Int J Burn Trauma 2022;12(6):251-260
www.IJBT.org /ISSN:2160-2026/IJBT0145769

Original Article

Initial treatment strategies in new-onset atrial fibrillation in critically ill burn patients

Mithun R Suresh[1], Alexander C Mills[2], Garrett W Britton[3], Wilson B Pfeiffer[4], Marissa C Grant[4], Julie A Rizzo[5,6]

[1]Department of Medicine, CentraCare-St.Cloud Hospital, 1406 6th Ave N, St. Cloud 56303, MN, USA; [2]Department of Surgery, University of Texas Health Science Center at Houston, 6410 Fannin Street, Houston 77030, TX, USA; [3]Burn Center, United States Army Institute of Surgical Research, 3698 Chambers Pass STE B, JBSA Ft. Sam Houston 78234, TX, USA; [4]Department of Anesthesiology, Brooke Army Medical Center, 3551 Roger Brooke Dr, JBSA Ft. Sam Houston 78234, TX, USA; [5]Department of Trauma, Brooke Army Medical Center, 3551 Roger Brooke Dr, JBSA Ft. Sam Houston 78234, TX, USA; [6]Department of Surgery, Uniformed Services University of The Health Sciences, 4301 Jones Bridge Rd, Bethesda 20814, MD, USA

Received August 5, 2022; Accepted December 5, 2022; Epub December 15, 2022; Published December 30, 2022

Abstract: Introduction: Atrial fibrillation is associated with increased morbidity and mortality in critically ill patients. Few studies have specifically examined this arrhythmia in burn patients. Given the significant clinical implications of atrial fibrillation, understanding the optimal management strategy of this arrhythmia in burn patients is important. Consequently, the purpose of this study was to examine rate- and rhythm-control strategies in the management of new onset atrial fibrillation (NOAF) and assess their short term outcomes in critically ill burn patients. Methods: We identified all patients admitted to our institution's burn intensive care unit between January 2007 and May 2018 who developed NOAF. Demographic information and burn injury characteristics were captured. Patients were grouped into two cohorts based on the initial pharmacologic treatment strategy: rate-(metoprolol or diltiazem) or rhythm-control (amiodarone). The primary outcome was conversion to sinus rhythm. Secondary outcomes included relapse or recurrence of atrial fibrillation, drug-related adverse events, and complications and mortality within 30 days of the NOAF episode. Results: There were 68 patients that experienced NOAF, and the episodes occurred on median days 8 and 9 in the rate- and rhythm-control groups, respectively. The length of the episodes was not significantly different between the groups. Conversion to sinus rhythm occurred more often in the rhythm-control group (P = 0.04). There were no differences in the incidences of relapse and recurrence of atrial fibrillation, and the complications and mortality between the groups. Hypotension was the most common drug-related adverse event and occurred more frequently in the rate-control group, though this difference was not significant. Conclusions: Conversion to sinus rhythm occurred more often in the rhythm-control group. Outcomes were otherwise similar in terms of mortality, complications, and adverse events. Hypotension occurred less frequently in the rhythm-control group, and although this difference was not significant, episodes of hypotension can have important clinical implications. Given these factors, along with burn patients having unique injury characteristics and a hypermetabolic state that may contribute to the development of NOAF, when choosing between rate- and rhythm control strategies, rhythm-control with amiodarone may be a better choice for managing NOAF in burn patients.

Keywords: Burns, new onset atrial fibrillation, rate-control, rhythm-control

Introduction

Atrial fibrillation is present when the following electrocardiographic rhythm occurs: 1) irregular R-R intervals when atrioventricular conduction is present, 2) no p-waves are present, and 3) atrial activity is irregular [1]. This is a common arrhythmia in the intensive care unit (ICU), as it can occur in nearly 50% of some cohorts of critically ill patients [2]. There are several important factors related to burn injuries and their management that may help to explain how atrial fibrillation can be triggered, including significant fluid shifts and electrolyte imbalances related to resuscitation [3, 4], severe tissue damage resulting in a significant inflammatory response and surge in inflammatory mediators and catecholamines [5], and post-operatively from the adrenergic stimulation and inflammation that can occur after surgical procedures [6]. Current treatment options include rate-(e.g., beta blockers, calcium channel blockers,

digoxin, etc.) or rhythm-control medications (e.g., antiarrhythmics) [7]. In terms of efficacy, Brown et al., found that rhythm-control medications were more successful in achieving rate- and rhythm-control in critically ill post-operative patients [8]. However, there is no difference in mortality when comparing rate- and rhythm-control strategies [9-11]. Furthermore, prior studies cite fewer adverse drug reactions [9, 12] and reduced need for hospitalization [9, 12, 13] with rate-control medications compared to rhythm-control medications. Regarding prognosis, appropriate management of atrial fibrillation is paramount, as previous studies have described the association of atrial fibrillation with an increased risk of cerebrovascular accidents (CVAs) [14, 15], longer ICU stays [2, 16-18], reductions in ejection fraction [19], need for mechanical ventilation [16], increased incidence of shock [16], and future hospitalizations for heart failure [15]. Importantly, while many studies characterize and assess atrial fibrillation in critically ill patients, a population commonly underrepresented in clinical assessment is that of burn injured patients, as few studies have reported on arrhythmias in these patients [20-23].

Given the significant clinical implications of this arrhythmia in critically ill patients, along with the various risks and benefits of rate-control and rhythm-control medications, determining the optimal management strategy for burn-injured patients in the ICU is important. Moreover, there is currently no consensus on how best to treat atrial fibrillation when it occurs in burn patients. Seguin et al., briefly listed multiple treatment strategies that were used in their study of trauma patients that developed atrial fibrillation following admission to the ICU [24]. Hadjizacharia et al., reported lower mortality in trauma patients with atrial arrhythmias that received beta-blockers [25]. As burn patients differ physiologically from trauma patients, perhaps due to the profound hypermetabolic response that occurs following thermal injury, the response to rate-versus rhythm-control strategies may also vary. The purpose of this study was to examine rate- and rhythm-control strategies in the management of new onset atrial fibrillation (NOAF), and assess their short term outcomes in critically ill burn patients.

Materials and methods

Ethics

This study was approved by the Research Regulatory Compliance Division of the United States Army Institute of Surgical Research and consent was waived due to the retrospective nature of this study along with the use of de-identified data (protocol number H-18-011nr).

Inclusion and exclusion criteria

For the inclusion criteria, we included all patients that were hospitalized in our institution's burn intensive care unit (BICU) between January 2007 and May 2018, and developed NOAF while in the BICU. Patients were excluded if they (1) had NOAF but did not require admission or transfer to the BICU or (2) had atrial fibrillation in the BICU, but it was not new onset.

Data collection

Demographic information was gathered, and burn injury characteristics that were captured include total body surface area (TBSA) burned, % full-thickness burned, and the presence of inhalation injury. Patients were included in the final study population if they developed NOAF while in the BICU. Atrial fibrillation was defined by an irregularly irregular rhythm with a variable ventricular rate and no p waves lasting for at least 30 minutes, and NOAF was defined as newly developed atrial fibrillation in patients without a previous history of atrial fibrillation. Patients who presented to the hospital in atrial fibrillation were excluded. The most recent mean arterial pressure (MAP) and heart rate (HR) prior to the beginning of NOAF were obtained and shock index was subsequently calculated. Patients with an echocardiogram completed prior to the beginning of NOAF had their ejection fraction captured. Features of the NOAF episode that were collected include length of episode as documented on continuous telemetry, along with the highest HR and lowest MAP during the episode. Laboratory values prior to the NOAF episode, including potassium, magnesium, and phosphorus, were also collected, with hypokalemia defined as potassium less than 4.0 mmol/L, hypomagnesemia defined as magnesium less than 2.0 mmol/L, and hypophosphatemia defined as phosphorus less than 3.0 mg/dL.

Cohorts and outcomes

Patients were cohorted into two groups based on the initial pharmacologic treatment strategy. The rate-control group consisted of patients who initially received metoprolol or diltiazem, and the rhythm-control group consisted of patients who initially received amiodarone. Treatment regimens with these medications were as follows: metoprolol 5 mg IV bolus repeated up to three times, diltiazem 0.25 mg/kg IV bolus followed by an infusion of 5-15 mg/hour, or amiodarone 150 mg IV bolus over 10 minutes followed by an infusion of 1 mg/minute for 8 hours, then 0.5 mg/minute for 16 hours. The primary outcome was conversion to sinus rhythm. Secondary outcomes included relapse (additional episode of atrial fibrillation within 24 hours of conversion to sinus rhythm) or recurrence (additional episode of atrial fibrillation after 24 hours of conversion to sinus rhythm). Data on complications associated with atrial fibrillation (defined as CVA, encephalopathy, myocardial infarction) that occurred within 30 days of the episode were collected. Mortality occurring within 30 days of the NOAF episode was recorded. Finally, adverse events that occurred within 60 minutes of medication administration were collected to determine any drug-related events.

Statistical analysis

Descriptive statistics were used to report the findings, and significance tests were used to compare the results in the rate- and rhythm-control groups. The Tukey-Kramer test was used for post-hoc adjustment of parametric data with a significant F test. Statistical significance occurred at $P < 0.05$. Analyses were performed using SAS version 9.4 (SAS Institute Inc., Cary, NC).

Results

Patient demographic data and burn injury characteristics

We identified 68 patients out of 2,491 patients admitted to the BICU that experienced NOAF during the study period, with 51 (75%) patients initially treated with rate-control medications and 17 (25%) patients treated with rhythm-control medications. There were 43 (63%) male patients and 25 (37%) female patients with ages between 18 and 94 years. **Table 1** describes the demographic and burn injury characteristics of the rate- and rhythm-control groups. Both groups had similar mean age, percentage of male patients, and BMI. Likewise, burn injuries in both groups were similar, as TBSA, % full-thickness, presence of inhalation injury, and etiology of burn were not significantly different between the groups. For comorbidities, both groups had similar incidences of coronary artery disease, hypertension, and congestive heart failure. Outpatient beta-blocker usage was also similar in both groups.

Echocardiographic and hemodynamic parameters, laboratory data, and characteristics of the NOAF episode

Table 2 describes the values of various parameters prior to and during the episode of NOAF. Both rate- and rhythm-control groups had a similar percentage of patients with a normal ejection fraction prior to the episode of NOAF. Likewise, shock index and the percentage of patients on vasoactive medications before the episode of NOAF were similar. For laboratory values, both groups had a similar percentage of patients with hypokalemia, hypomagnesemia, and hypophosphatemia. Hemoglobin prior to the episode of NOAF was also similar in both groups. The episodes of NOAF occurred on median hospital days 8 and 9 in the rate- and rhythm-control groups, respectively. The length of the NOAF episode was shorter in the rate-control group (3.7 hours) compared to the rhythm-control group (7.6 hours), but this difference was not statistically significant. Furthermore, both groups had similar maximum HRs and minimum MAPs during the episode.

Primary and secondary outcomes

Table 3 lists the outcomes. Conversion to sinus rhythm occurred more frequently in the rhythm-control group (12 patients, 71%) compared to the rate-control group (20 patients, 39%), and this difference was statistically significant ($P = 0.04$). Relapse and recurrence of atrial fibrillation occurred frequently, and there was no difference between the groups. Likewise, both groups had similar heart rates after getting either rate- or rhythm-control medications. When comparing mortality and complications associated with atrial fibrillation (CVA,

Table 1. Demographics and burn characteristics of the two cohorts

Demographics/Burn characteristics	All patients (n = 68)	Rate-control (n = 51)	Rhythm-control (n = 17)	*p*-value
Age	63±15	64±16	62±11	0.86
BMI	30±8	30±8	29±5	0.67
TBSA	21 (13-40)	22 (11-42)	18 (14-25)	0.56
% FT	10 (1-20)	10 (3-23)	3 (0.3-11)	0.09
Presence of inhalation injury	11 (16%)	7 (14%)	4 (24%)	0.22
Etiology of burn				
• Flame	58 (85%)	44 (86%)	14 (82%)	0.70
• Scald	2 (3%)	1 (2%)	1 (6%)	0.44
• Contact	3 (4%)	3 (6%)	0 (0%)	0.43
• Other	4 (6%)	2 (4%)	2 (12%)	0.26
CAD history	15 (22%)	11 (22%)	4 (24%)	0.26
HTN history	35 (51%)	25 (49%)	10 (59%)	0.17
CHF history	3 (4%)	3 (6%)	0 (0%)	0.43
Outpatient B-blocker	22 (32%)	17 (33%)	5 (29%)	0.23

BMI = body mass index, TBSA = total body surface area, % FT = percent full thickness burn, CAD = coronary artery disease, HTN = hypertension, CHF = congestive heart failure, EF = ejection fraction. Data presented as mean ± standard deviation or median (interquartile range) as appropriate.

Table 2. Parameters prior to and during the episode of new onset atrial fibrillation for the two cohorts

Parameters	All patients (n = 68)	Rate-control (n = 51)	Rhythm-control (n = 17)	*p*-value
Normal EF	61 (90%)	46 (90%)	15 (88%)	0.33
Shock index	1.5±0.6	1.6±0.6	1.5±0.5	0.66
Vasopressors before episode	17 (25%)	11 (22%)	6 (35%)	0.34
Hypokalemia	30 (44%)	23 (45%)	7 (41%)	0.21
Hypomagnesemia	10 (15%)	9 (18%)	1 (6%)	0.43
Hypophosphatemia	27 (40%)	21 (42%)	6 (35%)	0.77
Hemoglobin before episode	10±2	10±2	9±2	0.29
Episode hospital day	8 (3-19)	8 (3-21)	9 (6-15)	0.93
Episode total hours	4.3 (1-10)	3.7 (1-8.5)	7.6 (1.8-15.2)	0.14
Highest HR	149±23	149±23	148±24	0.85
Lowest MAP	63±14	63±16	63±9	0.97

EF = ejection fraction, HR = heart rate, MAP = mean arterial pressure. Data presented as mean ± standard deviation or median (interquartile range) as appropriate.

encephalopathy, myocardial infarction) within 30 days, there were no differences between both groups. Finally, there were 14 adverse events believed to be drug-related in the study population. Hypotension was the most common event, occurring in 9/51 (18%) patients in the rate-control group and 1/17 (6%) patients in the rhythm-control group (P = 0.43).

Discussion

This study examined NOAF in 68 patients with burn injuries to compare rate- and rhythm-control management strategies and their outcomes. The majority of the patients in the study population were initially treated with rate-control medications. With regards to the primary outcome, significantly more patients converted to sinus rhythm from atrial fibrillation in the rhythm-control group compared to the rate-control group. In addition, fewer patients in the rhythm-control group experienced hypotension after medication administration. Mortality was high, as nearly half of the patients in our study population died within 30 days of experiencing atrial fibrillation. Given the morbidity and mor-

Table 3. Episode features and outcomes comparison between the two cohorts

Episode Features & Outcomes	All patients (n = 68)	Rate-control (n = 51)	Rhythm-control (n = 17)	*p*-value
Cardioversion	32 (47%)	20 (39%)	12 (71%)	0.04*
Relapse	27 (40%)	20 (39%)	7 (41%)	0.22
Recurrence	40 (59%)	31 (61%)	9 (53%)	0.58
HR after treatment	87±20	88±18	86±27	0.73
Death	30 (44%)	19 (37%)	9 (53%)	0.27
CVA	4 (6%)	4 (8%)	0 (0%)	0.41
Encephalopathy	3 (4%)	3 (6%)	0 (0%)	0.43
MI	1 (1%)	1 (2%)	0 (0%)	0.44
Hypotension	10 (15%)	9 (18%)	1 (6%)	0.43

HR = heart rate, CVA = cerebrovascular accident, MI = myocardial infarction. Death and complications associated with atrial fibrillation (CVA, encephalopathy, MI) occurred within 30 days of the episode of new onset atrial fibrillation. Data presented as mean ± standard deviation or median (interquartile range) as appropriate. *Statistically significant.

tality in our study patients, understanding the optimal way to treat atrial fibrillation in burn patients is critical, as these patients are very sensitive to fluid shifts and hemodynamic changes. Therefore, in the setting of NOAF in burn patients, initial treatment with rhythm-control medications appears to be a safe alternative to rate-control medications.

O'Connor et al. provided the most descriptive study on elderly burn patients that developed NOAF while being treated at their institution [23]. The burn characteristics of the patients in their study were similar to our patients, with a median TBSA of 15% and inhalation injury occurring in 16% of the patients. Likewise, the median day of NOAF was similar at 7 days, and the mortality rate was also similar at 50%. However, there was no information provided on the pharmacological management strategies used in these patients. This study also did not provide the underlying comorbidities of the patients, vital signs, and laboratory values associated with the NOAF episode.

With regards to the primary outcome, significantly more patients converted to sinus rhythm from atrial fibrillation in the rhythm-control group compared to the rate-control group. This aligns with findings from other studies in critically ill patients, which demonstrate the superiority of amiodarone in achieving both rate- and rhythm-control [8]. There are several potential benefits with conversion to sinus rhythm and not remaining in atrial fibrillation. Even shortly after the onset of NOAF, there can be an elevated risk of cerebral thromboembolism [26]. Ongoing tachycardia from poor heart rate control can predispose patients to the development of tachycardia-induced cardiomyopathy and congestive heart failure [27]. In addition, the irregular atrial contractions are associated with a reduction in cardiac output [28], which could be harmful to burn patients due to the impact of hypoperfusion on wound healing [29]. Burn patients already have prolonged hospitalizations frequently [30], and given the association of atrial fibrillation with longer ICU stays in critically ill patients [2, 16-18], additional ICU days secondary to NOAF is an unneeded burden for burn patients. Furthermore, inhalation injury is a significant comorbidity in burn patients and these patients frequently require mechanical ventilation [31]. Atrial fibrillation is associated with an increased need for mechanical ventilation in some critically ill patients [16], so developing NOAF may further predispose burn patients with inhalation injury to needing mechanical ventilation. Finally, atrial fibrillation is associated with increased mortality in ICU patients [16-18, 25, 32-34]. We also found a fairly high mortality rate in our study population. Consequently, this further underscores the importance of determining the best way to treat atrial fibrillation and achieve conversion to sinus rhythm.

When examining complications within 30 days of the NOAF episode, they occurred with a similar incidence in both groups. Likewise, both groups were similar in terms of relapse and recurrence of atrial fibrillation. For drug-related adverse events, hypotension was the most common event. Although there was no statisti-

cal difference in the incidence of hypotension after medication administration in either group, the percentage difference was three times higher in the rate-control group, and this difference could be clinically relevant. Consequently, every episode of hypotension shortly after burn injury could be particularly detrimental given the significant intravascular hypovolemia and vasoplegia that occurs with severe burn injury [35]. Acute kidney injury occurs often following burn injuries [36], and hypotension can predispose or lead to worsening renal injury and dysfunction [37]. Hypotension causes peripheral vasoconstriction which results in inadequate perfusion of peripheral skin. This can cause existing wounds to worsen and may contribute to burn wound progression [38]. In addition, poor perfusion is detrimental to wound healing and can risk skin graft success [39], which can lead to the need for additional operations and contribute to an even longer hospital stay. Finally, hypotension associated with atrial fibrillation that does not resolve may ultimately require electrical cardioversion for resolution [1], which can cause progression from partial to full thickness injuries [40].

In terms of mortality, nearly half of the patients in the study population died. This finding aligns with previous studies that have described the association of atrial fibrillation with mortality in numerous groups of critically ill patients, including those with sepsis [14-18, 32], trauma [25, 33], and non-cardiac surgery [34] patients. Furthermore, there was no difference in mortality between the rate- and rhythm-control groups, which also aligns with previous studies [9-11]. It should be noted that many other studies that examined atrial fibrillation in the critically ill typically did not include burn patients.

The majority of the study population were initially treated with rate-control medications. This is not surprising, as contemporary management strategies of atrial fibrillation frequently employ rate-control medications as first-line agents [7]. Beta-blockers are used to treat many medical conditions, and in our study population, nearly one-third of the patients were already taking beta-blockers as an outpatient. Accordingly, with patients who are taking beta-blockers as an outpatient, these medications should be continued if possible in order to avoid rebound hypertension and tachycardia that may occur with their abrupt withdrawal [41]. There is also some evidence showing that continuation of outpatient beta-blocker therapy is associated with reduced mortality and healing time in burn patients [42]. Non-dihydropyridine calcium channel blockers are commonly used as second-line rate-control agents when beta-blockers are unsuccessful in achieving heart rate control, and additional caution is needed when using these medications due to their negative inotropic effects and risk of causing hypotension [7]. Furthermore, previous studies have suggested that calcium channel blockers are less successful in achieving early conversion to sinus rhythm than beta-blockers [43, 44]. If multiple rate-control medications are unsuccessful in controlling atrial fibrillation, treatment algorithms suggest trying anti-arrhythmic medications next. Amiodarone is commonly used as a third-line agent in these situations [7]. Importantly, in addition to its anti-arrhythmic properties, amiodarone can also help with rate control [45]. The difficulty with using amiodarone is its initial dosing is an infusion, which needs to be made and administered over 10 minutes. In contrast, the aforementioned rate-control agents are administered as intravenous pushes. Finally, digoxin can be given if other rate- or rhythm-control medications are unsuccessful. Advantages of digoxin include its positive inotropic effects [46] and synergism with beta-blockers and calcium channel blockers for rate control [47]. However, given its impaired efficacy in patients during states of increased adrenergic activity [48] along with its narrow therapeutic index [49], digoxin may not be effective in hypermetabolic burn patients, so it should only be considered when there are limited medication options remaining.

Our view is that when choosing between rate- and rhythm-control medications, since there were no significant differences when comparing complications and adverse effects between the groups, a rhythm-control medication such as amiodarone may be a better choice. There are some factors to help prove and support this conclusion. The first factor is the significantly greater frequency of conversion to sinus rhythm in the rhythm-control group compared to the rate-control group. Supporting this factor is our clinical experience that the pathophysiology of burn injuries is more conducive

to using rhythm-control medications for NOAF. In addition, further support for this conclusion is provided by the fact that the post-burn period is characterized by a surge of adrenergic activity and release of catecholamines [39]. Accordingly, rate-control medications may not be very effective during these hyperadrenergic states due to impaired β-adrenergic receptor responsiveness [50, 51]; instead, rhythm-control medications may need to be used. Another factor to help support this conclusion is that the duration of the catecholamine surge that accompanies burn injuries can be long-lasting, as hormone levels can be elevated for several months or years [52]. Catecholamines are the primary drivers of the profound hypermetabolism that characterizes burn injuries, and the resultant increases in heart rate and cardiac output can be seen more than 2 years after burn injuries [53]. As discussed, prior literature consists of very few studies that have exclusively examined atrial fibrillation in burn patients [20-23]. Goff et al., examined admissions to their burn unit that experienced cardiac complications, but their analysis examined a variety of complications, not just arrhythmias such as atrial fibrillation [20]. The studies by Meyers et al., and Iyah et al., consisted of only a few patients with atrial fibrillation (3 and 2 patients, respectively), and these studies provided limited information on the patients' demographics and outcomes [21, 22]. As discussed, O'Connor et al., provided the most descriptive study [23]. However, none of these studies provide any analyses or recommendations on medications for treating atrial fibrillation. Accordingly, the lack of literature with detailed recommendations for treating atrial fibrillation can be a limitation with regards to coming to the conclusion that amiodarone should be considered over other medications when treating NOAF because there is no consensus on managing this condition in burn patients. However, the finding of a significantly greater frequency of conversion to sinus rhythm in the rhythm-control group compared to the rate-control group in this study, combined with knowing that the post-burn period is characterized by hyperadrenergic activity and elevated catecholamine levels that can persist for months or years supports the conclusion of this study. Further support for the conclusion of this study is provided by the finding of hypotension being the most common drug-related adverse event and occurring more frequently in the rate-control group. Although this difference was not statistically significant, every episode of hypotension can be potentially harmful to burn patients. Going forward, additional prospective and multi-center studies will be helpful to continue investigating strategies to treat NOAF in burn patients.

The shortcomings of this study are related to its design, which are important due to their impact on our results. First, as a retrospective, observational study, causation and an accurate measurement of treatment effect cannot be established between rate- and rhythm-control medications, and any of the outcomes due to the inability to control for unknown confounders. Next, the accuracy of the data is dependent on the accuracy and available information in the BICU records. Another shortcoming is that this is a single institution study, so our findings may not be generalizable to other burn centers with different patient populations. Finally, our small sample size is another major shortcoming of this study. Accordingly, our expectation for future research is that studies will need to be larger and prospective, with patients from multiple institutions. This will allow for more detailed investigations of various treatment strategies and any acute adverse effects related to drug administration. Of particular relevance to drug administration is the fact that some patients may be on propranolol (which has rate-control properties as a beta blocker) when the NOAF episode occurs. Unfortunately, our data set that was created and pulled from the BICU records did not have information on which patients were receiving propranolol. This limitation should be accounted for in future studies by gathering information on which patients are receiving propranolol. For reference, at our institution, our standard practice is to start propranolol typically on or around post-burn day 5 in severely burned patients.

Conclusions

This study examined rate- and rhythm-control strategies in the management of NOAF in critically ill burn patients. Conversion to sinus rhythm occurred more often in the rhythm-control group. Hypotension occurred less frequently in the rhythm-control group, and although this difference was not statistically significant, episodes of hypotension can have significant

clinical implications. Most patients were initially treated with rate-control medications, and outcomes were otherwise similar between the rate- and rhythm-control groups in terms of the incidence of relapse and recurrence of atrial fibrillation, and mortality and complications within 30 days. The unique hypermetabolism and injury characteristics of burn patients that may contribute to the development of atrial fibrillation. There is a lack of consensus in the literature on the optimal way to manage NOAF in burn patients. But, since there were no significant differences between the rate- and rhythm-control groups when comparing complications and adverse events, based on our findings, rhythm-control medications such as amiodarone may be preferred over rate-control medications due to the significantly higher incidence of conversion to sinus rhythm and less frequent episodes of hypotension. Future prospective studies from multiple institutions will be helpful to corroborate our findings going forward.

Acknowledgements

The views expressed herein are those of the author(s) and do not reflect the official policy or position of Brooke Army Medical Center, Department of the Army, Department of the Air Force, Department of Defense, or any agencies under the U.S. Government.

Disclosure of conflict of interest

None.

Address correspondence to: Dr. Mithun R Suresh, Department of Medicine, CentraCare-St.Cloud Hospital, 1406 6th Ave N, St. Cloud 56303, MN, USA. E-mail: sure0015@umn.edu

References

[1] January CT, Wann LS, Alpert JS, Calkins H, Cigarroa JE, Cleveland JC Jr, Conti JB, Ellinor PT, Ezekowitz MD, Field ME, Murray KT, Sacco RL, Stevenson WG, Tchou PJ, Tracy CM and Yancy CW; ACC/AHA Task Force Members. 2014 AHA/ACC/HRS guideline for the management of patients with atrial fibrillation: a report of the American College of Cardiology/American Heart Association Task Force on practice guidelines and the Heart Rhythm Society. Circulation 2014; 130: e199-e267.

[2] Meierhenrich R, Steinhilber E, Eggermann C, Weiss M, Voglic S, Bogelein D, Gauss A, Georgieff M and Stahl W. Incidence and prognostic impact of new-onset atrial fibrillation in patients with septic shock: a prospective observational study. Crit Care 2010; 14: R108.

[3] Kazaure HS, Roman SA, Tyler D and Sosa JA. The significance of atrial fibrillation in patients aged ≥ 55 years undergoing abdominal surgery. World J Surg 2015; 39: 113-120.

[4] Walsh SR, Oates JE, Anderson JA, Blair SD, Makin CA and Walsh CJ. Postoperative arrhythmias in colorectal surgical patients: incidence and clinical correlates. Colorectal Dis 2006; 8: 212-216.

[5] Maesen B, Nijs J, Maessen J, Allessie M and Schotten U. Post-operative atrial fibrillation: a maze of mechanisms. Europace 2012; 14: 159-174.

[6] Joshi KK, Tiru M, Chin T, Fox MT and Stefan MS. Postoperative atrial fibrillation in patients undergoing non-cardiac non-thoracic surgery: a practical approach for the hospitalist. Hosp Pract (1995) 2015; 43: 235-244.

[7] Danelich IM, Lose JM, Wright SS, Asirvatham SJ, Ballinger BA, Larson DW and Lovely JK. Practical management of postoperative atrial fibrillation after noncardiac surgery. J Am Coll Surg 2014; 219: 831-841.

[8] Brown M, Nassoiy S, Chaney W, Plackett TP, Blackwell RH, Luchette F, Engoren M and Posluszny J Jr. Impact and treatment success of new-onset atrial fibrillation with rapid ventricular rate development in the surgical intensive care unit. J Surg Res 2018; 229: 66-75.

[9] Wyse DG, Waldo AL, DiMarco JP, Domanski MJ, Rosenberg Y, Schron EB, Kellen JC, Greene HL, Mickel MC, Dalquist JE and Corley SD; Atrial Fibrillation Follow-up Investigation of Rhythm Management (AFFIRM) Investigators. A comparison of rate control and rhythm control in patients with atrial fibrillation. N Engl J Med 2002; 347: 1825-1833.

[10] Van Gelder IC, Hagens VE, Bosker HA, Kingma JH, Kamp O, Kingma T, Said SA, Darmanata JI, Timmermans AJ, Tijssen JG and Crijns HJ; Rate Control versus Electrical Cardioversion for Persistent Atrial Fibrillation Study Group. A comparison of rate control and rhythm control in patients with recurrent persistent atrial fibrillation. N Engl J Med 2002; 347: 1834-1840.

[11] Roy D, Talajic M, Nattel S, Wyse DG, Dorian P, Lee KL, Bourassa MG, Arnold JM, Buxton AE, Camm AJ, Connolly SJ, Dubuc M, Ducharme A, Guerra PG, Hohnloser SH, Lambert J, Le Heuzey JY, O'Hara G, Pedersen OD, Rouleau JL, Singh BN, Stevenson LW, Stevenson WG, Thibault B and Waldo AL; Atrial Fibrillation and Congestive Heart Failure Investigators. Rhythm control versus rate control for atrial fibrillation and heart failure. N Engl J Med 2008; 358: 2667-2677.

[12] Hohnloser SH, Kuck KH and Lilienthal J. Rhythm or rate control in atrial fibrillation-Pharmacological Intervention in Atrial Fibrillation (PIAF): a randomised trial. Lancet (London, England) 2000; 356: 1789-1794.
[13] Opolski G, Torbicki A, Kosior DA, Szulc M, Wozakowska-Kaplon B, Kolodziej P and Achremczyk P; Investigators of the Polish How to Treat Chronic Atrial Fibrillation Study. Rate control vs rhythm control in patients with nonvalvular persistent atrial fibrillation: the results of the Polish How to Treat Chronic Atrial Fibrillation (HOT CAFE) Study. Chest 2004; 126: 476-486.
[14] Walkey AJ, Wiener RS, Ghobrial JM, Curtis LH and Benjamin EJ. Incident stroke and mortality associated with new-onset atrial fibrillation in patients hospitalized with severe sepsis. JAMA 2011; 306: 2248-2255.
[15] Walkey AJ, Hammill BG, Curtis LH and Benjamin EJ. Long-term outcomes following development of new-onset atrial fibrillation during sepsis. Chest 2014; 146: 1187-1195.
[16] Christian SA, Schorr C, Ferchau L, Jarbrink ME, Parrillo JE and Gerber DR. Clinical characteristics and outcomes of septic patients with new-onset atrial fibrillation. J Crit Care 2008; 23: 532-536.
[17] Salman S, Bajwa A, Gajic O and Afessa B. Paroxysmal atrial fibrillation in critically ill patients with sepsis. J Intensive Care Med 2008; 23: 178-183.
[18] Klein Klouwenberg PM, Frencken JF, Kuipers S, Ong DS, Peelen LM, van Vught LA, Schultz MJ, van der Poll T, Bonten MJ and Cremer OL; MARS Consortium. Incidence, predictors, and outcomes of new-onset atrial fibrillation in critically ill patients with sepsis. A cohort study. Am J Respir Crit Care Med 2017; 195: 205-211.
[19] Guenancia C, Binquet C, Laurent G, Vinault S, Bruyère R, Prin S, Pavon A, Charles PE and Quenot JP. Incidence and predictors of new-onset atrial fibrillation in septic shock patients in a medical ICU: data from 7-day holter ECG monitoring. PLoS One 2015; 10: e0127168.
[20] Goff DR, Purdue GF, Hunt JL and Cochran RP. Cardiac disease and the patient with burns. J Burn Care Rehabil 1990; 11: 305-307.
[21] Meyers DG, Hoestje SM and Korentager RA. Incidence of cardiac events in burned patients. Burns 2003; 29: 367-368.
[22] Iyah GRS, Reddy PC, El-Amin O and Caldito GC. Electrocardiographic abnormalities in patients with acute burn injuries. J La State Med Soc 2008; 160: 39-40, 42-43.
[23] O'Connor JM, Helmer SD and Khandelwal A. Atrial fibrillation in elderly burn patients. Am Surg 2014; 80: 623-624.
[24] Seguin P, Laviolle B, Maurice A, Leclercq C and Mallédant Y. Atrial fibrillation in trauma patients requiring intensive care. Intensive Care Med 2006; 32: 398-404.
[25] Hadjizacharia P, O'Keeffe T, Brown CV, Inaba K, Salim A, Chan LS, Demetriades D and Rhee P. Incidence, risk factors, and outcomes for atrial arrhythmias in trauma patients. Am Surg 2011; 77: 634-639.
[26] Procter NEK, Stewart S and Horowitz JD. New-onset atrial fibrillation and thromboembolic risk: cardiovascular syzygy? Heart Rhythm 2016; 13: 1355-1361.
[27] Lishmanov A, Chockalingam P, Senthilkumar A and Chockalingam A. Tachycardia-induced cardiomyopathy: evaluation and therapeutic options. Congest Heart Fail 2010; 16: 122-126.
[28] Clark DM, Plumb VJ, Epstein AE and Kay GN. Hemodynamic effects of an irregular sequence of ventricular cycle lengths during atrial fibrillation. J Am Coll Cardiol 1997; 30: 1039-1045.
[29] Merz KM, Pfau M, Blumenstock G, Tenenhaus M, Schaller HE and Rennekampff HO. Cutaneous microcirculatory assessment of the burn wound is associated with depth of injury and predicts healing time. Burns 2010; 36: 477-482.
[30] Taylor SL, Sen S, Greenhalgh DG, Lawless M, Curri T and Palmieri TL. Real-time prediction for burn length of stay via median residual hospital length of stay methodology. J Burn Care Res 2016; 37: e476-e482.
[31] Walker PF, Buehner MF, Wood LA, Boyer NL, Driscoll IR, Lundy JB, Cancio LC and Chung KK. Diagnosis and management of inhalation injury: an updated review. Crit Care 2015; 19: 351.
[32] Wells GL and Morris PE. Incidence and prognosis of atrial fibrillation in patients with sepsis. Cardiol Res 2011; 2: 293-297.
[33] Duby JJ, Heintz SJ, Bajorek SA, Heintz BH, Durbin-Johnson BP and Cocanour CS. Prevalence and course of atrial fibrillation in critically ill trauma patients. J Intensive Care Med 2017; 32: 140-145.
[34] Brathwaite D and Weissman C. The new onset of atrial arrhythmias following major noncardiothoracic surgery is associated with increased mortality. Chest 1998; 114: 462-468.
[35] Soussi S, Dépret F, Benyamina M and Legrand M. Early hemodynamic management of critically ill burn patients. Anesthesiology 2018; 129: 583-589.
[36] Clark A, Neyra JA, Madni T, Imran J, Phelan H, Arnoldo B and Wolf SE. Acute kidney injury after burn. Burns 2017; 43: 898-908.
[37] Izawa J, Kitamura T, Iwami T, Uchino S, Takinami M, Kellum JA and Kawamura T. Early-phase cumulative hypotension duration and severe-stage progression in oliguric acute kidney injury with and without sepsis: an observational study. Crit Care 2016; 20: 405.

[38] Rowan MP, Cancio LC, Elster EA, Burmeister DM, Rose LF, Natesan S, Chan RK, Christy RJ and Chung KK. Burn wound healing and treatment: review and advancements. Crit Care 2015; 19: 243.
[39] Jeschke MG, van Baar ME, Choudhry MA, Chung KK, Gibran NS and Logsetty S. Burn injury. Nat Rev Dis Primers 2020; 6: 11.
[40] Kennedy JM, Goldie C and Nickerson D. Burn progression secondary to cardioversion. J Burn Care Res 2011; 32: e143-5.
[41] Rangno RE and Langlois S. Comparison of withdrawal phenomena after propranolol, metoprolol and pindolol. Br J Clin Pharmacol 1982; 13 Suppl 2: 345S-351S.
[42] Arbabi S, Ahrns KS, Wahl WL, Hemmila MR, Wang SC, Brandt MM and Taheri PA. Beta-blocker use is associated with improved outcomes in adult burn patients. J Trauma 2004; 56: 265-271.
[43] Mooss AN, Wurdeman RL, Mohiuddin SM, Reyes AP, Sugimoto JT, Scott W, Hilleman DE and Seyedroudbari A. Esmolol versus diltiazem in the treatment of postoperative atrial fibrillation/atrial flutter after open heart surgery. Am Heart J 2000; 140: 176-180.
[44] Balser JR, Martinez EA, Winters BD, Perdue PW, Clarke AW, Huang W, Tomaselli GF, Dorman T, Campbell K, Lipsett P, Breslow MJ and Rosenfeld BA. Beta-adrenergic blockade accelerates conversion of postoperative supraventricular tachyarrhythmias. Anesthesiology 1998; 89: 1052-1059.
[45] Clemo HF, Wood MA, Gilligan DM and Ellenbogen KA. Intravenous amiodarone for acute heart rate control in the critically ill patient with atrial tachyarrhythmias. Am J Cardiol 1998; 81: 594-598.
[46] Gheorghiade M, Adams KF and Colucci WS. Digoxin in the management of cardiovascular disorders. Circulation 2004; 109: 2959-2964.
[47] Olshansky B, Rosenfeld LE, Warner AL, Solomon AJ, O'Neill G, Sharma A, Platia E, Feld GK, Akiyama T, Brodsky MA and Greene HL; AFFIRM Investigators. The Atrial Fibrillation Follow-up Investigation of Rhythm Management (AFFIRM) study: approaches to control rate in atrial fibrillation. J Am Coll Cardiol 2004; 43: 1201-1208.
[48] Lim HS, Hamaad A and Lip GY. Clinical review: clinical management of atrial fibrillation-rate control versus rhythm control. Crit Care 2004; 8: 271-279.
[49] Hirai T, Kasai H, Naganuma M, Hagiwara N and Shiga T. Population pharmacokinetic analysis and dosage recommendations for digoxin in Japanese patients with atrial fibrillation and heart failure using real-world data. BMC Pharmacol Toxicol 2022; 23: 14.
[50] Kaufman TM and Horton JW. Burn-induced alterations in cardiac beta-adrenergic receptors. Am J Physiol 1992; 262: H1585-H1591.
[51] Kaufman TM and Horton JW. Characterization of cardiac beta-adrenergic receptors in the guinea pig heart: application to study of beta-adrenergic receptors in shock models. J Surg Res 1993; 55: 516-523.
[52] Kulp GA, Herndon DN, Lee JO, Suman OE and Jeschke MG. Extent and magnitude of catecholamine surge in pediatric burned patients. Shock 2010; 33: 369-374.
[53] Williams FN, Herndon DN, Suman OE, Lee JO, Norbury WB, Branski LK, Mlcak RP and Jeschke MG. Changes in cardiac physiology after severe burn injury. J Burn Care Res 2011; 32: 269-274.