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New-onset atrial fibrillation and clinical outcome in non-cardiac intensive care unit patients

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ABSTRACT

Background: Data regarding new onset atrial fibrillation (nAF) in general, non-cardiac, intensive care unit (ICU) patients are limited. However, it has been suggested that nAF is associated with worse clinical outcome in these patients.
Objective: The purpose of the present work was to study the prognostic impact of nAF, in this setting.
Methods: We prospectively studied all patients admitted to a single ICU for a period of 12 months. Patients admitted for brief post-operative monitoring, patients with chronic, intermittent atrial fibrillation and atrial fibrillation present upon admission, were excluded. Death during ICU stay (ICUD) was the pre-specified study end-point. Length of stay (LOS) for survivors was also reported. A number of factors related to the occurrence of nAF and the present disease were recorded for each patient.
Results: The study population was comprised of 133 patients. Twenty (15%) of them manifested nAF. The end-point of ICUD was observed in 27.1% of the patients. The median LOS reported was 8 days. Patients with nAF seemed to have significantly worse prognosis, compared to those who did not manifest nAF (OR = 3.35, 95%CI:1.26–8.92; $P = 0.016$). Additionally, nAF patients appear to require significantly extended LOS ($P = 0.01$). Nevertheless, when the effect of nAF on ICUD was adjusted for sepsis, there was no statistically significant difference between those that manifested nAF and the rest of the patients.
Conclusion: Patients suffering nAF seem to have worse prognosis during ICU stay. However, a direct impact of nAF on mortality was not documented.

1. Introduction

Atrial fibrillation (AF) is one of the most frequent cardiac arrhythmias in the general population as well as in critically ill patients.[1] Despite being under-recognised for many years in the intensive care units (ICU), it seems that AF is far more frequent in these settings than the 2–4% estimated for the general population.[2] Furthermore, its incidence is reported to vary greatly depending on the type of ICU involved.[2,3]

At first, AF attracted the attention of researchers in ICUs treating post-cardiac surgery patients, 10–65% of whom seem to manifest AF.[4] Previously published data that supported the association of

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this particular arrhythmia with poor clinical outcome gave reason for the investigation of other critically ill populations as well. As a result, studies were conducted in patients submitted to non-cardiac surgery and, later, in patients that underwent non-thoracic surgery.[5–12] The reported frequency of AF in the former population ranges from 9 to 29% while in the latter population it reaches 8.9%. Concerning prognosis, it is suggested that new-onset AF (nAF) is associated with increased mortality and longer hospital stay in the aforementioned critically ill populations.[4,6,10,12]

However, data regarding the frequency of nAF in general ICUs and other non-cardiac and non-surgical populations are limited.[13–15] Moreover, it is uncertain whether the diagnosis of nAF conveys any prognostic information in this setting.[13,14] An accumulating body of evidence supports the concept that systemic inflammation might be a significant contributor to the manifestation of nAF.[16] Given the fact that sepsis is a common diagnosis in all ICUs, and has a direct impact on clinical outcome, it seems reasonable that this parameter should be evaluated in every investigation addressing the prognostic effect of nAF.

In this prospective observational study we attempted to investigate the incidence of nAF and its impact on prognosis, in the setting of a general ICU. Our intention was to address these issues in relation to the potential impact of inflammation.

2. Methods

The study was designed as a prospective single-centre observational study and was conducted in a non-cardiac general ICU over a 12-month period. The ICU admits primarily medical patients who require mechanical ventilation as well as trauma and non-cardiac surgery patients. The study complies with the Declaration of Helsinki and the ethics committee of the hospital has approved the research protocol.

Consecutive patients admitted to the ICU were included in the present study. Patients admitted for brief post-operative monitoring and patients with chronic or intermittent AF and AF present upon admission, were excluded from the final analysis. A number of variables were recorded for each patient at the time of admission including basic demographics and pre-existing morbidities. All patients were risk stratified at presentation according to APACHE II scoring system. During the ICU stay, conditions related to the occurrence of AF and the manifestation of systemic inflammatory response syndrome (SIRS) and sepsis in particular, were documented. In-ICU data were prospectively collected on predesigned case report forms.

All ICU patients were monitored by means of a continuous 3-lead electrocardiogram (ECG) and a 12-lead ECG was acquired where there was a heart rate increase and/or arrhythmia. The diagnosis of AF was made by ECG interpretation, based on the observation of R–R wave interval irregularity without repetitive pattern and the absence of distinct P waves or the replacement of P waves with fibrillatory atrial waves. In addition, diagnosis was confirmed by the absence of previously documented A waves in the transmitral flow doppler signal of a contemporary transthoracic echocardiogram. All ECGs and echocardiographic studies were also analysed off-line and diagnosis was confirmed by a cardiologist blinded to the patients' clinical and biochemical data. On the occurrence of new-onset AF, clinical and laboratory circumstances, as well as cardioversion success and relapse, were reported. SIRS and sepsis were defined according to the American College of Chest Physicians/Society of Critical Care Medicine Consensus Conference.[17] Apart from the manifestation of SIRS, adequate evidence of infection was required to document the diagnosis of sepsis. Specifics of sepsis severity, such as the use of vasopressors and corticosteroids, were reported in all cases.

Table 1
Patient characteristics (N = 133).

Age (years ± SD)	52.5 ± 19.6
Gender (%m/%f)	67.7/32.3
APACHE II (points ± SD)	16.0 ± 6.6
Cause of admission (%)	
Medical	53.3
Trauma	36.7
Non-thoracic surgery	10.0
Cardiovascular risk factors (%)	
Smoking	51.1
Arterial hypertension	38.4
Diabetes mellitus	18.1
Dyslipidemia	10.5
History of heart disease (%)	21.1
History of lung disease (%)	18.1
History of neurological disorders (%)	9.0
History of rheumatologic disease (%)	2.3
History of thyroid hormone disorders (%)	3.8

The management of most diagnoses in the ICU was protocol-based, at least regarding the indications for major interventions and further medical therapy was left to the discretion of the attending physician who was unaware of the study protocol. Sepsis was treated with a stepwise protocol based on the principles of the Surviving Sepsis Campaign Guidelines.[18] However, the treatment of nAF did not follow a pre-specified protocol except for hemodynamic destabilisation which should be treated with electrical cardioversion. In the rest of the cases, efforts to re-establish sinus rhythm were made by electrical cardioversion or medication according to the decision of the intensivist. This was also the case after a relapse when rate or rhythm control should be decided. The choice of antiarrhythmic and antithrombotic drugs was also left to the discretion of the physician. All decisions were recorded in the patients' case report forms.

All-cause death during ICU stay (ICUD) was the pre-specified end-point of the present study, while the total length of stay in the ICU (LOS) was also reported for all surviving patients.

2.1. Statistical analysis

The categorical variables were expressed as percentages, while the continuous variables were expressed as mean ± SD when normally distributed and otherwise as median (25th, 75th percentile). Normal distribution was tested using the Kolmogorov–Smirnov test. Continuous variables were compared using the t-test or the Mann–Whitney U-test, as appropriate. Associations of dichotomous variables were tested by chi square or Fisher's exact test, as appropriate. All tests were 2-tailed, and $p < 0.05$ was considered significant. The predictive effect of nAF before and after adjustment for covariates was estimated by logistic regression analysis. Statistical analysis was performed with Statistical Package for Social Sciences software (release 17.0, SPSS Inc., Chicago, Illinois).

3. Results

A total of 171 patients were admitted to our ICU and were enrolled in the present study registry. Thirty-two patients were admitted for brief post-operative monitoring during the study period and 6 patients were found to have chronic AF and were excluded. Thus the population of the final analysis consisted of the remaining 133 patients. The observed mean age was 52.5 (±19.6) years. Of the study cohort, 67.7% were male. The disease severity was estimated by a mean APACHE II risk score of 16.0 (±6.6). The patient characteristics are presented in Table 1.

Twenty patients developed AF during their stay in the ICU, which corresponds to a 15% of the study sample. The incidence of new-onset AF was 15.6% and 14.0% in male and female

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