

Withdrawal of Life-Sustaining Therapy in Intensive Care Unit Patients Following Out-Of-Hospital Cardiac Arrest: An Australian Metropolitan ICU Experience

Nilesh Anand Devanand

drnileshanand@gmail.com

Northern Adelaide Local Health Network, Adelaide, Australia

Mohammed Ishaq Ruknudeen

Northern Adelaide Local Health Network, Adelaide, Australia

Natalie Soar

Northern Adelaide Local Health Network, Adelaide, Australia

Suzanne Edwards

University of Adelaide

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Abstract

Objective: To determine factors associated with withdrawal of life-sustaining therapy (WLST) in intensive care unit (ICU) patients following out-of-hospital cardiac arrest (OHCA).

Methods: A retrospective review of ICU data from patient clinical records following OHCA was conducted from January 2010 to December 2015. Demographic features, cardiac arrest characteristics, clinical attributes and targeted temperature management were compared between patients with and without WLST. We dichotomised WLST into early (ICU length of stay <72 hours) and late (ICU length of stay \geq 72 hours). Factors independently associated with WLST were determined by multivariable binary logistic regression using a backward elimination method, and results were depicted as odds ratios (OR) with 95% confidence intervals (CI).

Results: The study selection criteria resulted in a cohort of 260 ICU patients post-OHCA, with a mean age of 58 years and the majority were males (178, 68%); 151 patients (58%) died, of which 145 (96%) underwent WLST, with the majority undergoing early WLST (89, 61%). Status myoclonus was the strongest independent factor associated with early WLST (OR 38.90, 95% CI 4.55–332.57; $p < 0.001$). Glasgow Coma Scale (GCS) motor response of <4 on day 3 post-OHCA was the strongest factor associated with delayed WLST (OR 91.59, 95% CI 11.66–719.18; $p < 0.0001$).

Conclusion: The majority of deaths in ICU patients post-OHCA occurred following early WLST. Status myoclonus and a GCS motor response of <4 on day 3 post-OHCA are independently associated with WLST.

1. Introduction

Cardiac arrest is the single leading cause of death in Australia.¹ The Australian Resuscitation Outcomes Consortium (Aus-ROC) epidemiological registry² reported a crude incidence of 99.4 per 100,000 population of out-of-hospital cardiac arrest (OHCA) in 2015.³ Despite an overall decline in the cardiac arrest trends between 2010 – 2018, the annual incidences remains high at 57,000 cases per year.^{4,5} Generally, about 60% of OHCA patients admitted to the intensive care unit (ICU) remain comatose⁶ for more than 24 hours, of which two-thirds sustain hypoxic–ischaemic brain injury.^{1,7} However, only a minority of these patients die from brain death secondary to neuronal damage.⁸ Instead, a large proportion (about 80%)⁹ of deaths occur following early withdrawal of life-sustaining therapy (WLST) post-OHCA.¹⁰

WLST is a highly delicate and ethically complex process influenced by multiple clinical and non-clinical factors.¹¹ These variables often make neuroprognostication and WLST challenging, requiring concerted clinical and imaging assessments alongside numerous family discussions to make a timely, unified decision. Standard practices based on the Australian Resuscitation Council¹² and the European Society of Intensive Care Medicine¹³ prognostication guidelines advocate neuroprognostication after 72 hours of

arrest and at the very least 12 hours following cessation of sedation. Prior practices of targeted temperature management further complicated this process as it obscured the optimal timing of clinical assessments due to the effects of hypothermia on the clearance of sedatives.¹⁴ Additionally, family preferences, cultural beliefs and patients' own advance care directives add to the challenges of appropriate WLST.

The influence of these multiple factors can lead clinicians to prematurely define a patient's outcome earlier than the guideline-endorsed 72-hour period.¹⁵ A false impression of poor early neurological recovery inculcates the 'self-fulfilling prophecy' notion, which skews clinical perception for a meaningful outcome, inevitably leading to early WLST.^{16 17}

Strict guideline compliance in such multifaceted, complex situations is challenging. Awareness of WLST factors may provide clinicians an additional insight into the prognostication process, thus avoiding common trappings that traditionally lead to higher incidences of withdrawal and mortality rates. This renewed perspective allows intensivists to manoeuvre the post-cardiac phase confidently without being influenced by false-positive clinical findings while concurrently acknowledging predictors that signal poor outcomes.

In order to better understand this crucial facet of post-resuscitative care, we aimed to identify factors that predicted withdrawal of life sustaining therapy in the early and late phases following out-of-hospital cardiac arrest.

2. Methods

2.1 Study design and setting

This retrospective, single-centre, observational study was undertaken at Lyell McEwin Hospital in South Australia from January 2010 to December 2015. The Central Adelaide Local Health Network Human Ethics Committee approved this study with a waiver of consent (HREC/16/TQEH/17). Lyell McEwin is a major metropolitan public hospital that serves a population of approximately 450,000. The ICU accommodates 20 beds, with the ability to invasively ventilate 14 patients. It has an average annual admission of approximately 1600 patients, with an 80–90% bed occupancy rate.

2.2 Study variables and data collection

2.2.1 Inclusion and exclusion criteria

All adult patients (age ≥ 18 years) admitted to the ICU after the return of spontaneous circulation (ROSC) following cardiopulmonary resuscitation (CPR) for non-traumatic OHCA were included. In-hospital and paediatric (age < 18 years) cardiac arrest, along with patients with missing data on ROSC times, were excluded (Fig. 1). Patient selection were based on pre-defined criteria for in and out-of-hospital cardiac arrest (See 2.2.3 Definitions).

2.2.2 Data Collection

ICU data submitted to the ANZICS-APD, the hospital case mix and the coronary care database were utilised to screen and identify patients admitted to the ICU following OHCA. The ANZICS-APD remains one of the largest binational databases in the world, with contributions from 124 ICUs. It currently contains more than one million intensive care patient submissions collected from ICUs in Australia and New Zealand¹⁸.

We collected data on (1) patient demographics; (2) comorbidities (Charlson Comorbidity Index); (3) cardiac arrest characteristics (provision of bystander CPR, cardiac arrest precipitant, arrest causes [cardiac and non-cardiac], arrest rhythms [shockable (ventricular tachycardia [VT], ventricular fibrillation [VF]), non-shockable (pulseless electrical activity [PEA]) and asystole]), (4) duration of cardiac arrest (ROSC time, minutes); (5) targeted temperature management; and (6) neurology at hospital discharge (Cerebral Performance Category and end of life care [timings and tools used to determine neurological prognoses, such as brainstem reflexes (pupillary, corneal and cough reflex) and decision to withdraw life-sustaining treatment]) by reviewing patients' case notes. We also obtained data on the severity of illness (Acute Physiology and Chronic Health Evaluation [APACHE II]), mortality (ICU and hospital, hours), and length of stay (ICU and hospital) from the ANZICS-APD.

2.3 Definitions

We defined *OHCA* as cardiac arrest in (i) persons not occupying an in-patient hospital bed and/or (ii) persons in the Emergency Department (ED) who have not been formally assessed and admitted by the medical team¹⁹. *WLST* was defined as the cessation of life-sustaining treatment in the form of termination of inotrope and/or vasopressors and/or ventilatory support²¹. *Early WLST (EWLST)* was defined as the withdrawal of life-sustaining treatment within 72 hours following OHCA⁸. Conversely, *late WLST (LWLST)* was defined as withdrawing life-sustaining therapy at or after 72 hours post-ICU admission⁸. *Cardiac cause of cardiac arrest* was defined as cardiac arrest secondary to a primary cardiac-related disease, including myocardial infarction, arrhythmia, cardiomyopathies and cardiogenic pulmonary oedema²². *Non-cardiac cause of cardiac arrest* was defined as cardiac arrest not related to cardiac disease, including but not limited to causes such as trauma, sepsis, exsanguination, drug overdose, metabolic disorders and endocrinopathies²². *ROSC* was defined as the resumption of normal heart rhythm with a detectable pulse¹⁹.

2.4 Objectives

The primary objective was to determine the factors associated with WLST in post-resuscitated OHCA ICU patients. The secondary objectives were to compare the demographic features, cardiac arrest characteristics, clinical attributes and targeted temperature management between patients with and without WLST.

2.5 Statistical analysis

The proportion of patients undergoing WLST was given as frequency (percentage). Continuous data were reported as mean with standard deviation (SD) or median with interquartile range (IQR) and were compared between WLST groups by the Student's *t*-test or Mann–Whitney *U*-test, depending on the normality of the variable. Categorical data were reported as frequency (percentage) and groups were compared using the Chi-square test or Fisher's exact test, as appropriate. Initially, multivariable binary logistic regressions were used for all data to investigate the association between WLST and eleven *a priori* predictors, including ICU LOS (binary). Backward elimination was performed by eliminating the variables with the highest *p*-value one model at a time until all *p*-values were less than 0.5 (Harrell 2015)²³.

Then, multivariable binary logistic regression was used for data relating to ICU length of stay <72 hours to investigate the association between WLST and ten *a priori* predictors by performing backward elimination once again. For data relating to ICU length of stay ≥72 hours (delayed WLST), brain stem reflexes on days 2 and 3 post-cardiac arrest were removed due to collinearity, and then backward elimination was performed.

A Hosmer–Lemeshow goodness-of-fit test was performed for all three final models. A *p* value of ≤0.05 was considered to be statistically significant. All statistical analyses were performed using SAS, version 9.4 (SAS Institute Inc., Cary, NC, USA).

3. Results

3.1 Derivation of the study cohort

During the study period, 346 patients with cardiac arrest were admitted to the ICU, including 77 with IHCA and 269 with OHCA. Overall, 17 patients were excluded because of lack of ROSC times, out of which 9 were from the OHCA cohort. The final study cohort that was analysed consisted of 260 OHCA patients (Fig. 1).

3.2 Patient characteristics

The mean age was 58 years (SD = 17), with most patients (156, 60%) being less than 65 years old. Most of the patients were male (178, 68%). There were 109 patients (42%) who survived hospital discharge. Of the 151 patients who died, 145 (96%) died following WLST, including 89 patients (61%) within the first 72 hours of ICU admission—the 'early' cohort. Cardiac causes accounted for the majority of OHCA (141/260, 54.5%), with myocardial infarction as the leading cause. Asphyxia and pneumonia were the major non-cardiac causes of OHCA (Table 1 and 2).

The non-shockable cohort accounted for 52% of the 260 patients enrolled in the study. Of these, 26% of PEA patients and 41% of the asystole group underwent WLST. In contrast, most patients from the shockable group (78/125, 68%) did not receive WLST (Table 3).

3.3 Withdrawal of life-sustaining treatment

Patients in whom life-sustaining treatment was withdrawn had higher severity of illness scores on admission than survivors (mean (SD) APACHE II score 35 (7) vs. 29 (8); $p < 0.001$) (Table 2). They also had longer median arrest times before ROSC than survivors (27 (IQR 19–40) vs. 16 (IQR 11–26) minutes; $p = 0.006$) (Table 3).

Out of the 260 patients in the study cohort, 161 (62%) received targeted temperature management, of which a target of 32–34°C and 34–36°C were given to 91 (35%) and 70 (27%), respectively. There was no association between WLST and targeted temperature management. However, the median duration of core body temperature $>36^{\circ}\text{C}$ in the first 24 hours post-OHCA was higher in the non-withdrawal group compared to those sustaining WLST (10 (IQR 1–18) vs. 3.5 (IQR 0–12) hours; $p < 0.001$) (Additional File 1).

Although the overall proportion of WLST remained relatively the same over the study period, the gap between early and late WLST widened (Fig. 2). Interestingly, the trend of hospital death appeared to decline with an increased proportion of survivors, which is both unexpected and challenging to explain (Fig. 3).

3.4 Multivariable analysis for WLST

3.4.1 Total cohort

Out of the study cohort of 260 patients, age (OR 1.03, 95% CI 1.01–1.06; $p=0.01$), ROSC time (OR 1.04, 95% CI 1.01–1.07; $p = 0.003$), APACHE II score (OR 1.07, 95% CI 1.02–1.13; $p = 0.005$), absent brainstem reflexes on day 1 post-OHCA (OR 13.12, 95% CI 4.14–41.54; $p < 0.001$), non-shockable rhythm (OR 4.10, 95% CI 1.41–11.94; $p = 0.01$) and status myoclonus (OR 20.86, 95% CI 5.47–79.56; $p < 0.001$) were independently associated with WLST, adjusting for all other covariates in the model (Table 4).

3.4.2 Early WLST

For patients with ICU length of stay <72 hours, ROSC time (OR 1.05, 95% CI 1.01–1.09; $p = 0.01$), APACHE II score (OR 1.09, 95% CI 1.01–1.16; $p = 0.02$), absent brainstem reflexes on day 1 post-OHCA (OR 18.47, 95% CI 3.53–96.64; $p = 0.001$), status myoclonus (OR 38.9, 95% CI 4.55–332.57; $p = 0.001$) and non-shockable rhythm (OR 3.22, 95% CI 1.06–9.82; $p = 0.04$) were independently associated with early WLST, adjusting for all other covariates in the model (Table 4). The factors related to WLST were identical in the total cohort and the early WLST cohort, albeit differences in the effect size (Table 4).

3.4.3 Late WLST

For patients with ICU length of stay ≥ 72 hours, age (OR 1.06, 95% CI 1.00 - 1.12; $p=0.03$) and Glasgow Coma Scale (GCS) motor response of <4 (OR 91.59, 95% CI 11.66–719.18; $p < 0.001$) was independently associated with late WLST, adjusting for all other covariates in the model (Table 4).

4. Discussion

Based on our research, WLST factors can be broadly categorised into: *neurological* (status myoclonus, brain stem reflexes and motor response of GCS) and *non-neurological* (age, ROSC time, non-shockable rhythm, APACHE II score) factors. Within the early cohort, we found a combination of neurological and non-neurological factors to be associated with WLST. The mortality following these withdrawals was due to cardiovascular instability and multiorgan failure. Conversely, in the late cohort, we noted GCS motor response <4 as the main factor for WLST, possibly due to sustained hypoxic brain injury.

In our study, most of the analysed patient cohort underwent WLST (145/260, 55%), with 61% having an ICU length of stay less than 72 hours. We noted WLST was responsible for 151/260 (58%) deaths in patients admitted following OHCA. Within that cohort, 96% of the patients died following early WLST. The significant mortality outcome confirms previously published evidence of the role of WLST as a common mode of death in OHCA patients.⁸ In comparison to previous research by Albaeni et al.⁸ in the United States in 2014, our study reported higher rates of WLST and mortality.

The key to explain this discrepancy required us to retrospectively review the growing research of withdrawal practices that occurred between 2006 and 2015.^{13,27} Parallel with these developments were serial updates on therapeutic hypothermia, which at that time showed significant improvement in neurologic function and survival.^{25,28} Despite these developments, the striking outcome in our study was that the majority of patients had life support withdrawn outside of current recommended guidelines. Firstly, the high proportion of post-OHCA mortality from early withdrawal was likely a consequence of unstandardized withdrawal practices. Treating intensivists may have applied their own professional judgement and actioned what was thought to be the most appropriate treatment for the patient. Secondly, many of these patients received therapeutic hypothermia, which is known to confound early clinical assessments.²⁹

Unfortunately, the combined effect of the above factors led to the creation of the '*self-fulfilling prophecy*' which falsely predicts poor outcome, thus leading to high early withdrawal rates. This phenomenon explains the differences in our withdrawal rates, with the absence of brainstem reflexes and status myoclonus driving this decision-making. We conclude that the lack of a protocolised withdrawal model with ever-changing recommendations on therapeutic hypothermia resulted in an array of individualised treatments rather than a standardised approach.

A resounding theme from previously published research, including ours, highlights one foundational concept—that WLST and neuroprognostication are inherently connected,³⁰ and the association resembles a cause-and-effect relationship. Repeatedly, multiple studies have shown poor neuroprognostication practices (*cause*) lead to higher rates of WLST³¹ (*effect*). This relationship was illustrated in our study, wherein of 67 patients with absent brainstem reflexes on day 1 post-OHCA, 93% underwent early WLST. This trend continued on days 2 and 3 post-arrest, with 100% of the patients with absent brainstem reflexes having their care withdrawn. This striking observation raises a crucial point: Survival outcome

determined solely by neurological examination using brainstem reflexes within 72 hours led to early WLST, with a high mortality outcome.³⁰

A common presenting feature following cardiac arrest is post-hypoxic myoclonus status epilepticus (MSE). This occurrence has historically been viewed as a marker of poor prognosis.³⁵ Our data confirms this with a strong association of withdrawal, especially within 72 hours of cardiac arrest. However, contrary to the perception of MSE as an 'agonal phenomenon', recent research³⁵ has shown some good outcomes following post-arrest myoclonus. These conflicting outcomes raise an essential question: Should status myoclonus be viewed as a clinical sign of futility? Recent advances in phenotyping practices with electroencephalography have significantly influenced patients' management and survival rates with status myoclonus. Good outcomes have also been associated with ICU length of stay of ≥ 8 days,³⁵ in contrast to our patient cohort with MSE, which had withdrawal of care within 72 hours. Hence, we believe that status myoclonus should not be viewed as a poor prognostic sign at face value until appropriately stratified.

The challenges of WLST further continue with the incorporation of targeted temperature management. Having undergone large serial trials, the targeted temperature management practices continue to evolve from the proposed adoption of 33–36°C²⁵ and, most recently, to normothermia²⁶ with the avoidance of fever. Although these hypothermic practices did not increase the likelihood of withdrawal in our study, we found a longer duration of exposure to hypothermia led to a higher incidence of WLST. This correlation confirms prior pharmacokinetics research on the delayed clearance of sedative medications due to hypothermia.³⁴

Overall, the clinical implications of these factors steer intensivists to form pessimistic clinical perceptions, thus leading them to arrive at hasty decisions on patients' survival outcomes. This '*self-fulfilling prophecy*' is now a widely recognised conundrum that bridges poor and untimely neuroprognostication practices with withdrawal of life support. Acknowledging the presence of this intrinsic clinical bias is vital. Only then can these patients undergo rigorous objective evidenced-based assessments and outcomes determined on the merits of their actual neurological status.

4.1 Limitations

Our study has several significant limitations. The first major limitation was its single-centre, retrospective design, which culminated in a small sample size. Second, the data collected from 2010 to 2015 may not be reflective of recent clinical practices. Third, our review did not include and thus lacked data on patients' advanced care directives. Additionally, it was evident from our clinical records review that there was a lack of protocolised management for WLST. Fourth, in versus out-of-hospital cardiac arrest definitions remain controversial and lack universal consensus³⁶. Different definitions can potentially alter the sample sizes of both populations, thus risking misrepresentations of the case-mix. In order to prevent enrolment bias from misclassification, we delineated these two cohorts with a clear and sensible definition of ours. Lastly, there were challenges with extracting information from the patients' case notes.

Some of the sought-after variables were not legible, inaccurately documented or missing entirely. These made the abstracting process difficult as the required information had to be sourced from other avenues, such as ICU charts, ED documentation and discharge summaries.

5. Conclusion

Early WLST is a significant contributor to OHCA deaths. From our analysis, APACHE II score, status myoclonus, absent brainstem reflexes on day 1 post-cardiac arrest, non-shockable rhythm and prolonged ROSC time predict early withdrawal of care. Future research incorporating post-OHCA patients receiving normothermia and undergoing protocolised neuroprognostication, considering other variables such as advance care directives, family wishes and cultural variances, may more accurately capture the actual proportions of patients receiving withdrawal of care and their predictors in these current times of intensive care practice.

Declarations

Conflicts of Interest

Nilesh Anand Devanand, Mohammed Ishaq Ruknudeen, Natalie Soar and Suzanne Edwards declare they have no conflict of interest.

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Ethics Approval and Consent to Participate

Our manuscript does not report on an investigational therapy, nor does it involve using animal or human tissue in any experiment. The study site human and ethics committee has reviewed the study protocol along with its annual progress and has approved the study to proceed as planned.

Consent for Publication

We have obtained publication consent from the ethics committee.

Availability of Data and Material

Data are available on request.

Authors' Contributions

NA collected the patients' data by reviewing clinical records and ICU charts, and prepared the manuscript. IR performed the preliminary statistical analysis and provided intellectual input in finalising the manuscript. NS assisted with data collection and administrative affairs related to this study. All of the above authors were collectively involved in the study design, protocol development and data management. SE performed and finalised the statistical analysis of our data. All authors have read and approved the final manuscript.

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Tables

Table 1: Cardiac arrest aetiologies for the OHCA cohort ($n = 260$)

Aetiologies	<i>n</i> (%)
Cardiac	141 (54.5)
Acute coronary syndrome	101 (38.9)
STEMI	95 (36.6)
NSTEMI	6 (2.3)
Cardiomyopathy ^a	18 (7)
Arrhythmias	16 (6.2)
Ischaemic heart disease	3 (1.2)
Cardiogenic APO	1 (0.4)
Others	2 (0.8)
Right atrial mass	1 (0.4)
Cor pulmonale secondary to PAH	1 (0.4)
Non-cardiac	119 (45.5)
Asphyxia	26 (10.2)
Hanging	17 (6.6)
Acute asthma	5 (2.0)
Choking	3 (1.2)
Angioedema	1 (0.4)
Pneumonia	25 (9.9)
Community acquired pneumonia	16 (6.3)
Hypoxic respiratory failure	6 (3.2)
Aspiration pneumonia	2 (0.8)
Drug overdose	12 (4.8)
Sepsis syndromes	11 (4.3)
Septic shock	5 (2.0)
Sepsis	4 (2.0)
Urosepsis	2 (0.8)
Acute exacerbation of COPD	8 (3.1)
CNS diseases	6 (2.4)

Stroke	3 (1.2)	
Intracranial bleed	3 (1.2)	
Haemorrhagic Shock	4 (2.4)	
Endocrine disorders		3 (1.2)
DKA	1 (0.4)	
Hypoglycaemia	2 (0.8)	
Dyselectrolytaemia		3 (1.2)
Hyperkalaemia	2 (0.8)	
Hypokalaemia	1 (0.4)	
Others		6 (2.4)
Chronic liver disease	2 (0.8)	
Chronic renal failure	1 (0.4)	
Bowel ischaemia	1 (0.4)	
Multiple myeloma	1 (0.4)	
Alcohol-withdrawal seizures	1 (0.4)	
Self-harm (lacerations)	1 (0.4)	
Unknown		11 (4.2)

Note: OHCA = out-of-hospital cardiac arrest; STEMI = ST elevation myocardial infarction; NSTEMI = non-ST elevation myocardial infarction; APO = acute pulmonary oedema; PAH = pulmonary arterial hypertension; COPD = chronic obstructive airway disease; DKA = diabetic ketoacidosis.

^a: includes all forms of cardiomyopathies.

Table 2: Baseline characteristics of the patients in the WLST vs. non-WLST groups

Clinical characteristics	Total cohort (<i>n</i> = 260)	WLST		<i>p</i> -value
		Yes (<i>n</i> = 145)	No (<i>n</i> = 115)	
Age, mean (SD), years	58 (17)	59 (18)	56 (16)	0.13**
Age group ^a				0.005
<65 years	156 (60)	76 (52)	80 (70)	
≥65 years	104 (40)	69 (48)	35 (30)	
Gender (male)	178 (68)	98 (67)	80 (70)	0.73
Charlson Comorbidity Index grade ^b				0.05
No comorbidities	68 (26)	36 (25)	32 (28)	
Grade 1	80 (31)	36 (25)	44 (38)	
Grade 2	91 (35)	59 (40)	32 (28)	
Grade 3	21 (8)	14 (10)	7 (6)	
APACHE II score, mean (SD)	32 (8)	35 (7)	29 (8)	<0.001**
Length of stay				
ICU, median (IQR), hours	51 (28-88)	52 (27-86)	48 (28-92)	0.81***
Hospital, median (IQR), hours	96 (48-240)	72 (48-96)	240 (144-360)	<0.001
ICU <72 hours	165 (63)	89 (61)	76 (66)	0.43**
Neurological characteristics				
Status myoclonus	54 (1)	51 (35)	3 (3)	<0.001*
Absent brainstem reflexes				
Day 1 post-CA	67 ^a (27)	62 (45)	5 (4)	<0.001
Day 2 post-CA	38 ^b (18)	38 (34)	0	<0.001*
Day 3 post-CA	26 ^c (16)	26 (18)	0	<0.001*
Motor response <4 day 3 post-CA	66 ^d (39)	63 (80)	3 (3)	<0.001*
Brain dead	28 (11)	28 (19)	0	<0.001*
Hospital discharge alive	109 (42)	0	109 (95)	<0.001*
Hospital death	151 (58)	145 (96)	6 (4)	

Note: All results are *n* (%) unless otherwise specified. WLST = withdrawal of life-sustaining therapy; APACHE = Acute Physiology and Chronic Health Evaluation; CA = cardiac arrest.

^{a,b,c,d}: the missing values for the neurological characteristics were due to the patients' death and therefore could not be measured = 8, 48, 95, 91, respectively.

* Fisher's exact test *p*-value; ** independent *t*-test *p*-value; *** Wilcoxon rank-sum test *p*-value

Table 3: Cardiac arrest characteristics of the WLST vs. non-WLST groups

Cardiac arrest characteristics	Total cohort (<i>n</i> = 260)	WLST		<i>p</i> -value
		Yes (<i>n</i> = 145, 56%)	No (<i>n</i> = 115, 44%)	
Provision of bystander CPR	149 (57)	81 (56)	68 (59)	0.60
Initial cardiac arrest rhythm				
Pulseless VT	7 (3)	2 (1)	5 (4)	<0.001
VF	119 (46)	46 (32)	73 (63)	
PEA	64 (25)	38 (26)	26 (23)	
Asystole	70 (27)	59 (41)	11 (10)	
Shockable	125 (48)	47 (32)	78 (68)	<0.001
OHCA aetiology				
Acute myocardial infarction	100 (40)	49 (35%)	51 (46%)	0.08
Hypoxia	68 (27)	50 (36%)	18 (16%)	0.001
Cardiac cause of OHCA	138 (53)	66 (45)	72 (63)	0.006
ROSC time, median (IQR), min	23 (15-32)	27 (19-40)	16 (11-26)	<0.001***

Note: All results are *n* (%) unless otherwise specified. WLST = withdrawal of life-sustaining therapy; CPR = cardiopulmonary resuscitation; VT = ventricular tachycardia; VF = ventricular fibrillation; PEA = pulseless electrical activity; OHCA = out-of-hospital cardiac arrest; ROSC = return of spontaneous circulation.

*** Wilcoxon rank-sum test *p*-value.

Table 4: Predictors of WLST: Multivariable binary logistic regression

Sample	Predictor	Comparison	Odds ratio* (95% CI)	DF	Chi-square	p-value
All patients						
	Age (years)	Per 1 year increase	1.03 (1.00–1.06)	1	5.23	0.02
	APACHE II score	Per 1 unit increase	1.08 (1.02–1.14)	1	8.02	0.005
	BSR D1 post-CA	Absent vs Present	11.99 (3.85–37.36)	1	18.35	<0.001
	Bystander CPR	Yes vs No	1.31 (0.60–2.86)	1	0.48	0.49
	Cardiac cause of arrest	Cardiac vs Non-cardiac	1.97 (0.58–6.74)	1	1.17	0.28
	Hypoxic arrest	Yes vs No	2.86 (0.91–8.94)	1	3.26	0.07
	ICU length of stay	<72 hours vs ≥72 hours	0.58 (0.27–1.25)	1	1.92	0.17
	Myoclonic jerks	Yes vs No	23.13 (6.00–89.11)	1	20.83	<0.001
	Total downtime	Per 1 minute increase	1.04 (1.01–1.07)	1	8.46	0.004
	Sex	Male vs Female	1.55 (0.65–3.66)	1	0.99	0.32
	Shockable rhythm	Non-shockable vs shockable	4.21 (1.39–12.70)	1	6.48	0.01
ICU LOS < 72 hours						
	Age (years)	Per 1 year increase	1.02 (0.98–1.05)	1	1.07	0.30
	APACHE II score	Per 1 unit increase	1.09 (1.01–1.16)	1	5.58	0.02
	BSR D1 post-CA	Absent vs Present	18.47 (3.53–96.64)	1	11.92	0.001
	Myoclonic jerks	Yes vs No	38.90 (4.55–332.57)	1	11.18	0.001
	Total downtime	Per 1 minute increase	1.05 (1.01–1.09)	1	6.52	0.01

Shockable rhythm	Non-shockable vs shockable	3.22 (1.06–9.82)	1	4.22	0.04
ICU LOS ≥ 72 hours					
Age (years)	Per 1 year increase	1.06 (1.00–1.12)	1	4.54	0.03
APACHE II score	Per 1 unit increase	1.10 (0.95–1.28)	1	1.56	0.21
BSR D1 post-CA	Absent vs Present	6.55 (0.97–44.28)	1	3.71	0.05
Bystander CPR	Yes vs No	2.86 (0.59–13.90)	1	1.70	0.19
Cardiac cause of arrest	Cardiac vs Non-cardiac	3.27 (0.26–40.97)	1	0.84	0.36
Hypoxic arrest	Yes vs No	7.59 (0.73–78.40)	1	2.89	0.09
Motor response	<4 vs ≥4	91.59 (11.66–719.18)	1	18.46	<0.001
Myoclonic jerks	Yes vs No	5.18 (0.62–43.04)	1	2.32	0.13
Sex	Male vs Female	0.25 (0.03–1.85)	1	1.83	0.18
Shockable rhythm	Non-shockable vs shockable	2.23 (0.27–18.37)	1	0.55	0.46

Note: APACHE = Acute Physiological and Chronic Health Evaluation; BSR = brainstem reflex; CA = cardiac arrest; CPR = cardiopulmonary resuscitation; LOS = length of stay; ICU = intensive care unit.

*Modelling the probability that WLST = 'Yes'

Figures

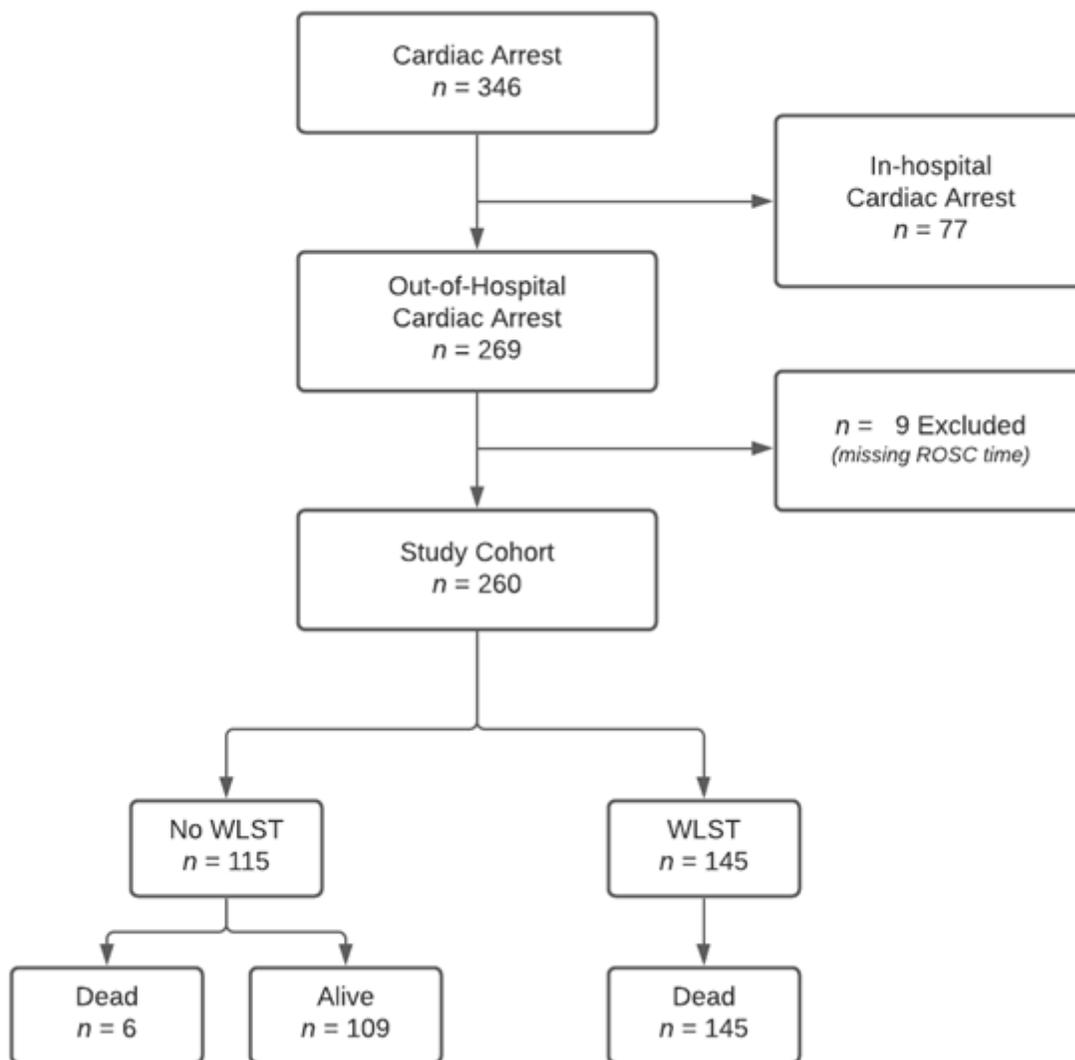


Figure 1

Study flow chart. WLST = withdrawal of life-sustaining therapy; ROSC = return of spontaneous circulation.

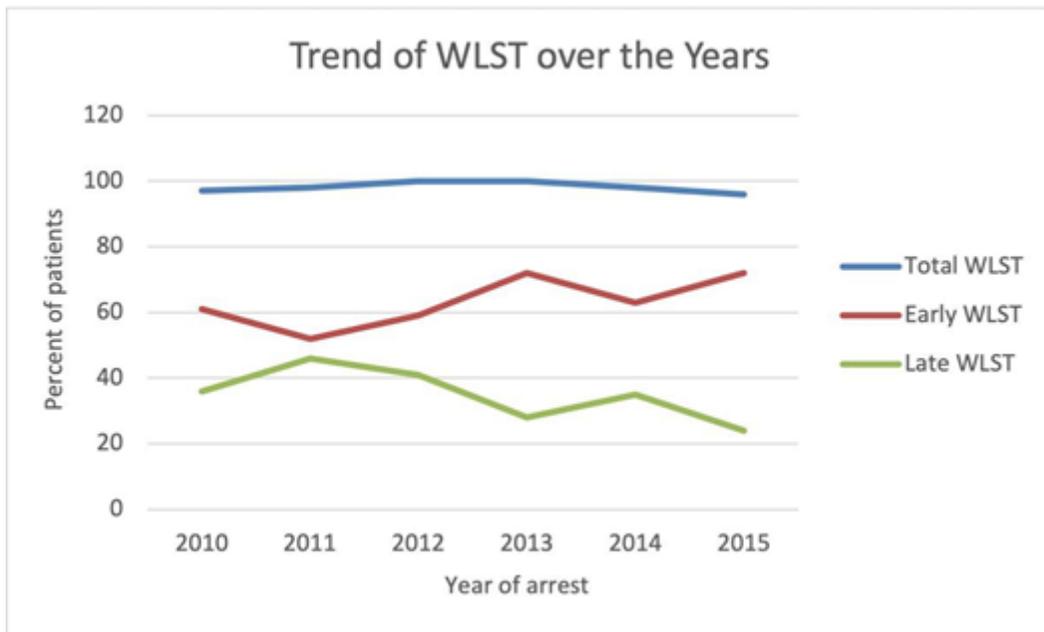


Figure 2

The graph above demonstrates the trend of total, early and late WLST from 2010 to 2015.

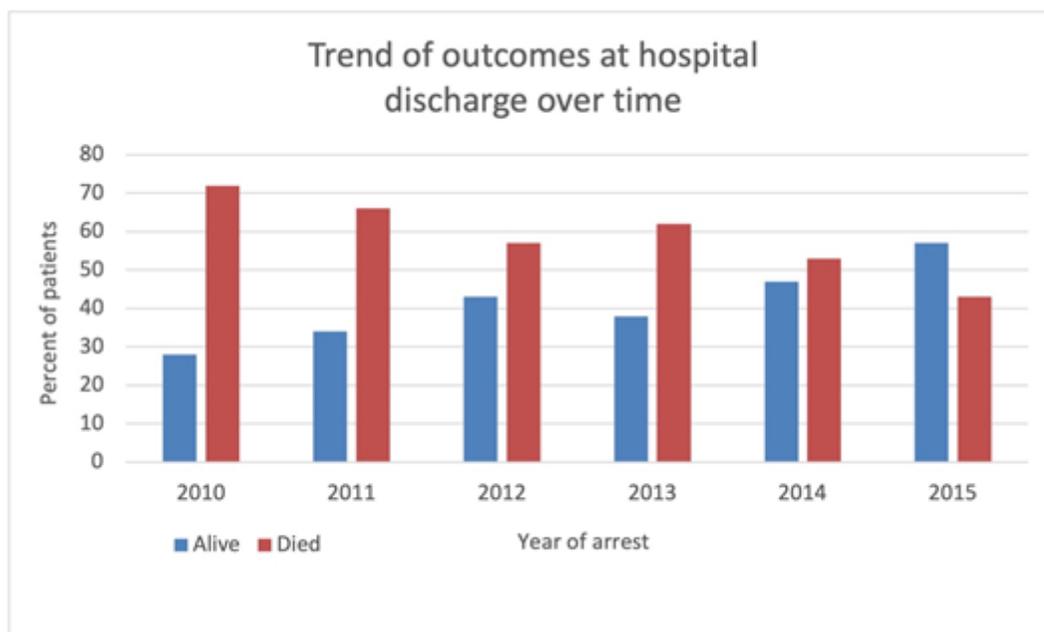


Figure 3

The graph above demonstrates the trend of outcomes at hospital discharge from 2010 to 2015.

Supplementary Files

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