Clinical course after identification of new-onset atrial fibrillation in critically ill patients: a multicenter prospective cohort study

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Research

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Abstract

Background

New-onset atrial fibrillation (AF) in critically ill patients is reportedly associated with poor outcomes. However, epidemiological data in intensive care units (ICUs) after new-onset AF identification are lacking. This study aimed to describe the clinical course after the identification of new-onset atrial fibrillation.

Methods

This prospective cohort study of 32 ICUs in Japan during 2017-2018 enrolled adult patients with new-onset AF. We collected data on patient comorbidities, physiological information before and at the AF onset, interventions, transition of cardiac rhythms, adverse events, and in-hospital death and stroke.

Results

The incidence of new-onset AF in the ICU was 2.9% (423 patients). At the AF onset, the mean atrial pressure decreased, and the heart rate increased. Sinus rhythm returned spontaneously in 84 patients (20%), and 328 patients (78%) were treated with pharmacological interventions (rate-control drugs, 67%; rhythm-control drugs, 34%). In total, 173 (40%) patients were treated with anticoagulants. Adverse events were more frequent in nonsurvivors than in survivors (bleeding: 14% vs 5%; p = 0.002, arrythmia other than AF: 6% vs 2%; p = 0.048). There were 92 (22%) and 15 patients (4%) patients who continued to have AF at 48 hours and 168 hours after onset, respectively. The hospital mortality rate of those patients were 32% and 60%, respectively. The overall hospital mortality was 26%, and the incidence of in-hospital stroke was 4.5%.

Conclusions

Although the proportion of patients continued to have AF within 168 hours decreased with various treatments, these patients were at a high risk of death. Moreover, adverse events occurred more frequently in nonsurvivors than in survivors. Further research to assess the management of new-onset AF in critically ill patients is strongly warranted.

Background

New-onset atrial fibrillation (AF) in critically ill patients is the most frequent arrhythmia in intensive care units (ICUs) [1, 2]. Most previous studies of new-onset AF in the ICU compared between patients with and without new-onset AF [3–5] and reported that critically ill patients who developed new-onset AF may be at higher risk of a long duration of hospital stay, stroke, and death [1, 6, 15, 16, 7–14]. Although several observational studies on patients who developed new-onset AF have been published, there is no high-quality clinical trial that has evaluated the strategy for managing new-onset AF [17–19]. Therefore, the optimal management strategy for new-onset AF is unknown.

Designing a good clinical trial needs comprehensive information on the clinical course after the identification of a disease. Regarding the clinical course after the identification of new-onset AF in critically ill patients, various strategies for new-onset AF management were reported [17–20]. However, no single study has included comprehensive information after the identification of new-onset AF: information of rhythm transition, interventions for new-onset AF, adverse events with those interventions, and outcome.

Accordingly, we conducted the Atrial Fibrillation Treatment Evaluation Registry in ICU (AFTER-ICU) study that prospectively investigated new-onset AF patients in a multicenter cohort of general ICU patients. The current study aimed to describe the clinical course after the identification of new-onset AF in critically ill patients.

Methods

Study design and setting

The prospective cohort AFTER-ICU study was conducted in 32 ICUs in Japan. The study was registered at UMIN-CTR (UMIN000026401), and the study protocol was approved by the Jikei University Institutional Review Board (28–200[8443]) and the ethics committees of all other participating hospitals with an opt-out policy from the patient or their proxy. We enrolled patients admitted to the ICU between April 1, 2017 and March 31, 2018. All study patients were followed up until hospital discharge. This study is reported in accordance with the Strengthening the Reporting of Observational Studies in Epidemiology statement [21].

Participants

We included patients who developed new-onset AF during their ICU stay. The exclusion criteria were as follows: (i) age < 18 years; (ii) history of AF; (iii) discharged from the ICU within 24 hours after ICU admission; (iv) admitted to the ICU after cardiac surgery or cardiac arrest; (v) with a pacemaker at the AF onset; (vi) withheld or withdrew medical therapy at the AF onset; and (vii) declined enrollment in this study. AF was defined as an arrhythmia with irregular R-R intervals without apparent P waves or with F waves that persisted longer than 5 minutes or with recurrent episodes within 5 minutes, as confirmed using 12-lead electrocardiograms or continuous 3-lead electrocardiograms [4, 9, 16, 22–24]. New-onset AF was diagnosed by physicians (intensivists or cardiologists) in the participating hospitals.

Variables and measurements

The following information were collected immediately after the initial AF onset: age, sex, body mass index, comorbidities, CHADS2 score [25], previous medications, patient category, infection status at AF onset, most damaged organ system, Acute Physiology and Chronic Health Evaluation II score [26] at ICU admission, Sequential Organ Failure Assessment score [27] at AF onset, physiological data, vasopressors use and dose, inotrope use and dose, antiarrhythmic drug use, sedative drug use, anticoagulant use, mechanical ventilation (MV) use, noninvasive positive pressure ventilation use, high-flow nasal canula

use, and renal replacement therapy. We also recorded the following information within 7 days after initial AF onset or during ICU stay, whichever was shorter: restoration of sinus rhythm (SR), antiarrhythmic drug use, direct-current cardioversion, anticoagulant use, adverse events (bleeding events or cardiac arrhythmia other than AF), AF recurrence, and total AF length. Within 7 days after AF onset, we also examined hospital mortality for the following patients: those with sustained AF, those with recurrent AF, those with SR, and those who survived after ICU discharge. Sustained AF was defined as continued AF without restoration of SR from the AF onset. Restoration of SR was defined as the sustained SR for longer than 24 hours after the conversion from AF to SR. Spontaneous restoration of SR was defined as the restoration of SR without any antiarrhythmic drugs. Recurrent AF was defined as the repeated occurrence of AF after restoration of SR. Data on cardiac rhythm at ICU discharge and in-hospital stroke were also collected. In-hospital stroke was defined as a symptomatic cerebral infarction diagnosed by a neurologist or a neurosurgeon or determined via new computed tomography or magnetic resonance imaging findings [22]. The occurrence of stroke in the general ward was confirmed by manually reviewing the medical records according to this definition. Other definitions of the collected variables are detailed in Table S1.

Statistical analysis

The study results are presented as median and interquartile range or as absolute numbers with percentage. Variables that are presented for all study patients compare the survivors and the nonsurvivors during their hospital stay. In all analyses, the number of missing data was reported if we had missing data, and cases with missing data were excluded from each analysis. Comparisons between the two groups were conducted using chi-square test or Fisher's exact test for categorical variables and Mann-Whitney U test for continuous variables. P values less than 0.05 were considered to be significant. All analyses were performed using SPSS ver. 25.0 (IBM Corp., Armonk, NY, USA).

Results

A total of 14,348 adult patients except cardiac surgery patients were admitted to the ICU for longer than 24 hours during the study period. Of them, 423 (2.9%) had new-onset AF and met the eligibility criteria for this study. In total, 112 (26%) patients of the study cohort died during the hospital stay.

The patients' demographic and clinical characteristics are shown in Table 1. Body mass index (one patient) and Sequential Organ Failure Assessment score (10 patients) data were missing. Almost half of the study patients had a previous history of hypertension, and one-third had diabetes. In total, 267 (63%) were medical patients, and 295 (70%) patients had an infection at the AF onset. The proportion of medical patients and those with infection at the AF onset were greater among the nonsurvivors than among the survivors. The nonsurvivors also had worse disease severity scores (Acute Physiology and Chronic Health Evaluation II and Sequential Organ Failure Assessment) than survivors.

Table 1

Clinicodemographic patient characteristics

	Overall (n = 423)	Survivors (n = 311)	Nonsurvivors (n = 112)	p value
Age, years	75 (67–81)	75 (67–81)	76 (66–82)	0.706
Male sex, n (%)	286 (68)	204 (66)	82 (73)	0.158
Body mass index, kg/m^2 †	22 (20–25)	23 (20–25)	22 (19–24)	0.110
Comorbidity, n (%)				
Hypertension	199 (47)	150 (48)	49 (44)	0.441
Diabetes	112 (26)	79 (25)	33 (29)	0.454
Congestive heart failure	43 (10)	38 (12)	5 (5)	0.018
Ischemic heart disease	43 (10)	33 (11)	10 (9)	0.717
Stroke or TIA	45 (11)	30 (10)	15 (13)	0.285
Chronic hemodialysis	24 (6)	16 (5)	8 (7)	0.476
CHADS2 score	1 (1–2)	1 (1–2)	1 (0–2)	0.564
Previous medication, n (%)				
Calcium-channel blockers	141 (33)	101 (32)	40 (36)	0.560
β-blocking agents	56 (13)	47 (15)	9 (8)	0.073
ACE inhibitors	22 (5)	21 (7)	1 (1)	0.013
ARBs	89 (21)	70 (23)	19 (17)	0.279
Antidiabetic agents	97 (23)	68 (22)	29 (26)	0.432
Anticoagulants	31 (7)	24 (8)	7 (6)	0.679
Antiarrhythmic drugs	5 (1)	5 (2)	0 (0)	0.331
Patient category, n (%)				0.026

TIA: transient ischemic attack, CHADS2: one point: recent congestive heart failure, hypertension, age at least 75 years, diabetes mellitus; two points: transient ischemic attack or a prior stroke, ACE: angiotensin converting enzyme, ARBs: angiotensin II receptor blockers, APACHE II: Acute Physiology and Chronic Health Evaluation II, SOFA: Sequential Organ Failure Assessment, ICU: intensive care unit, AF: atrial fibrillation.

† One missing data

†† Ten missing data

	Overall (n = 423)	Survivors (n = 311)	Nonsurvivors (n = 112)	p value
Non-scheduled surgical	95 (22)	71 (23)	24 (21)	
Scheduled surgical	61 (14)	53 (17)	8 (7)	
Medical	267 (63)	187 (60)	80 (71)	
Infection at AF onset, n (%)	295 (70)	205 (66)	90 (80)	0.004
Most damaged organ system, n (%)				< 0.001
Gastrointestinal	118 (28)	86 (28)	32 (29)	
Respiratory	110 (26)	73 (23)	37 (33)	
Cardiovascular	55 (13)	41 (13)	14 (13)	
Trauma	26 (6)	22 (7)	4 (4)	
Neurological	24 (6)	19 (6)	5 (5)	
Urogenital	21 (5)	20 (6)	1 (1)	
Musculoskeletal	20 (5)	12 (4)	8 (7)	
Metabolic	13 (3)	11 (4)	2 (2)	
Hematological	9 (2)	2 (1)	7 (6)	
Others	27 (6)	25 (8)	2 (2)	
APACHE II score at ICU admission	23 (18–29)	22 (17–28)	26 (22–33)	< 0.001
SOFA score at AF onset ††	7 (4–9)	6 (3–8)	8 (6–12)	< 0.001
Days from ICU admission to AF onset	1.6 (0.6–3.0)	1.3 (0.6–2.7)	2.5 (1.3–5.2)	< 0.001

TIA: transient ischemic attack, CHADS2: one point: recent congestive heart failure, hypertension, age at least 75 years, diabetes mellitus; two points: transient ischemic attack or a prior stroke, ACE: angiotensin converting enzyme, ARBs: angiotensin II receptor blockers, APACHE II: Acute Physiology and Chronic Health Evaluation II, SOFA: Sequential Organ Failure Assessment, ICU: intensive care unit, AF: atrial fibrillation.

† One missing data

†† Ten missing data

The physiological data before and at the AF onset are shown in Table 2 and Fig. 1. Regardless of whether patients died or not, the heart rate significantly increased and the blood pressure decreased during the

development of AF. Nonsurvivors had a higher heart rate before AF onset and a lower mean arterial pressure at the AF onset than survivors.

Table 2
Physiological data before and at the onset of atrial fibrillation

	Overall (n = 423)	Survivors (n = 311)	Nonsurvivors (n = 112)	p value
Physiological data before AF onset				
Heart rate, bpm	95 (83–107)	93 (81–105)	100 (92–111)	< 0.001
Systolic arterial pressure, mmHg	122 (104–141)	122 (105–141)	122 (103–141)	0.737
Mean arterial pressure, mmHg	80 (71–92)	81 (71–93)	79 (70–90)	0.459
Diastolic arterial pressure, mmHg	59 (52–69)	60 (52–70)	58 (51–69)	0.491
Physiological data at AF onset				
Heart rate, bpm	130 (112–148)	130 (110–147)	136 (116–157)	0.054
Systolic arterial pressure, mmHg	111 (91–133)	112 (94–134)	108 (87–129)	0.029
Mean arterial pressure, mmHg	76 (64–89)	78 (65–91)	73 (61–87)	0.015
Diastolic arterial pressure, mmHg	58 (48–70)	59 (50–70)	57 (46–68)	0.028
Respiratory rate, /min	20 (16–24)	20 (16–24)	20 (15–25)	0.852
Glasgow Coma Scale	14 (12–15)	15 (13–15)	14 (9–15)	< 0.001
AF: atrial fibrillation, bpm: beats per minute.				

Medications and organ support taken at the AF onset are shown in Table 3. Laboratory data are shown in Table S2. In total, 192 (45%) patients were taking a vasopressor at the AF onset. Meanwhile, 255 (60%) patients received MV, and 104 patients (25%) were treated with renal replacement therapy at the AF onset. The proportions of patients who required vasopressors, MV, and renal replacement therapy at the AF onset were higher among nonsurvivors than that among survivors.

Table 3

Medications and ICU management at the onset of atrial fibrillation

	Overall (n = 423)	Survivors (n = 311)	Nonsurvivors (n = 112)	p value
Medications at AF onset				
Vasopressors, n (%)	192 (45)	128 (41)	64 (57)	0.004
Noradrenaline, n (%)	182 (43)	119 (38)	63 (56)	0.158
Noradrenaline, μg/kg/min †	0.12 (0.05–0.22)	0.12 (0.05–0.22)	0.13 (0.05–0.22)	0.993
Adrenaline, n (%)	14 (3)	8 (3)	6 (5)	0.001
Adrenaline, μg/kg/min †	0.05 (0.03–0.25)	0.05 (0.03–0.28)	0.06 (0.05–0.15)	0.651
Dopamine, n (%)	32 (8)	18 (6)	14 (13)	0.021
Dopamine, μg/kg/min †	3.4 (2.1–4.9)	3.1 (2.0–4.8)	3.8 (2.3–5.6)	0.287
Vasopressin, n (%)	39 (9)	18 (6)	21 (19)	< 0.001
Inotropes, n (%)	52 (12)	33 (11)	19 (17)	0.093
Dobutamine, n (%)	41 (10)	25 (8)	16 (14)	0.063
PDE inhibitors, n (%)	12 (3)	9 (3)	3 (3)	1.000
Diltiazem, n (%)	4 (1)	3 (1)	1 (1)	1.000
β-blocking agents, n (%)	34 (8)	26 (8)	8 (7)	0.840
Amiodarone, n (%)	3 (1)	2 (1)	1 (1)	1.000
Other antiarrythmic drugs, n (%)	2 (1)	2 (1)	0 (0)	1.000
Dexmedetomidine, n (%)	84 (20)	61 (20)	23 (21)	0.890
Propofol, n (%)	87 (21)	61 (20)	26 (23)	0.416
Midazolam, n (%)	47 (11)	31 (10)	16 (14)	0.222
Anticoagulants, n (%)	83 (20)	61 (20)	22 (20)	1.000
Heparin intravenous injection, n (%)	60 (14)	45 (14)	15 (13)	0.875

AF: atrial fibrillation, PDE: phosphodiesterase, MV: mechanical ventilation, NPPV: noninvasive positive pressure ventilation, HFNC: high flow nasal canula, RRT: renal replacement therapy

† Mean dose only for the patients administrated.

	Overall (n = 423)	Survivors (n = 311)	Nonsurvivors (n = 112)	p value
Heparin subcutaneous injection, n (%)	22 (5)	15 (5)	7 (6)	0.620
Warfarin, n (%)	1 (0)	1 (0)	0 (0)	1.000
MV at AF onset, n (%)	255 (60)	166 (53)	89 (79)	< 0.001
NPPV at AF onset, n (%)	12 (3)	10 (3)	2 (2)	0.740
HFNC at AF onset, n (%)	14 (3)	13 (4)	1 (1)	0.126
RRT at AF onset, n (%)	104 (25)	56 (18)	48 (43)	< 0.001
AF: atrial fibrillation, PDE: phosphodiesterase, MV: mechanical ventilation, NPPV: noninvasive positive pressure ventilation, HFNC: high flow nasal canula, RRT: renal replacement therapy				
† Mean dose only for the patients administrated.				

The interventions for new-onset AF and outcomes are shown in Table 4 and Table S3. SR was spontaneously restored in 84 patients (20%), while 328 patients (78%) required a pharmacological intervention. There were 282 (67%) and 145 (34%) patients who were treated with rate-control and rhythm-control drugs, respectively. Meanwhile, 173 (41%) patients were administered anticoagulant drugs in the ICU; 19 patients (4.5%) experienced ischemic stroke during the hospital stay. Adverse events (bleeding, cardiac arrhythmia other than AF) occurred more frequently in nonsurvivors than in survivors.

Table 4

Interventions and outcomes after the onset of atrial fibrillation

	Overall (n = 423)	Survivors (n = 311)	Nonsurvivors (n = 112)	p value
Pharmacological intervention, n (%)	328 (78)	237 (76)	91 (81)	0.294
Rate control drugs, n (%)	282 (67)	206 (66)	76 (68)	0.816
Beta blocking agents, n (%)	220 (52)	162 (52)	58 (52)	1.000
Landiolol, n (%)	172 (41)	123 (40)	49 (44)	0.501
Bisoprolol, n (%)	70 (17)	57 (18)	13 (12)	0.106
Propranolol, n (%)	2 (1)	1 (0)	1 (1)	0.460
Carvedilol, n (%)	8 (2)	8 (3)	0 (0)	0.117
Calcium-channel blockers, n (%)	127 (30)	99 (32)	28 (25)	0.188
Diltiazem, n (%)	74 (17)	56 (18)	18 (16)	0.772
Verapamil, n (%)	58 (14)	47 (15)	11 (10)	0.200
Digoxin, n (%)	14 (3)	8 (3)	6 (5.4)	0.214
Rhythm control drugs, n (%)	145 (34)	104 (33)	41 (37)	0.563
Magnesium sulfate, n (%)	76 (18)	50 (16)	26 (23)	0.114
Amiodarone, n (%)	50 (12)	36 (12)	14 (13)	0.865
Pilsicainide, n (%)	42 (10)	32 (10)	10 (9)	0.854
Others, n (%)	35 (8)	24 (8)	11 (10)	0.549
Both rate and Rhythm control drugs, n (%)	108 (26)	76 (24)	32 (29)	0.448
Direct-current cardioversion, n (%)	65 (15)	39 (13)	26 (23)	0.009
Anticoagulants, n (%)	173 (41)	136 (44)	37 (33)	0.057
Heparin intravenous injection, n (%)	124 (29)	98 (32)	26 (23)	0.116

SR: sinus rhythm, DC: direct-current cardioversion, DOAC: direct oral anticoagulants, AF: atrial fibrillation, ICU: intensive care unit

† Among patients who survived at ICU discharge.

†† Length from AF onset to ICU discharge.

* Length from AF onset to hospital discharge.

	Overall (n = 423)	Survivors (n = 311)	Nonsurvivors (n = 112)	p value
Heparin subcutaneous injection, n (%)	42 (10)	30 (10)	12 (11)	0.716
DOAC, n (%)	20 (5)	19 (6)	1 (1)	0.034
Warfarin, n (%)	5 (1)	5 (2)	0 (0)	0.331
Adverse events				
Bleeding, n (%)	30 (7)	14 (5)	16 (14)	0.002
Cardiac arrhythmias other than AF, n (%)	13 (3)	6 (2)	7 (6)	0.048
Spontaneous restoration of SR, n (%)	84 (20)	66 (21)	18 (16)	0.271
Length until spontaneous restoration, hours	11 (3.0–36)	11 (2.9–33)	9.9 (3.3–51)	0.987
AF recurrence, n (%)	89 (21)	55 (18)	34 (30)	0.007
Total AF length, hours	21 (5.1–53)	18 (4.7–44)	24 (6.3–67)	0.172
AF at ICU discharge †, n (%)	62 (17)	51 (16)	11 (19)	0.230
ICU length of stay ††, days	5.6 (2.6–11.2)	4.6 (2.4–9.2)	9.0 (3.9–15.7)	< 0.001
Hospital length of stay *, days	26 (13–49)	34 (16–56)	15 (8–29)	< 0.001
Stroke after AF onset, n (%)	19 (5)	13 (4)	6 (5)	0.600
Days from AF to stroke, days	5.1 (1.4–11.0)	8.6 (1.9–21.3)	1.3 (0.6–5.1)	0.291

SR: sinus rhythm, DC: direct-current cardioversion, DOAC: direct oral anticoagulants, AF: atrial fibrillation, ICU: intensive care unit

† Among patients who survived at ICU discharge.

†† Length from AF onset to ICU discharge.

* Length from AF onset to hospital discharge.

The clinical course over 168 hours after AF onset is summarized in Fig. 2. At 168 hours after AF onset, 53% of the patients were discharged from the ICU, 36% restored and remained in SR, 4% had sustained AF, 2% had recurrent AF, and 5% died.

The hospital mortality of patients with sustained AF, recurrent AF, restored SR, and of those who survived after ICU discharge every 24 hours until 168 hours after AF onset are shown in Fig. 3. The in-hospital mortality were 9% for patients who survived to ICU discharge, 38% for patients with SR, 33% for patients with recurrent AF, and 60% for patients with sustained AF at 168 h).

Discussion

In this multicenter prospective cohort study, we enrolled 423 patients with new-onset AF and described the clinical course after the identification of new-onset AF. In this general ICU population that excluded post-cardiac surgery patients, the incidence of new-onset AF was 2.9%. At the AF onset, the mean arterial pressure was lower and vasopressor requirement was higher among nonsurvivors than that among survivors. After the AF onset, almost all patients were treated with some pharmacological interventions for new-onset AF (78%), except for those who restored SR spontaneously (20%). Anticoagulants were given to approximately 40% of the study patients. Both bleeding and cardiac arrhythmia other than AF occurred more frequently in nonsurvivors than in survivors. Although the proportion of patients who had any AF decreased within 168 hours after the identification of new-onset AF, they had higher hospital mortality than those with SR. The overall hospital mortality was 26%, while the incidence of in-hospital stroke was 4.5% among patients with new-onset AF.

Few studies have investigated the hemodynamic impact of new-onset AF. A post-hoc analysis of a sepsis registry of 418 new-onset AF patients reported a decrease in blood pressure and an increase in heart rate at the AF onset [9]. Our study also found hemodynamic deterioration at the AF onset in this diverse ICU population. Although there was no significant difference in the mean arterial pressure before the AF onset between survivors and nonsurvivors, the mean arterial pressure after the AF onset was lower in nonsurvivors than that in survivors. Nonsurvivors were also more frequently treated with vasopressors at the AF onset than survivors. These findings suggest that the degree of blood pressure decrease may reflect the underlying status of critical illness that was hidden prior to the AF onset. That is, patients who have uncontrolled underlying critical illness may be at risk of experiencing a direct hemodynamic impact of new-onset AF.

Several studies in the 1990s reported that the conversion rates to SR with various drugs ranged from 1 hour to 24 hours [3, 4, 28]. The rates reported in these studies were around 70% within 24 hours, which were consistent with our findings. Meanwhile, the rhythm transition after 24 hours has not been reported. In our study, almost all patients received interventions for new-onset AF, except for those with spontaneous restoration of SR. Consequently, in the overall cohort, the proportion of those who had any AF decreased to less than 10% within 168 hours after the identification of new-onset AF. However, patients who had any AF within 168 hours had higher hospital mortality than those with SR. These findings suggest that the resistance to AF therapy may be associated with poor outcome. Moreover, cardiac arrythmias other than AF occurred more frequently in nonsurvivors than in survivors. One explanation may be the difficulty of treating new-onset AF in patients who had poor prognosis due to their uncontrolled underlying disease.

Although anticoagulation is a common therapy for AF in the general ward [29], few studies have assessed anticoagulation for treating new-onset AF in the ICU [4, 17, 19]. ICU physicians may consider anticoagulation for prolonged AF duration based on indirect evidence in the general ward setting [20]. Several studies reported various proportions (16–58%) of anticoagulant administration for new-onset AF patients in the ICU [1, 18, 30]. To the best of our knowledge, only one study inclusively reported the proportion of anticoagulant use, incidence of bleeding events, and incidence of ischemic stroke [18]. This was a single-center prospective cohort study of 108 new-onset supraventricular arrythmia patients in a mixed ICU that reported the proportion of anticoagulant use for new-onset AF (58%), incidence of hemorrhagic events (40%), and incidence of embolic stroke (4.6%) [18]. Compared with this study, our study showed a lower proportion of patients treated with anticoagulants (41%) and a lower incidence of hemorrhagic events (7.1%). Moreover, in our study, although nonsurvivors were less frequently treated with anticoagulation than survivors, bleeding events occurred more frequently in nonsurvivors than in survivors. These findings suggest that anticoagulation for new-onset AF in the ICU should be provided cautiously at least for those with possible poor prognosis.

Our findings provide several implications for future intervention studies. We need to identify the best timing for initiating AF interventions. In the current study, the median time from AF onset to the spontaneous restoration of SR (20% of all new-onset AF patients) was 11 hours. We should consider this duration as an interval before starting AF interventions. Regarding pharmacological interventions, our study showed that the majority of patients received drugs for new-onset AF, and the number of patients who remained in AF markedly decreased within 48 hours. These findings suggest that new-onset AF may be treatable. However, the pharmacological interventions for new-onset AF varied in our study as well as in previous studies [3, 4], which partly contributes to the difficulty in conducting intervention studies for new-onset AF in the ICU. Therefore, a specific intervention that is effective for the restoration of SR should be identified first.

To the best of our knowledge, this is the largest study of new-onset AF patients in the ICU setting and provides the most detailed information after the identification of new-onset AF. However, several limitations should be acknowledged. First, the incidence of new-onset AF in our study (2.9%) was relatively low (2.9%) compared to those of previous studies (1.7–43.9%) [4]. Because we manually detected new-onset AF without using automatic systems, we may have missed some new-onset AF cases that could not be clinically recognized. However, a retrospective cohort study using an automated analysis of continuous electrocardiography to detect AF reported that subclinical AF (detected by the algorithm but missed by clinicians) was not associated with poor hospital outcome [7]. Moreover, populations, settings, detection methods for new-onset AF, and definitions of the denominator for calculating the incidence (e.g., including vs excluding patients with a prior history of AF) reported in previous studies varied. Because only post-cardiac surgery patients were excluded in the calculation of the incidence, the denominator in our study might be larger than that in previous studies. Second, we did not use a validated definition of new-onset AF. However, although previous studies also used various definitions of new-onset AF [4], the hospital mortality in our study (26%) was similar to those in previous studies (20–69%) [3, 5, 7, 9, 12, 24, 31]. Third, we collected detailed information for new-onset AF only

within 7 days after its onset. However, to the best of our knowledge, this observation period for AF was the longest among new-onset AF studies that described its clinical course in detail after its onset in the ICU [8, 9, 12]. Finally, we did not evaluate specific interventions or exposures for new-onset AF in critically ill patients using multivariable regression models, although we plan to conduct post-hoc analyses of new-onset AF management in the near future.

Conclusions

This multicenter prospective cohort study evaluated the clinical course after the identification of new-onset AF in critically ill patients. Although the proportion of patients who remained in AF decreased with various treatments over time, those patients were at a high risk of death. Moreover, adverse events occurred more frequently among non-survivors than among survivors. Further research to assess the management of new-onset AF in critically ill patients is strongly warranted.

Abbreviations

AF = atrial fibrillation; ICU = intensive care unit; MV = mechanical ventilation; SR = sinus rhythm

Declarations

Ethics approval and Informed consent

The study protocol was approved by the Jikei University Institutional Review Board (28-200[8443]) and the ethics committees of all other participating hospitals with an opt-out policy from the patient or their proxy.

Consent for publication

Not applicable

Conflicts of interest

All the authors declare that they have no conflicts of interest.

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The AFTER-ICU study group

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Availability of data and materials

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Authors' contributions

TY has full access to all study data and takes responsibility for its integrity. Study concept and design: TY, SU, and YS. Data acquisition: TY and SU. Data analysis and interpretation: TY, SU, and YS. Manuscript drafting: TY. Critical revision of the manuscript for important intellectual content: TY, SU, and YS.

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Figures

Figure 1

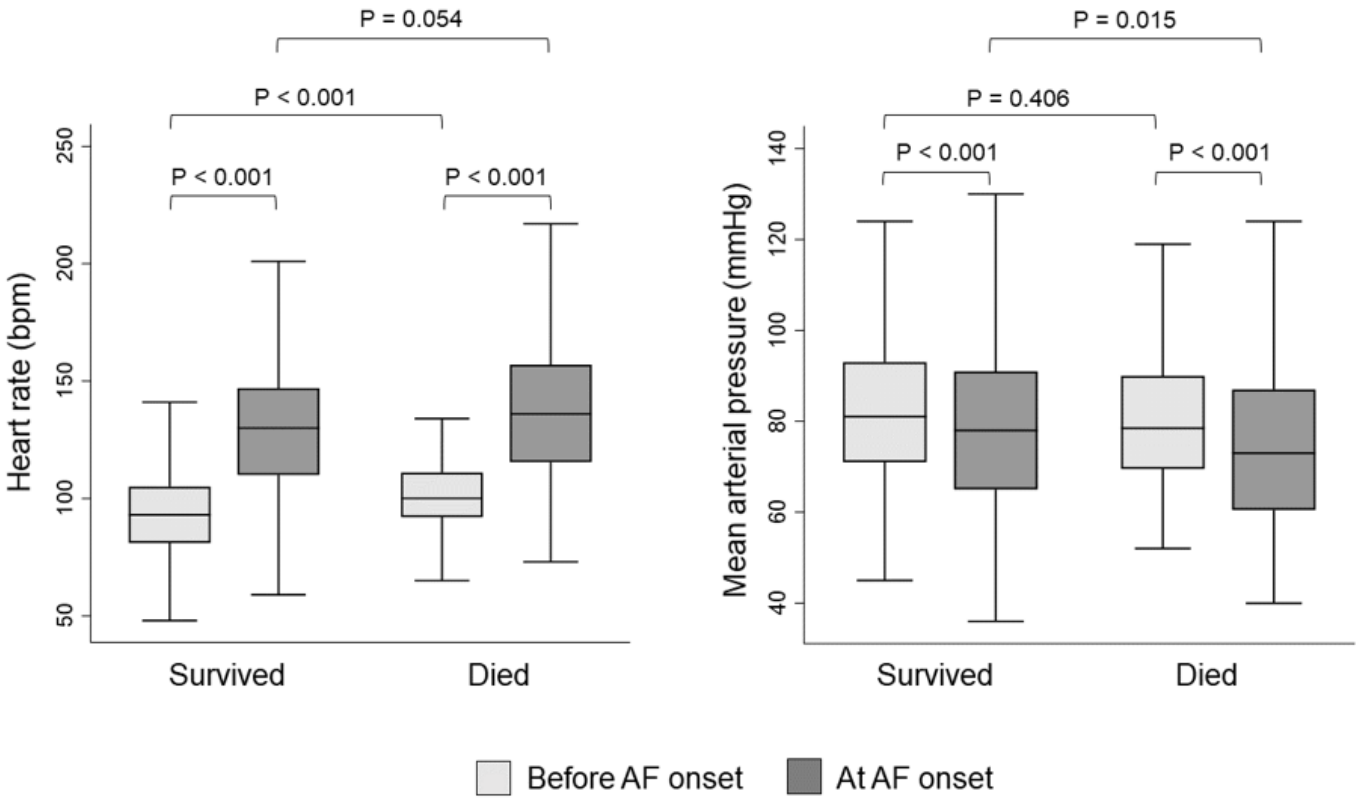
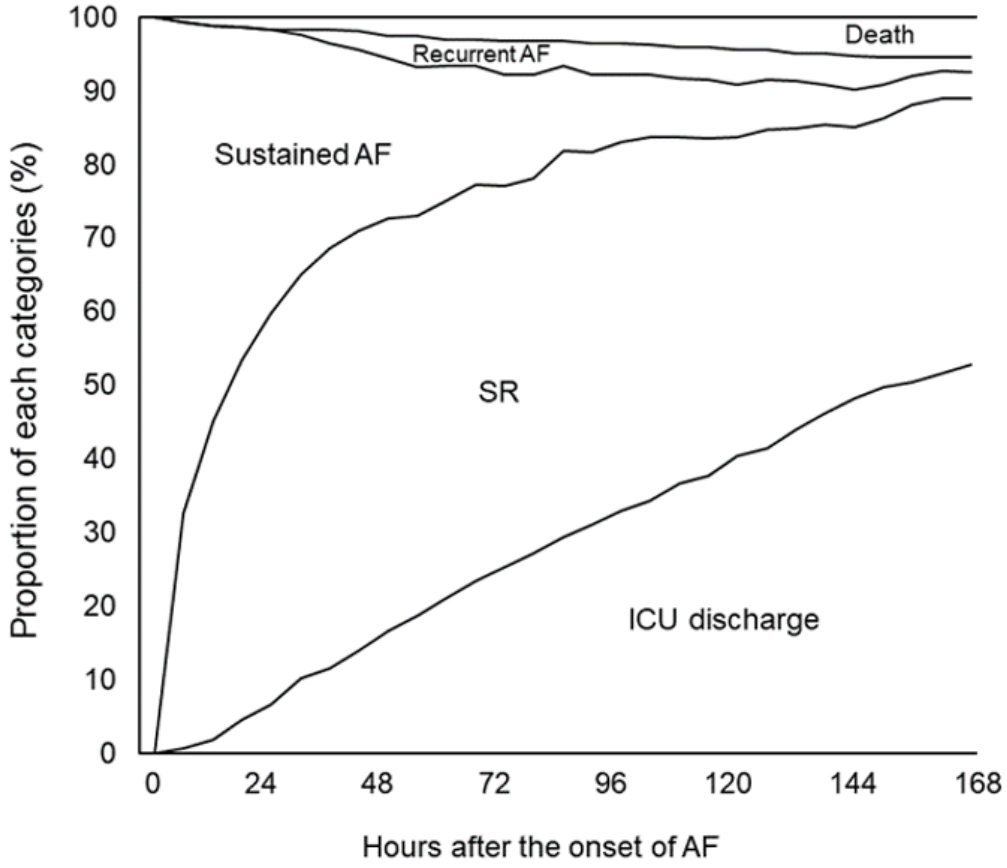


Figure 1

Changes in hemodynamic variables during the development of AF AF, atrial fibrillation; bpm, beats per minute

Figure 2

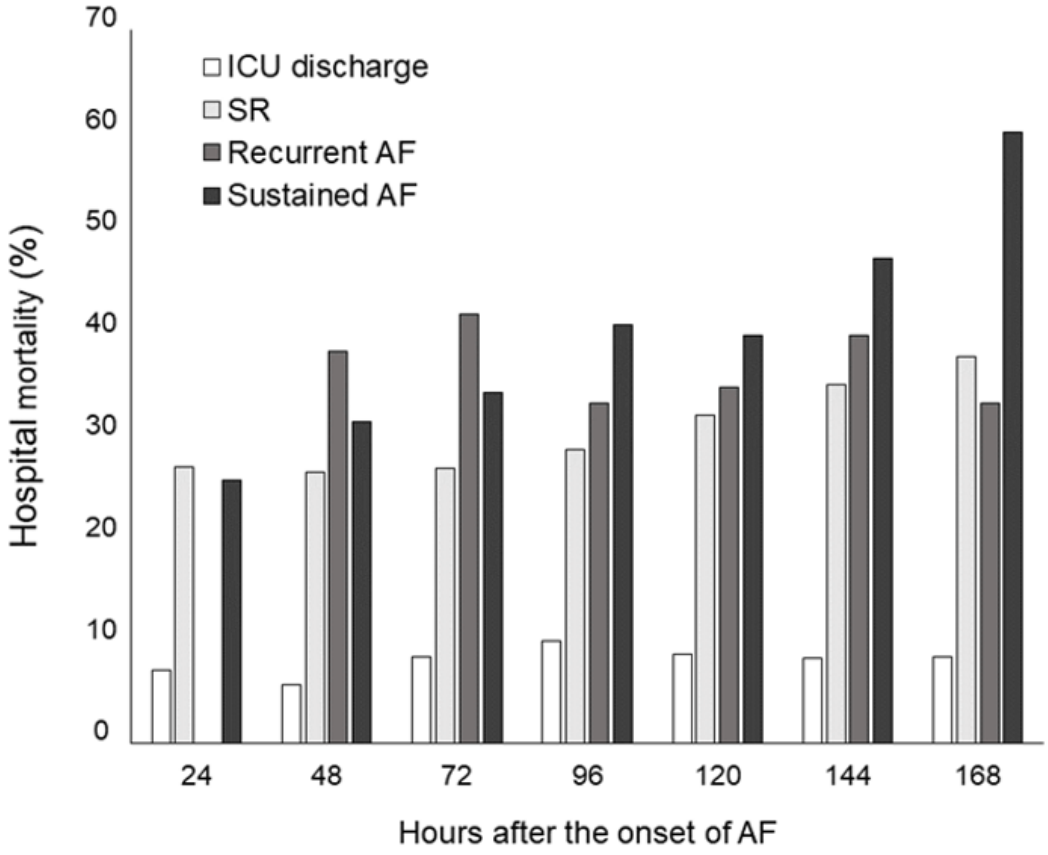


Patients (%)							
Death	2	3	3	4	4	5	5
Recurrent AF	0	3	4	4	5	5	2
Sustained AF	39	22	15	9	7	5	4
SR	53	56	52	50	43	37	36
ICU discharge	7	17	25	33	40	48	53

Figure 2

Rhythm transition and clinical course after AF onset AF, atrial fibrillation; SR, sinus rhythm; ICU, intensive care unit

Figure 3



Hospital mortality (%)							
ICU discharge	7	6	8	10	9	8	9
SR	27	27	27	29	32	35	38
Recurrent AF		38	42	33	35	40	33
Sustained AF	26	32	34	41	40	48	60

Figure 3

In-hospital mortality after AF onset AF, atrial fibrillation; SR, sinus rhythm; ICU, intensive care unit

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