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Perioperative & Critical Care: Short Report

New-Onset Postoperative Atrial Fibrillation and Preoperative Sleep in Cardiac Surgical Patients

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ABSTRACT

BACKGROUND New-onset postoperative atrial fibrillation is associated with adverse clinical outcomes in older adults. Poor preoperative sleep quality is a putative modifiable risk factor. The relationships between new-onset postoperative atrial fibrillation and preoperative sleep structure in older adults undergoing elective cardiac surgery were investigated at a single center.

METHODS This was a prespecified substudy within a prospective observational study of perioperative electroencephalographic markers (ClinicalTrials.gov; NCT03291626). We analyzed preoperative sleep recordings from 71 cardiac surgical patients aged ≥60 years without a prior history of atrial fibrillation. Overnight recordings were acquired using a consumer-grade headband and underwent manual sleep staging. Electroencephalographic slow wave activity (power in the 0.5–4 Hz frequency band) was computed in 1-minute intervals for non-rapid eye movement sleep stages. Associations between new-onset postoperative atrial fibrillation incidence and sleep measures were evaluated using univariate logistic regression models and multivariate logistic regression models including age and sex.

RESULTS New-onset postoperative atrial fibrillation was present in 22 of 71 (31%) patients. A higher preoperative percentage of total sleep time in non-rapid eye movement stage 1 was associated with new-onset postoperative atrial fibrillation (median difference of 5.4%, $P = .0002$, Mann-Whitney U-test), independent of age and sex. No associations were observed between new-onset postoperative atrial fibrillation and other sleep metrics, including slow wave activity (all $P > .05$, Mann-Whitney U-test).

CONCLUSIONS Excess preoperative non-rapid eye movement stage 1 sleep, consistent with greater sleep fragmentation, is a potential modifiable target for mitigating new-onset postoperative atrial fibrillation risk in older adults undergoing elective cardiac surgery requiring cardiopulmonary bypass.

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New-onset postoperative atrial fibrillation (POAF) is a common cardiac dysrhythmia after cardiac surgery with adverse clinical sequelae.[1] New-onset POAF is associated with increased rates of morbidity and mortality,[1,2] with additional treatment costs of $10,000-

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$20,000 per patient.[1] Established risk factors fail to predict more than half of POAF cases.[3] Many risk factors, including advanced age, are nonmodifiable. Understanding potential modifiable risk factors, such as poor sleep, is important for presurgical optimization.

Poor sleep is a putative contributor to new-onset POAF, but relationships remain unclear.[4] Because sleep regulates the autonomic nervous system and cardiovascular function, poor sleep may confer vulnerability to POAF.[5] Sleep is categorized into rapid eye movement (REM) and the non-REM sleep stages—N1, N2, and N3. N1 is predominant in poor quality fragmented sleep. N3, with its dominant sleep slow waves and heightened parasympathetic activity, may have cardioprotective qualities.[6] In ambulatory nonsurgical patients, reduced durations of total sleep time (TST), N2, N3, and REM were associated with an increased risk of atrial fibrillation.[7] Whether these findings can be extrapolated to the preoperative electroencephalographic (EEG) sleep of older adults undergoing elective cardiac surgery remains unknown.

IN SHORT

- An electroencephalographic consumer-grade headband allowed investigation of associations between preoperative sleep structure and new-onset postoperative atrial fibrillation in older adults undergoing cardiac surgery.
- Sleep fragmentation, characterized by a higher percentage of N1 sleep and indicative of poor sleep quality, is significantly associated with increased risk of new-onset postoperative atrial fibrillation.

PATIENTS AND METHODS

This is a substudy of Prognosticating Delirium Recovery Outcomes Using Wakefulness and Sleep Electroencephalography (P-DROWS-E, ClinicalTrials.gov NCT03291626).[8] Patients were enrolled at Barnes-Jewish Hospital in St Louis, Missouri, between December 2019 and December 2021. Inclusion criteria were (1) English-speaking, (2) 60 years of age and older, and (3) elective major cardiac surgery requiring cardiopulmonary bypass. Exclusion criteria were (1) surgery requiring deep hypothermic circulatory arrest, (2) preoperative delirium, and (3) deafness or blindness. For this substudy, patients with a preoperative diagnosis of atrial fibrillation were also excluded. Incidence of new-onset POAF was determined via manual review of the electronic medical record up to postoperative day 7.

Preoperative overnight sleep EEG recordings were acquired utilizing a wearable wireless headband (Dreem, Rhythm) that bypasses technical limitations of PSG and actigraphy.[8] Participants completed up to 2 nights of preoperative unattended overnight sleep recordings.

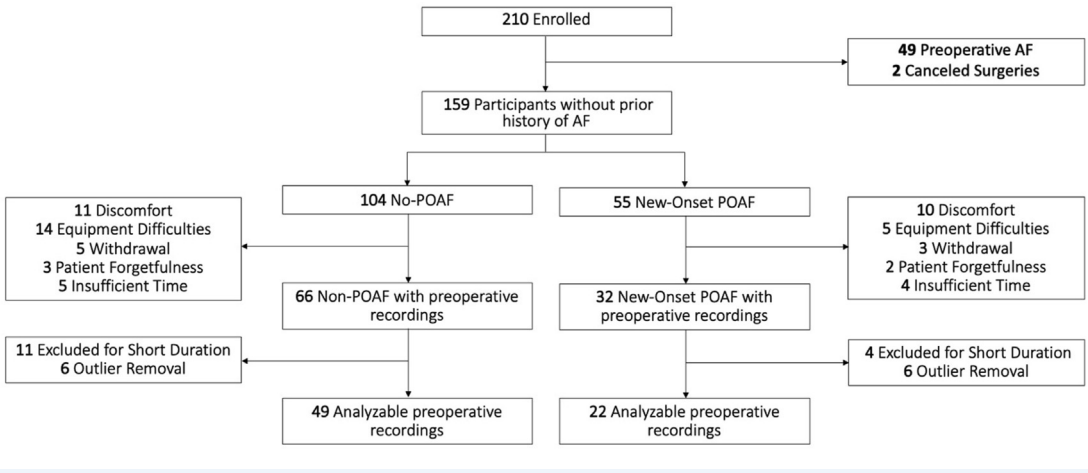

FIGURE 1 Consort flow diagram. Patients enrolled in the parent study with a history of atrial fibrillation (AF) were excluded. Attrition occurred due to electroencephalographic headband discomfort, equipment difficulties, withdrawal from the parent study, patient forgetfulness, or insufficient time. Patients were excluded due to sleep recordings of insufficient duration or position as outliers. (POAF, postoperative atrial fibrillation.)

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TABLE 1 Cohort Demographic and Perioperative Characteristics

Characteristics	No-POAF n = 49	New-onset POAF n = 22
Demographic		
Age	66.0 (10.0)	66.5 (8.0)
Sex		
Race		
White	43 (87.8)	19 (86.4)
Black	5 (10.2)	3 (13.6)
Asian	1 (2.0)	0
Education, y	18 (7)	16 (7)
Preoperative		
Admission status, outpatient	30 (61.2)	14 (63.6)
BMI, kg/m^2	29.2 (8.9)	29.4 (5.0)
CCI	6 (4)	7 (3)
CAD	37 (75.5)	17 (77.3)
Hypertension	44 (89.8)	17 (77.3)
OSA	13 (26.5)	4 (18.2)
STOP-Bang (OSA risk)	4 (1.5)	4 (2.0)
Non-OSA sleep disorder	0	1 (4.6)
Prescribed sleep medication[a]	9 (18.4)	0
Beta blocker	34 (69.4)	13 (59.1)
Calcium channel blocker	19 (38.8)	5 (22.7)
Intraoperative		
Surgery type		
CABG	24 (49.0)	9 (40.9)
CABG and valve	1 (2.0)	2 (9.1)
Single valve	18 (36.7)	8 (36.4)
Multiple valve	3 (6.1)	1 (4.6)
Other	3 (6.1)	2 (9.1)
Cross-clamp duration, min	86.0 (31.5)	77.5 (44.0)
Bypass duration, min	116.0 (45.0)	122.0 (45.0)
Surgery duration, min	380.0 (177.5)	462.0 (183.0)
Postoperative		
Number of inotropes	1 (0)	1 (0)
Inotrope duration, d	2 (2.0)	2 (2.0)
Number of vasopressors	1.0 (1)	1 (1)
Vasopressor duration, d	1 (1.0)	1 (2.0)
Pulmonary vasodilator, d	0	0
Intubation duration, d	0.4 (0.4)	0.5 (0.7)
ICU length of stay, d	2 (3.3)	3 (4.0)
Hospital length of stay, d[a]	8 (7)	12 (9.5)

[a]$P \leq .05$. Characteristics were compared between the No-POAF and new-onset POAF groups using the Mann-Whitney U-test, Fisher's exact test, or the χ^2 test. Values are presented as median (interquartile range) or n (%). BMI, body mass index; CABG, coronary artery bypass grafting; CCI, Charlson Comorbidity Index; CAD, coronary artery disease; ICU, intensive care unit; OSA, obstructive sleep apnea, STOP-Bang, Snoring history, Tired during the day, Observed stop breathing while sleep, High blood pressure, BMI more than 35 kg/m^2, Age more than 50 years, Neck circumference more than 40 cm, and male Gender.

Raw EEG data were preprocessed using custom-coded MATLAB (The MathWorks) scripts and EEGLAB.[9] Registered polysomnographic technologists scored channels Fpz-F8, Fpz-F7, and F8-F7 in 30-second epochs, using Philips Respironics Sleepware G3 Software, based on the modified criteria of the American Academy of Sleep Medicine.[8] Staff were blinded to clinical outcomes. Poor quality recordings were excluded if the TST was less than 60 minutes or if derived sleep measures were positioned outside of the 5th to 95th percentile range.

To evaluate sleep slow wave strength, slow wave activity (SWA) was calculated in 1-minute intervals as the total 0.5-4 Hz spectral power during N2 and N3 sleep stages. Relative SWA power was determined as the absolute SWA divided by total EEG power. Analyses were conducted with custom-written MATLAB scripts and multitaper methods via the Chronux toolbox.[9]

Relationships between EEG sleep markers and new-onset POAF incidence were evaluated using a univariate logistic regression model. Secondary analyses for demographic covariates were performed via Mann-Whitney U-test (continuous measures) or Fisher's exact/χ^2 tests (categorical variables). A logistical regression model included sex and age as covariates. No power/sample size calculations or corrections of alpha for multiple comparisons were conducted.

COHORT CHARACTERISTICS. A total of 210 patients were recruited (Figure 1), with exclusions based on preoperative atrial fibrillation diagnosis or cancelled surgeries. Of the remaining 160 and exclusions due to missing data, 22 and 49 participants remained in the new-onset POAF and no-POAF cohorts, respectively.

Baseline demographic and perioperative characteristics are shown in Table 1. Patients who did not develop POAF were more likely to be prescribed preoperative sleep medications ($P = .031$). Hospital length of stay was 4 days longer in patients with new-onset POAF ($P = .049$). As with other factors, the risk of obstructive sleep apnea, assessed by the STOP-Bang (Snoring history, Tired during the day, Observed stop breathing while sleep, High blood pressure, BMI more than 35 kg/m^2, Age more than 50 years, Neck circumference more than 40 cm, and male Gender) measure, did not differ between cohorts. There were no significant differences in preoperative transthoracic echocardiographic indices (Supplemental Table).

ASSOCIATIONS BETWEEN PREOPERATIVE SLEEP MACROSTRUCTURE AND NEW-ONSET POAF. Compared with the no-POAF cohort, the percentage of TST in N1 was 5.4% greater in the new-onset POAF cohort (Figure 2A; New-onset POAF group median (interquartile range) 10.5% (6.1%) and No-POAF group median (interquartile range) 5.2% (4.5%); $P = .0002$, Mann-Whitney U-test). No significant differences were observed for the

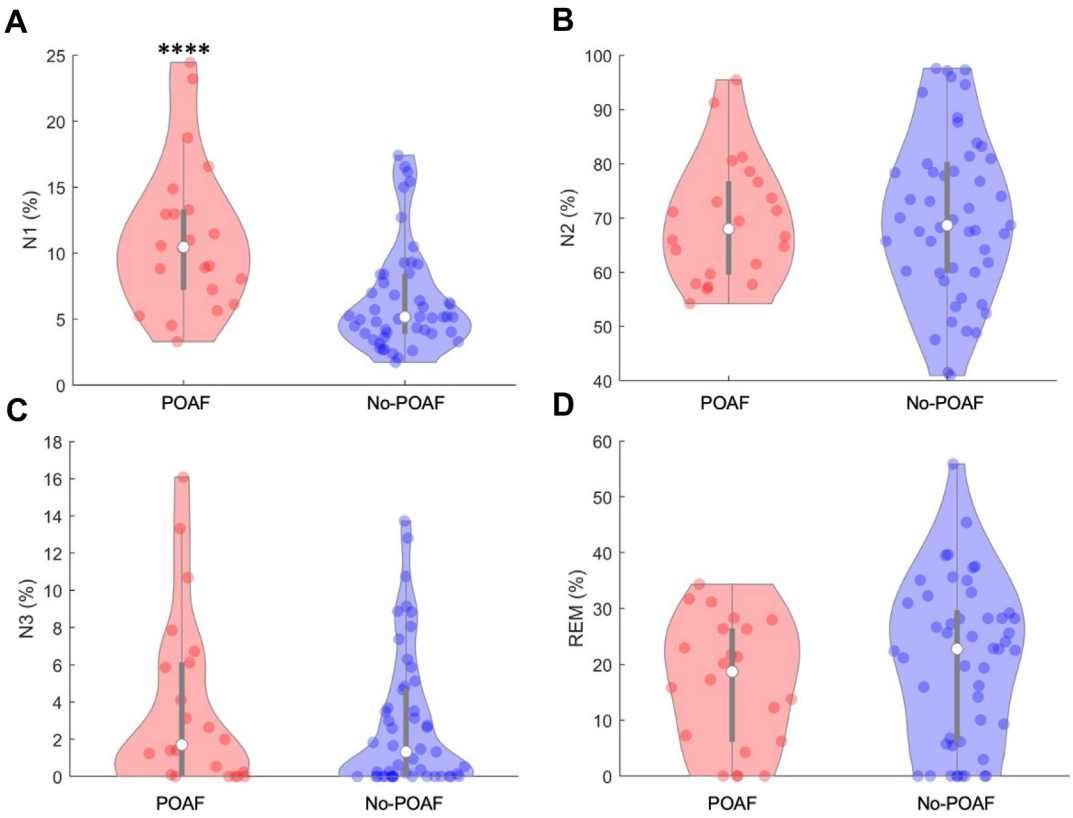

FIGURE 2 New-onset postoperative atrial fibrillation (POAF) was associated with a greater median percentage of total sleep time in N1 sleep. (A) Violin plots showing that percentage of total sleep time in N1 sleep was greater ($p = .0002$) in the New-onset POAF group, median (interquartile range) 10.5% (6.1%), compared with the No-POAF group, median (interquartile range) 5.2% (4.5%). In contrast, no associations were observed for other sleep stages, including (B) N2 sleep ($P = .74$), (C) N3 sleep ($P = .43$), and (D) rapid eye movement sleep (REM) ($P = .32$).

median percentages of TST in N2, N3, or REM (Figures 2B-2D).

A multivariate logistical regression was performed, incorporating percentage of TST in N1, age, and sex (intercept -0.30, $p = 0.91$). Only percentage of TST in N1 was associated with new-onset POAF incidence ($\beta = -0.21$, $P = .0008$), whereas this outcome was not linked to age ($\beta = 0.04$, $P = .27$) or sex ($\beta = -0.06$, $P = .92$).

ASSOCIATIONS BETWEEN EEG SLOW WAVE ACTIVITY AND NEW-ONSET POAF. EEG sleep slow waves arise during N2 and dominate N3 sleep. When comparing SWA between groups, no associations with new-onset POAF were observed for either N3 sleep (Figure 3A) or N2/N3 sleep combined (Figure 3B). Furthermore, there were no statistical differences in median absolute and relative power (Supplemental Figure).

COMMENT

N1 sleep defines the transition from wakefulness to sleep, contributing to 8% to 15% of overall sleep in the elderly population.[9] A higher percentage of TST in N1 suggests poor quality fragmented sleep[9] that may heighten the risk for POAF in combination with other factors.[2] Chronic sleep fragmentation deprives the body of restorative processes conferred REM, N2, and N3 sleep. Deficiencies in cellular homeostatic processes in the heart and a heightened baseline level of inflammation could contribute to POAF vulnerability. Alternatively, fragmented sleep might indicate anxiety and stress related to impending cardiac surgery, necessitating larger prospective studies. If confirmed, clinical trials targeting new-onset POAF risk by reducing N1 sleep could explore pharmacologic (ie, dexmedetomidine or suvorexant) or nonpharmacologic approaches towards maximizing consolidated sleep.

Prior work has associated atrial fibrillation with N2 and N3 sleep durations in nonsurgical populations.[4,6] Thus, the lack of association between new-onset POAF incidence and SWA was unexpected. The pathophysiology of new-onset POAF

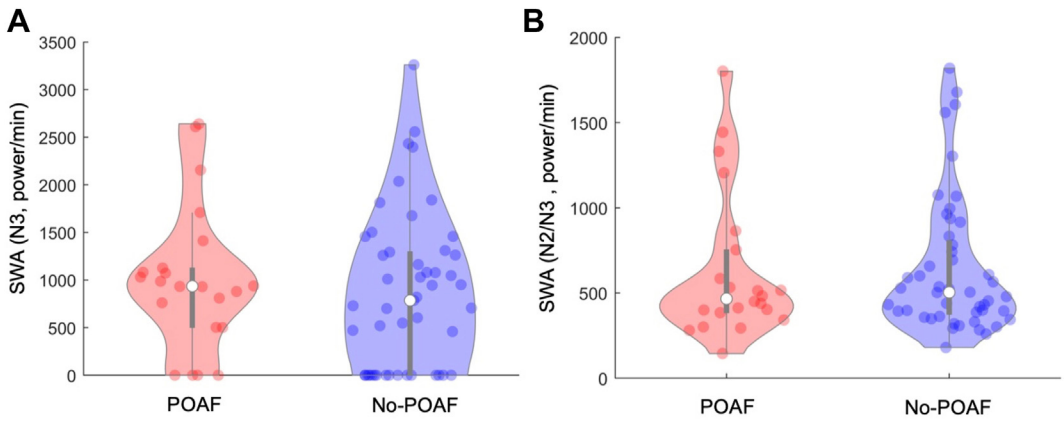

FIGURE 3 New-onset postoperative atrial fibrillation (POAF) was not associated with slow wave activity (SWA). SWA measures strength of sleep slow waves that define N3 sleep and can occur in N2 sleep. (A) Violin plots measures of SWA for only N3 with no significant differences (n = 71, median difference −37.336, $P = .47$). (B) Similar measures of SWA combined across N2 and N3 for both New-onset POAF and No-POAF cohorts (n = 70, median difference 149.59, $P = .74$).

likely combines abnormal sleep structure with surgical stress factors such as tissue injury, inflammation, and pain. Differential modulation of sympathetic and parasympathetic activity during specific sleep stages might also contribute to an arrhythmogenic substrate.[10]

LIMITATIONS AND STRENGTHS. As this study was observational, causality cannot be determined. The limited sample size restricted the investigation's scope and power. Participant selection bias may exist, as those comfortable with the headband might differ from lighter sleepers who may not tolerate the headband. Finally, while a greater rate of preoperative sleep medication use was observed in the no-POAF group, larger studies are needed to investigate this further.

Despite limitations, no previous exploration of preoperative sleep microarchitecture has been conducted. Additionally, our study utilized new technology, overcoming challenges associated with traditional polysomnography in investigating sleep.

CONCLUSIONS. In a cohort of older adults undergoing major cardiac surgery requiring cardiopulmonary bypass, a greater percentage of TST in N1 was associated with an elevated risk of new-onset POAF. Excessive N1 sleep/sleep fragmentation may be a modifiable risk factor for new-onset POAF.

The Supplemental Material can be viewed in the online version of this article [https://doi.org/10.1016/j.atssr.2024.07.010] on http://www.annalsthoracicsurgery.org.

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DISCLOSURES

Ralph J. Damiano, Jr, reports a relationship with AtriCure Inc that includes: funding grants and speaking and lecture fees; with Medtronic Inc that includes: consulting or advisory and speaking and lecture fees; and with Edwards Lifesciences Corp that includes: speaking and lecture fees.

REFERENCES

1. Greenberg JW, Lancaster TS, Schuessler RB, Melby SJ. Postoperative atrial fibrillation following cardiac surgery: a persistent complication. *Eur J Cardiothorac Surg*. 2017;52:665–672.

2. Dobrev D, Aguilar M, Heijman J, Guichard JB, Nattel S. Postoperative atrial fibrillation: mechanisms, manifestations and management. *Nat Rev Cardiol*. 2019;16:417–436.

3. Methangkool E, Howard-Quijano K, Mahajan A. The problem with predicting postoperative atrial fibrillation. *J Cardiothorac Vasc Anesth*. 2015;29:1115–1116.

4. Genuardi MV, Ogilvie RP, Saand AR, et al. Association of short sleep duration and atrial fibrillation. *Chest*. 2019;156:544–552.

5. Malhotra A, Loscalzo J. Sleep and cardiovascular disease: an overview. *Prog Cardiovasc Dis*. 2009;51:279–284.

6. Kwon Y, Gharib SA, Biggs ML, et al. Association of sleep characteristics with atrial fibrillation: the multi-ethnic study of atherosclerosis. *Thorax*. 2015;70:873–879.

7. Mehra R, Marcus GM. Novel Insights into sleep disorder and atrial fibrillation risk: more than sleep apnea. *Chest*. 2019;156:421–423.

8. Smith SK, Nguyen T, Labonte AK, et al. Protocol for the Prognosticating Delirium Recovery Outcomes Using Wakefulness and Sleep Electroencephalography (P-DROWS-E) study: a prospective observational study of delirium in elderly cardiac surgical patients. *BMJ Open*. 2020;10:e044295.

9. Edwards BA, O'Driscoll DM, Ali A, Jordan AS, Trinder J, Malhotra A. Aging and sleep: physiology and pathophysiology. *Semin Respir Crit Care Med*. 2010;31:618–633.

10. Zafeiropoulos S, Doundoulakis I, Farmakis IT, et al. Autonomic neuromodulation for atrial fibrillation following cardiac surgery: JACC review topic of the week. *J Am Coll Cardiol*. 2022;79:682–694.