	0.62 [0.45–0.86]	0.68 [0.48–0.96]	0.72 [0.50–1.04]	0.75 [0.50–1.13]
	CCI = 2	36.0	0.45 [0.33–0.62]	0.49 [0.35–0.69]	0.57 [0.42–0.77]	0.46 [0.31–0.69]
	CCI = 3	30.3	0.35 [0.25–0.48]	0.43 [0.30–0.61]	0.53 [0.38–0.74]	0.46 [0.31–0.69]
Scale 2%	No comorbidity	61.2	1	1	1	1
	1	47.0	0.56 [0.39–0.82]	0.65 [0.44–0.98]	0.70 [0.47–1.03]	0.67 [0.42–1.06]
	2	43.6	0.49 [0.34–0.72]	0.60 [0.39–0.91]	0.66 [0.45–0.97]	0.59 [0.36–0.95]
	3	33.9	0.32 [0.21–0.50]	0.45 [0.28–0.72]	0.54 [0.34–0.85]	0.47 [0.28–0.82]
	over 4	31.0	0.28 [0.18–0.44]	0.42 [0.26–0.68]	0.51 [0.32–0.82]	0.40 [0.23–0.69]
Scale 3%	>=0	55.3	1	1	1	1
	[0–(−7)]	41.9	0.58 [0.48–0.77]	0.67 [0.49–0.90]	0.72 [0.55–0.95]	0.67 [0.47–0.95]
	[(−7) to (−15)]	28.0	0.31 [0.23–0.43]	0.41 [0.29–0.57]	0.48 [0.34–0.67]	0.38 [0.26–0.57]
	<(−15)	14.5	0.14 [0.07–0.24]	0.23 [0.11–0.50]	0.34 [0.17–0.66]	0.25 [0.11–0.57]

IPW: inverse probability weight; CCI = Charlson Comorbidity Index.
%Summary of scale scoring is provided in Fig. 1. Scale 2 is the cumulative comorbidity scale (+1 point for every comorbidity +1 additional point for congestive heart failure). Scale 3 is assigns specific scores to each medical condition.
[a] Odds ratio adjusted on Utstein covariates (age, gender, time response, location, witnessed and bystander CPR status).
[#] Test for trend significant at p < 0.01 for each scale in the multivariable adjusted models.

and EMS response interval) to demographics (AUC increase from 0.64 to 0.66). Collectively a multivariable model that incorporated demographic, cumulative comorbidity, OHCA circumstances, and prehospital Utstein treatment characteristics achieved an AUC of 0.73. (Fig. 2)

Discussion

In this cohort of ventricular fibrillation OHCA, cumulative comorbidity was associated with a substantially lower likelihood of survival even after adjustment for Utstein data elements. This inverse comorbidity-survival association demonstrated a dose-dependent trend, observed across different clinical outcomes (survival, functional survival, and 30-day and 1-year survival), and was consistent across 3 scales. Cumulative comorbidity helped explain some of the variability in survival as evidenced by the receiver operating curves, similar in magnitude to basic Utstein circumstance variables or prehospital care variables. Collectively, the Utstein elements and cumulative comorbidity accounted for nearly half of the variability in survival for this cohort.

Table 4
Association between cumulative comorbidity and different clinical outcomes (logistic regression).

		Admitted to hospital		CPC1/CPC2		30 days Mortality		1 year mortality	
		%	Adjusted Odds Ratio*	%	Adjusted Odds Ratio*	%	Adjusted Odds Ratio	%	Adjusted Odds Ratio
Charlson Index	CCI = 0	71.2	1	52.1	1	55.3	1	54.9	1
	CCI = 1	64.2	0.78 [0.54–1.12]	39.7	0.66 [0.47–0.94]	43.5	0.66 [0.48–0.97]	42.5	0.68 [0.48–0.97]
	CCI = 2	60	0.65 [0.46–0.91]	34.0	0.52 [0.37–0.74]	34.4	0.46 [0.32–0.65]	33.1	0.45 [0.32–0.64]
	CCI = 3	54.8	0.58 [0.41–0.82]	25.1	0.38 [0.26–0.55]	28.0	0.39 [0.27–0.56]	22.6	0.30 [0.21–0.45]
Scale 2	No comorbidity	74.2	1	58.2	1	61.0	1	60.8	1
	1	67.1	0.83 [0.54–1.27]	44.8	0.68 [0.45-1.01]	47.0	0.67 [0.45–1.01]	46.4	0.69 [0.46–1.04]
	2	65.6	0.82 [0.53–1.27]	38.1	0.53 [0.35–0.81]	41.8	0.57 [0.37–0.87]	40.6	0.57 [0.37–0.87]
	3	60.3	0.73 [0.45–1.18]	29.6	0.42 [0.26–0.67]	32.8	0.44 [0.27–0.72]	29.4	0.40 [0.25–0.66]
	over 4	55.6	0.62 [0.38–1.0]	27.8	0.41 [0.25–0.66]	29.1	0.39 [0.24–0.64]	25.0	0.35 [0.21–0.57]
Scale 3	>=0	71.9	1	51.8	1	55.1	1	54.2	1
	[0-(−7)]	64.3	0.80 [0.59–1.09]	38.0	0.65 [0.48–0.88]	40.7	0.64 [0.47–0.87]	38.7	0.62 [0.45–0.84]
	[(−7) to (−15)]	54.7	0.60 [0.43–0.83]	24.4	0.39 [0.28–0.56]	25.9	0.37 [0.26–0.53]	23.4	0.35 [0.24–0.51]
	<(−15)	48.4	0.57 [0.32–1.0]	11.3	0.20 [0.09–0.47]	11.7	0.19 [0.08–0.44]	10.2	0.18 [0.07–0.43]

Utstein characteristics: Age, gender, location, witnessed and bystander CPR status, time response.
CPC = Charlson Comorbidity Index; CPC = Cerebral Performance Category; Scores are detailed in Fig. 1.
All comparisons between full model with or without comorbidity were significant ($p < 0.05$).

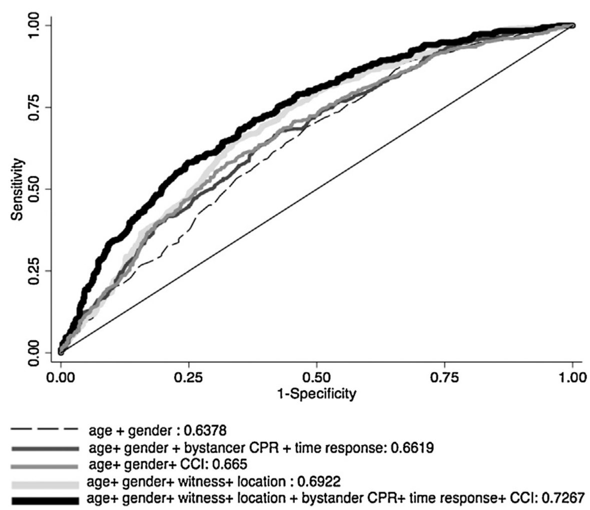

Fig. 2. Receiver Operating Curves of demographic, cumulative comorbidity, Utstein circumstance, and Utstein prehospital care characteristics.

We used the EMS report to ascertain chronic health conditions and symptoms. However exclusion of patients who are declared dead in the field and do not have a complete hospital record would bias the association toward the null since cumulative comorbidity influences survival in part by influencing the association between comorbidity and hospital admission (Table 4).

Even with this limitation, we observed that over half of patients had some form of clinically-recognized heart disease and over three-quarters had at least one non-cardiac chronic health condition prior to the OHCA. This prevalence of chronic health conditions is comparable to other population-based prevalence reports [16].

In the current investigation, we highlight the Charlson index given its widespread evaluation in other medical conditions. We also evaluated a previously-published scale specific to OHCA and developed a new more extensive scale that incorporated symptoms. Specific symptoms of chest pain and seizure improve prediction though scale 3 adds additional parameters to the model without external validation or generalizability. Regardless of which scale was evaluated, we observed a trend association between cumulative comorbidity and outcome that was robust across a range of clinically-important outcomes.

The findings from the current study contrast with a handful of prior investigations that have not observed a clear relationship between cumulative comorbidity and outcome. This difference may be attributable to study design and populations. Prior studies have restricted to patients >70 years, restricted to those with hospital information [17], or included all patients regardless of initial rhythm [18]. We a-priori chose to include all adult patients who presented with an initial rhythm of ventricular fibrillation [6]. In the current cohort, we did not observe an interaction between cumulative comorbidity and age that would indicate a lack of prognostic influence among older adults [18]. As noted, we chose to use the EMS record to ascertain chronic clinical conditions so as not to exclude patients who did not survive to hospital admission and potentially bias the relationship. With regard to initial rhythm, survival can vary >10-fold according to initial rhythm and could challenge the ability to detect important prognostic influence of comorbidity given the potential confounding of initial rhythm. Moreover, few characteristics influence prognosis in asystole. We selected ventricular fibrillation as the study population given its designation as the Utstein comparator group that could provide the greatest fidelity when evaluating the comorbidity-outcome relationship. An understanding of differences between current and past studies helps inform interpretation of the current findings.

Prior research suggests that the basic data elements account for only about a quarter of the survival variability [2]. Using a comparable method, we observed that cumulative comorbidity helped explain outcome variability to a similar extent as the basic Utstein elements involving OHCA circumstances or care, and collectively cumulative comorbidity and the core Utstein data elements accounted for nearly half of variability. The results indicate that cumulative comorbidity provides important prognostic information that may help explain outcome variation and in turn could help improve prediction. While the current study indirectly supports the potential for cumulative comorbidity to affect pathophysiology and response to treatment, the study does not identify if and how comorbidity might alter treatment approaches to improve outcome.

The study is observational given the focus on chronic health conditions and OHCA; thus there may be unmeasured confounders that account for the relationship between cumulative comorbidity and outcome. The biologic mechanism for the relationship remains uncertain. The study rigorously evaluated cumulative scales as opposed to specific individual health conditions. Specific conditions may be more directly related to particular biologic pathways that would in turn be amenable to distinct treatments. As noted, ascertainment of chronic health conditions relied on EMS records. The approach undoubtedly produced some misclassification most likely by under-ascertainment of chronic conditions. Such misclassification would tend to attenuate the comorbidity–survival relationship, suggesting that the true magnitude of the relationship may be even greater than observed in this study. Finally, the results are drawn from a single large metropolitan community with a mature EMS system and may not be generalizable to all communities. These limitations should be balanced against the study's strengths: a large cohort of ventricular fibrillation OHCA that uses a uniform approach to classify chronic health conditions, rigorously tests multiple scales using a variety of outcomes, and provides context regarding the extent of prognosis relative to the Utstein data elements.

In conclusion, cumulative comorbidity as assessed from EMS records and tested using 3 different scales was consistently associated with lower likelihood of favorable clinical resuscitation outcome even after accounting for Utstein data elements. Based on these results, cumulative comorbidity can help explain survival variability and improve prognostic accuracy. Whether information about cumulative comorbidity or specific chronic health conditions can inform resuscitation treatment is uncertain, though the current results suggest cumulative comorbidity may influence acute pathophysiology and response to treatment.

Conflict of interest

None to disclose

Acknowledgment

We thank the EMS providers of King County for their ongoing commitment to rigorous evaluation in order to improve patient care.

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.2017.08.239.

References

[1]. Go AS, Mozaffarian D, Roger VL, Benjamin EJ, Berry JD, Blaha MJ, et al. Heart disease and stroke statistics–2014 update: a report from the American Heart Association. Circulation 2014;129:e28–92.

[2]. Rea TD, Cook AJ, Stiell IG, Powell J, Bigham B, Callaway CW, et al. Predicting survival after out-of-hospital cardiac arrest: role of the Utstein data elements. Ann Emerg Med 2010;55:249–57.

[3]. Weisfeldt ML, Becker LB. Resuscitation after cardiac arrest: a 3-phase time-sensitive model. JAMA 2002;288:3035–8.

[4]. Atwood C, Eisenberg MS, Herlitz J, Rea TD. Incidence of EMS-treated out-of-hospital cardiac arrest in Europe. Resuscitation 2005;67:75–80.

[5]. Carew HT, Zhang W, Rea TD. Chronic health conditions and survival after out-of-hospital ventricular fibrillation cardiac arrest. Heart 2007;93:728–31.

[6]. Soholm H, Hassager C, Lippert F, Winther-Jensen M, Thomsen JH, Friberg H, et al. Factors associated with successful resuscitation after out-of-hospital cardiac arrest and temporal trends in survival and comorbidity. Ann Emerg Med 2015;65:523–31, e2.

[7]. Kleinman ME, Brennan EE, Goldberger ZD, Swor RA, Terry M, Bobrow BJ, et al. Part 5: adult basic life support and cardiopulmonary resuscitation quality: 2015 American Heart Association guidelines update for cardiopulmonary resuscitation and emergency cardiovascular care. Circulation 2015;132:S414–35.

[8]. Rea TD, Helbock M, Perry S, Garcia M, Cloyd D, Becker L, et al. Increasing use of cardiopulmonary resuscitation during out-of-hospital ventricular fibrillation arrest: survival implications of guideline changes. Circulation 2006;114:2760–5.

[9]. Dumas F, White L, Stubbs BA, Cariou A, Rea TD. Long-term prognosis following resuscitation from out of hospital cardiac arrest: role of percutaneous coronary intervention and therapeutic hypothermia. J Am Coll Cardiol 2012;60:21–7.

[10]. Perkins GD, Jacobs IG, Nadkarni VM, Berg RA, Bhanji F, Biarent D, et al. Cardiac Arrest and Cardiopulmonary Resuscitation Outcome Reports: Update of the Utstein Resuscitation Registry Templates for Out-of-Hospital Cardiac Arrest: A Statement for Healthcare Professionals From a Task Force of the International Liaison Committee on Resuscitation (American Heart Association, European Resuscitation Council, Australian and New Zealand Council on Resuscitation, Heart and Stroke Foundation of Canada, InterAmerican Heart Foundation, Resuscitation Council of Southern Africa, Resuscitation Council of Asia); and the American Heart Association Emergency Cardiovascular Care Committee and the Council on Cardiopulmonary, Critical Care, Perioperative and Resuscitation. Circulation 2015;132:1286–300.

[11]. Charlson ME, Pompei P, Ales KL, MacKenzie CR. A new method of classifying prognostic comorbidity in longitudinal studies: development and validation. J Chronic Dis 1987;40:373–83.

[12]. Ajam K, Gold LS, Beck SS, Damon S, Phelps R, Rea TD. Reliability of the cerebral performance category to classify neurological status among survivors of ventricular fibrillation arrest: a cohort study. Scand J Trauma Resusc Emerg Med 2011;19:38.

[13]. Phelps R, Dumas F, Maynard C, Silver J, Rea T. Cerebral performance category and long-term prognosis following out-of-hospital cardiac arrest. Crit Care Med 2013;41:1252–7.

[14]. van Buuren S. Multiple imputation of discrete and continuous data by fully conditional specification. Stat Methods Med Res 2007;16:219–42.

[15]. Seaman SR, White IR. Review of inverse probability weighting for dealing with missing data. Stat Methods Med Res 2013;22:278–95.

[16]. Rea TD, Pearce RM, Raghunathan TE, Lemaitre RN, Sotoodehnia N, Jouven X, et al. Incidence of out-of-hospital cardiac arrest. Am J Cardiol 2004;93:1455–60.

[17]. Terman SW, Shields TA, Hume B, Silbergleit R. The influence of age and chronic medical conditions on neurological outcomes in out of hospital cardiac arrest. Resuscitation 2015;89:169–76.

[18]. Beesems SG, Blom MT, van der Pas MH, Hulleman M, van de Glind EM, van Munster BC, et al. Comorbidity and favorable neurologic outcome after out-of-hospital cardiac arrest in patients of 70 years and older. Resuscitation 2015;94:33–9.