Can Heparin Improve Clinical Outcomes in Cardiac Arrest? A Retrospective Cohort Study from the EICU Collaborative Research Database

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Research

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Abstract

Background: Studies indicate that heparin can improve survival in patients with out-of-hospital cardiac arrest. Thus, we aimed to investigate the effect of heparin on hospitalized patients with cardiac arrest.

Methods: Clinical data of cardiac arrest patients from the eICU Collaborative Research Database V2.0 were retrospectively analyzed. We compared neurological prognosis and primary outcomes in a heparin group that received unfractionated heparin or low molecular weight heparin with a non-heparin group. Additionally, we compared the two heparin sub-groups.

Results: After propensity score matching, there were 673 patients in the heparin group and 1346 patients in the non-heparin group. The Glasgow Coma Scale score was significantly better in the heparin group ($P<0.05$). There were no significant differences in terms of spontaneous respiratory function recovery, dementia, or vegetative state between the two groups ($P>0.05$). Intensive care unit (ICU) mortality and hospital mortality rates were significantly lower in the heparin group ($P<0.05$). The duration of mechanical ventilation, length of stay in ICU, and length of stay in hospital were significantly longer in the heparin group ($P<0.05$). Median survival time was significantly longer in the heparin group ($P<0.001$). In the comparison of patients who received unfractionated heparin and low molecular weight heparin (267 in each group), there were no significant differences in Glasgow Coma Scale score, ICU mortality, hospital mortality, or median survival time between the two groups ($P>0.05$).

Conclusions: Heparin administration may be beneficial in reducing the mortality rate and prolonging the survival time of in-hospital patients with cardiac arrest. It may also improve the prognosis of neurological function to a certain extent. Outcomes were not significantly different between patients who received unfractionated heparin and those who received low molecular weight heparin.

Background

Cardiac arrest is a common and lethal condition frequently encountered by emergency medicine providers. Achieving improvements in survival rates and good neurological outcomes remains a challenge [1]. There have many studies on drug therapy for cardiac arrest; however, currently there exists a lack of drugs with definite efficacy for improving the prognosis of neurological function and clinical outcomes in patients with cardiac arrest [2–5].

Animal studies have shown that cardiac arrest is accompanied by extensive microthrombosis in the brain [6]. Clinical reports suggest that thrombosis is often seen in the heart, pulmonary vessels, and other areas in a cardiac arrest [7–9]. Coronary thrombosis and pulmonary embolism are also common causes of cardiac arrest [10, 11]. Furthermore, current guidelines recognize thrombosis as a potential (and reversible) cause of cardiac arrest [12]. Moreover, hypothermia and hypercoagulability are common pathophysiological processes following cardiac arrest [13, 14]. Therefore, treatment of the coagulation state and thrombosis may become one of the effective measures for the treatment of cardiac arrest.

Thrombolytic is not overly recommended and routine used in cardiac arrest [15, 16], with the difficulty in determining early etiology, inability of thrombolytic therapy in improving survival, and the increased risk of bleeding events being the main reasons [9, 15]. However, anticoagulant therapy is considered to be associated with significantly fewer bleeding-related complications than thrombolytic therapy [17]. Animal experimental studies have shown that heparin anticoagulant therapy can significantly improve the prognosis of cardiopulmonary resuscitation model rats [18]. Moreover, small retrospective studies have shown that aspirin and heparin (AH) can significantly improve survival in patients with out-of-hospital cardiac arrest [19, 20]. Therefore, we aimed to establish whether heparin anticoagulant

therapy can improve the prognosis of patients' neurological function and the patients' clinical outcomes. This study retrospectively analyzed the relationship between the use of unfractionated heparin (UFH) or low molecular weight heparin (LMWH) in patients with cardiac arrest from a multicenter electronic intensive care unit (ICU) database, and to explore patient prognosis and the prospect of the clinical application of heparin in these patients.

Materials And Methods

Study design and database

We conducted a retrospective cohort study using the eICU-CRD V2.0 database. Because all patient records in this database are anonymous, the Review Committee of this study determined that there was no need to obtain informed consent from individual patients. The eICU-CRD V2.0 database was released on 17 May 2018. The database contains clinical data from 200,859 patients in multiple ICUs in the United States between 2014 and 2015. In this study, the corresponding author completed the training on 'Protection of Human Subjects' and obtained permission to use the database (certification number: 36026306). The study was approved by the Research Ethics Committee of Wuxi People's Hospital (KS202112).

Study subjects

All subjects were derived from the eICU-CRD V2.0 database. The inclusion criteria were: (1) Age ≥ 18 years and (2) a diagnosis of cardiac arrest. The exclusion criteria were: (1) missing information on one of sex, age, height, weight, acute physiology and chronic health evaluation score (APACHE-IV), initial simplified acute physiology score (SAPS-II), or Glasgow Coma Scale (GCS) score; and (2) lack of information on ICU and discharge outcomes. Admission venues included emergency department, floor, operation room, and direct admission. Therefore, both in- and out-of-hospital cardiac arrest events were included.

Data extraction

All data in this study were extracted from the database using Structured Query Language (SQL) scripts and *Navicat for PostgreSQL* (11.2.9) software [21]. The extracted variables included: (1) baseline characteristics: sex, age, height, weight, APACHE IV, SAPS Ⅱ score, GCS score, race, type of ICU; (2) diagnosis, initial rhythm types, witnessed or not, and whether or not 15 min have passed before CPR was started; (3) treatment status, including the application of various vasoactive drugs, mechanical ventilation and length, acute renal failure (ARF), and hemodialysis; (4) neurological outcomes, including the highest GCS score, change in mental status, encephalopathy (post-anoxic), seizures, dementia, persistent vegetative state, ventilation (spontaneous-adequate); and (5) mortality and length of stay (LOS), including the status of ICU discharge, LOS in ICU, the status of hospital discharge, and LOS in hospital.

Statistical analysis

Continuous variables that were normally distributed were described as mean ± standard deviation (SD), comparison between the two groups was performed using the independent sample t-test, and comparison among multiple groups was performed using an analysis of variance (ANOVA). Counting data and classification variables were described by frequency and percentage, and a chi-square test was used for comparison between these groups. To reduce the confounding influence of the differences in baseline characteristics, propensity score matching (PSM) (1:2 in heparin group and non-heparin group, 1:1 in UFH and LMWH) was performed using 'nearest neighbor' matching, with a caliper width of 0.02 across sex, age, BMI, APACHE-Ⅳ, SAPS-Ⅱ, initial heart rhythm, and the presence of witnesses. A Kaplan-Meier survival curve (log rank method) was used to evaluate the difference in survival time between the two groups. A significance level was set at 0.05 (for a two-tailed analysis). All analyses were performed with the use of IBM SPSS

Statistics software (version 26.0; IBM Corp., Armonk, NY, USA), and R software (version 2.15.3; The R Foundation for Statistical Computing, Vienna, Austria) was used for PSM.

Results

Patient characteristics

A total of 5995 patients were studied, including 4890 in the non-heparin group and 1105 in the heparin group (755 in the UFH group and 350 in the LMWH group) (Fig. 1). ANOVA showed that there were no significant differences in age, sex, GCS score, presence of a witness, CPR time, or mechanical ventilation among the three groups (all $P > 0.05$). BMI, APACHE-Ⅱ, APS-Ⅲ, race, type of ICU, initial rhythm, vasopressor, and the incidence of ARF and hemodialysis were significantly different (all $P < 0.05$). In the heparin and non-heparin groups, which were matched 1:2 (673 cases for heparin group and 1346 cases for the non-heparin group), there were no significant differences between the two groups in terms of age, sex, BMI, severity of the disease, initial rhythm, witnesses, vasopressor used, ARF, or rate of hemodialysis (all $P > 0.05$) (Table 1).

Table 1
Demographic characteristics and basic characteristic

Variables	Before PSM				After PSM		
	non-Heparin N = 4890	UFH N = 755	LMWH N = 350	*P value*	non-Heparin N = 1346	Heparins N = 673	*P* value
Age(years), mean ± sd	63.44±15.44	63.55±14.81	63.26±14.92	0.88	63.38±14.94	63.42±15.22	0.95
Sex(male), n (%)	2874(58.77)	452(59.87)	198(56.57)	0.63	802(59.58)	397(58.99)	0.79
BMI (kg/m2), mean ± sd	28.67 ± 10.62	30.17 ± 10.01	29.78 ± 11.49	< 0.001	30.35 ± 8.37	30.59 ± 8.86	0.56
Disease severity scores (worst within 24 hours), mean ± sd							
APACH-IV	97.03 ± 7.67	93.47 ± 36.19	89.21 ± 4.15	< 0.001	92.9 ± 37.27	94.14 ± 35.26	0.48
APS-II	85.73 ± 6.41	81.99 ± 34.86	77.31 ± 3.06	< 0.001	81.29 ± 6.82	82.6 ± 34.68	0.44
GCS	6.22 ± 4.31	6.39 ± 4.34	6.77 ± 4.41	0.12	9.77 ± 4.5	9.83 ± 4.31	0.62
Ethnicity, n (%)				< 0.001			< 0.001
African American	652(13.33)	122(16.16)	1(0.29)		177(13.15)	128(19.02)	
Asian	73(1.49)	16(2.12)	10(2.86)		15(1.11)	7(1.04)	
Caucasian	3605(73.72)	523(69.27)	232(66.29)		1024(76.08)	463(68.8)	
Hispanic	164(3.35)	46(6.09)	33(9.43)		36(2.67)	37(5.5)	
Native American	40(0.82)	3(0.4)	1(0.29)		13(0.97)	4(0.59)	
Other/Unknown	356(7.28)	45(5.96)	16(4.57)		81(6.02)	34(5.05)	
Initial rhythm, n (%)				0.003			0.07
Asystole	484(9.9)	92(12.19)	38(10.86)		133(9.88)	58(8.62)	
PEA	842(17.22)	179(23.71)	74(21.14)		211(15.68)	134(19.91)	
VF	500(10.22)	140(18.54)	58(16.57)		184(13.67)	133(19.76)	
VT	256(5.24)	70(9.27)	11(3.14)		138(10.25)	70(10.4)	
unknown	170(3.48)	28(3.71)	10(2.86)		48(3.57)	24(3.57)	
Witnessed, n (%)				0.22			0.53

Abbreviations: UFH = Unfractionated heparin, LMWH = Low molecular weight heparin, PSM = Propensity Score Match, BMI = body mass index, APACHE-IV: acute physiology and chronic health evaluation score, APS-II = simplified acute physiology score, GCS = Glasgow Coma Score, MV = Mechanical ventilation, PEA = pulseless electrical activity, VF = ventricular fibrillation, VT = ventricular tachycardia, CPR = cardiopulmonary resuscitation, AMI = acute myocardial infarction, ARF = acute renal failure, DVT = deep vein thrombosis

Variables	Before PSM				After PSM		
	non-Heparin N = 4890	UFH N = 755	LMWH N = 350	*P value*	non-Heparin N = 1346	Heparins N = 673	*P* value
witnessed, < 15 min CPR	1190(24.34)	278(36.82)	104(29.71)		317(23.55)	209(31.05)	
witnessed, > 15 min CPR	446(9.12)	84(11.13)	34(9.71)		97(7.21)	64(9.51)	
un-witnessed	246(5.03)	40(5.3)	19(5.43)		75(5.57)	39(5.79)	
Vasopressor, n (%)	2035(41.62)	337(44.64)	120(34.29)	0.005	695(51.63)	333(49.48)	0.36
Early Defibrillation, n (%)	129(2.64)	17(2.25)	7(2.00)	< 0.001	32(2.38)	12(1.78)	0.389
AMI, n (%)	111(2.27)	31(4.11)	3(0.86)	< 0.001	29(2.15)	19(2.82)	0.353
MV, n (%)	3652(74.68)	567(75.1)	264(75.43)	0.93	974(72.36)	543(80.68)	< 0.01
ARF, n (%)	988(20.2)	192(25.43)	67(19.14)	0.003	287(21.32)	166(24.67)	0.10
Dialysis, n (%)	526(10.76)	109(14.44)	27(7.71)	0.001	131(9.73)	83(12.33)	0.08
DVT prophylaxis	2380	680	311	< 0.001	980	620	< 0.001
Drug therapy	0	359	175	-	0	368	-
Compression devices	2380	256	111	< 0.001	980	252	< 0.001
Dialysis	526	109	27	0.001	131	83	0.08

Abbreviations: UFH = Unfractionated heparin, LMWH = Low molecular weight heparin, PSM = Propensity Score Match, BMI = body mass index, APACHE-IV: acute physiology and chronic health evaluation score, APS-II = simplified acute physiology score, GCS = Glasgow Coma Score, MV = Mechanical ventilation, PEA = pulseless electrical activity, VF = ventricular fibrillation, VT = ventricular tachycardia, CPR = cardiopulmonary resuscitation, AMI = acute myocardial infarction, ARF = acute renal failure, DVT = deep vein thrombosis

Clinical outcomes between heparin and non-heparin groups

Neurological prognosis

The heparin group was significantly better than the non-heparin group for three measures: the maximum GCS score, various GCS scores (motor, verbal, and eyes), and GCS score classification (the degree of consciousness disturbance (13–15 was mild, 9–12 was moderate, and 3–8 was severe) ($P < 0.05$). The incidence of changed mental status, encephalopathy (post-anoxic), seizures, and the duration of mechanical ventilation were higher in the heparin group than in the non-heparin group ($P < 0.05$). There was no significant difference in the incidence of ventilation (spontaneous-adequate), dementia, or persistent vegetative state ($P > 0.05$) (Table 2).

Table 2
Clinical outcomes between Heparins and non-Heparins, UFH and LMWH.

Clinical outcomes	Heparins N = 673	non-Heparins N = 1346	*P* value	UFH N = 267	LMWH N = 267	*P* value
GCS (max), mean ± sd	11.89 ± 4.4	11.29 ± 4.75	0.007	12.06 ± 4.48	11.96 ± 4.16	0.81
GCS (motor), mean ± sd	5.02 ± 1.73	4.75 ± 1.94	0.003	5.02 ± 1.79	5.13 ± 1.6	0.51
GCS (verbal), mean ± sd	3.59 ± 1.81	3.39 ± 1.87	0.025	3.72 ± 1.78	3.53 ± 1.81	0.28
GCS (eyes), mean ± sd	3.43 ± 1.12	3.24 ± 1.24	0.001	3.39 ± 1.15	3.49 ± 1.06	0.38
GCS 13–15, n (%)	422(62.7)	792(58.84)	0.041	147(55.06)	135(50.56)	0.21
GCS 9–12, n (%)	67(9.96)	153(11.37)		18(6.74)	29(10.86)	
GCS 3–8, n (%)	161(23.92)	395(29.35)		48(17.98)	50(18.73)	
Mental status changed, n (%)	226(33.58)	327(24.29)	< 0.001	65(24.34)	118(44.19)	< 0.001
Encephalopathy (post-anoxic), n (%)	86(12.78)	108(8.02)	0.001	19(7.12)	47(17.6)	< 0.001
Seizures, n (%)	92(13.67)	71(5.27)	< 0.001	23(8.61)	51(19.1)	< 0.001
Dementia, n (%)	6(0.89)	11(0.82)	0.86	2(0.75)	4(1.5)	0.41
Persistent vegetative state, n (%)	15(2.22)	20(1.49)	0.23	5(1.87)	6(2.25)	0.76
Ventilation (Spontaneous-adequate), n (%)	392(58.25)	779(57.88)	0.87	166(62.17)	161(60.3)	0.66
Ventilation LOS (days), mean ± sd	6.04 ± 6.05	4.63 ± 4.63	< 0.001	5.26 ± 4.46	6.36 ± 6.39	0.021
ICU mortality, n (%)	209(31.05)	503(37.37)	0.005	78(29.21)	86(32.21)	0.45
ICU LOS (days), mean ± sd	7.07 ± 8.38	4.94 ± 5.8	< 0.001	5.94 ± 5.41	7.29 ± 9.85	0.05
Hospital mortality, n (%)	272(40.42)	622(46.21)	0.013	100(37.45)	115(43.07)	0.19
Hospital LOS (days), mean ± sd	12.25 ± 11.12	9.47 ± 9.74	< 0.001	10.37 ± 9.01	12.36 ± 11.58	0.027

Abbreviations: UFH = Unfractionated heparin, LMWH = Low molecular weight heparin, GCS = Glasgow Coma Score, LOS = Length of stay, ICU = Intensive care unit

Mortality and LOS

The ICU mortality rate (31.05% vs. 37.37%, P = 0.005) and hospital mortality rate (40.42% vs. 46.21%, P = 0.013) in the heparin group were significantly lower than that in the non-heparin group (P < 0.05). However, the LOS was significantly longer in the heparin group compared to the non-heparin group for mechanical ventilation LOS (4.63 ± 4.63 days vs. 6.04 ± 6.05 days, P < 0.001), ICU LOS (4.94 ± 5.80 days vs. 7.07 ± 8.38 days, P < 0.001), and total hospital LOS (9.47 ± 9.74 days vs. 12.25 ± 11.12 days, P < 0.001) (Table 2).

Clinical outcomes in UFH and LMWH

The UFH group and LMWH group were matched 1:1 according to sex, age, BMI, APACHE-Ⅱ, and SAPS-Ⅱ. Finally, 267 pairs of patients were successfully matched.

Neurological prognosis

There was no statistical significance in the maximum GCS score, various GCS scores, and GCS classification between the two groups (P > 0.05). The incidence of changed mental status, encephalopathy (post-anoxic), seizures, and the duration of mechanical ventilation were significantly higher in the LMWH group than in the UFH group (P < 0.05). There was no significant difference in the incidence of ventilation (spontaneous-adequate), dementia, or persistent vegetative state (P > 0.05) (Table 2).

Mortality and LOS

There were no significant differences in ICU mortality (29.21% vs. 32.21%, P = 0.45), ICU LOS (5.94 ± 5.41 days vs. 7.29 ± 9.85 days, P = 0.05), and hospitalization mortality (37.45% vs. 43.07%, P = 0.19) between the UFH and LMWH groups. The LOS for mechanical ventilation (5.26 ± 4.46 days vs. 6.36 ± 6.39 days, P = 0.021) and hospital LOS (10.37 ± 9.01 days vs. 12.36 ± 11.58 days, P = 0.027) were significantly shorter in the UFH group compared to the LMWH group, as shown in Table 2.

Survival time

The median survival time of the heparin group (20.75 ± 2.37 days) was longer than that of the non-heparin group (14.63 ± 1.26), and this difference was significant (P < 0.001). There was no statistically significant difference in the median survival time between the UFH group (20.96 ± 5.09 days) and the LMWH group (19.54 ± 3.73 days) (P = 0.89), as shown in Fig. 2.

Discussion

In this study, patients in the heparin group had significantly improved neurological outcomes (GCS score), ICU mortality, hospital mortality, and survival time compared with those in the non-heparin group. There was no significant difference in the prognosis of some neurological outcomes (spontaneous-adequate ventilation, dementia, and persistent vegetative status). There was no significant difference between the UFH group and the LMWH group for these clinical outcomes.

The study cohort was from a United States database. Data show that approximately 30–40% of hospitalized cardiac arrest patients die in the ICU and 40–50% die in the hospital, which is consistent with previous reports [1, 20]. Because the guidelines do not recommend heparin for the treatment of cardiac arrest, only 18.43% (1105 patients) in this cohort received heparin for a variety of reasons, and UFH use was about twice as high as LMWH use. In a retrospective study of 384 patients by Grabmaier and his colleagues, the use of AH in patients with out-of-hospital cardiac arrest improved survival from 34–59.4%. AH was found to be an independent predictor of discharge survival in the regression model (hazard ratio 0.60 [0.44–0.82], P = 0.002) [20]. In this study, the survival rate of the control group was 44.79%, higher than that of the placebo group in the previous study by Grabmaier, and the final discharge survival rate of the heparin group was 59.58%, which was similar to that of the AH group in the Grabmaier study. Although some studies have suggested that the combination of anticoagulant and antiplatelet is not necessary for most situations, the combination of the two studies suggests that the combination of anticoagulant and antiplatelet may improve patient and clinical outcomes. If the treatment levels in the two studies were similar, aspirin's

contribution to survival would be about 10%, and heparin's contribution to survival would be about 15%, without taking into consideration any cross-actions. More rigorous prospective, double-blind, crossover studies are needed to further clarify the separate effects of aspirin and heparin and whether there is a synergistic interaction between them. In addition, the current study found that heparin significantly extended the survival time of patients with cardiac arrest, which has not been reported in previous studies; however, heparin patients also had longer hospital stays.

Neurological outcome is another important clinical outcome in patients with cardiac arrest. The maximum GCS score during the disease was used to evaluate the patient's state of consciousness. Both the mean value of the maximum GCS and the mean value of each item (motor, verbal, or eyes) were better in the heparin group. A stratified GCS analysis also showed that the heparin group had a higher ratio of good cerebral performance (GCS score of 13–15) (62.7% vs. 58.84%). Moreover, Grabmaier's research showed that pre-hospital AH administration was associated with favorable neurological outcomes (odds ratio [OR] 2.25 [1.31–3.87], P = 0.003). Patients with AH were more likely to gain return of the spontaneous circulation (OR 2.22 [1.45–3.42], P < 0.001) [19]. However, it was also found that the incidence of changed mental status, encephalopathy (post-anoxic), seizures, and the duration of mechanical ventilation was longer in the heparin group. This may be associated with an increase in the survival rate of patients who do not have a good neurological outcome under current treatment but whose prognosis is clearly better than that of death.

As common anticoagulants, in addition to large differences in molecular weight, UFH and LMWH also have large differences in terms of mechanism of action, pharmacokinetics, and risk of adverse reactions [22]. UFH can act on variety of thrombin enzymes and can also act on platelets, which have a shorter half-life, lower bioavailability, and pose a higher risk of bleeding [23]. To further determine whether there is a difference between the two types of heparin, we investigated their effects on clinical outcomes. The results showed that there was no significant difference in the major clinical and neurological outcomes between the two groups. However, UFH was associated with a tendency towards lower ICU and hospital mortality rates compared to LMWH. The same trend was observed for GCS scores. Whether this trend is related to the antiplatelet effect of ordinary heparin needs further study. Because we did not analyze bleeding-related complications, it is unclear whether the common heparin group had a higher risk of bleeding. However, Grabmaier's study showed that AH did not increase the risk of bleeding in patients with cardiac arrest [19].

Animal studies have shown that a marked activation of blood coagulation occurs and that microthrombi are found in the cerebral vessels after a cardiac arrest of 5 to 10 min [18]. Microthrombosis, microcirculation disorder, secondary tissue ischemia and hypoxia, and oxygen metabolism disorder followed by a series of nerve cell injury are some of the important influences on the neurological prognosis of cardiac arrest [24–26], and the formation of systemic microthrombosis is also an important mechanism affecting tissue oxygen metabolism and organ function damage [25]. Resolving the influence of microthrombosis on various organs of cardiac arrest may be an important mechanism for heparin to improve the prognosis of cardiac arrest patients. In addition, the cause of cardiac arrest in most patients is related to thrombosis of blood vessels in the heart or lungs [11]. Furthermore, the anticoagulant and antiplatelet effects of heparin have a good effect on the improvement of heart or pulmonary vascular infarction. Cardiac arrest is not a contraindication to the use of heparin in clinical practice; however, the occurrence of bleeding complications is a concern. Interestingly, some studies have shown that heparin does not significantly increase the risk of bleeding in cardiac arrest [27, 28].

Our study had some limitations. First, heparin may be used for hemodialysis, thrombosis, hemodynamic monitoring, hypercoagulability, or disseminated intravascular coagulation; as this study was limited by data extraction, we could not analyze the reasons for administration of heparin. Second, when heparin anticoagulants are used for different

reasons, the frequency, dose, and cycle of medication vary greatly; hence, the total dose of each sample was difficult to obtain, and the dose-response analysis was limited. Third, due to data limitations, we could not determine which bleeding complications were causally associated with heparin; therefore, no comparison of bleeding-related complications was made. Fourth, lack of heparin administration in some cases may stem from a decision to discontinue care due to poor prognosis. Data on the proportion of cases with limited or discontinued treatment because of poor prognosis was unavailable in the database. Finally, coagulation status, D-dimer, and other indicators may directly affect the use of heparin in some patients. Patients' thrombosis risk score may also be an important basis for the prevention of deep vein thrombosis. The distribution of these factors among each group, the use of heparin, and the effect on outcomes represents a more complex interaction, and this was not covered in this study. Therefore, further research is needed.

Conclusions

According to the findings of this retrospective cohort study, heparin (UFH or LMWH) may be a promising option for treating hospitalized patients with cardiac arrest because heparin reduced mortality rates and prolonged survival times of in-hospital patients with cardiac arrest and improved prognosis of neurological function to a certain extent. Furthermore, outcomes were not significantly different between patients who received UFH and those who received LMWH. Prospective, randomized controlled studies with larger sample sizes are needed to clarify the value of heparin in treating patients with cardiac arrest.

List Of Abbreviations

AH, aspirin and heparin; ANOVA, analysis of variance; APACHE-IV, Acute Physiology and Chronic Health Evaluation Score; ARF, acute renal failure; GCS, Glasgow Coma Scale; ICU, intensive care unit; LMWH, low molecular weight heparin; LOS, length of stay; OR, odds ratio; PSM, Propensity Score Matching; SAPS-II, Simplified Acute Physiology Score; SD, standard deviation; SQL, Structured Query Language; UFH, unfractionated heparin.

Declarations

Ethics approval and consent to participate

The corresponding author (YZ) completed the training on 'Protection of Human Subjects' and obtained permission to use the database (certification number: 36026306). The study was approved by the Research Ethics Committee of Wuxi People's Hospital (KS202112). Because all patient records in the database are anonymous, the Review Committee of this study waived the requirement to obtain informed consent from individual patients.

Consent for publication

Not applicable.

Availability of data and material

The data used in this research is available from the eICU website: https://eicu-crd.mit.edu/.

Competing interests

The authors declare that they have no competing interests.

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Authors' contributions

FG was responsible for data validation and writing of the manuscript, and YZ was responsible for research design, data extraction, and analysis. All authors have read and approved the final manuscript.

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Figures

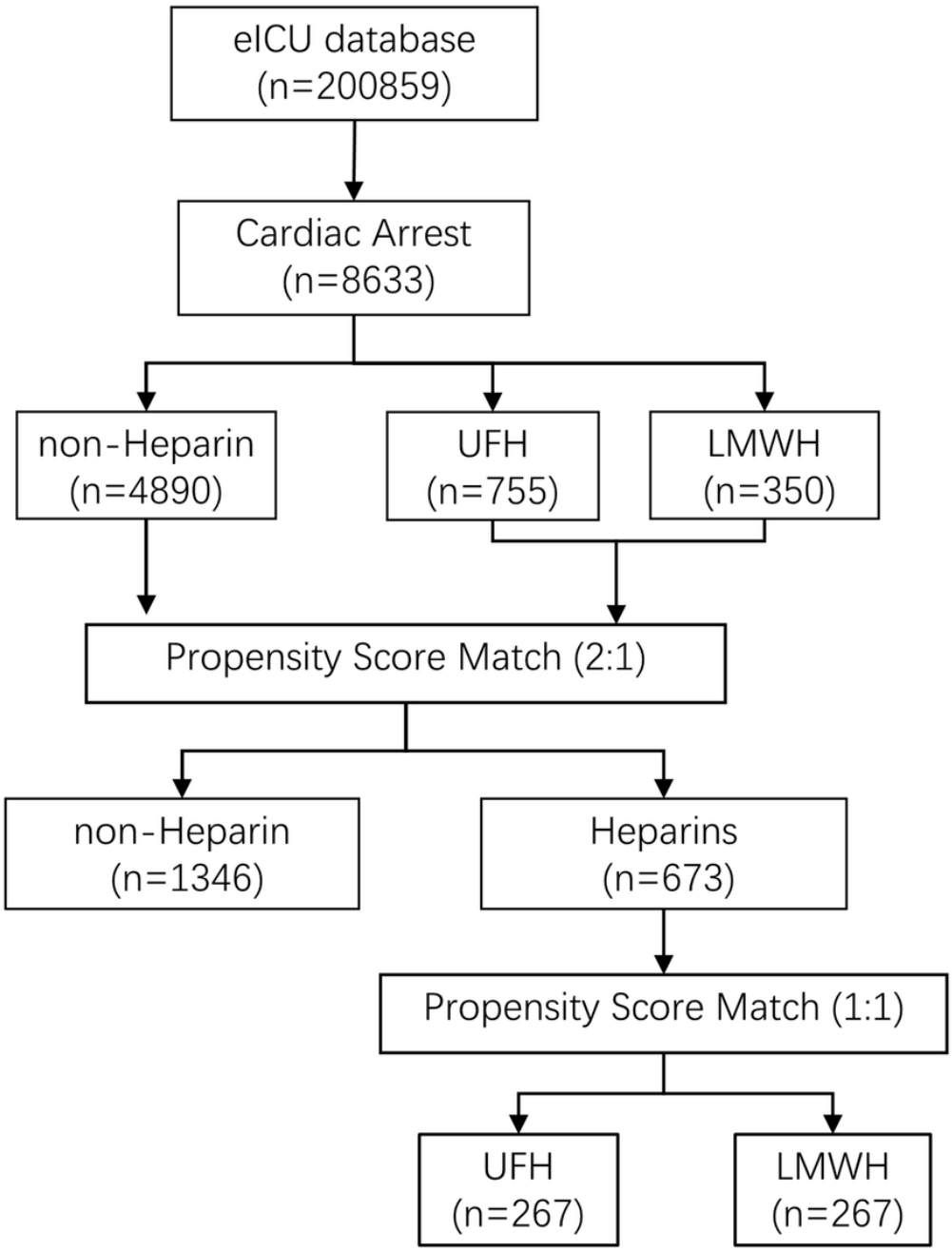

Figure 1

Process of selecting the study subjects. eICU=The Philips Electronic ICU, UFH=unfractionated heparin, LMWH=Low molecular weight heparin

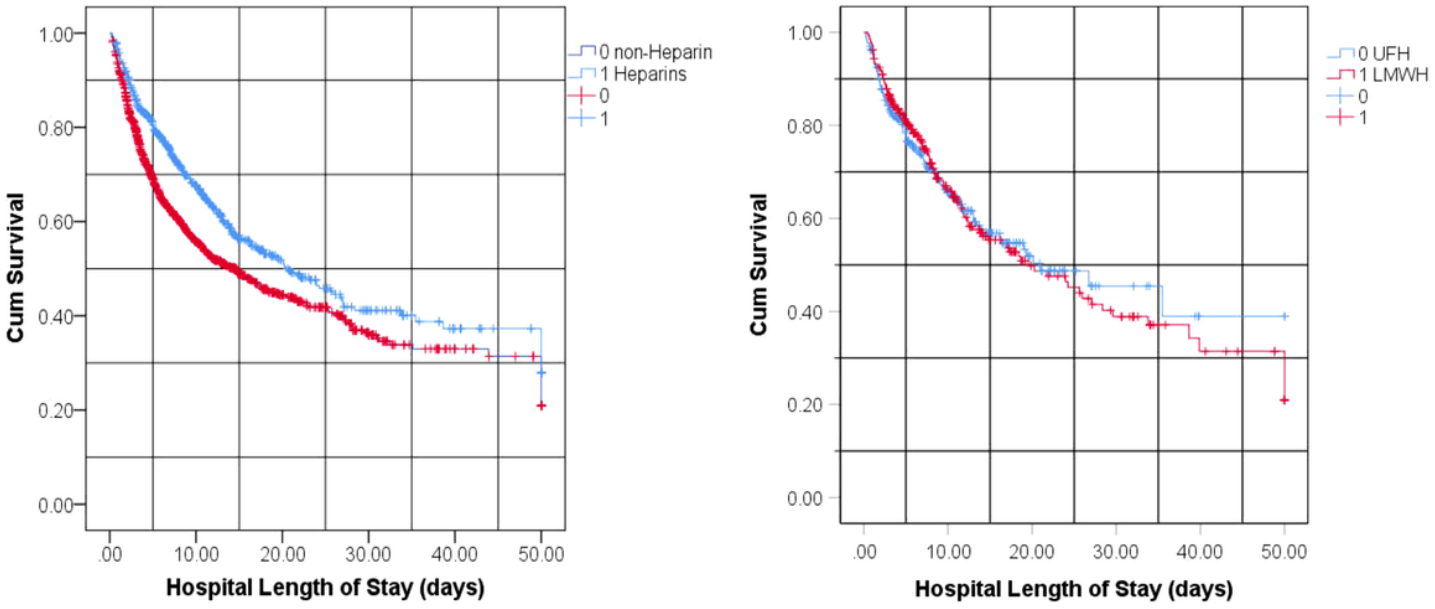

Figure 2

Kaplan-Meier survival curves depict cumulative survival to hospital discharge. A. The median survival time of the heparin group and the non-heparin group are 20.75±2.37 days and 14.63±1.26 days. The survival time of the heparin group is longer than that of the non-heparin group (P<0.001). B. The median survival time of the UFH group and the LMWH group (after matching) are 20.96±5.09 days and 19.54±3.73 days, and this difference is not significant (P=0.89). UFH=unfractionated heparin, LMWH=Low molecular weight heparin