Intensive Care Med (2019) 45:928–938
https://doi.org/10.1007/s00134-019-05633-x

REVIEW

New-onset atrial fibrillation in adult critically ill patients: a scoping review

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Abstract

Purpose: New-onset atrial fibrillation (NOAF) is common and associated with increased morbidity and mortality. However, its clinical importance and management in critically ill patients are not well described. The aim of this scoping review is to assess the epidemiology and management strategies of NOAF during critical illness.

Method: The review was conducted in accordance with the PRISMA extension for scoping reviews. We searched PubMed, EMBASE and the Cochrane Library for studies assessing the incidence, outcome and management strategies of NOAF in adult critically ill patients. The quality of evidence was evaluated using the Grading of Recommendations Assessment, Development, and Evaluation (GRADE) approach.

Results: A total of 99 studies were included, of which 79 were observational and 20 were interventional. The incidence of NOAF varied from 1.7% to 43.9% with considerable inter-population variation (very low quality of evidence). Commonly identified risk factors for NOAF included higher age, cardiovascular comorbidities and sepsis. The occurrence of NOAF was associated with adverse outcomes, including stroke, prolonged length of stay and mortality (very low quality of evidence). We found limited data on the optimal management strategy with no evidence for firm benefit or harm for any intervention (very low/low quality of evidence).

Conclusions: The definition and incidence of NOAF in critically ill patients varied considerably and many risk factors were identified. NOAF seemed to be associated with adverse outcomes, but data were very limited and current management strategies are not evidence-based.

Keywords: Atrial fibrillation, Arrhythmias, Cardiac, Tachycardia, Critical illness, Intensive care units, Risk factors, Stroke, Thromboembolism, Mortality, Review

Introduction

Atrial fibrillation (AF) is the most common tachyarrhythmia worldwide [1]. The risk of AF increases with advanced age, hypertension and different heart diseases [2]. Evidence derived from non-critically ill populations has shown that AF contributes to negative short- and long-term outcomes such as haemodynamic instability, risk of stroke, heart failure and increased mortality [3].

New-onset AF (NOAF) is often seen in critically ill patients, but with variable frequency [4]. It has been suggested that the pathophysiology and etiology of NOAF during critical illness differ from AF in non-critically ill patients because of the presence of potential reversible factors including inflammation, electrolyte disturbance and use of proarrhythmic drugs [5]. However, the clinical importance of NOAF and whether NOAF is a marker of disease severity or independently associated with worse outcomes remain unclear. Also, knowledge about management strategies for NOAF including pharmacological

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rhythm or rate control, direct current (DC) cardioversion and anticoagulant therapy is sparse [6, 7].

Accordingly, in this scoping review we aimed to describe the incidence, risk factors, outcomes and management strategies related to NOAF during critical illness.

Method

Protocol and registration

We followed the methodology of the Preferred Reporting Items for Systematic reviews and Meta-Analyses extension for Scoping Reviews (PRISMA-ScR) statement [8] (the filled-in checklist is available in the Electronic Supplementary Material, ESM).

We prospectively registered our protocol in the Prospective Register of Systematic Reviews (PROSPERO), no. CRD42016052652.

Eligibility criteria

We framed the following research question: in adult critically ill patients, what is the incidence and outcomes of NOAF and what risk factors and treatment strategies exist?

We used a population, intervention, comparator and outcomes-based (PICO) approach to define eligibility criteria:

Population	Critically ill adults, defined as being in high-dependency units, emergency rooms, intensive care units (ICUs) or undergoing major non-cardiac thoracic surgery.
Intervention	Pharmacological and non-pharmacological (including DC cardioversion) treatment of NOAF.
Comparator	Any, including placebo and no treatment
Outcomes	Mortality, adverse events including thromboembolic events and length of stay in the ICU and hospital.

Definition of new-onset atrial fibrillation

We defined NOAF as AF diagnosed during hospital stay in patients with no prior history of persistent or permanent AF and with a duration of less than 1 week.

We included studies in which a proportion of the patient population had a history of paroxysmal AF.

Information sources and search strategy

We systematically searched PubMed, EMBASE and the Cochrane Library for relevant literature (ESM B) in December 2018, without any limitations on publication date and language.

We used the following search string:

1. "Atrial fibrillation" OR "atrial flutter" OR "supraventricular arrhythmia" OR "tachyarrhythmia"
2. "Critical care" OR "intensive care" OR ICU
3. #1 AND #2

We included observational studies and randomized clinical trials (RCTs). We excluded studies in animals and children, studies in populations of patients who had undergone cardiac surgery, who were not critically ill, who had persistent or permanent AF or other arrhythmias, and studies without original data.

Selection of sources and data extraction

The study selection process was completed using Covidence (www.covidence.org). Two authors (M.W., N.H.) independently screened titles and abstracts of the identified references. Potentially relevant articles were reviewed in full text and any disagreements were resolved with co-authors (M.H.M., A.P.). One author (M.W.) extracted data using a standardized data extraction form. The following study characteristics were extracted: study design, year of publication, type of population, interventions, comparator, incidence, risk factors and clinical outcomes.

Outcome measures

Our outcomes of interest included mortality at longest follow-up, thromboembolic events, adverse events, proportion of patients achieving rhythm control (conversion to sinus rhythm) or rate control, and length of stay in ICU or hospital. All outcomes were defined as per the included studies.

Assessment of risk of bias and quality of evidence

We assessed risk of bias of the included studies using the Cochrane Collaboration risk of bias tool for RCTs and the Risk of Bias In Non-randomized studies–of Interventions (ROBIN-I tool) for observational studies [9, 10].

The overall quality of evidence was evaluated using the Grading of Recommendations Assessment, Development, and Evaluation (GRADE) approach [11]. In brief,

Take-home message

New-onset atrial fibrillation is common during critical illness and may be associated with adverse outcomes, and current management strategies are not evidence-based.

we assessed the following domains: (1) risk of bias, (2) imprecision, (3) inconsistency, (4) indirectness and (5) publication bias. Accordingly, the overall quality of evidence was rated as high, moderate, low, or very low.

Data synthesis

Study characteristics, extracted data and results are presented descriptively. We grouped studies according to study design and type of population. Additionally, interventional studies were subgrouped with respect to whether prophylactic or active treatment regimens were investigated.

Results

We included a total of 99 studies, of which 79 were observational and 20 were interventional (Fig. 1).

Characteristics of studies

Of the 79 observational studies, 59 studies were conducted in a ICU setting, nine studies in non-cardiac thoracic surgery and 11 studies in other hospital settings (ESM D).

Out of the 20 interventional studies, nine studies were done in an ICU setting, six studies in non-cardiac thoracic surgery and five studies in emergency department setting (ESM E).

The majority of studies included patients from mixed ICUs ($n=25$) [12–36] and patients with varying severity of sepsis ($n=21$) [37–57] (Table 1). The remaining studies were in surgical settings ($n=15$) [58–72], patients undergoing non-cardiac thoracic surgery ($n=9$) [73–81] and acute medical illness ($n=9$) [82–90] (Table 1).

We identified 25 prospective observational studies [13–15, 21, 24, 25, 27, 30–32, 38, 41, 43, 47, 49, 58, 59, 61, 64, 69, 72, 74, 83, 88, 89] and 55 retrospective observational studies [12, 16, 17, 19, 20, 22, 23, 26, 28, 29, 33–37, 39–42, 44–46, 48, 50–57, 60, 62, 63, 65–68, 70, 71, 73, 75–82, 84–87, 90].

In the observational studies, NOAF was most commonly defined as detected or reported episodes of AF identified by chart review, electrocardiography (ECG) and/or use of hospital records. In 25 observational studies, NOAF was diagnosed by continuous telemetry and/or confirmed by 12-lead ECG [13–15, 17, 21, 24, 26, 30, 38, 43, 45, 47, 49, 59, 64, 69, 72–76, 78, 82, 83, 89].

We identified 20 interventional studies; six studies assessed different prophylactic regimens [91–96] and 14 studies therapeutic regimens [97–110]. Of the 20 studies, 15 were RCTs [91–96, 99, 100, 102–104, 106, 108–110].

In the interventional studies, NOAF was primarily defined as a rapid and irregular heart rhythm with varying definitions of heart rate and duration.

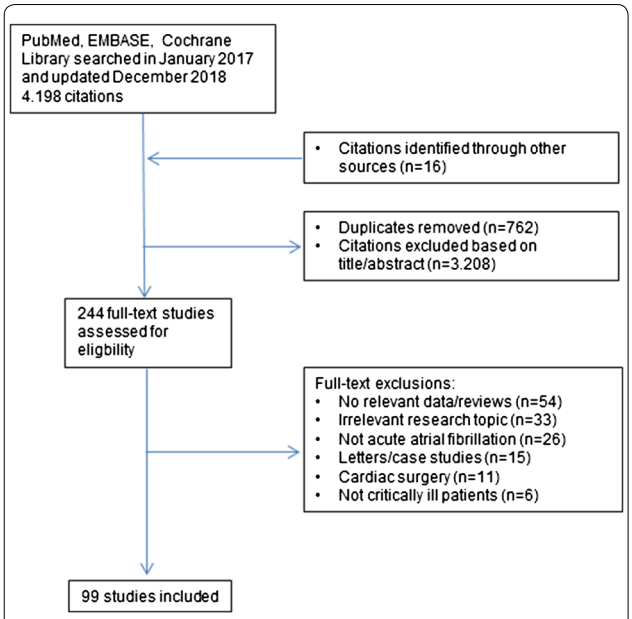

Fig. 1 Flowchart

Incidence

The overall reported incidence of NOAF varied from 1.7% to 43.9% (Table 1). We observed considerable inter-population variation depending on case-mix, the definition of NOAF and the detection method used.

Studies using continuous monitoring or ECGs reported a median (interquartile range) of NOAF of 14.2% (9–25%), as compared to 7.2% (5.4–14.8%) in studies assessing NOAF by chart review, medical records or administrative data (ESM D).

Patients with severe sepsis or septic shock, those with non-cardiac thoracic surgery and patients undergoing organ transplant seemed to have the highest incidences of NOAF [15, 38, 40–43, 45–49, 56, 74, 75, 80, 81] (Table 1). In general, there was lack of a uniform definition of NOAF in the included studies. Two observational studies, which used continuous monitoring devices, reported that subclinical/silent NOAF undetected by clinicians was present in between 8% and 34% of the patients [26, 38].

The overall quality of evidence in the studies assessing the incidence of NOAF was very low because of risk of bias, inconsistency and imprecision.

Risk factors

Twenty-three studies performed multivariate analysis of risk factors associated with NOAF [12, 15, 19, 25, 26, 38, 44, 49, 51, 52, 63–65, 71–76, 78, 81, 82, 89].

The reported risk factors for the development of NOAF were within four categories: (1) baseline demographic

Table 1 Observational studies assessing the incidence of NOAF and its impact on LOS and mortality

Population	Total number of studies	Incidence of NOAF	Absolute increase in LOS Median [interquartile range]	Absolute increase in mortality Median [interquartile range]	GRADE (quality of evidence)
Non-cardiac thoracic surgery [73–81]	9	9.9–43.5%	In-ICU – In-hospital 3 days [3–5 days]	In-ICU – In-hospital – 28/30-day 2.6% [1.6–8%]	Low/very low
Mixed ICU [12–36]	25	1.7–29.5%	In-ICU 5.6 days [3–6 days] In-hospital 10 days [3–14 days]	In-ICU 15.4% [9.5–30.2%] In-hospital 23.5% [11.8–28.4%] 28/30-day –	Low/very low
Acute medical illness [82–90]	9	5.4–21.7%	In-ICU – In-hospital 3.3 days [2–8 days]	In-ICU – In-hospital 27.2% [19.4–39.1%] 28/30-day –	Low/very low
Mixed populations with varying severity of sepsis [37–57]	21	1.9–43.9%	In-ICU 5 days [3.2–10.3 days] In-hospital –	In-ICU 14.8% [5.2–21.3%] In-hospital 25.2% [16.9–36.4%] 28/30-day –	Low/very low
Surgical ICU/[a]other [58–72]	15	4.1–14.9%	In-ICU 2 days [0.3–10 days] In-hospital 7.5 days [4–10.1 days]	In-ICU 15.5% [11.3–21.8%] In-hospital 17.4% [16.4–19.2%] 28/30-day –	Low/very low

GRADE Grading of Recommendations, Assessments, Development, and Evaluation, *ICU* intensive care unit, *LOS* length of stay, *NOAF* new-onset atrial fibrillation

[a] Including major surgery and trauma patients

characteristics, (2) organ failures and/or acute conditions, (3) laboratory findings and (4) interventions (Fig. 2).

Baseline characteristics associated with NOAF included higher age [13–15, 21, 24, 26, 30, 32, 35, 38, 41, 42, 44, 45, 47, 52–54, 56–58, 64, 65, 69–72, 75–78, 80–85, 89, 90], male sex [14, 30, 41, 52, 54, 71, 76, 77, 80, 84, 90] and co-existing cardiovascular disease [13, 14, 17, 18, 21, 24, 30, 41, 44, 45, 47, 48, 52–54, 56, 57, 62, 64, 65, 70, 76, 78, 80, 82–84] (ESM C).

Sixteen studies reported significantly higher severity of illness in patients with NOAF as compared to patients without NOAF [13–15, 21, 30, 32, 45, 48, 59, 63, 64, 70, 72, 84, 85, 87].

Organ dysfunctions and acute conditions associated with NOAF were respiratory failure [22, 26, 41, 44, 52, 57, 73, 89, 90], circulatory failure and/or shock [21–23, 26, 30, 41, 45, 64, 72], acute kidney injury and/or use of renal replacement therapy [14, 17, 21, 22, 30, 41, 45, 49, 52, 64, 65, 72, 84, 87], trauma [13, 32, 64, 70–72] and sepsis [14, 15, 20–22, 24, 26, 30, 32, 42, 63, 64, 72, 87, 89] (ESM C).

Laboratory variables associated with NOAF were elevated white blood cell count, elevated C-reactive protein [14, 24, 33, 41, 45, 47, 75], elevated brain natriuretic peptide [14, 19, 38, 76], and disturbances in sodium, potassium or magnesium balance [12, 14, 23, 24, 41, 51, 58, 59, 70]. In addition, dilatation of the right or left atrium on echocardiography, low left ventricular ejection fraction

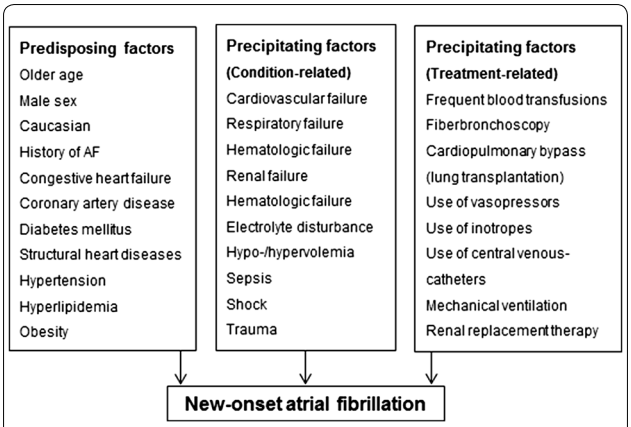

Fig. 2 Identified risk factors for atrial fibrillation in critically ill patients

and functional mitral regurgitation [24, 30, 38, 45, 82, 90] were associated with NOAF (ESM C).

Interventions associated with NOAF included use of vasopressors/inotropes [13–15, 21, 23, 30, 47, 49, 63–65, 72, 77, 80, 84], mechanical ventilation [13, 15, 37, 44, 53, 67, 68, 70, 71, 80, 84, 87], use of pulmonary artery and/or central venous catheters [23, 37, 52, 53, 58, 64, 71], fluid overload [23, 30, 59, 64, 70, 72] and blood transfusion [71, 72, 78] (ESM C).

The overall quality of evidence in the studies assessing risk factors for NOAF was very low because of risk of bias and inconsistency.

Outcomes

In general, patients with NOAF had worse outcomes than those without NOAF, including higher mortality [13–16, 21, 26, 30, 34, 37, 41, 44, 45, 48, 50, 56, 58, 59, 61, 64, 66, 67, 71, 73, 78, 80, 82, 84–87, 89] and prolonged ICU [14, 21, 22, 25–27, 30, 32, 37, 41, 47, 48, 59, 61, 64, 70–72, 77, 80, 84–87] and hospital stay [13, 21, 26, 27, 30, 44, 59, 64, 65, 69–71, 73–75, 77, 79–82, 84–87] (Table 1).

NOAF was independently associated with increased mortality in some studies [12, 14, 30, 45, 71, 85] but not in all [13, 25, 44, 84]. The studies evaluating the prognostic impact of NOAF by adjusted analysis varied in sample size, population, classification of NOAF, the number of clinical variables used in the adjusted analysis, and in follow-up. The quality of evidence was very low because of risk of bias, imprecision and inconsistency.

We observed no consistent association with thromboembolic events [23, 34, 35, 38, 39, 42, 48–50, 54, 59, 66, 67, 70]. However, the occurrence of NOAF seemed to increase the risk of ischemic stroke [35, 52, 54, 57, 67]. The use, indication for and effect of anticoagulant therapy were limited reported [13, 20, 22, 23, 34, 35, 38, 42, 48–50, 57, 67, 68]. The overall quality of evidence was very low because of risk of bias, imprecision and inconsistency.

Prophylactic and therapeutic management strategies

Of the 20 included interventional studies, ten assessed rhythm control with nine different drugs [97–106], four assessed rate control with five different drugs [107–110] (Table 2) and six focused on prophylactic interventions using five different drugs [91–96] (Table 3).

Four of the 20 interventional studies used a placebo-controlled design [91, 92, 94, 109]. Three of the studies were conducted in non-cardiac thoracic populations assessing prophylactic strategies [91, 92, 94] and one study in emergency departments assessing therapeutic strategy [109]. One study examined the interventions' impact on length of stay and/or mortality [91]. The quality of evidence was low because of considerable risk of bias due to inadequate randomization [92, 94] and inconsistency [91, 92, 94, 109].

The studies on rhythm control assessed procainamide, cibenzoline, flecainide (class I antiarrhythmic agents) [98–100], esmolol (class II) [104, 106], amiodarone, ibutilide (class III) [97, 98, 100–103, 105], verapamil, diltiazem (class IV) [99, 103, 104, 106] or magnesium (class V) [102] (Table 2).

The rate control strategy was evaluated with amiodarone (class III) [110], diltiazem, verapamil (class IV) [107, 108, 110], magnesium or digoxin (class V) [109, 110] (Table 2).

Prophylactic regimens included acebutolol (class II) [92], amiodarone (class III) [93, 95, 96], diltiazem, verapamil (class IV) [91, 92, 94] and magnesium (class V) [93] (Table 3). Three RCTs suggested a reduction in the length of hospital stay [93, 95, 96]; four RCTs suggested a reduction in mortality [91, 95, 96, 106] using active treatment. Most of the RCTs had unclear or high risk of bias, especially due to inadequate randomization and/or blinding method in studies assessing treatment regimens [99, 100, 103, 104, 106, 108, 110] or prophylactic regimens [92–96].

The overall quality of evidence of the different pharmacological interventions varied from very low to low because of risk of bias and imprecision (ESM F–G).

In the observational studies, the management strategies were inconsistently reported with associated risk of bias, indirectness and imprecision (very low quality of evidence). Spontaneous resolution of NOAF was reported in five studies, and it varied from 9% to 25% [21, 60, 64, 72, 78]. DC cardioversion was primarily used in patients with haemodynamic instability or when previous medical treatment had failed to convert NOAF to sinus rhythm [23, 47, 81, 88].

Table 2 Interventional studies assessing therapeutic strategies for NOAF

Study	Population Study design Number of patients	Intervention/comparator	Primary outcome		
			Rhythm control	Rate control	Mortality
[97]	ICU NRT 72	Amiodarone PO Amiodarone IV	64% 67%	–	–
[98]	ICU NRT 46	Cibenzoline Amiodarone	72% 71%	–	–
[99]	ICU RCT 30	Flecainide Verapamil	80% 33%	–	–
[100]	ICU RCT 24	Procainamide Amiodarone	71% 70%	–	–
[101]	ICU NCT 26	Amiodarone	81%	–	–
[102]	ICU RCT 42	Magnesium Amiodarone	78% 50%	–	–
[103]	ED/IM RCT 24	Amiodarone Verapamil	77% 0%	–	–
[104]	ED/IM RCT 45	Esmolol Verapamil	50% 12%	–	–
[105]	ED/IM NRT 34	Ibutilide	79%	–	–
[106]	Surgical ICU RCT 64	Esmolol Diltiazem	85% 62%	–	31% 38%
[107]	ICU postop. NCT 10	Verapamil	–	100%	–
[108]	ICU RCT 60	Diltiazem Amiodarone bolus Amiodarone inf.	–	70% 55% 75%	35% 35% 35%
[109]	ED/IM RCT 199	Magnesium Placebo	–	65% 34%	–
[110]	ED/IM RCT 150	Diltiazem Digoxin Amiodarone	–	90% 74% 74%	–

ED emergency department, *ICU* intensive care unit, *IM* internal medicine, *INF* infusion, *IV* intravenous, *NCT* non-controlled trial, *NOAF* new-onset atrial fibrillation, *NRT* non-randomized trial, *PO* per os, *Postop* postoperative, *RCT* randomized controlled trial

Discussion

In this scoping review, we observed considerable variation in the incidence of NOAF in adult critically ill patients, and we identified several risk factors associated with NOAF.

NOAF seemed to be associated with adverse outcomes, including mortality, stroke, and increased ICU and hospital length of stay. However, the evidence on the optimal management strategy was limited and of low/very low quality.

Considerable variation was observed in the reported incidences of NOAF. The large variation in the reported incidence may be due to variation in the used definitions, monitoring intensity and lack of standardized detection method of NOAF, which may have resulted in underdetection in some studies. However, the extent and clinical impact are unknown.

A standardized approach to the definition and method of detection of NOAF is likely needed. First-time detected AF and newly detected episodes in patients with paroxysmal AF, confirmed either by telemetry or ECG,

Table 3 Interventional studies assessing prophylactic strategies for preventing NOAF

Study	Population Study design Number of patients	Intervention comparator	Primary outcomes		
			Incidence (NOAF)	LOS median or mean (± SD)	Mortality
[91]	Thoracic surgery RCT 330	Diltiazem (D) Placebo (P)	14.9% 24.5%	Hospital D: 8.9 (± 7.9) days P: 8.7 (± 7.8) days	D: 0.6% P: 2.0%
[92]	Thoracic surgery RCT 117	Acebutolol Diltiazem Placebo	5.1% 23.1% 20.5%	–	–
[93]	Thoracic surgery RCT 657	Amiodarone (A) Magnesium (M) Control (C)	9.6% 12.5% 20.5%	ICU A: 24.8 (± 0.86) h M: 32.5 (± 0.94) h C: 43.8 (± 1.2) h Hospital A: 4.2 (± 0.17) days M: 6.1 (± 0.19) days C: 8.3 (± 0.17) days	–
[94]	Thoracic surgery RCT 199	Verapamil Placebo	8% 15.1%	–	–
[95]	Thoracic surgery RCT 130	Amiodarone (A) Control (C)	13.8% 32.3%	ICU A: 46 h C: 84 h Hospital A: 7 days C: 8 days	A: 3.1% C: 1.5%
[96]	Thoracic surgery RCT 80	Amiodarone (A) Control (C)	15% 40%	ICU A: 68 h C: 77 h Hospital A: 11 days C: 12 days	A: 0% C: 5%

ICU intensive care unit, *LOS* length of stay, *NOAF* new-onset atrial fibrillation, *RCT* randomized controlled trial, *SD* standard deviation

could be a pragmatic and clinically relevant definition of NOAF in future studies.

NOAF during critical illness is common and probably the result of a higher susceptibility due to critical illness and concurrent presence of predisposing and precipitating risk factors [111, 112]. We identified several risk factors for NOAF and the most common factors were higher age, cardiovascular comorbidities, sepsis, multi-organ failure and life-sustaining interventions (ESM C). However, it may be difficult to assess whether risk factors are chronic or acutely developed when NOAF is diagnosed.

It has been suggested that the combination of arrhythmogenic substrates and triggers may induce structural and cardiac changes causing NOAF [5], especially in patients with a previous history of AF or other chronic conditions who may have a lower threshold for developing NOAF. However, most of the identified risk factors associated with NOAF are common in ICU patients and often present concurrently, thereby lowering the discriminative value of the individual factors for guiding clinical decision-making.

Most studies showed an association between NOAF and poorer outcome. However, NOAF may be a marker of poor outcome rather than an independent prognostic factor. Residual confounders may lead to overestimations of the impact of NOAF on outcomes, even in adjusted analyses. Only a minority of studies assessed NOAF as an independent risk factor for mortality, and conflicting results were reported. This could be explained by risk of bias and clinical heterogeneity among the studies or different adjustments for predisposing factors. It seems reasonable that NOAF could increase the mortality as demonstrated in two prospective cohort studies conducted in ICUs [14, 30], but the evidence is still too limited to draw any firm conclusion. Thus, it is unclear whether NOAF is a transient phenomenon during critical illness or a truly independent causal factor, and whether treatment of NOAF improves outcome.

We observed considerable clinical heterogeneity among the included interventional studies; most were single-centre and at high risk of bias. We found no high-quality RCTs assessing the impact of using active therapeutic

intervention vs. no treatment or placebo in critically ill patients on patient-important outcomes.

The overall aim in the management of NOAF is to prevent related complications, including haemodynamic instability, development of stroke or heart failure by targeting for sinus rhythm or reducing rapid ventricular rate to stabilize the haemodynamics by improving ventricular filling, and thereby increasing cardiac output [113–115]. In addition, assessing the need of anticoagulant therapy to lower the risk of ischemic stroke and improve long-term patient-important outcomes, including quality of life. However, we found no high-quality RCT of therapeutic interventions on patient-important outcomes. Instead, we found mostly small, single-centre trials with high risk of bias, no use of placebo, considerable clinical heterogeneity and haemodynamic surrogate outcomes such as rhythm and rate control. Neither rhythm nor rate control is established as a validated outcome of real importance to patients.

Thus, interventions that look beneficial in such trials may have an undetected overall negative impact on patients and it is still unclear whether the haemodynamic stable patient benefits from active treatment or if a more conservative non-pharmacological approach is superior. This is especially a concern in vulnerable critically ill patients and because antiarrhythmic drugs all have well-known adverse effects [116, 117]. The European Society of Cardiology recommends the use of beta-blockers or calcium channel blockers for rate control [118], but amiodarone or digoxin might be advantageous in patients with structural heart diseases or low left ventricular ejection fraction owing to a positive or fairly less negative inotropic effect. However, rhythm and rate control of AF have not led to significantly different outcomes in non-critically ill patients [119–121]. Whether this is the same in critically ill patients is unknown because of differences in disease severity, interventions, polypharmacy and type of AF, which could have an impact on outcomes. Most guidelines are derived from non-critically ill populations and cannot be extrapolated to critically ill patients, and our findings suggest that only low-quality evidence exists for the management of NOAF during critical illness.

The concurrent correction of electrolyte and fluid disturbances may alone facilitate conversion of NOAF, and thereby reduce the risk of adverse drug reactions from antiarrhythmic drugs [117]. Since most trials omitted placebo they are at risk of detecting a false positive effect of antiarrhythmic drugs.

In non-critically ill patients, evidence has shown that AF increases the risk of stroke [113]. However, few studies have assessed anticoagulant therapy in critically ill patients, including timing, agents and optimal dosages, and their balance between effects and side effects. Anticoagulant therapy is a challenge in critically ill patients considering the presence of organ failures, risk of bleeding, coagulopathy, polypharmacy and potential need for invasive interventions. Meanwhile, different pro-inflammatory states [122] such as sepsis, surgery and trauma may also increase the risk of thrombosis. The burden of silent or subclinical NOAF and the risk of thrombosis were also largely unknown [123, 124].

The strengths of our scoping review include the comprehensive and systematic search, the pre-registration on PROSPERO, adherence to the PRISMA-ScR statement [8] and assessment of the quality of evidence according to GRADE [11].

Our review also holds limitations. Only one author (M.W.) extracted data, but it is unlikely that this had any influence on the overall conclusion that the evidence for treatment of NOAF in critically ill patients is of low quality. In addition, we cannot be sure that our search string identified all relevant studies. We included patients from emergency departments and patients with a previous history of AF, which may share some similarities including the presence of acute critical illness and potential risk factors, e.g. hypoxemia, electrolyte disturbances and sepsis. It may be argued that these patients differ from ICU patients, but as a result of the lack of standardized detection method and variation in the used definitions of NOAF and critical illness, we found it reasonable to include a broader range of studies so that we would not miss any important information. However, we excluded studies on cardiac surgical and non-acutely ill outpatients because of assumption of a different background for NOAF, and thus our results are not generalizable to these populations.

In this scoping review, we observed considerable variation in the incidence of NOAF in adult critically ill patients, and we identified several risk factors associated with NOAF. NOAF seemed to be associated with adverse outcomes, including mortality, stroke, and increased ICU and hospital length of stay. However, the evidence on the optimal management strategy was limited and of low/very low quality. Therefore, high-quality RCTs are warranted to assess the balance between the benefits and harms of different management strategies in critically ill patients.

Electronic supplementary material

The online version of this article (https://doi.org/10.1007/s00134-019-05633-x) contains supplementary material, which is available to authorized users.

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Author contributions
MW, NH, AP and MHM contributed to the study design. MW and NH contributed to the study selection. MW performed the data extraction. All the authors contributed to the revision of the manuscript.

Funding
MW's salary is paid by the Research Council of Rigshospitalet.

Compliance with ethical standards

Conflicts of interest
The authors have received no specific funding for this study. The Department of Intensive Care at Rigshospitalet receives support for other research projects from Ferring Pharmaceuticals, Denmark; and the Novo Nordisk Foundation, Denmark.

Publisher's Note

Received: 14 February 2019 Accepted: 29 April 2019
Published online: 14 May 2019

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