

New-onset Atrial Fibrillation In Sepsis No Correlation With Inflammatory Cytokines in Real-life Clinical Setting

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Research

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Abstract

Background

New-onset atrial fibrillation (new-onset AF) is one of the most common tachyarrhythmia in critically ill patients and is associated with increased morbidity and mortality. Unfortunately, risk factors for new-onset AF in sepsis have not been clearly elucidated. This study aims to determine the association of new-onset AF with circulating inflammatory cytokine concentrations.

Methods

This is a retrospective analysis of the relationship between new-onset AF in sepsis and inflammatory cytokine concentrations. The study included patients with sepsis diagnosed in the Emergency Intensive Care Unit (EICU) of The First Affiliated Hospital of Xinjiang Medical University. This study was conducted on data submitted from June 2016 through May 2019. The patients were classified based on the new-onset AF into Control group (n = 100) Non New-onset AF in sepsis group (n = 182) New-onset AF in sepsis group (n = 89). We aimed to investigate whether new-onset AF in sepsis can be explained by increased circulating inflammatory cytokine concentrations.

Results

Unadjusted analysis of the 371 observations from the retrospective cohort study demonstrated that serum cytokine concentrations do not correlate with new-onset AF in sepsis, despite the fact that cytokines predict mortality and correlate with organ dysfunction and sepsis severity (APACHE II and SOFA scores). On multivariable analysis, the present study shows that hypertension, BMI, fibrinogen and hs-Troponin-T strongly correlated with the new-onset AF in sepsis. Besides, none of the cytokine concentrations correlated with any of the hs-Troponin-T or fibrinogen.

Conclusions

Our study shows that risk factors for new-onset AF in sepsis are mainly factors that are associated with the pre-admission comorbidity, coagulation, cardiac biomarkers. none of the measured inflammatory cytokines correlates with new-onset AF in sepsis.

Background

Sepsis is defined as life-threatening organ dysfunction caused by a dysregulated host response to infection (1). Mortality rate of sepsis is high despite the best available treatments, and is mostly the result of septic shock and multiorgan failure. Patients admitted to intensive care units (ICU) with sepsis are prone to developing cardiac dysrhythmias, most commonly AF (2); approximately one-fourth of patients 65 years or older hospitalized with sepsis have concomitant AF (3). Furthermore, the occurrence of AF is independently associated with both a prolonged stay and increased mortality in the ICU. Although AF can be a debilitating illness with potentially catastrophic complications such as thromboembolic stroke and heart failure, these risks can be substantially mitigated by anticoagulation and by control of heart rate or rhythm (4). Numerous experimental in vitro studies attempted to explore the complex molecular-cellular inflammatory pathways potentially leading to new-onset AF (5–7). They found that mediators of the inflammatory response can alter atrial electrophysiology and structural

substrates, thereby leading to increased vulnerability to AF. Inflammation also modulates calcium homeostasis and connexins, which are associated with triggers of AF and heterogeneous atrial conduction. However, despite intensive laboratory efforts, the mechanisms responsible for new-onset AF remain elusive, and the paucity of clinical evidence for an association of circulating cytokines with new-onset AF is notable.

We have demonstrated that AF is the most common new-onset arrhythmia in patients hospitalized with sepsis. In this study we aimed to investigate whether new-onset AF in sepsis can be explained by increased circulating inflammatory cytokine concentrations.

Materials And Methods

This retrospective cohort study was approved by the Institutional Review Board of The First Affiliated Hospital of Xinjiang Medical University with a waiver of informed consent(K202001-22). The total consecutive population of 394 patients admitted through the Emergency Department(ED) at The First Affiliated Hospital of Xinjiang Medical University from June 1, 2016, to May 31, 2019, had an International Classification of Diseases, 9th Edition (ICD-9) diagnosis code for sepsis. Sepsis was defined as life-threatening organ dysfunction caused by a dysregulated host response to infection, which is compatible with the sepsis-3 definition(1). AF detection was based on hourly recordings of the observed heart rhythm in the electronic patient record by the bedside nurse. We defined new-onset AF as the observation of AF for > 1 hour continuously, or the documentation of shorter periods of AF initiating either pharmacological treatment or electrical cardioversion. We excluded patients with a history of chronic or paroxysmal AF or flutter, and patients following recent cardiomy or cardiac arrest. We also excluded observations occurring within 12 hours prior to hospital mortality to guard against the possibility of analyzing terminal rhythms. Patients were divided into two groups according to their heart rhythm, one is new-onset AF in sepsis, the other is non new-onset AF in sepsis.

Case Collection

According to the inclusion criteria and exclusion criteria of this study, patients with sepsis were included in the new-onset AF in sepsis group according to electrocardiogram or ECG monitoring within EICU 24 hours, and those without new-onset atrial fibrillation were included in the non new-onset AF in sepsis group. And collect the biochemical results of all patients within 24 hours after admission (collect patients with sepsis within 24 hours of admission to minimize the effect of anti-infective therapy on inflammatory indexes). Laboratory examination: liver function, kidney function, cardiac biomarkers: high-sensitivity (hs) troponin-T and N-terminal pro-B-type natriuretic peptide (NT-proBNP) (Roche Diagnostics), cytokines: TNF- α , IL-1 β , IL-6, IL-8, IL-10, CRP, and monocyte chemoattractant protein-1 (MCP-1)(normal values: ≤ 2 pg/mL, ≤ 5 pg/mL, ≤ 7 pg/mL, ≤ 21 pg/mL, ≤ 3 pg/mL, ≤ 7 mg/L, and ≤ 722 pg/mL, respectively). Cytokines were measured by solid phase enzyme-linked immunosorbent assay kits (R&D Systems, Inc). These particular cytokines were chosen because they were most frequently cited in the literature in relation to sepsis and to new-onset AF.

Clinical Data

All primary information, vital signs, monitoring parameters, laboratory results, and 28-day mortality were prospectively collected. Admission Acute Physiology and Chronic Health Evaluation (APACHE) score and daily Sequential Organ Failure Assessment (SOFA) were calculated on the days of examination of blood samples.

Statistics

Statistical analyses were performed using SPSS 22.0 software (IBM) and GraphPad Prism 6. Student t-test, χ^2 , or Mann-Whitney U tests were used to compare the distributions of continuous and dichotomous variables. Normality of distribution of all continuous variables was explored by examining skewness, kurtosis, and Q-Q plots. Pearson linear correlation and Spearman rank nonparametric correlation were used to assess correlations among all continuous variables. Univariate and multivariate (backward stepwise selection method with probability for removal of 0.05) logistic regressions and cox regression were used to determine the association of variables with new-onset AF in sepsis mortality, respectively. Kaplan-Meier log-rank test were used to compare survival curves.

Results

A total of 394 patients (healthy people 100), 235 males and 159 females, and 23 cases were excluded due to the incomplete information and prior AF. Finally 89 patients with new-onset AF in sepsis were included, as well as 182 cases of sepsis without new-onset AF, and 100 people were included in the normal control group. Patients with sepsis were 70.730 ± 14.249 years of age, at least one source of infection was identified in 262 patients (96.7%), and 142 (52.4%) had positive blood cultures. Patients with new-onset AF were 70.930 ± 13.709 years of age, 58.4% were men, Hypotension (systolic BP < 90 mmHg for > 1 h) occurred in 11 patients (12.35%). Seventy-one patients (26.2%) died during follow-up (28 days), 32 (36.0%) died with New-onset AF in sepsis, and 39 (21.4%) died with Non New-onset AF in sepsis.

Table 1 summarizes the variables significantly associated with new-onset AF in sepsis. No significant differences were found among the three groups in any of the age, gender, type 2 diabetes, chronic obstructive pulmonary disease and hypercholesterolemia (all $P > 0.05$). In contrast, significant differences were found among the groups in hypertension, coronary heart disease, respiratory rates, heart rates, systolic blood pressure, diastolic blood pressure, white blood cell count, procalcitonin, TNF- α , IL-1 β , IL-6, IL-8, IL-10, CRP, MCP-1 (all $P < 0.05$). Compared to normal control group, patients with sepsis who had higher incidence in hypertension and coronary heart disease, higher serum concentration in white blood cell count, procalcitonin, TNF- α , IL-1 β , IL-6, IL-8, IL-10, CRP, MCP-1. None of the cytokine concentrations correlated with the new-onset AF in sepsis: white blood cell count, procalcitonin, TNF- α , IL-1, IL-6, IL-8, IL-10, CRP, MCP-1 (all $P > 0.05$). The percentage of hypertension and coronary heart disease in patients with new-onset AF was significantly higher compared to patients who never developed AF (Hypertension: $\chi^2 = 9.400$, $p = 0.002$; Coronary heart disease: $\chi^2 = 8.320$, $p = 0.004$). Figure 2 shows the survival curves of all patients divided into quartiles by serum cytokine concentrations.

Table 1
Baseline Demographics of People With and Without New-onset Atrial Fibrillation in sepsis and Control group

Measure	Control group(n = 100)	Non New-onset AF in sepsis(n = 182)	New-onset AF in sepsis(n = 89)	F / χ^2	P Value
Age (years)	68.530 ± 15.105	70.630 ± 14.542	70.930 ± 13.709	0.854	0.427
Male [n(%)]	60(60.0%)	118(64.8%)	52(58.4%)	1.273	0.529
Preadmission comorbidity					
Hypertension [n(%)]	27(27.0%)	48(26.4%)	40(44.9%)*	10.660	0.005
Coronary heart disease[n(%)]	21(21.0%)	36(19.8%)	32(36.0%)*	9.247	0.010
Type 2 diabetes [n(%)]	20(20.0%)	33(18.1%)	17(19.1%)	0.151	0.927
Chronic obstructive pulmonary disease [n(%)]	12(12.0%)	27(14.8%)	12(13.5%)	0.444	0.801
Hypercholesterolemia[n(%)]	22(22.0%)	44(24.2%)	23(25.8%)	0.388	0.824
Respiratory rates (times/min)	15.510 ± 2.963	20.490 ± 4.495*	20.240 ± 4.695*	50.009	< 0.001
Heart rates (beats/min)	75.700 ± 8.250	88.460 ± 15.507*	92.010 ± 15.800*	37.996	< 0.001
Systolic blood pressure(mm Hg)	111.00 ± 8.316	97.740 ± 8.763*	96.650 ± 6.479*	102.546	< 0.001
Diastolic blood pressure(mm Hg)	77.170 ± 7.070	66.970 ± 10.820*	64.610 ± 8.682*	51.298	< 0.001
White blood cell count (× 10 ⁹ /L)	5.926 ± 1.728	17.160 ± 9.470*	16.329 ± 9.627*	65.721	< 0.001
Procalcitonin (ng/mL)	0.234 ± 0.191	18.434 ± 4.892*	18.418 ± 4.789*	700.194	< 0.001
TNF- α (pg/mL)	0.400[0.320–0.457]	27.575[16.688–39.645]*	26.220[16.385–39.640]*	218.639	< 0.001
IL-1 β (pg/mL)	0.610[0.532–0.700]	2.810[2.367–3.212]*	2.800[2.455–3.050]*	218.447	< 0.001
IL-6(pg/mL)	4.100[3.302–4.535]	249.905[120.105–293.795]*	250.600[80.270–345.295]*	217.026	< 0.001
IL-8(pg/mL)	10.380[7.817–12.732]	75.820[20.095–112.753]*	78.490[18.345–122.765]*	133.594	< 0.001
IL-10(pg/mL)	0.470[0.322–0.650]	7.865[4.930–12.780]*	7.650[3.200–16.180]*	213.054	< 0.001
CRP(mg/L)	5.900[3.917–7.837]	65.735[32.275–111.245]*	64.200[15.895–127.895]*	198.088	< 0.001
MCP-1(pg/mL)	15.950[11.157–20.807]	1340.015[599.527–1185.113]*	1325.200[678.885–2163.915]*	219.724	< 0.001
VS Normal Control group *P<0.05					

The characteristics between patients with sepsis with/without AF are summarized in Table 2. We found significant differences between two groups in Body Mass Index(BMI), fibrinogen, HS-Troponin-T and 28-day mortality(all $P < 0.05$). Figure 3 shows the survival curves of two groups for 28-day mortality.

Table 2

Comparison of Biochemical Indicators among people With and Without New-onset Atrial Fibrillation in sepsis

Measure	Total(n = 271)	Non New-onset AF in sepsis(n = 182)	New-onset AF in sepsis(n = 89)	<i>t</i> Test/ χ^2	<i>P</i> Value
Body Mass Index(BMI)	22.54 ± 2.938	21.65 ± 2.422	24.38 ± 3.059	-7.968	< 0.001
Hemoglobin (g/L)	137.15 ± 16.958	137.51 ± 17.486	136.40 ± 15.893	0.504	0.615
Platelet count (× 10 ⁹ /L)	128.572 ± 14.232	128.280 ± 14.572	129.171 ± 13.571	-0.483	0.629
Lactic acid (mmol/L)	2.682 ± 0.888	2.671 ± 0.818	2.705 ± 1.021	-0.299	0.765
INR	2.121 ± 0.511	2.134 ± 0.503	2.094 ± 0.528	0.613	0.540
Fibrinogen (g/L)	5.154 ± 1.949	4.602 ± 1.651	6.284 ± 2.031	-7.287	< 0.001
HS-Troponin-T(ug/L)	0.569 ± 0.230	0.533 ± 0.212	0.643 ± 0.248	-3.786	< 0.001
NT-pro BNP(pg/mL)	249.042 ± 91.517	248.007 ± 92.002	251.160 ± 90.998	-0.266	0.791
K ⁺ (mmol/L)	3.976 ± 0.461	3.987 ± 0.486	3.955 ± 0.406	0.537	0.591
Na ⁺ (mmol/L)	140.036 ± 5.975	140.256 ± 4.808	139.587 ± 7.854	0.864	0.388
Ca ²⁺ (mmol/L)	2.233 ± 0.338	2.220 ± 0.295	2.260 ± 0.415	-0.906	0.366
Serum creatinine (μmol/L)	84.359 ± 10.021	84.212 ± 9.432	84.660 ± 11.182	-0.345	0.731
Alanine aminotransferase (U/L)	31.104 ± 8.345	30.868 ± 8.385	31.588 ± 8.289	-0.667	0.506
SOFA score	7.22 ± 1.985	7.21 ± 1.945	7.22 ± 2.077	-0.041	0.968
APACHEⅡscore	11.30 ± 2.614	11.30 ± 2.529	11.31 ± 2.794	-0.053	0.958
Source of infection [n(%)]	262(96.7%)	174(95.6%)	88(98.9%)	1.104	0.293
Positive blood cultures [n(%)]	142(52.4%)	93(51.1%)	49(55.1%)	0.375	0.540
28-day mortality[n(%)]	71(26.2%)	39(21.4%)	32(36.0%)	6.523	0.011

Table 3 summarizes the independent predictors of new-onset AF in sepsis within the following categories: hypertension, coronary heart disease, BMI, fibrinogen, HS-Troponin-T. The multivariate logistic regression showed that hypertension, BMI, fibrinogen, HS-Troponin-T strongly correlated with the new-onset AF in sepsis, and represented the independent risk factors for the new-onset AF in sepsis (all P < 0.05).

Table 3
The Multivariate Logistic Regression of Independent Variables Associated With New-onset Atrial Fibrillation in sepsis

Variable	B	SE	Wals	P	Exp(B)	95%CI
BMI	0.376	0.062	36.410	< 0.001	1.456	1.289–1.645
Hypertension	-0.807	0.352	5.262	0.022	0.446	0.224–0.889
Coronary heart disease	-0.688	0.372	3.430	0.064	0.503	0.243–1.041
Fibrinogen	0.516	0.097	28.303	< 0.001	1.675	1.385–2.025
HS-Troponin-T	2.390	0.750	10.147	0.001	10.915	2.508–47.502

None of the cytokine concentrations correlated with any of the HS-Troponin-T or fibrinogen, by linear nonlinear correlations tests among continuous variables (Table 4). All the cytokine concentrations, except IL-1 β , correlated with both SOFA scores and APACHE II scores calculated for the specific days of echocardiography and blood sampling.

Table 4
Correlations of Cytokine With Sepsis Severity, Cardiac Biomarker Concentrations and Coagulation (Pearson Linear and Spearman rank [P] Nonlinear Correlation-the Stronger of the Two)

Variable	SOFA score	APACHE II score	HS-Troponin-T	NT-pro BNP	Fibrinogen
TNF- α	0.429*	0.359*	0.042	-0.072	0.064
IL-1 β	0.050	0.045	0.037	-0.052	-0.077
IL-6	0.442*	0.401*	-0.003	-0.136#	0.064
IL-8	0.375*	0.339*	0.052	-0.082	0.067
IL-10	0.427*	0.442*	-0.009	-0.155#	0.084
CRP	0.352*	0.301*	0.000	-0.096	-0.010
MCP-1	0.395*	0.385*	0.064	-0.144#	0.104
*P < 0.01					
#P < 0.05					

Discussion

Atrial fibrillation is the most common cardiac arrhythmia and is associated with detrimental consequences. In addition to worsening patient's quality of life, AF is associated with stroke, heart failure, and increased mortality (8). Sepsis is characterized by a systemic release of pro-inflammatory cytokines, high levels of circulating stress

hormones, autonomic dysfunction, intravascular volume shifts and cardiovascular compromise(9), all of which are plausible risk factors for the development of AF(10).

New-onset AF in sepsis was defined as presence of AF in patients without prior AF, and the occurrence of AF was associated with sepsis. Some studies have assessed the relationship between new-onset AF and outcomes in ICU patients. A meta-analysis has shown that patients with sepsis who developed new-onset AF have higher mortality(11). Studies done in the ICU have shown that critically ill patients with new-onset AF have higher mortality and longer hospital stay (12–16). AF is also associated with mechanical ventilator weaning failure (17). Therefore, we aimed to gain a better understanding of the incidence and investigate whether new-onset AF in sepsis can be explained by increased circulating inflammatory cytokine concentrations.

Yu-Feng Hu et al(18) showed that inflammation has an important role in the initiation and maintenance of AF, and the electrophysiology and structural properties of the atria are critically affected by inflammatory processes, and the efficacy of the proposed anti-inflammatory drugs remains far from satisfactory. And, Nicholas A. Bosch et al(19) demonstrated that they identified two inflammation-related factors associated with AF risk during sepsis, increased inflammation, elevated C-reactive protein(greater than 70 mg/L) or WBC count (greater than $15 \times 10^9/L$) associated with increased AF risk. Some other experimental studies suggested that cytokines cause new-onset AF via mechanisms such as atrial remodelling(20, 21) or calcium overload in atrial myocytes(22, 23). However, no clinical study examined the association of circulating cytokine concentrations with new-onset AF in sepsis in patients. Our present study shows that circulating inflammatory cytokines are probably not the dominant causes of new-onset AF in real-life sepsis. Rather, cytokines probably have a weaker clinical role in the pathophysiology of new-onset AF in sepsis than suggested by the in vitro experiments, or their mechanisms are more complex and indirect than can be detected by correlations between cytokine concentrations and new-onset AF. However, other explanations are also possible. The pathophysiology of new-onset AF in sepsis is far from being fully understood.

In this study, we have revealed that BMI, hypertension, fibrinogen, hs-Troponin-T strongly correlated with the new-onset AF in sepsis, and clarification of the risk factors for AF during sepsis may improve our understanding of the mechanisms of arrhythmia development and help guide clinical practice.

Body Weight and New-Onset AF

Overweight and obesity are known risk factors for new-onset AF(24). Yun Gi Kim et al(25) found that the degree and duration of hypertension, as well as the presence of hypertension, were important factors for new-onset AF. Body weight status was significantly associated with new-onset AF and acted synergistically with hypertension. In a study of 34 patients, high-dominant frequencies or complex atrial fractionated electrogram sites were located adjacent to epicardial fat areas, which suggest that epicardial fat might maintain AF by releasing paracrine inflammatory mediators(26, 27). And free fatty acid overload in patients with obesity induces lipid accumulation within cardiomyocytes and apoptosis, which might also trigger regional inflammation(28). The potential pathophysiological mechanism of body weight and new-onset AF is that obesity-induced immune cell infiltration into the adipose tissue, particularly by M1 macrophages, as well as inflammation of adipose tissue and secreted proinflammatory cytokines occurs in patients with obesity.

Hypertension and New-Onset AF

The association between hypertension and AF in patients with sepsis is not yet established. However, based on the framingham heart study, hypertension increases the risk of AF by ≈ 1.5 -fold(29). And the hypertensive people who

have required medication for > 5 years had the highest risk of new-onset AF. Hypertension, if uncontrolled and long-standing, can lead to LVH, decreased diastolic function, and elevated LA pressure that will eventually lead to LA dilation and fibrosis(30). Those adverse changes in the LV and LA contribute to the development of new-onset AF(31, 32). Atrial stretch, owing to elevated left ventricular diastolic pressure in patients with hypertension, might activate regional RAAS, cardiac apoptosis, and oxidative stress, which can subsequently induce regional inflammation in the heart and correlated with new-onset AF in sepsis(33).

In our date, We found significant differences between two groups in hypertension, non new-onset AF in sepsis 48(26.4%), new-onset AF in sepsis 40(44.9%), ($P < 0.05$). Therefore, uncontrolled and long-standing hypertension is especially dangerous in terms of the occurrence of new-onset AF. Furthermore, the risk of new-onset AF showed a linear relationship with SBP and DBP. However, in our study, the SBP and DBP in patients with new-onset AF were not significantly higher compared to patients who never developed AF (SBP:t = 1.037, $p = 0.301$; DBP:t = 1.794, $p = 0.074$), because the inclusion criteria were different, and the patients with sepsis would affect heart function, reduce cardiac ejection function and affect blood pressure.

Fibrinogen and New-Onset AF

As a member of the coagulation system, fibrinogen plays an important role in the occurrence and development of sepsis. The earliest evidences about the role of coagulation activation during sepsis included histological demonstration of microvascular thrombosis in target organs of septic patients and the progressive decrease in platelet counts and coagulation factor levels in the late stages of sepsis, attributed to a “consumption coagulopathy”(34). In addition, fibrinogen was associated with the occurrence of AF. Fu R(35)found that compared with the controls, patients with AF had higher levels of fibrinogen (AF vs control: 3.3 ± 0.9 vs 3.0 ± 0.6 g/L, $P = 0.02$). Besides, Wei CC’s study (36)and Hu X’s study(37)also found the relationship between fibrinogen and AF. Our study shows that fibrinogen strongly correlated with the new-onset AF in sepsis, and the independent risk factors for the new-onset AF in sepsis.

According to relevant clinical studies(34), we considered that in patients with sepsis, blood coagulation disorder and microvascular thrombosis lead to cardiac microcirculation disturbance, affect myocardial blood supply, induce electrophysiological disorders of cardiomyocytes, and produce arrhythmias and AF, and Allan J. Walkey (38)found that the intensity and regulation of coagulation activation in sepsis seems to play a major role in the determination of patients’ outcome. Therefore, coagulation dysfunction may be one of the important causes of new-onset AF in sepsis, and our results provide targets for future studies focused on new-onset AF in sepsis prevention and treatment.

HS-Troponin-T and New-Onset AF

Information on the hs-TnT level has improved the prognostic information not only in patients with chest pain and acute coronary syndromes but also in patients with conditions such as congestive heart failure and stable atherosclerotic disease and even in apparently healthy elderly subjects. And Ziad Hijazi et al (39)found that hs-TnT levels can be detected in almost all patients (93.5%) with AF, levels of hs-TnT are often elevated in patients with AF, and the hs-TnT level is independently associated with an increased risk of stroke and cardiac death. However, Horjen AW et al (40)found that hs-TnI correlated weakly with biomarkers representing myocardial wall tension, inflammation and haemostasis in persistent AF, and hs-TnI release is an independent process parallel to other pathophysiological mechanisms associated with AF.

Based on the findings of the present study, we found that hs-TnT correlated with the new-onset AF in sepsis, and represented the independent risk factors for the new-onset AF in sepsis. And our results are consistent with those of Ziad Hijazi(39). There are several potential mechanisms that might explain this association between new-onset AF and HS-Troponin-T. One of the most important mechanisms is that atrial myocardial infarction, or ischaemia which will increase level of myocardial markers (such as HS-Troponin-T et al), will also induce atrial inflammation during the healing process, and might consequently induce AF(41).

Study Limitations

This project is a single-center study, the number of cases included is limited, the results of the study may be different from other studies to some extent, further research and multi-center study are required for better confirmation. Some of the patients with sepsis in the study have taken antibiotics by themselves previously outside the hospital, and if they come to our hospital for treatment without improvement, it may have a certain effect on the level of inflammatory factors detected at admission. Therefore, this study can only record the effect of inflammatory factors on new-onset AF in patients with sepsis.

Conclusions

Although circulating inflammatory cytokine concentrations predict mortality and correlate with sepsis severity, they do not seem to have a dominant effect on new-onset AF in real-life sepsis. In contrast, compared to patients without AF, patients who developed AF in sepsis were corpulent, suffered abnormal coagulation(fibrinogen), cardiac biomarkers(hs-Troponin-T) increasement, and preadmission comorbidity(hypertension and coronary heart disease). Besides, the main causes for new-onset AF in sepsis should be searched from other potential aspects, such as the response to acute physiologic-pharmacologic stimulations during sepsis and effects of vasoactive drugs on cardiac electrical activity.

Declarations

Ethics approval and consent to participate:This retrospective cohort study was approved by the Institutional Review Board of The First Affiliated Hospital of Xinjiang Medical University with a waiver of informed consent(K202001-22).

Consent for publication:Not applicable.

Availability of data and materials:The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request.

Competing interests:The authors declare that they have no competing interests.

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Authors' contributions: ZYL analyzed and interpreted the patient data regarding the sepsis and new-onset atrial fibrillation, and was a major contributor in writing the manuscript. DDL, YGC and JML performed the laboratory examination of the serum. JZY and PP directed the experiment. All authors read and approved the final manuscript.

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Figures

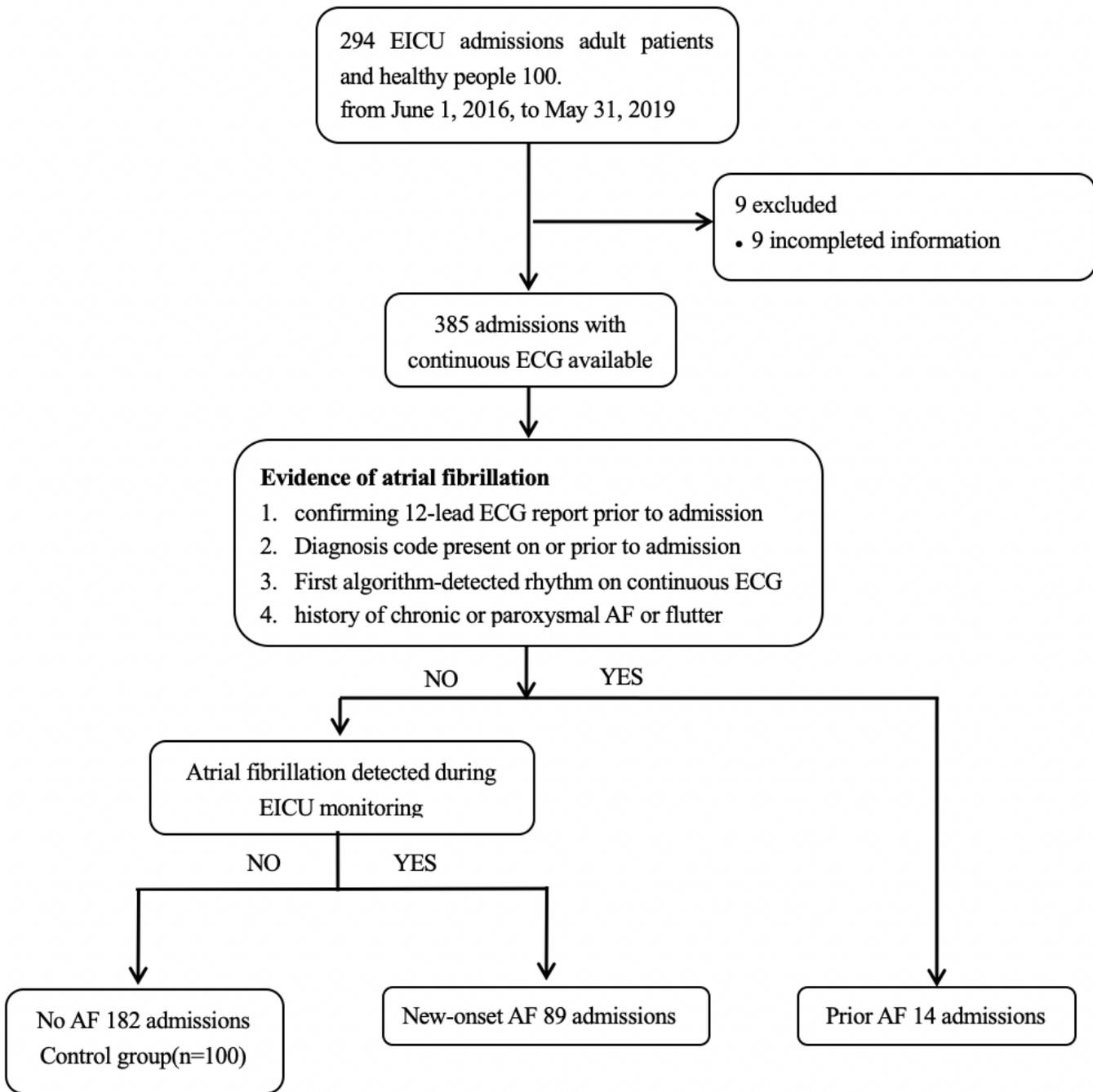


Figure 1

Flowchart of Patient Inclusion Into Primary Analysis Cohort

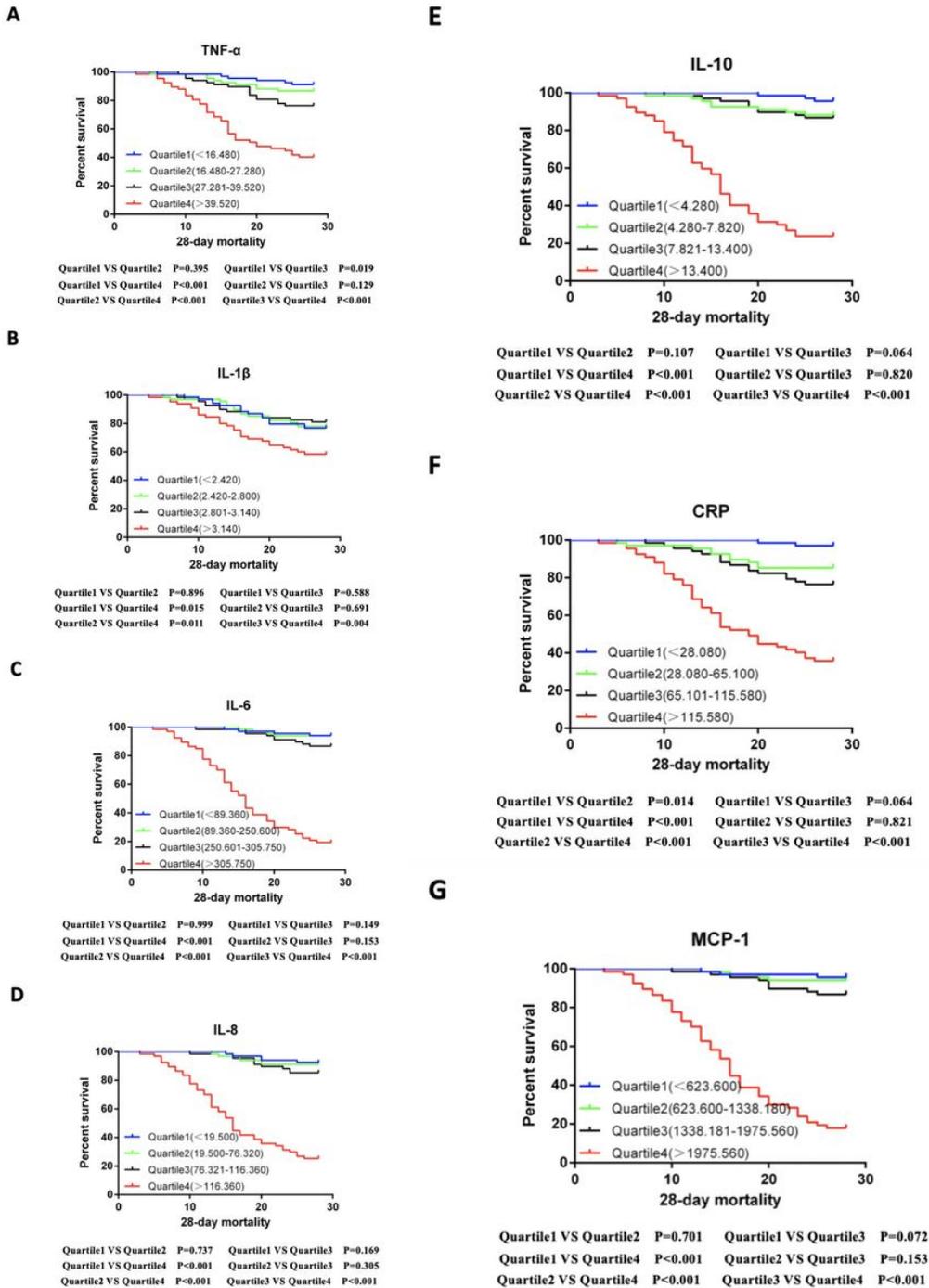
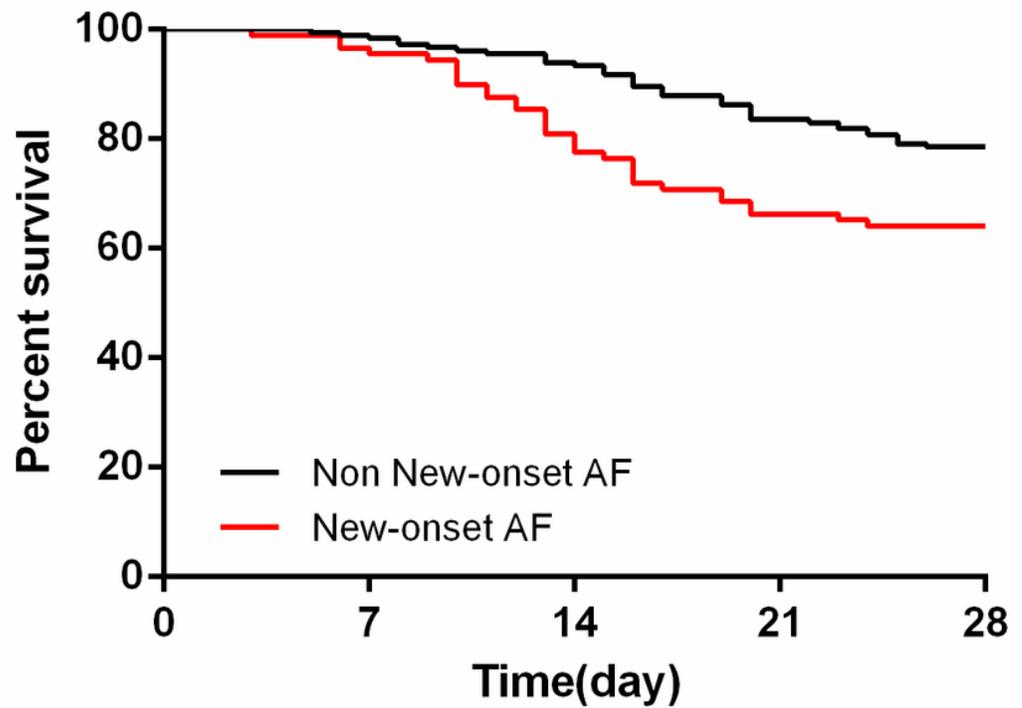


Figure 2

Kaplan-Meier survival curves and log-rank tests for comparisons when all patients were grouped according to their cytokine serum concentrations. A, Patients with different quartiles of TNF- α concentrations. B, Patients with different quartiles of IL-1 β concentrations. C, Patients with different quartiles of IL-6 concentrations. D, Patients with different quartiles of IL-8 concentrations. E, Patients with different quartiles of IL-10 concentrations. F, Patients with different quartiles of CRP concentrations. G, Patients with different quartiles of MCP-1 concentrations. TNF- α =tumor necrosis factor- α ; CRP=C-reactive protein; MCP=monocyte chemoattractant protein;



New-onset AF	89	86	72	61	57
Non New-onset AF	182	180	171	157	143

Figure 3

The Survival Curves of Two Groups for 28-day Mortality Hazard Ratio 1.938 95CI(1.267-3.507); log-rank P=0.004)