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NEW TACHYCARRHYTHMIAS IN CRITICAL CARE POPULATION

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НОВЫЕ ТАХИАРИТМИИ У КРИТИЧЕСКИХ ПАЦИЕНТОВ

Прогрессирующее сердечно-сосудистое ухудшение играет главную роль в патогенезе множественной органной недостаточности, вызванной сепсисом. Доказательства наличия различных сердечных аритмий у септических пациентов были продемонстрированы несколькими клиническими отчетами и наблюдениями. Описаны различные типы тахиаритмий у тяжелых пациентов с сепсисом.

Новые эпизоды фибрилляции предсердий были связаны с высокой смертностью и плохими результатами (инсульт, сердечная недостаточность, длительное использование вазопрессора и т. д.) у пациентов с тяжелыми заболеваниями септического типа по сравнению с несептическими больными. Потенциальные механизмы развития новых сердечных аритмий при сепсисе сложны и недостаточно изучены. Сердечные аритмии у критически больных с сепсисом, скорее всего, являются показателем тяжести предшествующей болезни.

Ключевые слова: сердечные аритмии, фибрилляция предсердий нового типа, сепсис, септический шок.

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Progressive cardiovascular deterioration plays a central role in pathogenesis of multiple organ failure (MOF) caused by sepsis. Evidence of various cardiac arrhythmias in septic patients has been demonstrated by multiple clinical reports and observations. Different types tachyarrhythmias in septic critically ill population have been described.

New onset atrial fibrillation episodes were associated with high mortality rates and poor patients' outcome (new episodes of stroke, heart failure, long vasopressor usage etc.) in critically ill septic patients compared to non-septic persons. Potential mechanisms of development new cardiac arrhythmias in sepsis are complex and poor understood. Cardiac arrhythmias in critically ill septic patients are most like an indicator of severity of preexisting critical illness.

Key words: cardiac arrhythmias, new-onset atrial fibrillation, sepsis, septic shock.

Introduction

In sepsis both systolic and diastolic biventricular myocardial dysfunction in might be present [1–12]. Several authors [13–15; 16–20] described autonomic system dysfunction as a part myocardial dysfunction pathogenesis in systemic inflammatory response syndrome. It is characterized by reduction in heart rate variability due to loss of the balance and attenuation in both sympathetic and vagal signals [15]. In presence of severe proinflammatory response in SIRS/Sepsis patients, the cholinergic vagal activity is remarkably overdrived by sympathetic tone resulting increased heart rate in over 24 hour ECG monitoring [13–16]. Such sepsis-related tachycardia might lead to tachycardia-related cardiomyopathy and remarkable myocardial dysfunction.

Evidence of various cardiac arrhythmias in septic patients has been demonstrated by multiple clinical reports and observations [21–25]. Those arrhythmias might be explained as by autonomic dysfunction, and also by impairment and involvement of cardiac conduction system unless to preexisting cardiac comorbidities [26; 27].

In this paper we will focus on clinical features of arrhythmias in septic patients and potential pathophysiologic mechanism of cardiac conduction system dysfunction.

Prevalence and Risk Factors

The clinical evidence and significance of cardiac arrhythmias as an early sign of sepsis were described first by Kirpatrick et al. in 1973 [28]. Since those different types of supraventricular, ventricular tachyarrhythmiasin septic critically ill population have been described [21; 29–32]. Most of clinical data has been based on mixed ICU population investigations and evaluated prevalence of supraventricular cardiac tachycarrhythmias (8–13.6%) [24; 25; 33–37; 40–44] than ventricular tachycarrhythmias (~ 2%) [40, 43]. Atrial fibrillation has been demonstrated as a most common arrhythmia associated with sepsis/septic/shock [36; 37; 41; 44]. Christian et al. [22] investigated mixed ICU population and showed overall new AF evidence about 5.8% in septic patients. New atrial fibrillation episodes have been established more frequently in surgical than medical patients (7.7% vs 5.4%). Salman et al. [37] and Arora et al. [38] have been found that evidence of new paroxysmal atrial fibrillation is up to 30% of all arrhythmic episodes related to sepsis. Walkey et al. [24] demonstrated that evidence of new onset AF associated with sepsis had been suggested in 14% from all hospital-associated events of AF. Risk factors for developing new onset tachycarrhythmias include preexisting factors (chronic heart failure, valvular disease, coronary artery disease, endocrine disease etc), acute metabolic disturbances (electrolyte abnormalities — hypophosphatemia, hypomagnesaemia etc.), and severity of illness (sepsis) and usage of vasopressors [35; 39; 42; 45]. Salman et al. [37] found strong correlation between paroxysmal atrial fibrillation (PAF) episodes and advanced age, previous medical history of PAF, high severity illness and lower left ventricular ejection fraction. Christian et al. [22] described advanced age as major risk factors in septic patients (65 years older) for development atrial fibrillation. Other risk factors for new onset AF has been related to gender (male), a history of hypertension (16–17 vs 11) and SOFA score more than 12 during ICU [35; 39; 42; 43].

Epidemiology

Epidemiologically, most of septic patients who developed new atrial fibrillation were in septic shock [22]. Pneumonia was determined as a most likely source of infection in septic patients with new atrial fibrillation [22]. Other sources of sepsis were presented less frequently [22]. Rarely, septic patients had multiple sites of infection [22].

Meierhenrich et al. [23] and Walkey et al. [24] demonstrated high prevalence of patients with septic shock. Finally, in large clinical database Walkey et al. [24] showed high respiratory tract infection prevalence (49%) over other sources of sepsis (urinary 40.3%, primary bacteremia 32.8%, abdominal 25.4% and skin/soft tissue — 7.9%) in patients with new onset AF. Gram-positive sepsis associated more frequently (28.4%) with new onset AF than gram-negative (23.4%) and fungal 1.6 vs 3.6% pathogens [24].

Morbidity and Mortality

New onset atrial fibrillation episodes were associated with high mortality rates in critically ill septic patients compared to non-septic persons [22–24; 37; 40].

Christian et al. [22] found mortality rate with new AF at 68.8% vs 39.8% in patients with no arrhythmias. Annane et al. [40] showed mortality rate of 20% of septic persons (from all ICU patients) had higher in-hospital death rates. Meierhenrich et al. [23] evaluated a mortality rates at in-ICU, at 28 and 60 days. There was a trend towards increase mortality in arrhythmic individuals with septic shock in ICU mortality (44%) 28 day mortality (39%) and 60 day mortality (48%) compared to non-shock septic patientswith AF (15%, 15% and 23% respectively) and septic individuals who maintained sinus rhythm (22%, 22% and 26% respectively). In the same study it has been demonstrated longer ICU stay in arrhythmic group rather than those who maintained sinus rhythm and new onset AF without shock. In Walkey et al. [24] study mortality rates were also higher in individuals with severe sepsis and new onset AF (56.3%) compared to patients with preexisting AF (43.8%) and without new onset AF (38.2%). However, Koyfman et al. [46] found no difference in ICU mortality rate between septic patients who had previous AF episodes and patients with no previous past medical history of any cardiac arrhythmias.

New onset AF was found also to correlate with new neurologic compromise. Annane et al. [40] showed both atrial fibrillation (15%) and ventricular arrhythmias (38%) in general ICU population has significant correlation with new neurologic events (focal neurological deficit and diffuse axon injury) compared to patients without arrhythmias (6%). Walkey et al. [24] showed higher occurrence in-hospital strokes in severe sepsis individuals with new onset AF (2.6%) compared with preexisting AF (0.57%) and without AF (0.69%).

In recent study Walkey et al. [25] found new-onset AF during sepsis have increased long-term risks of heart failure, ischemic stroke, and death after discharge from the sepsis hospitalization. High risk of ischemic stroke in septic patients with new onset AF was argued and explained by potential hemodynamic collapse, coagulopathy and inflammatory reaction.

Potential Mechanisms of Cardiac Arrhythmias and Cardiac Conduction System Dysfunction in Sepsis

As soon as atrial fibrillation is a most frequent heart rate disturbance in septic critically ill population we will focus on its potential pathophysiological pathways. The development of cardiac arrhythmias is associated with evidence of three factors: the arrhythmogenic substrate, the trigger factor and the modulation factors such as autonomic nervous system or inflammation [48]. Triggered activity has been shown in the musculature of all atrial structures (pulmonary vein, musculature of the coronary sinus, superior vena cava etc.). An imbalance in autonomic nervous system activity, accelerated sympathetic tone/increased adrenergic stimulation has been suggested to be one of responsive mechanisms of development heart disturbances [48–50].

The significance of inflammatory component in theory of development new atrial fibrillation events also has been supported by existence strong correlation between elevation of C-reactive protein, IL-6 and TNF-α blood levels and onset of AF [54].

Unopposed sustained atrial tachycardia during the sepsis/septic shock will further increase calcium influx through L-type Ca^{2+} channels. With each action potential, Ca^{2+} enters the cell through L-type Ca^{2+} channels (Calcium (Ca^{2+}) influx through the L-type Ca^{2+} channels is the main current to produce the plateau phase of the atrial action potential). Increased intracellular calcium load leads to marked shortening of the atrial refractory period and elicited triggered activity. These changes may facilitate the AF mechanism [48; 55]. Moreover, recent animal studies data [56–60] showed an enhanced response of the L-type calcium current itself to β-adrenergic stimulation after endotoxin application (ventricular myocytes model).

The β-adrenergic stimulation of ICa increased in early 12 h after EDTX (endotoxin) injection in the rat [60]. A similar finding was obtained in guinea pig hearts as early as 4 h after EDTX injection [59]. These findings might explain high sensitivity of cardiac pacemaker cells to positive inotropic effect of adrenergic stimulation and most likely development new AF episode especially in early septicstage. Abi-Gerges et al. [60] also showed attenuation of β-adrenergic stimulation effect with a reduction in the apparent sensitivity on ICa current after 36-h EDTX myocytes' exposure.

Clinical Strategy in Sepsis-Induced Cardiac Arrhythmias

New onset atrial fibrillation events in septic patients generate different clinical interests and significance. First, it has to be mentioned as a sign of early septic/SIRS state [21; 29; 41]. Thus, continuous cardiovascular monitoring and simple daily 12-lead ECG might be extremely helpful in addition to clinical exams and laboratory findings. Evidence of new AF episode might give us important clinical information about the probability of on-going sepsis and relevance of ECHO study (assessment of myocardial function), new cultures and antibiotic strategies and "early-goal directed therapy" decision.

Second, it might to be an important prognostic sign. It is correlated with increasing mortality and new neurologic events [23; 24; 40]. Thus, keeping it in mind, the heart-rate variability performance might be become a relevant part of clinical assessment potentially septic patient [15; 61].

The new AF event needs to be treated by electrical (synchronized shock) or pharmacological (amiodaron etc.) cardioversion. At least, it has to be delayed with available antiarrhythmic therapy (β-blockers, Ca channel blockers etc.). Amiodarone has less negative inotropic and proarrhythmic effect and found was single most frequently used drug for control of tachycarrhythmias [23]. In this large prospective study of 629 ICU patients with septic shock [23] authors presented extremely remarkable treatment data. Amiodarone (36 patients, n=49), digitalis (31 patients), beta blockers (25 patients) and electrical cardioversion have been used successfully to restore sinus rhythm.

In contrast, Walkey et al. [62] analyzed initial type of treatment (beta blockers, calcium channel-blockers, digoxin, or amiodarone) new onset AF in septic population. They demonstrated that beta-blockers were associated with better clinical outcomes.

Importantly, the inability to restore sinus rhythm was strongly correlated with ICU mortality. It has to be well understood that inability to restore sinus rhythm could compromise acutely patient's hemodynamic status and even increase mortality.

However, the restoration of sinus rhythm in septic patients does not automatically imply an improvement in clinical outcome.

Conclusions

Management of arrhythmias is undoubtedly one of the major problems in emergency and critical care medicine associated with worse patients' prognosis and clinical outcome. Arrhythmias only rarely appear to be a diagnosis for primary admission to the ICU rather arrhythmias occur during the ICU stay. Cardiac arrhythmias in critically ill patients are most like an indicator of severity of preexisting critical illness rather than independent on-going pathophysiological process.

Drs. Brotfain and Kuts contributed equally to the manuscript.

Ключові слова: серцеві аритмії, фібриляція передсердь нового типу, сепсис, септичний шок.

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