Review

Clinical review: Treatment of new-onset atrial fibrillation in medical intensive care patients – a clinical framework

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Abstract

Atrial fibrillation occurs frequently in medical intensive care unit patients. Most intensivists tend to treat this rhythm disorder because they believe it is detrimental. Whether atrial fibrillation contributes to morbidity and/or mortality and whether atrial fibrillation is an epiphenomenon of severe disease, however, are not clear. As a consequence, it is unknown whether treatment of the arrhythmia affects the outcome. Furthermore, if treatment is deemed necessary, it is not known what the best treatment is. We developed a treatment protocol by searching for the best evidence. Because studies in medical intensive care unit patients are scarce, the evidence comes mainly from extrapolation of data derived from other patient groups. We propose a treatment strategy with magnesium infusion followed by amiodarone in case of failure. Although this strategy seems to be effective in both rhythm control and rate control, the mortality remained high. A randomised controlled trial in medical intensive care unit patients with placebo treatment in the control arm is therefore still defendable.

Introduction

Atrial fibrillation (AF) is frequently observed in the medical intensive care unit (MICU) [1], with up to about 15% of MICU patients showing periods of AF [2-4]. AF directly leads to loss of the atrial kick and, as a consequence, reduces ventricular loading. Especially if the ventricular compliance is decreased, as is the case in sepsis and many other medical conditions, this reduction results in decreased cardiac performance. By performance, we mean the capacity to meet pressure and volume requirements. The irregular and mostly rapid ventricular response also shortens the ventricular filling time, and thereby shortens the preload. AF therefore reduces cardiac performance. The reduction is more serious in patients with pre-existing cardiac dysfunction due to decreased ventricular compliance. A persistent high ventricular rate may lead to tachycardia-mediated cardiomyopathy [5]. Conversion to sinus rhythm (SR) improves ventricular function in patients with heart failure [6]. These findings urge most intensivists to treat AF.

Most intensivists may have adopted an AF treatment modality based on their individual experience combined with extrapolation of the treatment of other, mostly unrelated, but well-defined and well-established, patient groups. In most cases this means that, after correction of assumed or perpetuating factors, treatment directly aimed at the rhythm disorder itself will be started. To date, treatment of AF in the MICU cannot be supported by sufficient evidence from the literature. Notwithstanding the large number of patients involved, thorough research in this field is scarce [7]. There are important reasons to believe that MICU patients are different from other patients with AF and therefore require a more tailored therapy. Fundamental questions that remain unanswered for MICU patients are summarised in Table 1.

To find answers for these questions we searched for direct clinical evidence and – when not available – searched for evidence from related areas. Direct evidence will be considered all results derived from randomised controlled trials or well-conducted epidemiological studies in MICU patients. The aim of the present paper is to improve insight, to explore future research goals and to define an optimal treatment mode based on current knowledge for the population admitted in MICU. We will describe the evidence found per question presented in Table 1 according to the patient group from which it is derived. Each section will start with MICU patients, followed by mixed intensive care unit (ICU) patients, surgical ICU patients and cardiothoracic surgery ICU patients, and will end with the least related patient category – outpatients.

AF = atrial fibrillation; CTS = cardiothoracic surgery; ICU = intensive care unit; LOS = length of stay; MICU = medical intensive care unit; SR = sinus rhythm.

Table 1

Questions regarding the prevalence and treatment of atrial fibrillation in medical intensive care unit patients

What is the pathophysiology of atrial fibrillation in medical intensive care unit patients?

Does atrial fibrillation attribute to mortality?

Does atrial fibrillation attribute to morbidity?

Can atrial fibrillation be treated or prevented?

What are the adverse effects of any treatment?

Can (preventive) treatment of atrial fibrillation improve survival?

Can (preventive) treatment of atrial fibrillation improve morbidity?

Should we aim for rate control or rhythm control?

Does atrial fibrillation increase stroke incidence in medical intensive care unit patients?

Can atrial fibrillation-associated stroke be prevented?

Methodology

We conducted a computer literature search in the databases of MEDLINE, EMBASE and the Cochrane Library, from 1966 to 2007, combining the following key words: 'intensive care' or 'critical care' or 'critically ill' and 'atrial fibrillation' or 'atrial tachyarrhythmia' and 'treatment' or 'aetiology' or 'risk factors'. Reference lists of all selected articles were reviewed to identify other relevant articles. For relevant articles the search was extended in PubMed with the 'related articles' search function. PubMed was checked for other publications by authors of key papers. Web of Science® was checked for papers citing key papers. All selected articles were reviewed by two different reviewers.

Definitions

AF is a supraventricular tachyarrhythmia characterised by uncoordinated atrial activation with subsequent deterioration of atrial mechanical function. On the electrocardiogram, AF is described by the replacement of consistent P waves with rapid oscillations or fibrillatory waves that vary in size, shape and timing, associated with an irregular, frequently rapid, ventricular response when atrioventricular conduction is intact [8]. Recurrent means at least two episodes of AF. Paroxysmal means self-terminating, and persistent means that self-termination is absent and that electrical or pharmacological conversion is necessary to end AF [9]. MICU patients are patients admitted to the ICU not for surgical or cardiological reasons.

What is the pathophysiology of atrial fibrillation?

There are no data on MICU patients specifically, nor data for surgical ICU patients. There are, however, risk factors identified in these patient categories. Risk factors due to causality can in general not be distinguished from epiphenomena. Risk factors can at least suggest a certain pathophysiology, however, and therefore they may help in the identification of a patient population. Independent risk factors for AF are age, disease severity, hypertension, hypoxia, previous AF, congestive heart failure, chronic obstructive pulmonary disease, chest trauma, shock, a pulmonary artery catheter, previous use of calcium-channel blockers, low serum magnesium, withdrawal of β-blocker or angiotensin-converting enzyme-inhibitor and withdrawal of catecholamine use [10-17].

In patients after noncardiac surgery, the right atrial pressure rather than fluid overload or right heart enlargement seems to be correlated with AF [14,18-20]. Cardiothoracic surgical (CTS) patients with AF, however, tend to have a more positive fluid balance [21,22]. Interestingly, systemic inflammatory response syndrome and sepsis are also independent risk factors [10,14]. A proinflammatory state, as measured by leucocytosis or monocyte activation, is associated with AF, although the mechanism is not clear [23-25]. AF is sometimes the first sign of sepsis [4]. A genetic predisposition for an increased inflammatory response is associated with an increased incidence of postoperative AF [26]. Catecholamines influence the susceptibility for AF [10,27]. Hypovolaemia is also a risk factor [28].

Most knowledge about AF is gained from studies in noncritically ill patients. AF is probably the final common pathway of structural changes in combination with a trigger leading to abnormal activation patterns in the atria [8]. Structural changes can be multiple; for example, fibrosis and amyloidosis. Structural changes increase with age, which might be the explanation for the fact that age is the most important risk factor for AF. There are numerous triggers that can lead to AF when combined with a substrate and a perpetuating factor. Ischaemia, and local (pericarditis or myocarditis) and generalised inflammation can affect the atria [29,30]. Hypovolaemia and hypervolaemia or a sudden increase in afterload, as in pulmonary embolism, and mitral or tricuspid valve dysfunction are examples of increased atrial workload that can cause AF. Nervous (both sympathic and parasympathic) tone, hormonal changes, electrolyte disturbances and also the preload and the afterload influence excitability and conduction in the atria and atrio–ventricular junction [27]. The cumulative effect of structural changes and one or more of these triggers and perpetuating factors will determine whether AF will occur and will persist [8,31].

Conclusion on pathophysiology

From human and animal studies it is clear that the cause of AF is multifactorial. There are more or less permanent changes in morphology and more or less temporary changes in haemodynamic balance, electrolyte balance, neural balance and hormonal balance that facilitate an appropriate environment and electrical stage for AF. Given the identified risk factors it is clear that the population admitted to a MICU

differs in prevalence of risk factors, and therefore differs in AF mechanism, from other ICU and non-ICU populations. Especially inflammation, haemodynamic changes, increasing age, comorbidity and neuroendocrine disturbances are more frequent in MICU patients. Extrapolation of data from non-MICU patients to MICU patients can only be done with caution.

Does atrial fibrillation attribute to mortality?

AF did not influence mortality significantly in a mixed medical–cardiac ICU [2]. In a general ICU population, however, patients with AF appeared to have a significantly higher mortality compared with patients without AF [3]. Furthermore, surgical patients with new-onset AF have a significantly higher disease severity and higher ICU mortality [4,11,32,33]. A persistent elevated increased heart rate, frequently due to AF, is associated with increased mortality [34]. In a large, retrospective, cohort study in cardiac surgery patients, AF was not an independent predictor for inhospital mortality [35]. Patients outside the ICU setting with AF have increased overall mortality and mortality of cardiovascular causes [36,37].

Conclusion on mortality

There is an association between AF and mortality in some patient groups. There is, however, no evidence for a causal relationship [38]. Both AF and mortality being a result of disease severity might be one of the explanations for the association [10]. A causal mechanism they have in common (for example, inflammation) might be another explanation.

Does atrial fibrillation attribute to morbidity?

AF did increase the length of stay (LOS) in a mixed medical–cardiac ICU [2]. Onset of AF in a patient in the surgical ICU increases their LOS in the ICU and in the hospital [11,16,32,33,39,40]. Onset of AF reduces the systolic blood pressure [41,42], and also decreases oxygen saturation and increases the pulmonary artery wedge pressure. An increased heart rate is associated with increased morbidity [34].

A number of symptoms in noncritically ill patients have been described [8]. Most relevant for ICU patients is the decreased cardiac output, which is caused by the loss of coordinated atrial contraction, by irregularity of ventricular contraction [43], by inadequate filling time for the left ventricle due to tachycardia, and by tachycardiomyopathy [8,44]. Tachycardiomyopathy can occur as soon as 24 hours after the start of AF [44].

Conclusion on morbidity

In all patient categories, AF is associated with increased morbidity. This is reflected by the number of reported symptoms and by the days spent in the ICU and in the hospital. Haemodynamic parameters also tend to be worse in patients with AF. As for mortality, the causality of increased morbidity is hard to prove.

Can atrial fibrillation be prevented?

Although advocated in the early days of intensive care, there is no evidence that digoxin or any other antiarrhythmic drug can prevent AF in critically ill patients [41,45]. There are no trials investigating prevention of AF in MICU patients.

In surgical ICU patients, and especially in CTS patients, there are trials and guidelines evaluating preventive measures [46,47]. Although prophylactic digoxin, verapamil and β-blockers all decrease the heart rate in cases of postoperative AF, only β-blockers decrease the incidence of postoperative AF as shown in a meta-analysis [48]. In CTS patients, β-blockers can reduce AF by 75% [12].

In randomised controlled trials, amiodarone prevented AF in patients undergoing CTS, and also reduced the hospital LOS and the ICU LOS [49-55]. There is no consensus, however, about the clinical relevance of this finding since data are conflicting [56,57]. Amiodarone, for example, was found to increase the ICU LOS and the need for vasoactive medication or other haemodynamic support in some studies [13,58]. More recent meta-analyses show that amiodarone prevents AF but the influence on the LOS or the mortality is not yet unequivocally established [59,60].

Magnesium and atrial pacing cannot prevent AF in CTS patients, as shown in several randomised controlled trials [13,52,61,62]. In a comparative trial, however, magnesium could prevent AF equally as effectively as sotalol; both drugs combined had a synergistic effect [63]. Amiodarone and magnesium are also synergistic [64], but synergism could not be shown for propranolol and magnesium [65]. Recent meta-analyses show that magnesium can prevent AF but without any effect on the LOS or on the mortality [66,67]. Cholesterol synthesis inhibitors and corticosteroids also are preventive, perhaps by interaction with inflammatory pathways [68-70].

Studies on prevention have extensively been reviewed recently [15,59,60,71]. Guidelines advise the prophylactic use of β-blocker or amiodarone for elective CTS patients [15,46,59,60]. Generalisation of prevention studies in CTS patients to MICU patients is unproven.

Can atrial fibrillation be treated?

There are no randomised placebo-controlled trials in MICU patients aimed at treating AF once it has occurred. There are, however, comparative trials between drugs that are supposed to be effective. Procainamide and amiodarone are equally effective; after 12 hours, 70% of the patients were in SR [72]. Magnesium, when compared with amiodarone, has been found to be more effective in restoration of SR, while the two treatments are equally effective in rate control [73]. Ibutilide, a relatively new class III agent, can restore SR in 70% of patients that fail rhythm control with amiodarone treatment [74]. Ibutilide can restore SR – with 80%

conversion to SR in haemodynamically unstable patients without unmanageable proarrhythmic side effects [75].

In the CTS population, 80% of patients with AF convert to SR within 24 hours. The use of β-blockers before the start of AF and the absence of diabetes and left ventricular hypertrophy were independent predictors of conversion to SR [76]. In a retrospective study of surgical patients with new-onset supraventricular tachycardia (93% with AF), 75% had SR within 48 hours after the start of continuous infusion of amiodarone [77]. In a mixed population with severe left ventricular dysfunction, amiodarone had no apparent negative effect on haemodynamics [78]. When compared with amiodarone, propafenone gives earlier conversion to SR but the ultimate conversion percentage was equal after CTS [79]. Ibutilide showed a dose-dependent conversion rate in a randomised controlled trial [80]. Ibutilide and amiodarone have an equal conversion rate to SR and an equivalent time to conversion, but amiodarone causes more hypotension – probably due to vasodilatation [81,82]. Direct-current cardioversion has a low rate of conversion to SR in postsurgical new-onset AF [10,83,84].

Treatment of AF in CTS patients has been the topic of several reviews and guidelines [85,86]. The studies in these patients are sufficiently powered to detect effectiveness for their primary end point, prophylaxis or treatment of AF, but are underpowered to detect differences in mortality or adverse effects due to the low incidence of these events.

There are also studies in mixed ICU populations. Diltiazem and amiodarone appeared equally effective in achieving rate control; however, discontinuation of the study drug because of hypotension occurred more often in the diltiazem group [87]. Ibutilide is effective for rapid conversion, but with potentially life-threatening proarrhythmic side effects [88]. Magnesium is more effective in rate control and probably in conversion than diltiazem in a mixed population with longstanding AF paroxysms [52]. With digoxin treatment, no rate control or rhythm control can be reached in a mixed ICU population [28,41]. The success rate of electric cardioversion is also low in this population [28,41].

The management of AF in noncritically ill patients has been studied and reviewed extensively [89,90]. New-onset AF has a high spontaneous conversion rate of 64–90% within 24 hours [91]. Treatment with digoxin has been replaced by treatment with β-blockers and calcium-channel blockers because better rate control can be achieved with these latter drugs. Especially in seriously ill patients, digoxin fails to achieve an adequate reduction of the ventricular rate [92]. Class I and class III antiarrhythmic drugs are effective in conversion of AF in recent-onset AF, especially when combined with verapamil [89,90,93]. Amiodarone is also an effective drug because high-dose oral or intravenous amiodarone has a higher conversion ratio to SR than placebo

[91,94-97]. A meta-analysis showed that class IA, class IC and class III antiarrhythmic agents are equally effective in obtaining SR [98]. Meta-analyses comparing amiodarone with class IC antiarrythmic drugs or placebo showed that treatment was equally effective, although conversion was earlier in class IC treatment [96,99]. None of the drugs was associated with an increased or a decreased mortality [98].

Depending on the AF duration, amiodarone is highly effective in conversion with no more adverse effects than other drugs [100]. In patients with severe congestive heart failure, amiodarone controls the heart rate immediately [101,102]. Magnesium is safe, reliable and cost-effective compared with diltiazem [52]. Ibutilide is a safe and effective drug in persistent AF [103]. Angiotensin-converting enzyme-inhibitors might be effective in preventing structural changes (for example, fibrosis) and might therefore enhance outcome in AF patients, even in patients with worse underlying heart disease [104]. Glucocorticoid therapy reduces the proinflammatory state as measured by C-reactive protein and probably, as a consequence, the incidence of AF [105].

Electrical cardioversion in noncritically ill patients is effective but has a high relapse rate [8]. The timing of treatment is important because applying electric cardioversion too early leads to an increased recurrence of AF [106]. Whether the findings in noncritically ill patients are relevant for MICU patients is uncertain, but this evidence gives us a direction for research in mechanisms and therapy.

Conclusion on prevention and treatment
The data to support a treatment strategy are insufficient in MICU patients. Patient heterogeneity and spontaneous conversion require randomised controlled trials against a placebo. This trial evidence is not available, so we have to use data from other patient groups. In these patients it appears that electric conversion is not useful because of the high relapse rate. Digoxin is not very effective for SR conversion or rate control. Calcium antagonists are modestly effective but have the serious adverse effect of inducting hypotension. Class IA, class IIC and class III antiarrhythmic drugs are effective but have a significant proarrhythmic effect. The same observation holds true for ibutilide and propafenon. Magnesium is safe and seems effective. Amiodarone is effective but hypotension is seen, although not very frequently. β-Blockers are effective in prevention but data on treatment are less robust. Steroids and statins may prevent AF in patients with a systemic inflammation.

Adverse effects of (preventive) treatment
Pharmacokinetics and pharmacodynamics are changed in ICU patients [107]. Multiple drug use may cause drug interactions [107]. These factors might render ICU patients more prone to side effects [107,108]. There are limited data, however, for MICU patients. Amiodarone-induced pulmonary toxicity has been described in postmortem MICU patients

suffering from acute respiratory distress syndrome [109,110]. In surgical ICU patients, amiodarone induces hypotension after intravenous loading [81,82]. Severe hepatoxicity due to amiodarone has been described [111]. Ventricular tachycardia occurred in CTS patients [80].

In non-ICU patients admitted for AF there is a high incidence of adverse events, mainly cardiac, from antiarrhythmic drugs [112]. On the other hand, the incidence of amiodarone-induced proarrhythmic effects is low [113-115]. Nevertheless amiodarone remains a drug with many side effects. Amiodarone pulmonary toxicity, especially in the previously damaged lung, is a hazardous adverse effect [108,110,116]. The occurrence is probably cumulative, dose dependent and duration dependent, but adverse pulmonary effects can also be seen within 3 days after the start of administration [110,114,115]. Drug interactions might be more frequent for amiodarone but have not extensively been studied [117]. The implications for the ICU patient of the effect of amiodarone on thyroid gland function, which is a major problem in outpatients, are not yet clear [118,119]. Amiodarone has a complex pharmacokinetic and pharmacodynamic profile [120].

Conclusion on adverse effects
Owing to the multiplicity of symptoms in ICU patients, adverse effects can be easily overlooked or attributed to the underlying disease. Reports on adverse effects of anti-arrhythmic drugs have mainly been described in non-ICU patients. The proarrhythmic effect is the most frequent and serious side effect. Hypotension, however, is also an important side effect described in ICU patients. An adverse effect of a specific drug is hard to detect in ICU patients because of the polypharmacy and because of the difficulty to distinguish between adverse effects, underlying disease and other nosocomial complications.

Can treatment of atrial fibrillation improve survival?
There are few data on the effect of treatment of AF on mortality in ICU patients. A meta-analysis in non-ICU patients showed that class IA, class IC and class III antiarrhythmic agents are equally effective in reaching SR. No impact, however, on the quality of life or the mortality could be found [98]. β-Blockers improve survival in patients with heart failure and AF [121]. Amiodarone treatment in patients with AF and congestive heart failure improved conversion to SR and survival [122].

Conclusion on improvement of survival
There are no studies in ICU patients showing a survival advantage in the treatment group; the advantage could either not be shown or was not an endpoint of the study. In non-ICU patients with heart failure and AF there is a survival advantage for β-blockers and amiodarone, which also has β-blocking activity. This might be related to the well-known effect of β-blockers on survival in patients with heart failure and not because of rate control or rhythm control.

Can treatment of atrial fibrillation improve morbidity?
There are no data on MICU patients. In a retrospective study in surgical patients with new-onset supraventricular tachy-cardia (93% with AF), continuous infusion of amiodarone did not lead to significant differences in haemodynamics in responders compared with nonresponders [77,123]. Another retrospective study in a selected population of critically ill patients showed that amiodarone improved haemodynamic parameters compared with pretreatment values [42].

In a mixed ICU patient population, conversion to SR did not increase the systolic blood pressure [73]. Most patients are already haemodynamically unstable before AF, and the contribution of AF is uncertain [124].

Conclusion on improvement of morbidity
The best available evidence comes from retrospective studies. The impact of conversion to SR or control of rhythm on haemo-dynamics is probably limited, although most clinicians intuitively would state that haemodynamics improve with treatment.

Should we aim for rate control or rhythm control?
There are no data in MICU patients. In a pilot trial in CTS patients there was no difference in the LOS or rhythm at discharge between rate control and rhythm control strategies [125,126]. After cardiac surgery in haemodynamically stable patients, rate control is preferred over rhythm control because almost all patients convert spontaneously within 6 weeks after surgery [12,86,125,127].

Five randomised-controlled trials in non-ICU patients did not show a beneficial effect of rhythm control over rate control in haemodynamically stable patients [128,129]. These studies have been described in three meta-analyses; rate control showed less adverse events and less hospitalisations [9,89,130]. These meta-analyses, however, do not sufficiently cover specific patient groups [124].

Conclusion on rate control or rhythm control
There are insufficient data in ICU patients to justify a choice between therapy directed on rate control or on rhythm control. Rhythm control clearly has no advantage above rate control, as measured both by morbidity or mortality, in non-ICU patients.

Does atrial fibrillation increase stroke incidence in medical ICU patients?
There are no data on stroke incidence in the MICU. Short-term postoperative AF is a risk factor for stroke in CTS patients [131]. Postoperative AF doubles the risk compared with patients without AF, despite the use of aspirin [22,32,131,132].

AF is an independent risk factor for stroke in non-ICU patients [133]. In patients with AF, an inflammatory response

is an independent risk for stroke [134]. The prothrombotic state due to inflammation is probably more important than the presence of AF [25]. An increased C-reactive protein level is a risk factor for thromboembolism in patients with AF [135].

Conclusion on stroke incidence

There are insufficient data in medical ICU patients, but in CTS patients it is clear that the stroke incidence is increased in patients with AF. Besides AF, a proinflammatory state is also a risk factor.

Can stroke be prevented?

Since there are no data on stroke incidence in MICU patients, there are also no data on prevention.

In elderly patients undergoing cardiothoracic surgery receiving preventive treatment with amiodarone in addition to β-blocker, the incidence of AF and stroke was significantly reduced but the mortality was not changed [53]. This effect was also shown in a meta-analysis [55].

The stroke incidence in non-ICU patients can be reduced with anticoagulation. The bleeding risk is outweighed by the advantage of a reduced stroke incidence in most patients [8]. There is no difference between rate control and rhythm control in stroke incidence when the patient is on anticoagulation treatment [130]. Treatment of the proinflammatory state can reduce the incidence of stroke.

Conclusion on stroke prevention

The incidence of stroke can probably be reduced in ICU patients with anticoagulation. There are no clear data that this risk reduction outweighs the increased bleeding risk in these patients. The proinflammatory state probably increases the risk for stroke and the risk for AF independently [136].

Discussion

Although AF is a frequent symptom associated with a high mortality in critically ill patients, there are still many lacunae in our knowledge. We evaluated the actual level of knowledge with the purpose to reach a treatment protocol based on best available evidence. There is no literature, however, presenting the criteria of evidence-based medicine. Even the questions of whether AF is the cause of mortality or just an epiphenomenon [3] and of whether treatment improves outcome are still not answered. A treatment protocol therefore has to be based on extrapolation of results from studies performed in other patient groups. But even in these patient groups, there is still a lot of debate about the optimal treatment protocol [137].

Because the beneficial effect of treatment is not certain, any protocol should at least not add serious adverse events; first, do no harm. Doing as little as possible is a defendable credo. This means optimising the fluid balance, correcting electrolyte disturbances, reducing sympaticus tonus and avoiding proarrhythmic drugs. Reduction of the systemic inflammatory state is tempting but is of course always the purpose of ICU treatment. The evidence for the use of steroids for this indication is insufficient. When the ventricular rate is arbitrarily judged acceptable and there is little haemodynamic compromise, no further action is probably required. If this condition is not met, we have to seek the balance between benefit and harm.

Direct-current cardioversion is not useful because of the high relapse rate. In some situations, however, judged to be desperate, direct-current cardioversion will be performed. It has also not been proven that electrical cardioversion does not damage a heart already involved in the multiorgan failure of critical illness. Although the effectiveness of magnesium has been questioned there are no reports on adverse effects. In nonacutely threatened patients, therefore, an attempt to achieve rate control and even rhythm control with intravenous infusion of magnesium is worthwhile. If further treatment is deemed necessary, a choice has to be made between various antiarrhythmic drugs. Class IA, class IC and class III antiarrhythmic drugs all are effective but are also proarrhythmic. Calcium-channel blockers are less effective and have the disadvantage of causing hypotension. Intensivists may have an emotional barrier to using β-blockers in patients also receiving vasopressors and inotropes, but β-blockers could be a rational choice. The choice made by most intensivists, however, is for amiodarone: this drug is effective, although not as fast acting as some other drugs. The acute adverse effects seem to be very limited, but the adverse effects in the long term might be a problem. We therefore advocate short-term use of amiodarone if treatment is deemed necessary.

A protocol concerning AF should also have a statement about stroke prevention. There are, however, no data to support such a statement. We have no data on the stroke incidence of medical ICU patients with AF. Owing to the proinflammatory state, this incidence is probably higher than in other patients with AF. On the other hand, there is also an increased, but unquantified, bleeding risk. Risks and benefits of anticoagulation can therefore not be weighed in general. This balance has to be estimated for individual patients, and an educated guess has to be made [136].

Conclusion

A rational treatment protocol could therefore consist of several steps. First, treatment of predisposing factors is necessary. Second, a short attempt at magnesium supplementation can be done. Third, amiodarone can be administered for a short-term period. Most patients will by then have an acceptable rate or rhythm; however, if the patient does not, ibutilide (a class III drug) can serve as rescue treatment.

We have treated 29 patients in a MICU with this protocol. Ninety per cent of the patients had SR after 24 hours and all

patients had an acceptable heart rate. We did not need to use ibutilide treatment, nor direct-current cardioversion. The inhospital mortality in this patient group, however, was still 38% [138].

Having a protocol with a reasonable success rate does not release us from doing further research. The high mortality rate could be caused by the fact that AF is just an epi-phenomenon in critically ill patients. The possibility that the mortality is in part caused by insufficient treatment of AF or, on the contrary, is caused by adverse effects of the treatment, however, is too realistic to be ignored. All we have stated about the treatment of AF in MICU patients is based on extrapolation and is therefore just a hypothesis. We should therefore explore the possibility of randomised controlled trials against placebo. These trials should be based on a better understanding of AF in critically ill patients.

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

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