

Original Contributions

LONG-TERM SURVIVAL AFTER DROWNING-RELATED CARDIAC ARREST

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Abstract—Background: Long-term outcomes after drowning-related cardiac arrest are not well characterized. **Objective:** Our aims were to estimate long-term survival and identify prognostic factors in a large, population-based cohort of drowning victims with cardiac arrest. **Methods:** We conducted a population-based prospective cohort study (1974–1996) of Western Washington Drowning Registry (WWDR) subjects with out-of-hospital cardiac arrest and attempted professional resuscitation. The primary outcome was long-term survival through 2012. We tabulated Utstein-style exposure variables, estimated Kaplan-Meier curves, and identified prognostic factors with Cox proportional hazard modeling. **Results:** Of 2824 WWDR cases, 407 subjects (median age 17 years [interquartile range 3–33 years], 81% were male) were included. Only 54 (13%) were still alive after 1663 person-years of follow-up. Most deaths occurred after termination of initial resuscitation or during initial hospitalization. Risk of subsequent death after hospital discharge was 9.6 (95% confidence interval [CI] 5.7–15.9) per 1000 person-years. Long-term survival differed by Utstein variables (older age, illicit substance use, pre-drowning activity, submersion duration, cardiopulmonary resuscitation duration, intubation, defibrillation, and medications) and inpatient markers of illness severity (vital signs, Glasgow Coma Scale, laboratory values, shock). In adjusted analyses, older age (hazard ratio [HR] 1.01; 95% CI 1.01–1.02), epinephrine administration (HR 1.92; 95% CI 1.31–2.80), antiepileptic administration (HR 0.53; 95% CI 0.35–0.81), initial arterial pH (HR 0.49; 95% CI 0.26–0.92), and shock (HR 2.19; 95% CI 1.16–4.15) were

associated with higher risk of death. **Conclusions:** Most cases of drowning-related cardiac arrest were fatal, but survivors to hospital discharge had a low risk of subsequent death that was independently associated with older age and clinical evidence of shock. © 2019 Elsevier Inc. All rights reserved.

Keywords—drowning; cardiac arrest; mortality; long-term follow-up; national death index

INTRODUCTION

Nearly 400,000 annual deaths worldwide are from unintentional drowning, although this may underestimate true mortality because fatalities from floods, tsunamis, and water-transport accidents are not included in this estimate, and International Classification of Diseases (ICD) codes can misclassify drowning fatalities (1,2). Cardiac arrest complicates drowning in approximately 10% of cases, and survival estimates after drowning-related cardiac arrest range from 0% to 12% (3,4). Factors associated with short-term survival and favorable neurologic outcome after drowning-related cardiac arrest include younger age, witnessed event, brief submersion duration, salt-water drowning, brief emergency medical services (EMS) response interval, brief resuscitation

interval, and shockable initial cardiac rhythm (5–10). Although 1-month survival and 1-year survival (for pediatric cases only) are reported occasionally, most outcomes after drowning-related cardiac arrest are limited to hospital discharge (5–7). Long-term outcomes are poorly described, which poses challenges to providing accurate prognostic information to caregivers of drowned patients, understanding the true burden of injury, and informing policy interventions.

Using data from a large regional drowning registry, we estimated long-term survival in a cohort of drowning subjects with both cardiac arrest and attempted professional resuscitation. We hypothesized that subjects with features or sequelae of more severe drowning injury were less likely to survive.

METHODS

The Michigan State University Institutional Review Board approved this study.

Data Source

The Western Washington Drowning Registry (WWDR) is a large, regional, drowning registry containing subjects with fatal and nonfatal drowning in King, Pierce, and Snohomish counties in Washington State between January 1974 and July 1996, and has been described previously (11,12). These counties include the city of Seattle and contained 2,559,136 residents in 1990 (13). Their western border is a temperate coastline along the Pacific Ocean, and their eastern edge is the Cascade Mountains, which feed major rivers, tributaries, and hundreds of lakes. Briefly, investigators ascertained WWDR cases by searching for keywords and ICD-9 codes in investigative and autopsy reports of each county's medical examiner office, hospital records from all 26 acute care hospitals (including tertiary care centers, the regional children's hospital, and regional trauma centers), incident reports from the four regional EMS agencies, Washington State death certificates, and state civilian hospital discharges. Research personnel abstracted detailed data about subjects, drowning events, prehospital course, and hospital course from these sources.

Study Design and Population

This is a secondary analysis of a previously developed cohort of subjects experiencing a drowning event. All subjects with drowning-related cardiac arrest (receiving professional cardiopulmonary resuscitation [CPR] in the prehospital or emergency department [ED] settings) were included. We excluded subjects without attempted professional resuscitation, and those who received CPR

solely in the inpatient setting because other factors may have contributed to an in-hospital cardiac arrest.

Study Definitions and Outcomes

Drowning is defined as some degree of primary respiratory impairment from submersion or immersion in a liquid medium (14). Utstein-style guidelines catalogued and organized the exposure variables in this registry (14). We collected data on the subject (sex, age, ethnicity, date of incident, precipitating event), scene (witnessed event, body of water, bystander resuscitation, EMS involvement, prehospital interventions, prehospital neurologic status), ED course (vital signs, interventions, neurologic status), and hospital course (ventilation requirements, complicating illnesses, final neurologic status at discharge). In this registry, the original investigators graded neurologic status at hospital discharge with the Pediatric Cerebral Performance Category (PCPC), listing 1) normal, 2) mild impairment, 3) moderate impairment, 4) severe impairment, 5) vegetative state, or 6) death (12,15). Even though PCPC has not been rigorously tested in adults, it provides nearly identical definitions to the Cerebral Performance Category (CPC) when assessing neurologic impairment. PCPC distinguishes "mild disability" from "normal cerebral performance," whereas CPC combines these into one category.

Our primary outcome was all-cause long-term survival through 2012. Deaths after hospital discharge were determined by linking registry data to the National Death Index (NDI) (National Center for Health Statistics, Hyattsville, MD) using subjects' given names and surnames, middle initials (if known), birth dates, and sex (16). After a preliminary search to identify potential matches (at least one matching criterion), NDI uses a probabilistic matching system to generate final results and denote high-probability matched cases.

Statistical Analyses

We performed analyses with STATA, version 12.0 (Stata-Corp, College Station, TX) and SAS, version 9.4 (SAS Institute, Cary, NC). After tabulating Utstein exposure variables (patient characteristics, drowning case features, EMS evaluation/treatment, ED evaluation/treatment, and hospital course) according to outcomes, we tested for differences in long-term survival using χ^2 , rank-sum, and *t*-tests appropriate to each variable. We estimated long-term survival among all survivors after hospital discharge by constructing Kaplan-Meier curves, and stratified by a priori selected subject characteristics (age, sex, and functional status at hospital discharge). We evaluated factors associated with subsequent death using Cox proportional hazard modeling.

Table 1. Subject and Drowning Characteristics

Variables	Drowning-Related Cardiac Arrest (n = 407)	Survival to Hospital Admission (n = 215)	Long-Term Survival (n = 54)
Subject characteristics			
Age, years, median (IQR)	16.7 (3.0–33.2)	11.2 (2.5–28.6)	4.5 (2.0–21.3)
Male sex	298 (73.2)	151 (70.2)	36 (66.7)
Ethnicity			
White	328 (80.6)	171 (79.5)	41 (75.9)
Black	34 (5.4)	15 (7.0)	4 (7.4)
Hispanic/Latino	17 (4.2)	7 (3.3)	2 (3.7)
Asian/Pacific Islander	7 (1.7)	10 (4.7)	3 (5.6)
Native American	10 (2.5)	4 (1.9)	2 (3.7)
Other	6 (1.5)	8 (3.7)	2 (3.7)
Precipitating illicit substances	45 (11.1)	20 (9.3)	2 (3.7)
Pre-existing illness			
Seizure	2 (8.9)	23 (10.7)	3 (5.6)
Diabetes	5 (1.2)	2 (0.9)	0 (0)
Heart disease	28 (6.9)	10 (4.7)	1 (1.9)
Mental health	20 (4.9)	13 (6.1)	5 (9.3)
Pre-event neurologic function			
Normal	374 (91.9)	200 (93)	52 (96.3)
Mild impairment	6 (1.5)	3 (1.4)	0 (0)
Moderate impairment	4 (1.0)	3 (1.4)	1 (1.9)
Severe impairment	2 (0.5)	2 (0.9)	0 (0)
Scene characteristics			
Other person present	353 (86.7)	186 (86.5)	46 (85.2)
Witnessed event	123 (30.2)	49 (22.8)	11 (20.4)
Public location	68 (16.7)	31 (14.4)	5 (9.3)
Body of water			
Pool	91 (22.4)	51 (23.7)	14 (25.9)
Lake/pond	134 (32.9)	67 (31.2)	19 (35.2)
Ocean/sound	54 (13.3)	29 (13.5)	9 (16.7)
Irrigation ditch/canal	12 (3.0)	10 (4.7)	4 (7.4)
River/stream	45 (11.1)	22 (10.2)	5 (9.3)
Bath tub	50 (12.3)	19 (8.8)	3 (5.6)
Hot tub/spa	14 (3.4)	10 (4.7)	0 (0)
Other	7 (1.8)	7 (3.2)	0 (0)
Ice on water	2 (0.5)	1 (0.5)	0 (0)
Pre-drowning activity			
Swimming	84 (20.6)	37 (17.2)	4 (7.4)
Bathing	44 (10.8)	16 (7.4)	2 (3.7)
Diving	7 (1.7)	6 (2.8)	4 (7.4)
Scuba diving	20 (4.9)	8 (3.7)	2 (3.7)
Boating/floating	31 (7.6)	15 (7.0)	1 (1.9)
Fishing	10 (2.5)	4 (1.9)	1 (1.9)
Working	5 (1.2)	2 (0.9)	0 (0)
Wading	9 (2.2)	6 (2.8)	2 (3.7)
Not in water (e.g., fell in)	142 (34.9)	87 (40.5)	24 (44.4)
Driving car	17 (4.2)	8 (3.8)	4 (7.4)
Other	24 (5.9)	26 (12.1)	4 (7.4)
Submersion interval,* min, median (IQR)	12.5 (5–49)	10 (5–15)	5 (3–10)
Bystander resuscitation			
Bystander type	263 (64.6)	154 (71.6)	38 (70.4)
Lifeguard	21 (5.2)	11 (5.1)	3 (5.6)
Health care professional	21 (5.2)	13 (6.1)	7 (13.0)
Other adult	213 (52.3)	127 (59.1)	27 (50.0)
Type of bystander resuscitation			
Mouth to mouth	131 (32.2)	76 (35.4)	19 (35.2)
Basic CPR	95 (23.3)	68 (31.6)	19 (35.2)
Non-standard method	5 (1.2)	4 (1.9)	0 (0)

CPR = cardiopulmonary resuscitation; IQR = interquartile range.

Values are n (%) unless otherwise indicated.

* > 25% missing data.

Because factors that affect short-term survival after cardiac arrest may have blunted or opposite relationships with later survival, we used two separate adjusted models: an “initial

resuscitation” model and an “inpatient” model (17). The initial resuscitation model contained all subjects but did not adjust for inpatient variables. The inpatient model

Table 2. Prehospital and Emergency Department Clinical Data

Variables	Drowning-Related Cardiac Arrest	Survival to Hospital Admission (n = 15)	Long-Term Survival (n = 54)
Prehospital course (n = 407)			
Initial GCS,* median (IQR)			
Eye	1 (1–1)	1 (1–1)	1 (1–1)
Verbal	1 (1–1)	1 (1–1)	1 (1–1)
Motor	1 (1–1)	1 (1–1)	1 (1–1)
Total	3 (3–3)	3 (3–3)	3 (3–3)
Prehospital CPR	404 (99.3)	214 (99.5)	53 (98.2)
CPR duration,† min, median (IQR)	25 (14–35)	21 (13–34)	15 (8–25)
Prehospital intubation attempted	324 (79.6)	190 (88.4)	47 (87.0)
Shockable initial rhythm	39 (9.6)	19 (8.8)	3 (5.6)
Defibrillation	89 (21.9)	50 (23.3)	6 (11.1)
External pacing	10 (2.5)	6 (2.8)	0 (0)
Prehospital i.v.	322 (79.1)	192 (89.3)	49 (90.7)
Prehospital drugs†			
Epinephrine	238 (58.5)	140 (65.1)	26 (48.2)
Atropine	133 (32.7)	83 (38.6)	19 (35.7)
Calcium	52 (12.8)	28 (13.0)	5 (9.3)
Bicarbonate	181 (44.5)	110 (51.2)	28 (51.9)
Lidocaine	51 (12.5)	40 (18.6)	7 (13.0)
Norepinephrine	37 (9.1)	33 (15.4)	3 (5.6)
Glucose	66 (16.2)	44 (20.5)	7 (13.0)
ED course (n = 351)			
Initial vital signs			
Temperature,† °C, mean ± SD	32.2 ± 3.9	32.6 ± 3.0	32.7 ± 3.0
Heart rate, beats/min, median (IQR)	0 (0–90)	77 (0–105)	80 (60–106)
Systolic blood pressure, mm Hg, median (IQR)	0 (0–94)	80 (0–114)	99 (44–130)
Diastolic blood pressure,† mm Hg, median (IQR)	0 (0–3)	0 (0–70)	54 (0–92)
Respiratory rate,† breaths/min, median (IQR)	0 (0–0)	0 (0–0)	0 (0–18)
Initial GCS,* median (IQR)			
Eye	1 (1–1)	1 (1–1)	1 (1–1)
Verbal	1 (1–1)	1 (1–1)	1 (1–1)
Motor	1 (1–1)	1 (1–1)	1 (1–2)
Total	3 (3–3)	3 (3–3)	3 (3–4)
Initial laboratory values			
Arterial pH, mean ± SD	6.9 ± 0.3	7.0 ± 0.3	7.1 ± 0.3
Arterial pCO ₂ , median (IQR)	45 (29–75)	41 (27–66.5)	38 (26–52)
Arterial pO ₂ , median (IQR)	126 (51–329)	180 (69–381)	203 (72–381)
Resuscitative measures			
Intubated in ED	28 (7.9)	208 (96.7)	6 (11.1)
CPR	186 (53.0)	74 (38.1)	8 (14.8)
CPR duration, min, median (IQR)	30.5 (17–55.5)	30 (14–50)	41 (34–64)
Shockable initial rhythm†	124 (35.3)	119 (71.3)	37 (68.5)
Defibrillated	39 (11.1)	26 (13.5)	1 (1.9)
External pacing†	6 (1.7)	1 (0.5)	0 (0)
Pharmacotherapy			
Epinephrine	140 (39.9)	66 (34.2)	10 (18.5)
Atropine	100 (28.5)	60 (31.1)	13 (24.1)
Calcium	47 (13.4)	29 (15.2)	3 (5.6)
Bicarbonate	200 (57.0)	139 (72.4)	28 (51.9)
Glucose	132 (37.6)	95 (54.3)	19 (35.2)
Norepinephrine	61 (17.4)	53 (27.3)	8 (14.8)
Lidocaine	36 (10.3)	30 (15.7)	3 (5.6)
Steroids	28 (8.0)	26 (13.5)	4 (7.4)
Antibiotics	13 (3.7)	12 (6.2)	3 (5.6)
Antiepileptics	21 (6.0)	18 (9.5)	12 (22.2)

CPR = cardiopulmonary resuscitation; ED = emergency department; GCS = Glasgow Coma Scale; IQR = interquartile range; pCO₂ = partial pressure carbon dioxide; pO₂ = partial pressure oxygen; SD = standard deviation.

Values are n (%) unless otherwise indicated.

* Subjects with long-term survival did have higher GCS values in the upper quartile.

† > 25% missing data.

contained only subjects that survived to hospitalization and was further adjusted for inpatient variables. Univariate screening identified potentially significant predictors

($p \leq 0.20$) among 28 Utstein variables of interest (Tables 1–3). Backwards variable selection ($p \leq 0.20$ to enter; $p \leq 0.05$ to stay) developed the final multivariable Cox

Table 3. Inpatient Clinical Data

Variables	Survival to Hospital Admission (n = 215)	Long-Term Survival (n = 54)
Mechanical ventilation	207 (59.0)	48 (88.9)
Seizure*	59 (16.8)	11 (20.4)
Pneumothorax	40 (11.4)	8 (14.8)
Pulmonary edema	130 (37.0)	30 (55.6)
Shock	124 (35.3)	11 (20.4)
Disseminated intravascular coagulation	33 (9.4)	5 (9.3)
Dialysis	6 (1.7)	1 (1.9)
Vasopressors	120 (34.2)	13 (24.1)
Antibiotics	137 (39.0)	40 (74.1)
Steroids	54 (15.4)	16 (29.6)
Antiepileptic therapy	109 (31.1)	27 (50.0)
Barbiturate coma	15 (4.3)	3 (5.6)
ICP monitoring	39 (11.1)	10 (18.5)
Hospital length of stay, days, median (IQR)	4 (1–13)	16 (8–34)
Functional status at discharge		
Normal	22 (6.3)	18 (33.3)
Mild/moderate impairment	17 (4.8)	15 (27.8)
Severe impairment/vegetative state	30 (8.5)	20 (37.0)

ICP = intracranial pressure; IQR = interquartile range.
 Values are n (%) unless otherwise indicated.
 * > 25% missing data.

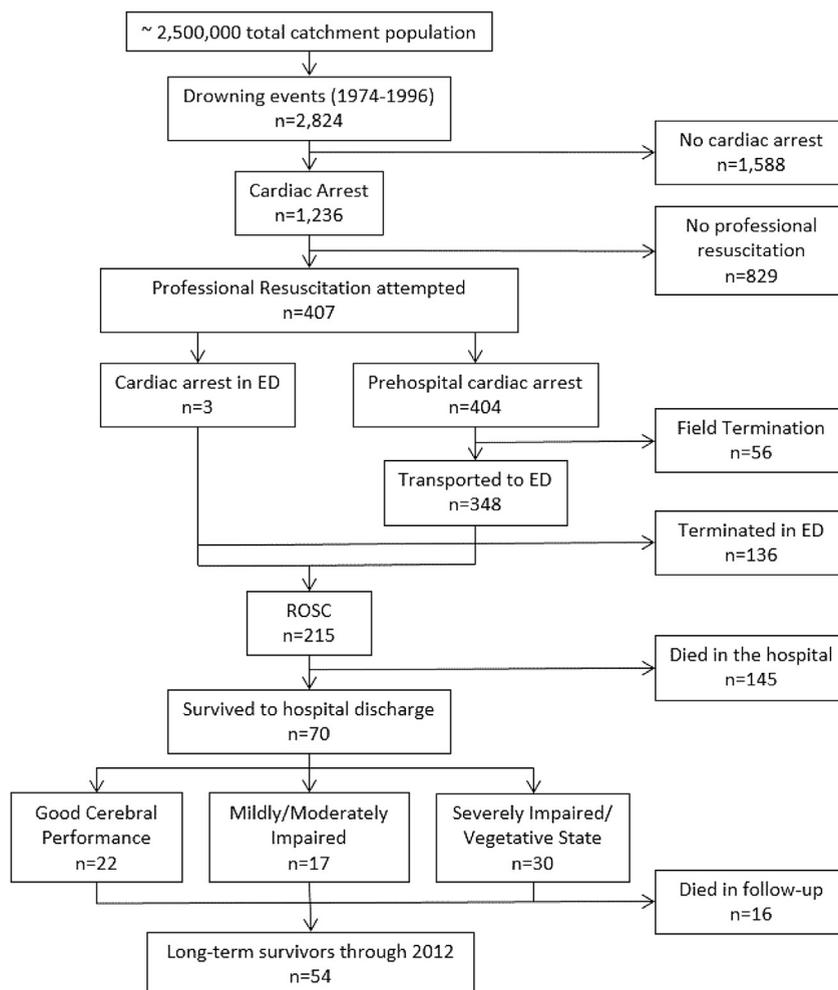


Figure 1. Study cohort and exclusions. ED = emergency department; ROSC = return of spontaneous circulation.

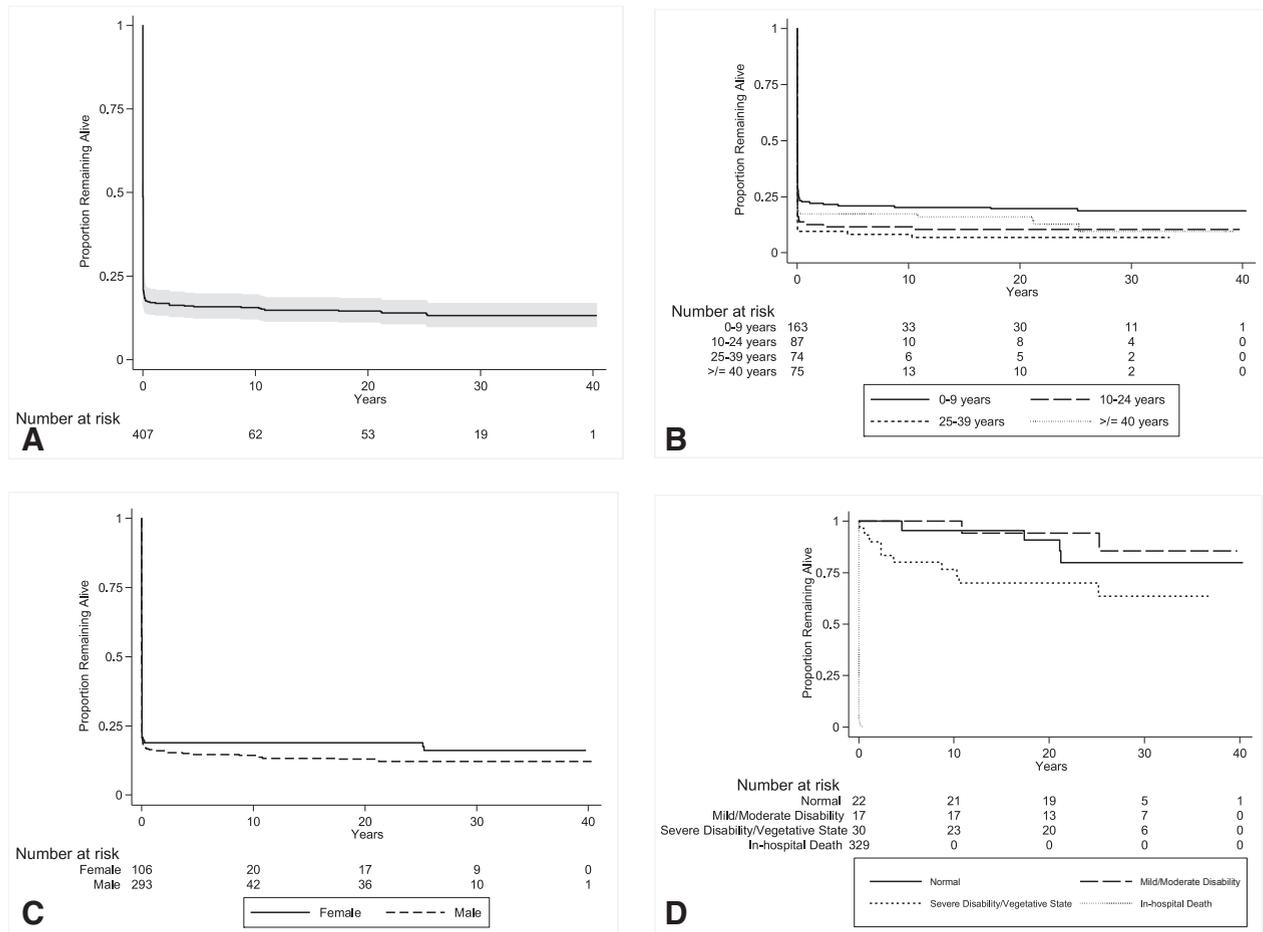


Figure 2. Kaplan Meier curves for long-term survival in whole cohort with 95% confidence interval (A), and stratified by age ($p = 0.001$) (B), sex ($p = 0.33$) (C), and functional outcome at hospital discharge ($p = 0.13$) (D).

models with those variables missing < 25% data. We assessed model fit with Harrell's *c*-statistic. Finally, we tabulated ICD codes listed as cause of death in NDI to discern whether the index drowning event was associated with specific causes of death or plausibly contributed to subsequent death.

RESULTS

Of 2824 subjects with drowning events, 1236 (44%) had drowning-related cardiac arrest. The final study cohort contained 407 (14%) subjects with attempted professional resuscitation (404 prehospital and 3 in the ED). Of these, 215 (53%) survived to hospital admission, 70 (17%) survived to hospital discharge, 39 (10%) survived to hospital discharge with favorable neurologic status, and 54 (13%) were still alive at long-term follow-up (Figure 1). The immediate case fatality rate (died prior to hospital admission) after drowning-related cardiac arrest was 83% (1021 of 1236) (95% confidence interval [CI] 80–85%) for all subjects, and 47% (192 of 407)

(95% CI 42–52%) for subjects with attempted resuscitation. The long-term mortality rate among those who survived to hospital discharge was 23% (16 of 70) (95% CI 13–34%).

Table 1 contains subject characteristics and drowning case features stratified by outcome. The study cohort was composed mostly of young (median age 17 years; interquartile range [IQR] 3–33 years) Caucasian (81%) males (73%) with normal pre-event neurologic function (92%) that drowned in summer months (46%) during the latter third of the registry (1990–1996) without a personal flotation device (99%). The events were usually unwitnessed (70%), in lakes/ponds (33%), but a bystander was typically present (87%) and performed some type of resuscitation intervention (65%). Table 2 contains prehospital and ED clinical data. EMS was uniformly summoned and most subjects (99%) received prehospital CPR (median 25 min; IQR 14–35 min), and prehospital intubation (80%). Few subjects had shockable initial cardiac rhythms (10%) or were defibrillated (22%). Epinephrine was the most common i.v. medication administered

Table 4. Univariate Cox Proportional Hazard Modeling for All-Cause Long-Term Mortality in the National Death Index

Variable	Hazard Ratio (95% CI)	p Value
Subject characteristics (n = 407)		
Age, years	1.01 (1.00–1.01)	0.03
Male sex	1.10 (0.87–1.40)	0.43
Drowning characteristics (n = 407)		
Witnessed drowning	1.28 (1.01–1.62)	0.04
Ice on water	1.01 (0.25–4.08)	0.98
Submersion interval,* min	1.002 (1.000–1.003)	0.02
Other person present	1.04 (0.73–1.45)	0.83
Personal flotation device	1.95 (0.62–6.11)	0.25
Bystander resuscitation	0.85 (0.67–1.08)	0.18
Prehospital course (n = 407)		
Attempted intubation	0.91 (0.64–1.23)	0.59
CPR duration, min*	1.01 (1.00–1.02)	<0.0001
Shockable initial rhythm	1.10 (0.77–1.56)	0.62
Epinephrine administered*	2.47 (0.67–3.34)	<0.0001
Prehospital ROSC	0.43 (0.32–0.59)	<0.0001
Emergency department course (n = 351)		
Body temperature, °C*	0.97 (0.93–1.01)	0.09
Glasgow Coma Scale	0.66 (0.52–0.85)	0.001
Arterial pH	0.29 (0.19–0.45)	<0.0001
Defibrillated	1.65 (1.16–2.34)	0.01
Epinephrine administered	2.01 (1.56–2.60)	<0.0001
Antiepileptics administered	0.24 (0.12–0.48)	<0.0001
Inpatient course (n = 215)		
Seizure*	0.99 (0.68–1.44)	0.97
Pneumothorax	1.06 (0.74–0.60)	0.68
Pulmonary edema	1.04 (0.75–1.44)	0.81
Shock	3.73 (2.60–5.37)	< 0.0001
Disseminated intravascular coagulation	1.37 (0.91–2.06)	0.14
Hemodialysis	1.02 (0.42–2.49)	0.96
Vasopressors	3.27 (2.30–4.65)	< 0.0001
Antiepileptic therapy	0.79 (0.57–1.08)	0.14
Barbiturate coma	0.89 (0.49–1.60)	0.69
Functional status at hospital discharge		
Normal	Reference	
Mild/moderate impairment	0.60 (0.11–3.30)	0.56
Severe impairment/vegetative state	2.18 (0.68–6.95)	0.19

CI = confidence interval; CPR = cardiopulmonary resuscitation; ROSC = return of spontaneous circulation.

* > 25% missing data.

(59%). In the ED, subjects were mildly hypothermic (mean temperature 32.2 ± 3.9°C), comatose (median Glasgow Coma Scale [GCS] 3), and acidemic (mean arterial pH 6.9 ± 0.3). Table 3 contains inpatient clinical data. During hospitalization, subjects manifested various sequelae of drowning-related cardiac arrest, including respiratory failure, lung injury, seizures, and shock.

Long-term survivors differed by subject characteristics (older age, use of illicit substances), drowning characteristics (pre-drowning activity, submersion duration), and clinical course (CPR duration, intubation, defibrillation, medications, initial vital signs, initial GCS, initial arterial blood gas, ongoing resuscitation in the ED, and subsequent shock). Interestingly, they did not differ in

Table 5. Adjusted Cox Proportional Hazard Modeling for All-Cause Long-Term Mortality in the National Death Index

Variable	Hazard Ratio (95% CI)	p Value
Age (years)	1.01 (0.99–1.02)	0.09
Witnessed drowning	1.43 (0.99–2.06)	0.05
ED Glasgow Coma Score	0.79 (0.62–1.02)	0.07
ED arterial pH	0.49 (0.26–0.92)	0.03
ED epinephrine administered	1.92 (1.31–2.80)	0.001
ED antiepileptics administered	0.32 (0.14–0.72)	0.01
Age (years)	1.01 (1.01–1.02)	0.03
Witnessed drowning	1.56 (0.96–2.53)	0.07
Bystander resuscitation	1.49 (0.90–2.47)	0.12
ED Glasgow Coma Scale	0.85 (0.66–1.08)	0.18
ED arterial pH	0.58 (0.27–1.26)	0.17
ED defibrillation	1.59 (0.92–2.75)	0.10
Inpatient shock	2.19 (1.16–4.15)	0.02
Inpatient vasopressors administered	2.01 (1.09–3.73)	0.03
Inpatient antiepileptics administered	0.53 (0.35–0.81)	0.003
Inpatient disseminated intravascular coagulation	0.66 (0.38–1.13)	0.13

CI = confidence interval; ED = emergency department.

submersion month, body of water, presence of ice in the water, personal flotation device, or bystander resuscitation (Tables 1–3).

Of the 70 subjects surviving to hospital discharge who were submitted to NDI, 16 (23%) with high probability of true match were classified as subsequent deaths beyond hospital discharge over 1663 person-years (mean duration 23.8 ± 10.2 years; range 0.1–40.3 years): 9.6 (95% CI 5.7–15.9) per 1000 person-years. Half of those 16 subsequent deaths occurred within the first 10 years after hospitalization. Older subjects were less likely to survive (p = 0.001), but we observed no difference by sex (p = 0.09) or neurologic status at hospital discharge (p = 0.13) (Figure 2). In post-hoc sensitivity analysis, after removing the aged older than 40 years quartile, subjects aged 25–39 years still had higher risk of long-term subsequent death (p < 0.001).

Tables 4 and 5 contain univariate and adjusted Cox proportional hazards models. In univariate analysis, older age, witnessed drowning, submersion duration, and clinical features (prehospital CPR interval, epinephrine administration, prehospital return of spontaneous circulation, initial GCS, initial arterial pH, shock, vasopressor administration, and antiepileptic medication administration) were each significantly associated with subsequent death. Given the larger proportion of missing data, submersion duration and CPR duration were excluded from the final models. Significant predictors of subsequent death in the final adjusted initial resuscitation model were initial arterial pH (HR 0.49; 95% CI 0.26–0.92), ED epinephrine administration (HR 1.92; 95% CI 1.31–2.80), and ED antiepileptic administration (HR 0.32; 95% CI 0.14–

0.72). Significant predictors of subsequent death in the final adjusted inpatient model were older age (HR 1.01; 95% CI 1.01–1.02), shock (HR 2.19; 95% CI 1.16–4.15), and inpatient antiepileptic administration (HR 0.53; 95% CI 0.35–0.81). The final models had acceptable fit (Harrell's *c*-statistic 0.77 and 0.78).

Supplementary Table 1 and Supplementary Figure 1 contain cause-specific mortality ICD codes. Median follow-up duration for 16 deceased subjects was 9.5 years (IQR 2.3–19.2 years). Causes of subsequent death were variable, but the most common categories were trauma (44%), cardiovascular disease (13%), drowning/submersion (13%), and liver disease (13%). Both subjects coded with “drowning” as cause of death died within 1 year of hospital discharge and had severe neurologic disability/vegetative state at discharge, suggesting that the initial drowning event may have been considered the cause of death.

DISCUSSION

In a large, regional drowning registry, only 13% of those with attempted professional resuscitation after drowning-related cardiac arrest survived more than 1600 person-years of follow-up. Of those who died, the vast majority occurred from termination of initial resuscitation efforts prior to hospital admission or during initial hospitalization; very few died after hospital discharge. In adjusted analysis, long-term survival was inversely associated with older age and clinical evidence of shock.

Strengths of our study include the size of the original cohort and length of follow-up. WWDR contains 2842 drowning subjects over a 22-year period, which is nearly twice as large as other large reported drowning cohorts (18,19). The subset of patients with drowning-related cardiac arrest is also larger than many previously reported cohorts (5,8,9). Our follow-up interval was 0.1–40 years, whereas the typical duration we found in the literature was 1 month and occasionally 1 year (5,6,10).

Other studies estimate 1-month survival from 1% to 28%, depending on subject age at the index cardiac arrest (5,6,9,10). One-year survival after pediatric drowning-related cardiac arrest approaches 20% and is primarily associated with shorter durations of CPR (7). A recent meta-analysis found that shorter submersion duration was most strongly associated with favorable outcomes, followed by shorter EMS response interval and salt-water (vs. fresh-water) exposure (20). Whereas the factors we identified in WWDR that were associated with subsequent death centered on older age and clinical markers of post-resuscitation shock (acidemia, additional epinephrine in the ED, and vasopressor administration). The association between increasing age and subsequent death may reflect propensity for comorbidities and less physiologic reserve,

or a simple function of normal aging. The association between clinical markers of post-resuscitation shock and subsequent death is a novel finding to the drowning literature, but carries face validity. We found an unexpected association between antiepileptic medication administration and lower risk of subsequent death that persisted in both adjusted models. Whether this is continuation of a subject's known antiepileptic medication or a new prophylactic or reactive therapy is unknown. Typically, we would expect reactive use of antiepileptic medications to be a surrogate for seizure and evidence of anoxic brain injury. Any prophylactic treatment of seizures could have been therapeutic or served as a marker for commitment to long-term care as opposed to withdrawal of life support. Alternatively, there may be an unknown mediating variable or this could be a coincidental association. Regardless, it requires further investigation before any substantive hypotheses can be generated.

The case fatality rate of drowning-related cardiac arrest with attempted professional resuscitation in the WWDR was 47% up to hospital admission and 83% up to hospital discharge. Drowning persons suffer aspiration, asphyxia, and associated hypoxemia with ultimate sequelae of unconsciousness, apnea, and cardiac arrest within minutes. Drowning-related cardiac arrest is typically asphyxial in nature and the initial cardiac rhythm is usually asystole or pulseless electrical activity (1). Occasionally, some other event (e.g., sudden cardiac death, traumatic injury, seizure) will precipitate drowning and contribute to the underlying pathophysiology. Resuscitation is complicated by risk of neurologic injury, unless environmental hypothermia affords some degree of neuroprotection by reducing brain metabolic activity. We do note an apparent non-statistical increase in long-term survival over the timeline of the drowning registry. This may reflect evolution in the treatment of cardiac arrest and post-resuscitation care. Unlike a recent study of hypothermic children post cardiac arrest from drowning, we have not found evidence in the WWDR for improved survival after drowning episodes during winter months, episodes with documented ice on the water, or episodes with lower water temperature (7,11). While bystander CPR has been associated with improved short-term outcomes, it was not associated with improved long-term survival in this cohort. This differential association with earlier vs. later outcomes has been demonstrated in observational studies of cardiac arrest (17). In other words, factors that affect short-term survival may have little or even opposite relationships with later death, whereas other factors that do not affect the initial resuscitation are associated with hazard of death after the initial phase of critical care (17).

It is difficult to infer from a single ICD code whether subsequent death was a direct consequence of the index

drowning event. Furthermore, coding data have limited precision in classifying disease and cause of death (21–23). Nevertheless, ICD code and the timing of death suggest an association with drowning, drowning-related complications, underlying medical condition, or risk-taking behavior that contributed to subsequent death (Supplementary Table 1 and Supplementary Figure 1).

The observed patterns of short-term and long-term survival in the WWDR cohort may differ in other regions. Nonetheless, the observed combination of high case fatality with low risk of subsequent death after index hospitalization in WWDR implies that prevention and mitigation of drowning injury are targets for improving clinical outcomes after drowning-related cardiac arrest. Short-term survival after drowning depends largely on the rapidity with which a person is removed from the water and resuscitated (24–26). The neutral trials of therapeutic hypothermia in pediatric subjects with cardiac arrest secondary to drowning emphasize the importance of early interventions that limit or, better yet, prevent anoxia (27). The World Health Organization recommends specific community-based actions and policies (controlled access to water, provision of safe places for young children, swimming and water safety education, bystander training in safe rescue, strengthening public awareness, safe boating regulations, managing flood risks, coordination of drowning prevention efforts, and development of a national water safety plan) to prevent drowning (24).

Limitations

Missing data were a limitation of our work (Tables 1 and 2), but we accounted for this to some degree by only including variables with lower prevalence of missing data (<25%) in the multivariable model. Furthermore, the majority of Utstein variables had low rates of missingness. Our primary outcome is subject to the accuracy of the NDI search, but NDI matching is an accepted method of ascertaining mortality in epidemiological research (28). NDI records include deaths associated with a state-issued death certificate, as well as those occurring outside the United States, provided the deceased is brought back to the United States for interment or cremation. The original investigators that established this registry used PCPC to classify neurologic outcome of all subjects at hospital discharge (12,15). As noted previously, PCPC has not been rigorously tested in adults, but provides nearly identical definitions to the CPC when assessing neurologic impairment. Most (52%) of the surviving cohort were under 18 years of age at the time of drowning. Finally, this study could not estimate long-term neurologic outcomes beyond hospital discharge.

Gross neurologic examination at the time of hospital discharge, especially in young children, may not reveal all the possible sequelae related to hypoxic brain injury (29). Suominen et al. found that 57% of 21 pediatric drowning survivors in Finland had some degree of dysfunction in long-term (median 8.1 years) neurocognitive outcomes (29). Moreover, 40% had low full-scale intelligence quotients (30).

CONCLUSIONS

In a large, regional drowning registry, half of all subjects experienced cardiac arrest. Among those with attempted professional resuscitation, the greatest risk of death occurred during initial resuscitation or index hospitalization. Risk of subsequent death was low beyond hospital discharge. Long-term survival was inversely associated with older age and clinical markers of shock. Replication of our findings in other populations is needed. The combination of high case fatality rate and low risk of subsequent death after drowning-related cardiac arrest supports implementation of drowning prevention measures. Epidemiological studies of long-term neurologic outcome after drowning-related cardiac arrest represent a large knowledge gap in the drowning literature.

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SUPPLEMENTARY DATA

Supplementary data related to this article can be found at <https://doi.org/10.1016/j.jemermed.2019.05.029>.

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ARTICLE SUMMARY

1. Why is this topic important?

At least 400,000 annual deaths worldwide are from unintentional drowning, and cardiac arrest complicates drowning in approximately 10% of cases. Survival estimates after drowning-related cardiac arrest range from 0% to 12%, but long-term outcomes are poorly described.

2. What does this study attempt to show?

This study attempts to estimate long-term survival in a large regional cohort of drowning subjects with both cardiac arrest and attempted professional resuscitation. It also attempts to determine factors associated with subsequent death.

3. What are the key findings?

Nearly half of subjects in a large regional cohort had drowning-related cardiac arrest, but 14% received attempted professional resuscitation. The immediate case fatality rate was substantial, but only 23% (95% CI 13–34%) of those subjects surviving to hospital discharge died during long-term follow-up (1663 person-years). In adjusted modeling, older age and indicators of shock were associated with subsequent death.

4. How is patient care impacted?

The observed pattern of high case fatality with low risk of subsequent death suggests that prevention and mitigation of drowning injury are the primary targets for improving clinical outcomes. The World Health Organization recommends specific community-based actions and policies to prevent drowning.