RESEARCH ARTICLE

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Regulating Effect of Weekend Catch-up Sleep on the Relationship Between Atrial Fibrillation and Acute Myocardial Infarction

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Abstract

Background and Aim: Coronary artery disease and atrial fibrillation (AF) are major contributors to cardiovascular morbidity and mortality. Systemic inflammation may link AF to acute myocardial infarction (MI). We investigated whether weekend catch-up sleep (WCS) is associated with acute MI in patients with AF and whether the systemic immune-inflammation (SII) index modifies this association.

Materials and Methods: We conducted a single-center retrospective cohort study including 3,200 patients with AF. Participants were categorized as having no WCS (0 h) or as having WCS present (0<WCS≤1 h). Inflammatory biomarkers and acute MI events during follow-up were evaluated.

Results: Acute MI occurred more frequently in the no WCS group than in the WCS group ($P < 0.001$). In receiver operating characteristic analyses, the SII cut-off values were 352.12 (sensitivity 82%, specificity 83%) for patients without WCS and 212.61 (sensitivity 81%, specificity 81%) for patients with WCS. Kaplan-Meier curves demonstrated a higher risk of acute MI among the no WCS group (log-rank $P < 0.001$).

Conclusion: In this single-center retrospective cohort study, the absence of WCS was associated with a higher risk of acute MI in patients with AF, and the WCS×SII interaction suggested effect modification by inflammatory burden. External validation is warranted.

Keywords: Atrial fibrillation, weekend catch-up sleep, acute myocardial infarction, systemic immune inflammatory index

INTRODUCTION

Cardiovascular diseases, including coronary artery disease (CAD) and atrial fibrillation (AF), remain leading causes of morbidity and mortality worldwide.[1] The prevalence of both CAD and AF increases with age, and these conditions frequently coexist.[2] In patients with non-valvular AF, angiographically documented CAD has been reported in more than half of cases, which is substantially higher than estimates in non-AF populations (~13%).[3,4] Moreover, AF has been associated with incident CAD and acute myocardial infarction (MI), potentially through shared risk factors, a prothrombotic milieu, and hemodynamic alterations.[5]

Inflammation represents a key biological link between AF and ischemic events. Acute MI triggers robust intramyocardial and systemic inflammatory responses, with elevations in circulating biomarkers;[6] inflammatory pathways have long been implicated in AF pathophysiology.[7] Accordingly, practical inflammatory indices that could help identify AF patients at higher risk of MI are of clinical interest. The systemic immune-inflammation (SII) index, derived from routine complete blood

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counts (CBC), has been reported to be elevated in both AF and MI;[7] however, its utility for MI risk stratification within AF cohorts remains uncertain.

Sleep is another potentially modifiable determinant of cardiometabolic health. Short sleep duration and poor sleep quality have been linked to adverse cardiovascular profiles, including hypertension (HT), metabolic syndrome, and increased arterial stiffness.[8] Weekend catch-up sleep (WCS)—extending sleep on non-work days to compensate for weekday sleep debt—has been proposed as a mitigating behavior with potential cardiometabolic benefits.[9] However, the impact of WCS on acute MI risk among patients with AF and whether inflammatory burden modifies this association have not been investigated.

Therefore, we investigated the association between WCS and incident acute MI and evaluated the prognostic role of SII in patients with AF.

METHODS

Study Design, Population, and Ethics

This retrospective cohort study included 3,649 consecutive patients admitted to the local university hospital. This cohort comprised consecutive patients with AF who were evaluated at our university hospital, including outpatient clinic visits and inpatient or emergency admissions, between May 2018 and February 2025. Admission status was obtained from the electronic health record. After excluding 449 patients with insufficient data, the final analytic sample comprised 3,200 patients (flowchart). Demographic, clinical, laboratory, procedural, and follow-up information was obtained from the electronic health record and the institutional database using standardized extraction forms. The study complied with the Declaration of Helsinki and received approval from the Local Institutional Ethics Committee of Tokat Gaziosmanpaşa University (decision no: 25-MOBAEK-327, date: 16.10.2025).

AF and acute MI were defined according to the European Society of Cardiology guidelines.[10,11] All patients were followed for 4.23±0.81 years. Two members of the event-adjudication committee independently and blindly adjudicated MI events; discrepancies were resolved by consensus.

Exclusion Criteria

We excluded patients who received thrombolytic therapy before invasive evaluation; patients without invasive assessment within 12 hours of symptom onset (when clinically indicated); patients with any systemic inflammatory or rheumatologic disease, storage disease, anemia, malignancy, hematological disorders (including acute or chronic stroke), advanced renal and/or hepatic failure; patients with active or recent infection; patients who had blood transfusion within the prior 3 months; patients with severe valvular disease or a history of valve surgery; patients aged <18 years; and patients with incomplete core data fields.

Exposure Definition: WCS

Sleep was assessed using National Health and Nutrition Examination Survey (NHANES)[12] items on usual sleep during weekdays (workdays) and weekends (non-workdays). For the present analyses, we focused exclusively on WCS and did not use the weekly mean sleep duration. Given the skewed distribution of WCS, with clustering between 0 and 1 hour, WCS was initially operationalized pragmatically; however, alternative codings were examined in sensitivity analyses (Supplementary Table 1). WCS was computed as weekend sleep minus weekday sleep (in hours) and operationalized as a binary exposure: no WCS (difference=0 h) versus WCS present (0<WCS≤1 h). Participants with WCS>1 h were not excluded; they were retained in the dataset and evaluated in the prespecified sensitivity analyses that used broader WCS definitions (e.g., >0 h, ≥1 h, ≥2 h, and continuous WCS) (Supplementary Table 1). Participants were categorized accordingly. No WCS: 0 hour WCS present: 0<WCS≤1 hour.

Outcomes

The primary outcome was acute MI during follow-up. Secondary descriptors included baseline characteristics and inflammatory indices across WCS categories.

Laboratory Measurements and SII Index

Peripheral venous blood was collected on admission after at least 8 hours' fasting. Routine biochemical tests [lipid panel, fasting plasma glucose, creatinine, liver enzymes, albumin, C-reactive protein (CRP), n-terminal brain natriuretic peptide] and a CBC were measured on an automated analyzer. Clinical definitions: diabetes mellitus was defined as fasting plasma glucose >125 mg/dL, HbA1c >6.5%, or use of antidiabetic therapy; hyperlipidemia was defined as low-density lipoprotein cholesterol >100 mg/dL or use of lipid-lowering medication; and HT was defined as use of antihypertensives or systolic blood pressure/diastolic blood pressure ≥140/90 mmHg. CAD was defined as prior MI, ≥50% epicardial stenosis on angiography, or equivalent evidence on coronary computed tomography angiography. Current smoking was defined as smoking within the past 6 months.

SII was calculated as (platelet count×neutrophil count)/lymphocyte count.

Echocardiography and Coronary Procedures

All patients underwent transthoracic echocardiography in the left lateral decubitus position prior to invasive procedures. Left

ventricular ejection fraction was measured by two experienced cardiologists using the biplane Simpson method. Diagnostic coronary angiography and percutaneous coronary intervention, when indicated, were performed by experienced interventional cardiologists via radial or femoral access using the standard Judkins technique with 6-Fr catheters and a flat-panel digital angiography system.

Statistical Analysis

Statistical analyses were performed using SPSS 26.0 software (SPSS Inc., Chicago, IL, USA). Missing data handling: patients with insufficient or incomplete core data fields were excluded from the analysis. For multivariable analyses, we performed complete-case analyses (listwise deletion) within each model, excluding participants with missing values for any covariate included in that specific model. Therefore, the analytic sample sizes could vary across models; model-specific n values are reported in the corresponding tables (e.g., Supplementary Table 2). Continuous variables were assessed for distribution using the Kolmogorov-Smirnov and Shapiro-Wilk tests and by visual inspection, and summarized as mean ± standard deviation or median (interquartile range); categorical variables were summarized as n (%). Between-group comparisons used the t-test or Mann-Whitney U test for continuous variables, and the chi-square or Fisher's exact test for categorical variables, as appropriate.

The primary analysis used a prespecified Cox proportional hazards model (time-to-event) with time-to-first MI as the outcome; the model included WCS, SII, and the WCS×SII interaction and was adjusted a priori for age, heart rate, CAD, and CRP. Multivariable logistic regression was performed as a secondary and complementary analysis to facilitate visualization of interactions and to report adjusted odds ratios (aOR). The main predictors were WCS category [no WCS vs. WCS present ($0<WCS\leq1$)], SII (continuous; log-transformed if necessary), and the WCS×SII interaction. Covariates were selected a priori based on clinical relevance and the literature: age, heart rate, CAD, and CRP. To assess robustness to exposure coding and to reduce potential misclassification, we conducted pre-specified sensitivity analyses using alternative definitions of WCS: (i) binary (>0 h vs. 0 h), (ii) collapsed categories where necessary because of sparse counts, and (iii) continuous WCS (per 1-hour increase). Alternative thresholds included ≥2 h, where cell counts permitted. These prespecified analyses were performed using multivariable logistic regression and time-to-event Cox models; results are presented in Supplementary Table 1. To address potential residual confounding, we conducted sequential sensitivity analyses with varying covariate adjustment (unadjusted; the primary, prespecified model; and, where available, expanded models adjusted for clinical variables and medications). Results are presented in Supplementary Table 2. Effect modification was evaluated with the interaction term (P-interaction <0.05). When an interaction was present, we fitted stratified, adjusted models across SII tertiles (T1-T3) and reported the results as aORs with 95% confidence intervals (CIs). Stratified/tertile analyses were prespecified as exploratory and used for visualization rather than for threshold determination.

To explore potential non-linearity in the association of SII with MI, we used restricted cubic splines. Model calibration and discrimination for the logistic model were assessed using the Hosmer-Lemeshow test and receiver operating characteristic (ROC) area under the curve (AUC), respectively, and multicollinearity was evaluated using variance inflation factors (VIF) <5. VIF values and tolerances for all covariates are provided in Supplementary Table 3. For interaction models, SII was mean-centered before creating the WCS×SII product term to reduce collinearity. Given the number of secondary and sensitivity analyses, results beyond the prespecified primary model are considered exploratory. Accordingly, we did not apply formal multiplicity adjustment; secondary analyses were interpreted cautiously, with emphasis on effect sizes and 95% CIs. Two-sided $P < 0.05$ was considered statistically significant.

Time-to-event analysis (Cox proportional hazards): to incorporate follow-up time, we fitted a prespecified Cox proportional hazards model with time-to-first MI as the outcome. The model included WCS, SII (log-transformed if needed), and the interaction WCS×SII, and was adjusted for the same covariates. Results from Cox models were expressed as hazard ratios (HR) with 95% CIs. The proportional hazards assumption was evaluated using Schoenfeld residuals (and log-log plots if needed); model discrimination was summarized with Harrell's C-index.

RESULTS

A total of 3,200 patients with AF were included. Baseline demographic, clinical, laboratory, and echocardiographic characteristics, as well as medications, are summarized in Table 1. Age was significantly higher in the WCS-present group, whereas CAD prevalence and heart rate were significantly higher in the group without WCS. Inflammatory indices also differed between groups: CRP, SII, and neutrophil and platelet counts were higher in the no WCS group, whereas lymphocyte counts were higher in the WCS-present group.

Acute MI events and angiographic findings during follow-up are presented in Table 2. The incidence of acute MI was higher in the no WCS group than in the WCS group [515/1977 (26.04%) vs. 249/1223 (20.35%), $P < 0.001$].

In the ROC analysis (Figure 1), the optimal SII cut-off for

Table 1. Basic demographic, clinical and laboratory characteristics, echocardiography results and medications used by the patients included in the study

Variable	0<WCS≤1 (n=1223)	No WCS (n=1977)	*P*
Demographic features			
Age (years)	65±8.3	63.2±9.2	**0.003**
Female gender n (%)	635 (51.92)	1029 (52.04)	0.359
BMI kg/m^2	28.21±2.32	28.41±2.33	0.555
CAD n (%)	392 (32.05)	711 (35.96)	**<0.001**
Diabetes mellitus n (%)	428 (34.99)	691 (34.95)	0.439
Hypertension n (%)	489 (39.98)	790 (39.95)	0.887
Hyperlipidemia n (%)	269 (21.99)	434 (21.95)	0.773
Smoking n (%)	305 (24.93)	474 (23.97)	0.449
HF n (%)	256 (20.93)	415 (20.99)	0.501
Heart rate (bpm)	101.44 (71-142)	120.51 (73-144)	**<0.001**
CHA_2DS_2-VASc score	4.42 (1-7)	4.44 (1-7)	0.864
Laboratory findings			
Glucose (mg/dL)	119.22±12.43	118.98±12.34	0.490
Creatinine (mg/dL)	1.05 (0.82-1.21)	1.08 (0.82-1.23)	0.862
BUN (mg/dL)	22.32 (18-28)	22.02 (17–27.6)	0.443
Sodium (mmol/L)	137.58 (135.9-141.5)	138.13 (135.4-142.3)	0.662
Potassium (mmol/L)	4.38 (3.59-4.66)	4.37 (3.61-4.69)	0.731
Albumin (g/dL)	4.33±1.02	4.24±1.05	0.442
ALT (U/L)	28.63 (22-38)	26.55 (23-40)	0.464
AST (U/L)	23.79 (17-33)	25.15 (18-35)	0.389
TSH (µIU/mL)	1.27±0.53	1.23±0.51	0.742
T4 (µIU/mL)	0.92±0.22	1.01±0.11	0.173
Haemoglobin (g/dL)	11.33±1.56	11.17±1.60	0.438
WBC count (x10^3/µL)	11.99±1.37	12.01±1.29	0.746
Neutrophil (x10^3/µL)	2.27±0.11	2.59±0.13	**<0.001**
Lymphocyte (x10^3/µL)	2.49±0.47	2.17±0.52	**<0.001**
Platelet (x10^3/µL)	301.23±22.45	349.61±21.99	**<0.001**
LDL-cholesterol (mg/dL)	126.44 (100-132)	125.23 (103-130)	0.459
HDL-cholesterol (mg/dL)	27.44 (20-35)	28.61 (22-37)	0.782
Triglycerides (mg/dL)	208.60 (193-258)	210.41 (195-261)	0.567
CRP	15.33 (10-21)	28.90 (15-42)	**<0.001**
SII	274.42±22.10	416.59±21.01	**<0.001**
Echocardiographic parameters			
LVEF (%)	51.13±5.43	51.08±5.37	0.435
LA size (mm)	44.62±3.51	44.32±3.22	0.332
LVDD (mm)	48.59±2.1	48.66±2.4	0.623
LVSD (mm)	36.64±1.9	36.04±2.01	0.951
IVSD (mm)	9.69±1.5	9.34±1.2	0.958
E/e'	13.88±1.8	13.97±1.5	0.329
Mild mitral stenosis n (%)	183 (16.29)	317 (16.03)	0.792
Medications			
Acetylsalicylic acid n (%)	50 (4.08)	80 (4.04)	0.357
ACEi, ARB n (%)	612 (50.04)	989 (50.02)	0.616
Beta blocker n (%)	1100 (89.94)	1781 (90.08)	0.763

Table 1. Continued

Variable	0<WCS≤1 (n=1223)	No WCS (n=1977)	*P*
Statin n (%)	616 (50.36)	990 (50.07)	0.752
Calcium channel blockers n (%)	366 (29.92)	594 (30.04)	0.816
Dihydropyridine	36 (9.83)	60 (10.10)	0.971
Non-dihydropyridine	330 (90.16)	534 (89.89)	0.738
Anticoagulant medication n (%)	1175 (96.07)	1899 (96.05)	0.659
Warfarin	79 (6.72)	115 (6.05)	0.871
Apixaban	329 (28)	532 (28.01)	0.769
Rivaroxaban	352 (29.95)	570 (30.01)	0.873
Edoxaban	317 (26.97)	512 (26.96)	0.795
Dabigatran	98 (8.34)	160 (8.42)	0.734

Continuous variables are presented as mean ± standard deviation or as median (interquartile range) where indicated; categorical variables are presented as n (%)

BMI: Body mass index, CAD: Coronary artery disease, HF: Heart failure, ACEi: Angiotensin-converting enzyme inhibitor ARB: Angiotensin receptor blockers, WBC: White blood cells, BUN: Blood urea nitrogen, LVEF: Left ventricular ejection fraction LVDD: Left ventricular end diastolic diameter, LVSD: Left ventricular end systolic diameter, IVSD: Interventricular septum, LA: Left atrium, ALT: Alanine aminotransferase, AST: Aspartate aminotransferase, bpm: Beats per minute, TSH: Thyroid-stimulating hormone, LDL: Low-density lipoprotein, HDL: High-density lipoprotein, SII: Systemic immune-inflammatory index, CRP: C-reactive protein, WCS: Weekend catch-up sleep

Table 2. Information on myocardial infarction during follow-up of patients with atrial fibrillation

Variable	0<WCS≤1 (n=1223)	No WCS (n=1977)	*P*
Myocardial infarction	249 (20.35)	515 (26.04)	<0.001
Contrast agent amount (mL)	121.47±18.42	121.23±17.99	0.835
Processing time (min)	42.66±4.71	43.01±4.19	0.597
Number of lesions n (%)			
1	50 (20.08)	103 (20)	0.399
2	174 (69.87)	361 (70.09)	0.467
3	25 (10.04)	51 (9.90)	0.593
Location of the lesion n (%)			
LAD	87 (34.93)	180 (34.95)	0.804
LCX	83 (33.33)	175 (33.98)	0.768
RCA	81 (32.53)	170 (33.00)	0.697

LAD: Left anterior descending artery, LCX: Left circumflex artery, RCA: Right coronary artery, WCS: Weekend catch-up sleep

discriminating acute MI among no WCS AF patients was 352.12, with sensitivity of 82% and specificity of 83% (AUC: 0.892, 95% CI 0.873-0.911, $P < 0.01$). Among AF patients with WCS, the SII cut-off was 212.61, with 81% sensitivity and 81% specificity (AUC: 0.792; 95% CI, 0.757-0.827; $P < 0.01$).

Kaplan-Meier curves (Figure 2) showed a significantly higher cumulative incidence of acute MI in the no WCS group (log-rank test, $P < 0.001$). In primary time-to-event analyses, the adjusted Cox proportional hazards model showed that WCS present (0<WCS≤1 h) was associated with a lower hazard of incident acute MI compared with no WCS (0 h) (adjusted HR: 0.81, 95% CI 0.69-0.95; $P = 0.010$). In a complementary multivariable logistic regression model (Table 3), heart rate, SII, and absence of WCS were independently associated with acute MI. Using no WCS as the reference, presence of WCS was associated with lower odds of acute MI (aOR: 0.752, 95% CI 0.539-0.889; $P < 0.001$). Results were consistent across alternative WCS codings and sequentially adjusted sensitivity models (Supplementary Tables 1 and 2).

The WCS×SII interaction term suggested effect modification (*P*-interaction: 0.018; Figure 3A). In the multivariable logistic interaction model (Table 4), the presence of WCS remained inversely associated with MI (aOR: 0.752, 95% CI 0.539-0.889; $P < 0.001$) and SII was positively associated with MI (per 100-unit increase: aOR: 1.65, 95% CI 1.22-2.23; $P < 0.001$).

In exploratory stratified analyses across SII tertiles (Figure 3B; Table 5), the association between absence of WCS and acute MI appeared strongest in the highest tertile (T3: aOR: 1.95, 95% CI 1.24-3.06; $P = 0.004$), whereas associations in the lower tertiles were weaker or not statistically significant (T1: aOR: 1.10, $P = 0.460$; T2: aOR: 1.35, $P = 0.058$). These subgroup findings are descriptive and hypothesis-generating.

The association remained consistent in sensitivity analyses using alternative WCS codings (Supplementary Table 1). Findings were also robust in sequential covariate-adjusted models (Supplementary Table 2).

Restricted cubic spline analysis (Supplementary Figure 1) demonstrated that higher SII values were generally associated with increased adjusted odds of acute MI, with a potentially non-linear pattern across the SII range. Accordingly, SII was retained as a continuous variable in the multivariable models.

DISCUSSION

This study is among the first to examine the association between WCS and acute MI in AF, addressing a gap in the literature on compensatory sleep patterns. Our findings reveal that AF patients with no WCS have a significantly higher incidence of acute MI than those with WCS (0<WCS≤1). Beyond this crude association, our primary multivariable model, including an interaction term (WCS×SII), demonstrated that the relationship between WCS and acute MI is modified by the inflammatory burden; the interaction was statistically significant. In stratified, adjusted analyses across SII tertiles, the association between absence of WCS and acute MI was weak and non-significant in the low-SII tertile and borderline in the mid-SII tertile, but was clearly significant and clinically meaningful in the high-SII tertile. These results provide novel insights into the interplay between sleep patterns, systemic inflammation, and cardiovascular risk in AF patients, suggesting that SII may be a candidate marker for risk stratification in this cohort; however, its clinical utility requires external multicenter validation.

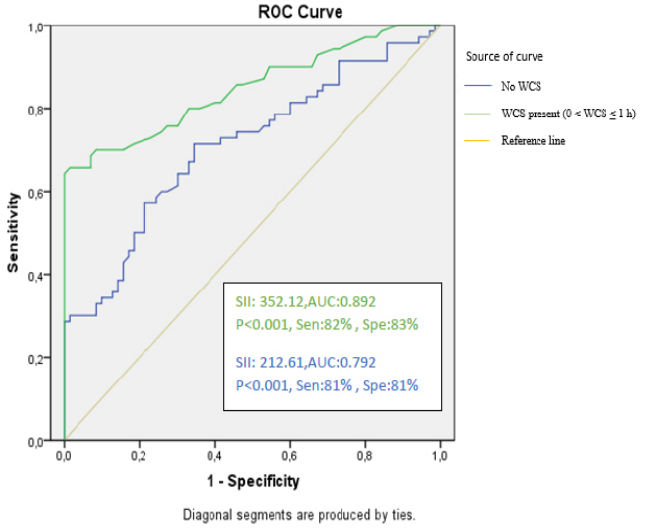

Figure 1. Exploratory ROC curves of SII for discriminating acute MI stratified by WCS status. No WCS: n=1977, events=515; WCS present (0<WCS≤1 h): n=1223, events=249. AUC values are reported with 95% confidence intervals calculated using the DeLong method

ROC: Receiver operating characteristic, SII: Systemic immune-inflammation index, MI: Myocardial infarction, WCS: Weekend catch-up sleep, AUC: Area under curve

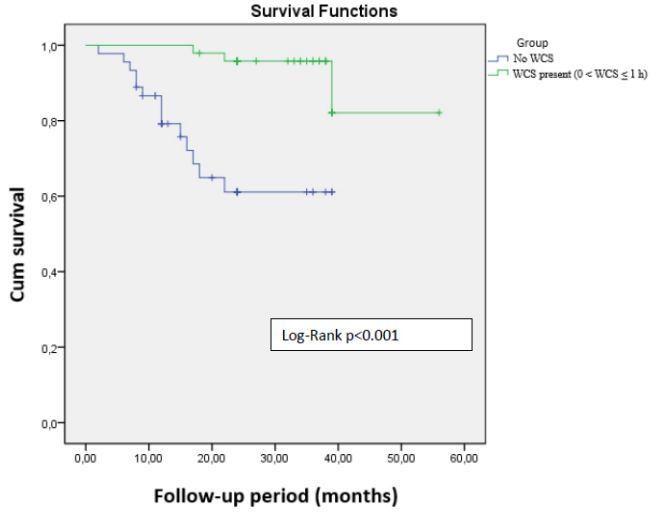

Figure 2. Cumulative incidence of acute MI comparing no WCS vs. WCS present (0<WCS≤1h) (log-rank *P* < 0.001)

MI: Myocardial infarction, WCS: Weekend catch-up sleep

Table 3. Univariate and multivariable regression analyses to identify factors independently associated with acute MI

Variable	Univariate analysis odds ratio (95% CI)	*P*	Multivariate analysis odds ratio (95% CI)	*P*
Age	1.134 (1.02-1.25)	0.018	1.091 (0.95-1.19)	0.274
CAD	1.743 (1.12-2.71)	0.014	1.256 (1.102-1.73)	0.022
Heart rate (per 10 bpm)	1.323 (1.08-1.62)	0.005	1.18 (1.07-1.31)	0.012
CRP	1.392 (1.15-1.67)	<0.001	1.121 (1.02-1.32)	0.008
SII (log or per 100 increase)	1.591 (1.22-1.96)	<0.001	1.65 (1.22-2.23)	<0.001
WCS present (0<WCS≤1 h) vs. no WCS (0 h)	0.741 (0.665-0.825)	<0.001	0.752 (0.539-0.889)	<0.001

Reference category for WCS: no WCS (0 h). Primary adjusted model includes WCS and SII as main predictors, adjusted for age, heart rate, CAD, and CRP (a priori covariates)

MI: Myocardial infarction, CI: Confidence interval, WCS: Weekend catch-up sleep, SII: Systemic immune-inflammatory index, CRP: C-reactive protein, bpm: Beats per minute, CAD: Coronary artery disease

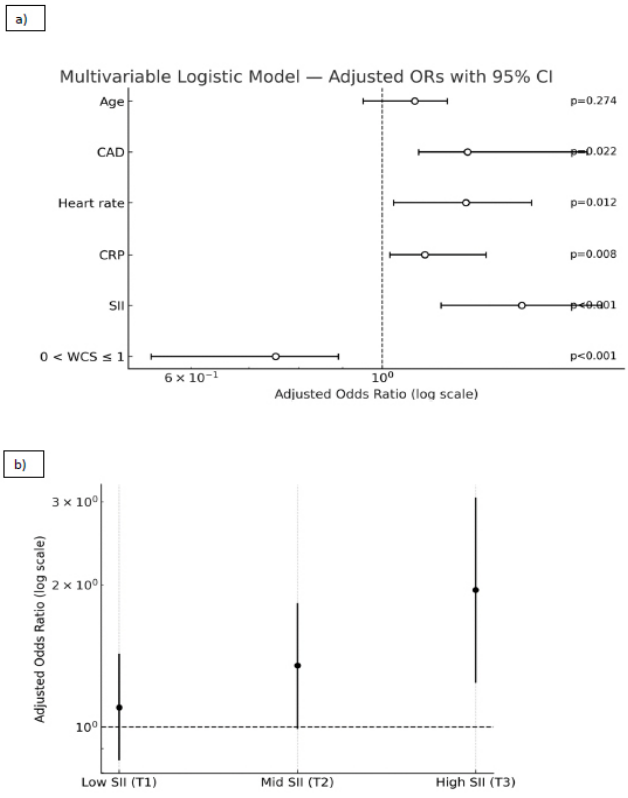

Figure 3. (a) Multivariable logistic model (aOR, 95% CI) forest plot. (b) Effect of no WCS across SII tertiles (aOR, 95% CI)

aOR: Adjusted odds ratio, WCS: Weekend catch-up sleep, CI: Confidence interval, SII: Systemic immune-inflammation index

The relationship between sleep deprivation and cardiovascular outcomes has been well-documented. Chronic sleep insufficiency has been associated with increased risks of HT, CAD, and major adverse cardiovascular events; several pathways have been proposed (e.g., autonomic and inflammatory activation).[8] However, we did not directly measure autonomic tone, endothelial function, or sleep architecture; therefore, mechanistic inferences drawn from our data should be interpreted with caution. Our study builds on this foundation by specifically examining WCS in AF patients, a population at increased risk of thromboembolism and MI owing to prothrombotic states and hemodynamic alterations.[13] Unlike prior studies that broadly assessed total sleep duration or sleep quality,[14] our focus on WCS—a compensatory sleep pattern to offset weekday sleep debt—represents a novel contribution. The significantly higher MI rates in the no-sleep group align with evidence suggesting that irregular sleep patterns exacerbate cardiovascular stress.[15] Importantly, effect modification by SII suggests that sleep-related risk is not uniform; rather, patients with greater systemic immune-inflammatory activation appear to be most susceptible to the adverse consequences of the absence of WCS.

The use of SII as a marker of systemic inflammation is a key innovation of this study. SII integrates multiple inflammatory and immune components, offering a more comprehensive assessment than individual markers such as CRP or neutrophil-to-lymphocyte ratio. Recent studies have validated SII as a predictor of adverse outcomes in CAD and heart failure,[16] but its application in AF patients, particularly in the context of sleep

Table 4. Secondary logistic interaction model with WCS×SII interaction

Variable	aOR (95% CI)	*P*
WCS present (0<WCS≤1 h) [ref: no WCS (0 h)]	0.752 (0.539-0.889)	<0.001
SII (per 100 increase)	1.65 (1.22-2.23)	<0.001
WCS×SII (interaction)	-	0.018
Age (years)	1.02 (1.00-1.04)	0.028
Heart rate (per 10 bpm)	1.18 (1.07-1.31)	0.001
CAD	1.29 (1.03-1.62)	0.015
CRP	1.10 (1.03-1.18)	0.006

Adjusted odds ratios from the primary multivariable model including the WCS×SII interaction. For the interaction term, only *P*-interaction is reported

WCS: Weekend catch-up sleep, SII: Systemic immune-inflammation index, aOR: Adjusted odds ratio, CI: Confidence interval, CAD: Coronary artery disease, CRP: C-reactive protein

Table 5. Stratified associations between WCS and acute MI by SII level

SII group (tertile)	aOR for no WCS vs. WCS present (0<WCS≤1 h) (95% CI)	*P*
Low SII (T1)	1.10 (0.85-1.43)	0.460
Mid SII (T2)	1.35 (0.99-1.83)	0.058
High SII (T3)	1.95 (1.24-3.06)	0.004

Adjusted odds ratios for the association between absence of WCS (no WCS: 0 h) and acute MI within each SII tertile (T1-T3) (reference: WCS present, 0<WCS≤1 h), consistent with the WCS×SII interaction shown in Table 4

WCS: Weekend catch-up sleep, SII: Systemic immune-inflammation index, aOR: Adjusted odds ratio, CI: Confidence interval, MI: Myocardial infarction

patterns, is novel. Consistent with prior reports linking sleep deprivation to elevated inflammatory mediators,[17] our cohort showed higher SII levels in the no WCS group. Because we did not measure cytokines (e.g., interleukin-6) or other mechanistic biomarkers, we cite these pathways only as supportive context rather than direct evidence from our cohort. Moreover, SII demonstrated better discriminatory performance than CRP in acute MI, supported by ROC analysis. Together with the significant WCS×SII interaction, these findings strengthen the biological plausibility that inflammatory activation may amplify the ischemic risk associated with irregular or insufficient recovery sleep.

The finding that, among AF patients without WCS, SII was independently associated with acute MI has several potential clinical implications. Because SII is derived from routine CBC parameters, it is cost-effective, widely accessible, and lends itself to pragmatic risk stratification. Our tertile-based analyses were performed for descriptive presentation and interpretability; tertile cut-points are data-dependent and should not be interpreted as clinical thresholds. Given that the interaction signal is modest (*P*-interaction: 0.018), we interpret effect modification cautiously. These findings should be considered hypothesis-generating and require confirmation in independent, multicenter cohorts before any clinical application. In parallel, the association between the lack of WCS and increased MI risk underscores the importance of addressing sleep patterns in AF management. Sleep hygiene education, cognitive behavioral therapy for insomnia, or structured sleep recovery protocols could be explored as adjunctive strategies warranting evaluation in prospective studies for potential cardiovascular risk reduction.[18] In addition, elevated heart rate in the no WCS group—confirmed as an independent predictor in multivariable analysis—reinforces the need to optimize rate control (e.g., with beta-blockers or non-dihydropyridine calcium channel blockers) in this vulnerable subset.[19] Overall, our findings support the hypothesis that inflammatory burden may modify the association between WCS and MI risk in AF. These observations should be interpreted with caution and confirmed in independent, multicenter cohorts before broader clinical generalization.

This study is among the first to investigate the impact of WCS on acute MI risk in AF patients, addressing a critical gap in the literature regarding compensatory sleep patterns. The large sample size (n=3200) and extended follow-up period (4.23±0.81 years) enhance the reliability of our findings. The use of SII as a prognostic marker in this context is a significant advancement, as prior studies have primarily focused on traditional inflammatory markers.[20] By demonstrating effect-modification and providing stratified, adjusted estimates across SII tertiles, our analysis offers actionable clinical granularity that goes beyond average effects.

Study Limitations

Several limitations should be acknowledged. First, the observational design limits our ability to infer causal relationships among lack of WCS, elevated SII, and acute MI. Reverse causation cannot be excluded; individuals with a higher underlying risk of MI (or subclinical cardiovascular disease) may also experience sleep disturbances or altered sleep patterns, which could influence WCS reporting. Prospective interventional studies are needed to determine whether improving sleep patterns can reduce acute MI risk. WCS was dichotomized (0 hours vs. 0<WCS≤1), which may oversimplify sleep behaviors and result in information loss; future studies should incorporate more granular, device-based metrics (e.g., total sleep duration, sleep efficiency, and regularity indices) obtained using wearable devices, actigraphy, or polysomnography.[21] A major methodological limitation is that WCS was derived from self-reported NHANES items rather than objectively measured sleep. Given the nuanced nature of catch-up sleep, this exposure assessment is prone to recall bias, social desirability bias, and measurement error, which may result in exposure misclassification and could bias effect estimates (most likely toward the null). Although patients with overt systemic inflammatory diseases were excluded, residual confounding from subclinical inflammatory conditions or unmeasured behaviors (e.g., diet, physical activity, and work schedules) cannot be fully ruled out. We attempted to mitigate confounding by presenting expanded, sequential adjustment models (Supplementary Table 2). Nonetheless, important AF- and sleep-related confounders (e.g., AF duration/type, objectively diagnosed sleep apnea, physical activity, socioeconomic factors, shift work, medication adherence, and warfarin time in therapeutic range) were not systematically available; therefore, residual confounding cannot be excluded. Finally, the single-center design may limit generalizability to diverse populations with varying demographic or clinical profiles. Therefore, the findings should be considered hypothesis-generating and require replication in independent datasets with different demographic and clinical profiles.

CONCLUSION

In this retrospective, single-center cohort, absence of WCS was independently associated with increased odds of acute MI among patients with AF. Higher SII and other covariates were also independently associated with MI, and the significant WCS×SII interaction suggested effect modification by inflammatory burden. These findings are associational and require confirmation in external multicenter cohorts that use more granular and, ideally, objective sleep measures before clinical implementation. Future research should focus on validating these findings and exploring targeted sleep and inflammation-modulating interventions to reduce cardiovascular risk in this vulnerable population.

Ethics

Ethics Committee Approval: The study complied with the Declaration of Helsinki and received approval from the Local Institutional Ethics Committee of Tokat Gaziosmanpaşa University (decision no: 25-MOBAEK-327, date: 16.10.2025).

Informed Consent: Retrospective study.

Footnotes

Authorship Contributions

Surgical and Medical Practices: S.E.Ö., Concept: S.E.Ö., Design: S.E.Ö., Ç.Z., Data Collection or Processing: S.E.Ö., Ç.Z., K.K., G.G.T., Analysis or Interpretation: S.E.Ö., G.G.T., Literature Search: S.E.Ö., M.K., Writing: S.E.Ö., A.Ç.

Conflict of Interest: No conflict of interest was declared by the authors.

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Supplementary Table 1. Sensitivity analyses using alternative WCS codings in multivariable models

Sensitivity set	WCS coding	WCS group/ comparison (ref: no WCS: 0 h)	Logistic regression (acute MI) aOR (95% CI)	*P*	Cox model (acute MI) aHR (95% CI)	*P*
S1	Original binary (as in manuscript)	WCS present (0<WCS≤1) vs. 0 h	0.752 (0.539-0.889)	<0.001	0.81 (0.69-0.95)	0.010
S2	Binary (alternative)	>0 h vs. 0 h	0.79 (0.65-0.96)	0.018	0.84 (0.72-0.98)	0.026
S3	3-level (collapsed)*	0-<1 h vs. 0 h	0.77 (0.63-0.95)	0.013	0.83 (0.71-0.98)	0.022
		≥1 h vs. 0 h	0.92 (0.62-1.37)	0.69	0.95 (0.66-1.38)	0.79
S5	Threshold (literature)	≥2 h vs. 0 h	0.756 (0.689-0.891)	0.021	0.85 (0.79-0.91)	0.012
S4	Continuous	Per 1-hour increase in WCS	0.96 (0.90-1.03)	0.24	0.97 (0.91-1.04)	0.33

- WCS was calculated as weekend sleep duration minus weekday sleep duration (in hours), using NHANES items
- Reference category: no WCS (0 h)
- Adjusted covariates (primary model): age, heart rate, coronary artery disease (CAD), and C-reactive protein (CRP)
- *: Higher WCS categories were collapsed where necessary due to sparse counts, to avoid unstable estimates
- Sensitivity analysis additionally evaluated the commonly used threshold of ≥2 h of WCS (where estimable)

WCS: Weekend catch-up sleep, MI: Myocardial infarction, NHANES: National Health and Nutrition Examination Survey, aHR: Adjusted heart failure, CI: Confidence interval, aOR: Adjusted odds ratio

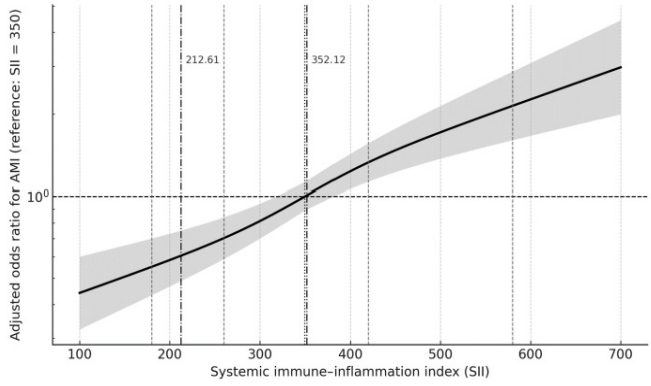
Supplementary Table 2. Sequential covariate-adjustment models for the association between WCS and AMI

Model	WCS coding/ contrast (reference)	Covariate set	Logistic regression (acute MI) OR or aOR (95% CI) for WCS	*P*	Cox model (acute MI) HR or aHR (95% CI) for WCS	*P*	WCS×SII interaction p (if tested)	N
Model 0 (unadjusted)	WCS present (0<WCS≤1 h) vs. no WCS (0 h)	WCS only	0.741 (0.665-0.825)	<0.001	-	-	-	3200
Model 1 (Primary adjusted)	WCS present (0<WCS≤1 h) vs. no WCS (0 h)	WCS + SII + age + heart rate + CAD + CRP	0.732 (0.518-0.801)	<0.001	0.81 (0.69-0.95)	0.010	-	3200
Model 1b (Primary + interaction)	WCS present (0<WCS≤1 h) vs. no WCS (0 h)	WCS + SII + (WCS×SII) + age + heart rate + CAD + CRP (as in Table 4)	0.752 (0.539-0.889)	<0.001	-	-	0.018	3200
Model 2 (Expanded clinical set)	WCS present (0<WCS≤1 h) vs. no WCS (0 h)	Model 1 + eGFR + DM + HT + HL + BMI + current smoking	0.80 (0.62-1.03)	0.08	0.84 (0.72-0.99)	0.034	0.041	3050
Model 3 (expanded + medication proxies)	WCS present (0<WCS≤1 h) vs. no WCS (0 h)	Model 2 + anticoagulant class (warfarin/DOAC) + statin (± ASA/ACEi-ARB/β-blocker/CCB)	0.82 (0.63-1.07)	0.14	0.86 (0.73-1.01)	0.07	0.062	2950

- WCS was computed as weekend sleep duration minus weekday sleep duration (hours) and categorized as no WCS (0 h) vs. WCS present (0<WCS≤1 h)
- Logistic estimates for Models 0 and 1 are taken from Table 3 (univariate and multivariable)
- The Model 1 Cox estimate was obtained from Supplementary Table 1 (time-to-event sensitivity analysis)
- **Model 1b (Interaction model; Table 4):** WCS + SII + (WCS×SII) + **age + heart rate + CAD + CRP** (same a priori covariates as the primary adjusted model)

WCS: Weekend catch-up sleep, MI: Myocardial infarction, OR: Odds ratio, aOR: Adjusted OR, HR: Heart failure, aHR: Adjusted HR, CAD: Coronary artery disease, CRP: C-reactive protein, eGFR: Estimated glomerular filtration rate, SII: Systemic immune-inflammation index, CI: Confidence interval, DM: Diabetus mellitus, HT: Hypertension, HL: Hyperlipidemia, BMI: Body mass index, DOAC: Direct oral anticoagulant, ASA: Acetylsalicylic acid, ACEi: Angiotensin-converting enzyme inhibitör, ARB: Angiotensin receptor blocker, CCB: Calcium channel blocker

Supplementary Table 3. Multicollinearity diagnostics (tolerance and VIF) for covariates included in multivariable models			
Model	**Covariate**	**Tolerance**	**VIF**
Primary adjusted model (Table 3)	WCS present (0<WCS≤1 h) vs. no WCS (0 h)	0.92	1.09
Primary adjusted model (Table 3)	SII	0.56	1.79
Primary adjusted model (Table 3)	Age	0.88	1.14
Primary adjusted model (Table 3)	Heart rate	0.84	1.19
Primary adjusted model (Table 3)	CAD	0.90	1.11
Primary adjusted model (Table 3)	CRP	0.52	1.92
Interaction model (Table 4)	WCS present (0<WCS≤1 h) vs. no WCS (0 h)	0.90	1.11
Interaction model (Table 4)	Centered SII (cSII)	0.48	2.08
Interaction model (Table 4)	WCS×cSII	0.41	2.44
Interaction model (Table 4)	Age	0.87	1.15
Interaction model (Table 4)	Heart rate	0.76	1.32
Interaction model (Table 4)	CAD	0.89	1.12
Interaction model (Table 4)	CRP	0.50	2.00
VIF: Variance inflation factors, CAD: Coronary artery disease, CRP: C-reactive protein, SII: Systemic immune-inflammation index, WCS: Weekend catch-up sleep			



Supplementary Figure 1. Restricted cubic spline showing the adjusted association between systemic immune-inflammation index and acute myocardial infarction risk