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Increase in white blood cell count is associated with the development of atrial fibrillation after an acute coronary syndrome☆

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ABSTRACT

Background: Evidence linking an elevated white blood cell count (WBCC), a marker of inflammation, to the development of atrial fibrillation (AF) after an acute coronary syndrome (ACS) is limited. We examined the association between WBCC at hospital admission, and changes in WBCC during hospitalization, with the development of new-onset AF during hospitalization for an ACS.
Methods: Development of AF was based on typical ECG changes in a systematic review of hospital medical records. Increase in WBCC was calculated as the difference between maximal WBCC during hospitalization and WBCC at hospital admission. Multiple logistic regression analysis was used to adjust for several potentially confounding demographic and clinical variables in examining the association between WBCC, and changes over time therein, with the occurrence of AF.
Results: The median age of study patients ($n = 1325$) was 60 years, 31.8% were women, and 80.1% were non-Hispanic whites. AF developed in 7.3% of patients with an ACS. Patients who developed AF, as compared with those who did not, had a similar WBCC at admission, but a greater increase in WBCC during hospitalization (6.0×10^9 cell/L vs. 2.7×10^9 cell/L, $p < 0.001$). After adjusting for several potentially confounding factors, an increase in WBCC was associated with the development of AF. This association was observed in patients with different ACS subtypes, types of treatment received, and according to time of acute symptom onset.
Conclusion: Increase in the WBCC during hospitalization for an ACS should be further studied as a potentially simple predictor for new-onset AF in these patients.

1. Background

The mechanisms leading to the development of AF after an acute coronary syndrome (ACS) are complex and are typically associated with myocardial ischemia and atrial reperfusion, increased left atrial pressure, autonomic dysregulation, and neurohumoral processes [1, 2]. Elevated serum levels of C-reactive protein (CRP), a marker of generalized inflammation, have been found to be associated with a greater risk of developing AF in general population samples and among patients who underwent coronary artery bypass graft (CABG) surgery [3, 4]. However, data linking an elevated white blood cell count (WBCC), a simple, inexpensive marker of generalized inflammation, with the development of AF after an ACS are sparse [3]. Although findings from the Framingham Heart Study and the Atherosclerosis Risk in Communities Study have shown that a high total WBCC was associated with a greater risk of developing AF in their general population samples [5, 6], most studies that have examined the association between WBCC and AF in patients with coronary artery disease have been limited to patients who have undergone coronary artery bypass graft surgery [7, 8], with the exception of two studies in Austria and Japan [9, 10]. These latter studies, however, were limited by their small sample size and the use of a single measure of WBCC [9, 10].

Using data from a large and socioeconomically diverse cohort of patients hospitalized with an ACS, we examined the association between WBCC at the time of hospital admission, and changes in serum levels

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of WBCC during the acute hospital stay, with the risk of developing AF during the patient's acute hospitalization.

2. Methods

2.1. Study design and population

We used data from The Transitions, Risks, and Action in Coronary Events-Center for Outcomes Research and Education (TRACE-CORE) study in the present investigation. The rationale, study design, patient recruitment practices, and data collection activities of TRACE-CORE have been previously described [11–13]. In brief, TRACE-CORE is a multi-center prospective cohort study which included adult men and women hospitalized with an ACS at three tertiary care and community medical centers in Worcester, MA, two hospitals in Atlanta, GA, and one hospital in Macon, GA, between April 2011 and May 2013. Each validated episode of ACS was categorized as either an ST-segment elevation acute myocardial infarction (STEMI), a non-ST-segment elevation myocardial infarction (NSTEMI), or as unstable angina [14, 15]. Institutional review board approval was obtained from all participating sites and study subjects provided written informed consent.

Trained study staff collected a wide range of information about patient's sociodemographic, lifestyle, and psychosocial characteristics at the time of baseline enrollment (in-person hospital interview) and at 1, 3, 6, and 12 months after discharge (via phone interview). We also collected information about patient's clinical presentation, laboratory test results, and receipt of coronary medications and revascularization procedures during their hospitalization for an ACS based on the abstraction of data from electronic medical records [13].

From the total sample of 1890 patients discharged from participating study hospitals between April 2011 and May 2013 with a confirmed ACS and serial WBCC tests, we excluded 152 patients who had a history of AF. To minimize the impact of concurrent infections on serum WBCC levels, we excluded 146 patients who had an active infection (ICD-9 codes: 001–139) during their hospitalization for an ACS. We also excluded 204 patients who did not provide data on the time of onset of their acute coronary symptoms as well as patients who had data missing on race/ethnicity ($n = 25$), body mass index ($n = 15$), systolic ($n = 8$) and diastolic ($n = 4$) blood pressure, heart rate ($n = 2$), and other laboratory tests ($n = 9$) at the time of hospital admission. The analytic sample for the present study consisted of a total of 1325 participants with a confirmed ACS who were discharged from the 6 hospitals at participating study sites in MA and GA.

2.2. White blood cell count

Blood samples were drawn on admission and during the hospital stay as part of the patient's standard workup, which included a complete blood count, cardiac enzymes, serum electrolytes, and coagulation parameters. The WBCC was estimated following standardized protocols at each participating hospital. Increases in the WBCC were calculated as differences between the WBCC recorded at the time of hospital admission from the highest WBCC measured at any time during the acute hospital stay. The relative increase in WBCC was calculated as 100% × (WBCC maximal − WBCC at admission) / WBCC at the time of hospital admission.

2.3. Atrial fibrillation

The development of AF was based on information available in hospital medical records and review of serial electrocardiographic findings. Patients were classified as having AF if this dysrhythmia was documented in the patient's progress notes, or if typical electrocardiographic changes consistent with a diagnosis of AF occurred during the acute hospital stay [2].

2.4. Other variables

Age was categorized as <55, 55–64, 65–74, and ≥75 years. Race/ethnicity was classified as either non-Hispanic white, non-Hispanic black, or other (including Asian and Hispanic). Hospital use of evidence-based medicines included the receipt of aspirin, P2Y12 inhibitors (clopidogrel, prasugrel, elinogrel, ticagrelor, or cangrelor), angiotensin converting enzyme inhibitors/angiotensin receptor blockers, beta blockers, and statins. Reperfusion treatment was defined as the receipt of either medical treatment or receipt of a percutaneous coronary intervention (PCI) or CABG surgery during the patient's index hospitalization.

2.5. Statistical analysis

The distribution of continuous variables in the study population was examined and non-normally distributed variables were reported with medians and interquartile ranges (IQR). We examined the relation between baseline hospital serum levels of WBCC, and changes during the acute hospitalization therein, in relation to the occurrence of AF using descriptive statistics. We compared the baseline characteristics of patients with an ACS who did and did not develop AF using chi-square tests and Fisher's exact tests for categorical variables and the Wilcoxon rank-sum test for non-normally distributed continuous variables. Consistent with the findings from prior studies [5, 6, 10, 16], we treated WBCC, and changes in WBCC during hospitalization, as continuous variables. Linearity assumptions for these continuous variables were verified using logit Locally Weighted Scatterplot Smoothing (LOWESS) plots.

We used multivariable logistic regression modelling to estimate the association between baseline WBCC, and WBCC changes during hospitalization, with the development of AF. We did not adjust for serum levels of C-Reactive Protein (CRP) and markers of acute myocardial necrosis (CK-MB and troponins) to avoid over-adjustment and because serum levels of CRP were infrequently measured in this patient population. We checked for multicollinearity among dependent variables using a variance inflation factor of 3 or more. Since the WBCC usually does not increase until 24–48 h after acute symptom onset, and the risk of AF may vary by subtype of ACS or type of treatment received, we also carried out several additional multiple regression analyses further stratified according to patient's time of arrival (early: <24 h vs. late: ≥24 h after acute symptom onset), type of ACS (STEMI and NSTEMI vs. unstable angina), and treatment received (CABG surgery vs. non-surgical therapy).

We a priori adjusted our principal study findings for patient's age, sex, race, time of arrival to the hospital, type of ACS, and hospital treatment received. The WBCC at the time of hospital admission was also included in the models for WBCC changes. All other potential confounders (shown in Table 1) were tested in our regression models in an iterative fashion and variables that changed the estimates of the effects of WBCC on AF by >10% were retained in the final models. All analyses were conducted on Stata Release 13 (College Station, TX: StataCorp LP).

3. Results

3.1. Study population

The median age of the 1325 patients with a confirmed ACS was 60.5 years (IQR = 52–69 years), 31.8% were women, 80.1% were non-Hispanic whites, and 12.8% were black. Approximately one half of study patients presented to the hospital within 12 h of acute symptom onset, while 28.2% presented after 48 h. Fifty-eight percent of patients had an NSTEMI while one fifth had unstable angina. Two-thirds of patients received a PCI and 12.2% underwent CABG surgery during their index hospitalization.

In this population, 96 (7.3%) patients developed new onset AF during their acute hospitalization. The frequency of AF did not significantly differ according to patient's hospital arrival time (arrival within first 24 h of acute symptom onset: 6.5% and ≥ 24 h: 8.5%; $p = 0.18$) and type of ACS (unstable angina: 7.2%, STEMI: 9.0%, or NSTEMI: 6.6%; $p = 0.38$), but was more commonly diagnosed in patients who underwent CABG surgery (24.1%) than in patients who received either a PCI (4.2%) or only medical therapy (7.3%) ($p < 0.001$).

3.2. Baseline patient characteristics according to the presence of AF

Patients who developed AF were approximately 7 years older than patients who did not develop this dysrhythmia (Table 1). Patients who developed AF were more likely to have developed important in-hospital complications including acute kidney injury, heart failure/cardiogenic shock, and ventricular tachycardia/fibrillation compared with patients who did not develop AF. A greater percentage of patients who did not develop AF received P2Y12 inhibitors while fewer of them received beta blockers compared with patients who developed AF during their hospitalization for an ACS. Patients who developed AF were significantly more likely to have undergone CABG surgery compared with patients who did not develop AF (Table 1).

3.3. Association between WBCC and occurrence of AF

The median WBCC at the time of hospital admission in patients who developed AF was 8.3×10^9 cells/L (IQR = 6.8–10.3×10^9 cells/L) while it was 9.0×10^9 cells/L (IQR = 7.1–11.5×10^9 cells/L) in patients who did not develop AF ($p = 0.10$). The median WBCC increased by 6.0×10^9 cells/L (IQR = 2.9–10.2×10^9 cells/L) in patients who developed AF, which was more than two-fold greater than in patients who did not develop AF (2.7×10^9 cells/L, IQR = 1.4–4.9×10^9 cells/L) ($p < 0.001$). In relative terms, the WBCC increased by 59.6% (IQR = 23.4–126.4%) during hospitalization, compared with the WBCC at the time of hospital admission, in patients who developed AF; this was two-fold greater than the increase in WBCC of 29.7% (IQR = 17.0–47.8%) which was observed in patients who did not develop AF.

Table 1
Baseline characteristics of patients discharged from the hospital after an acute coronary syndrome according to the presence of new-onset atrial fibrillation (AF).

Characteristics	AF present (n = 96)	AF absent (n = 1229)	p-Value
Age (years)	67 [60–74]	60 [52–68]	<0.001
Age (years)			<0.001
<55	13 (13.5%)	408 (33.2%)	
55–64	25 (26.0%)	400 (32.6%)	
65–74	36 (37.5%)	278 (22.6%)	
≥75	22 (22.9%)	143 (11.6%)	
Female	24 (25.0%)	397 (32.3%)	0.14
Race/ethnicity			0.64
White	81 (84.4%)	988 (80.4%)	
Black	10 (10.4%)	159 (12.9%)	
Other	5 (5.2%)	82 (6.7%)	
Medical history			
Acute coronary syndrome	23 (24.0%)	312 (25.4%)	0.76
Congestive heart failure	10 (10.4%)	134 (10.9%)	0.88
Chronic lung disease	15 (15.6%)	223 (18.1%)	0.54
Chronic kidney disease	11 (11.5%)	122 (9.9%)	0.63
Diabetes	26 (27.1%)	424 (34.5%)	0.14
Hypertension	75 (78.1%)	886 (72.1%)	0.20
Hypercholesterolemia	62 (64.6%)	803 (65.3%)	0.88
Pulmonary embolism	2 (2.1%)	13 (1.1%)	0.30*
Stroke	12 (12.5%)	97 (7.9%)	0.11
Valvular heart disease	5 (5.2%)	26 (2.1%)	0.05
Acute coronary syndrome type			0.38
Unstable angina	19 (19.8%)	246 (20.0%)	
ST-segment elevation myocardial infarction	27 (28.1%)	272 (22.1%)	
Non-ST-segment elevation myocardial infarction	50 (52.1%)	711 (57.9%)	
Hours from acute symptom onset			0.70
<2	17 (17.7%)	248 (20.2%)	
2–5.9	18 (18.8%)	269 (21.9%)	
6–11.9	7 (7.3%)	131 (10.7%)	
12–23.9	12 (12.5%)	127 (10.3%)	
24–47.9	11 (11.5%)	110 (9.0%)	
≥48	31 (32.3%)	344 (28.0%)	
Body mass index (kg/m^2)			0.45
<25	22 (22.9%)	218 (17.7%)	
25–<30	36 (37.5%)	491 (40.0%)	
≥30	38 (39.6%)	520 (42.3%)	
Physiologic findings at admission			
Systolic blood pressure (mm Hg)	136 [119–157]	142 [125–157]	0.19
Diastolic blood pressure (mm Hg)	80 [69–90]	80 [70–92]	0.48
Heart rate (beat/min)	79 [65–99]	76 [66–89]	0.20
Laboratory findings at admission			
Creatinine (mg/dl)	1.0 [0.8–1.3]	1.0 [0.8–1.2]	0.24
Glucose (mg/dl)	123.0 [105.0–156.5]	127.0 [107.0–166.0]	0.32
Potassium (mmol/l)	4.1 [3.7–4.4]	4.1 [3.8–4.4]	0.98
In hospital complications			
Acute kidney injury	11 (11.5%)	56 (4.6%)	<0.001
Heart failure/cardiogenic shock	10 (10.4%)	29 (2.4%)	<0.001
Ventricular tachycardia/fibrillation	14 (14.6%)	66 (5.4%)	<0.001
In hospital evidence-based medication use			
Aspirin	1198 (97.5%)	94 (97.9%)	0.79
P2Y12 inhibitors	1078 (87.7%)	67 (69.8%)	<0.001
ACE-I/ARBs	759 (61.8%)	53 (55.2%)	0.21
Beta-blockers	1121 (91.2%)	94 (97.9%)	0.022
Statins	1099 (89.4%)	89 (92.7%)	0.31
Reperfusion treatment received			<0.001
Medical treatment	20 (20.8%)	254 (20.7%)	
Percutaneous coronary intervention	37 (38.5%)	852 (69.3%)	
Coronary artery bypass graft surgery	39 (40.6%)	123 (10.0%)	

p-Value from Chi-square test and Fisher's exact test (*) for categorical variables and Wilcoxon rank-sum test for continuous variables. P2Y12 inhibitors include any of clopidogrel, prasugrel, elinogrel, ticagrelor, or cangrelor. Note: continuous variables are reported as median [interquartile range].

We failed to find an association between the occurrence of AF during the acute hospitalization and the WBCC at the time of hospital admission, either in the entire study population or in subgroups of patients further stratified according to duration of pre-hospital delay, ACS type, or type of hospital treatment received (Table 2).

On the other hand, the incidence rates of AF were higher in patients who had greater relative increases in their WBCC (Fig. 1). The odds ratio for developing AF was significantly >1.0 for each WBCC increase of 10^9 cells/L (multivariable adjusted odds ratio (aOR) = 1.14, 95% Confidence Interval (CI) = 1.07–1.21). This association was observed in patients who underwent CABG surgery, a PCI, or who were treated with medical therapy, in patients who arrived at the hospital within the first 24 h or thereafter following the onset of acute symptoms, as well as in patients with a STEMI or NSTEMI (Table 2).

4. Discussion

Excessive sympathetic stimulation, atrial ischemia, atrial stretch due to ventricular volume or pressure overload, electrolyte abnormalities, hypoxia, and concomitant lung disease have each been hypothesized as some of the underlying mechanisms contributing to the high incidence of AF observed in the context of acute coronary disease [15, 17]. Our study found that increases in the WBCC during hospitalization for an ACS were associated with greater odds for developing AF, supporting the hypothesis that a systemic inflammatory response may contribute to the development of AF in the setting of an ACS. Since AF after an ACS has adverse effects on both in-hospital and long-term outcomes [18–21], the association between the rise in WBCC and the onset of AF seen in the present study may partially explain the worse outcomes typically observed among patients with an elevated WBCC in the setting of an acute coronary event.

4.1. Association between WBCC and occurrence of AF

We found that a high WBCC at the time of hospital admission for an ACS was not associated with the development of new-onset AF. Although inconsistent with the results of previous community-based studies of general, apparently healthy, population samples [5, 6], prior studies of patients with an ACS have failed to demonstrate an association between baseline levels of WBCC and the development of AF [9, 10, 22]. In a study of 621 patients who underwent a PCI for an STEMI who were admitted to the hospital within 12 h of acute symptom onset, WBCC levels at the time of hospital admission were not associated with the subsequent development of AF during hospitalization [22]. A study of 259 Japanese patients admitted within the first 12 h of an acute myocardial infarction (AMI) also failed to find an association between WBCC at the time of hospital admission and the in-hospital development of AF [10].

On the other hand, we found that the odds of developing new onset AF were approximately 14% higher for every 10^9 cells/L increase in the WBCC during the patient's acute hospital stay. In the aforementioned Japanese study, although an increase in WBCC was not calculated, the peak WBCC at 5–7 days after admission was associated with a higher risk of AF, despite similar serum levels of WBCC at the time of hospital admission for patients who did and did not subsequently develop AF [10].

4.2. Potential mechanisms underlying the association between WBCC and AF

Atrial leukocyte infiltration and other markers of local inflammation are common histologic findings among patients with AF [23], and an elevated WBCC has been associated with a greater risk of developing AF in general community samples [5, 6, 16]. For example, among the 1401 participants in the original cohort of the Framingham Heart Study, a higher WBCC at the time of their baseline clinic examination was associated with a 2-fold greater risk of developing AF after 5 years [5]. In the Atherosclerosis Risk in Communities Study, among 14,500 adults free from AF, a higher WBCC at the time of baseline study enrollment was

Table 2
Odds ratio (95% confidence interval) for developing atrial fibrillation for every 1×10^9 cell/L of white blood cell count (WBCC) at admission or its increase among patients discharged from the hospital after an acute coronary syndrome.

Population	WBCC at admission				Increase in WBCC			
	Unadjusted		Multivariable adjusted		Unadjusted		Multivariable adjusted	
	OR	95% CI	OR	95% CI	OR	95% CI	OR	95% CI
All patients	0.96	0.90–1.02	0.97[a]	0.91–1.03	1.17	1.12–1.22	**1.14**[a]	**1.07–1.21**
Arrival time								
<24 h	0.95	0.88–1.04	0.96[b]	0.89–1.04	1.15	1.09–1.22	**1.17**[b]	**1.08–1.26**
≥24 h	0.97	0.88–1.07	0.97[b]	0.86–1.08	1.18	1.12–1.26	1.08[b]	0.84–1.06
ACS subtype								
AMI	0.95	0.89–1.02	0.97[c]	0.91–1.04	1.16	1.11–1.22	**1.13**[c]	**1.06–1.21**
Unstable angina	0.98	0.81–1.18	0.94[c]	0.76–1.16	1.20	1.11–1.30	**1.11**[c]	**1.00–1.30**
Reperfusion therapy								
Medical	0.98	0.86–1.10	0.98[d]	0.87–1.10	1.12	1.02–1.23	**1.13**[d]	**1.02–1.26**
PCI	0.93	0.83–1.03	0.90[d]	0.80–1.01	1.15	1.06–1.26	**1.12**[d]	**1.02–1.24**
CABG surgery	1.04	0.94–1.16	1.07[d]	0.95–1.20	1.05	0.98–1.13	**1.08**[d]	**1.00–1.18**

WBCC: white blood cell count (10^9 cell/L), OR: odds ratio, CI: confidence interval, ACS: acute coronary syndrome, AMI: acute myocardial infarction.
Note: white blood cell count at admission was additionally included in the models for increase in white blood cell counts.
Estimates are statistically significant if the 95% CIs do not contain 1 are shown in bold.
[a] Adjusted for age, sex, race, time of arrival, ACS subtype, and treatment received.
[b] Adjusted for age, sex, race, ACS subtype, and treatment received.
[c] Adjusted for age, sex, race, time of arrival, and treatment received.
[d] Adjusted for age, sex, race, time of arrival, and ACS subtype.

associated with a 9% greater risk of developing AF after 25 years of follow-up [6].

In general healthy populations, a high serum WBCC likely represents a long-standing underlying inflammatory process which is associated with the development of AF over the long-term. In the setting of an ACS, the development of AF may be strongly influenced by the acute inflammatory response to acute myocardial ischemia whereas the chronic inflammatory process may play a less important role. Since the WBCC only increases after the first 24–48 h of hospitalization for an ACS, and peaks at 2–4 days after symptom onset [10], it is possible that the WBCC at the time of hospital presentation has not yet increased in response to the development of acute myocardial ischemia. Inasmuch, a single measurement of the WBCC at the time of hospital admission for an ACS may not be associated with those mechanisms that give rise to the acute onset of AF during hospitalization as examined in the present study. This possible explanation is also supported by the similar WBCC findings observed at the time of hospital admission in patients who did and did not develop AF in the present study.

The association between new-onset AF and increases in WBCC that we observed is likely explained by the close relationship between systemic inflammation and AF. Unlike the WBCC at hospital admission, a rise in WBCC during hospitalization for an ACS likely reflects ongoing systemic inflammation after the acute coronary event. However, the role of the WBCC in the development of AF is not completely known. Prior studies have shown that WBCs release myeloperoxidase (MPO) which promotes atrial fibrosis and creates a substrate for the development of AF [24]. Another study has suggested that the frequency and duration of AF depends on the ability of the WBC to infiltrate cardiac tissue, which suggests a direct role for the WBC in the development of AF [25]. Nonetheless, atrial fibrosis is usually a latent and chronic process. Thus, its direct contribution to observed increases in WBCC and the onset of AF in the setting of an ACS is uncertain. Other mechanisms, such as acute oxidative injury due to the activation of WBCs after myocardial damage, may contribute to heterogeneity of electrical conduction in the myocardium and the occurrence of AF [26, 27]. However, evidence about these and other putative mechanisms is lacking in the

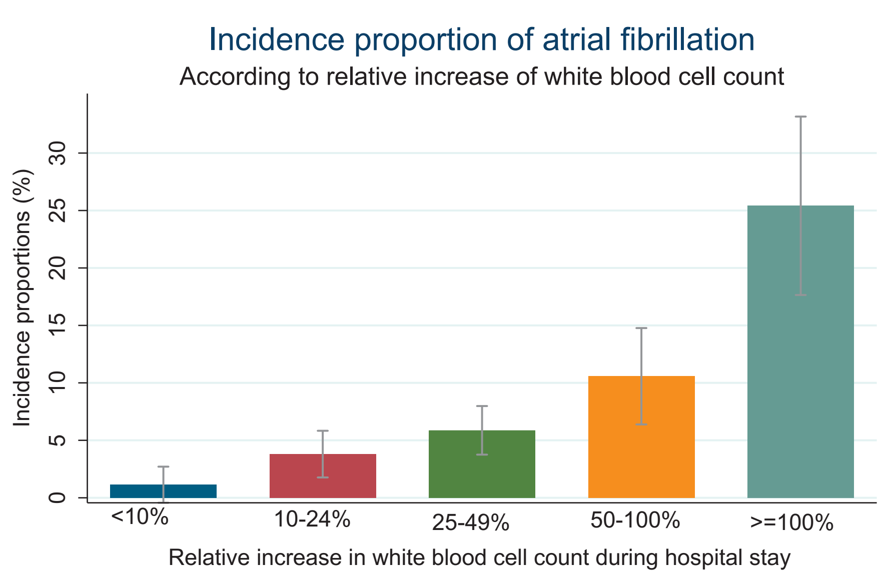

Fig. 1. Incidence proportions (95% confidence interval) of patients who developed atrial fibrillation according to the relative increase in white blood cell count (100% × (maximal counts − counts at admission) / counts at admission) in patients discharged from the hospital after an acute coronary syndrome.

setting of acute ischemic damage and further studies remain needed to better understand the link between increases in WBCC and the onset of AF.

4.3. Association between WBCC and AF in selected subgroups of patients with ACS

A systemic inflammatory response to undergoing cardiac surgery is common, and histologic studies have found an increase in the aggregability of WBCC following cardiac surgery [28–30]. Epidemiologic studies have found an association between elevated WBCC and the risk of developing AF among patients who underwent elective CABG surgery [3, 4]. In the present study, AF occurred in approximately one quarter of patients who underwent CABG surgery, a rate significantly higher than was observed in patients who underwent a PCI or who received only medical therapy. However, the association between a rise in serum WBCC levels and an increased risk of developing AF was also observed in a separate analysis restricted to patients who received medical treatment or a PCI only in the present study. Thus, the association observed between increases in WBCC and the development of AF may be due to the systemic inflammatory reaction to the acute coronary event rather to an acute inflammatory reaction that is associated with undergoing cardiac surgery. We also found a relatively similar association between increases in WBCC and the risk of developing AF in patients with unstable angina as well as in those who were diagnosed with either a STEMI or NSTEMI.

4.4. Study implications

While CRP and other non-specific biomarkers of inflammation, such as interleukin (IL)-6, IL-8, are more expensive to analyze and are not regularly assessed among patients hospitalized with an ACS, the WBCC is routinely repeated in patients with an ACS; this is especially the case among those who have undergone an invasive procedure for purposes of monitoring the potential risk of bleeding complications and infections. Indeed, our findings suggest that a rise in WBCC can be a readily available and cost-effective tool associated with the onset of AF. Since most patients who develop AF after an ACS are asymptomatic [31], the development of AF after hospital discharge for an ACS may go undiagnosed in some patients where continuous home monitoring is not available. Therefore, awareness of increases in the WBCC during hospitalization for an ACS may alert providers to more closely monitor these patients for the future development of AF.

4.5. Study strengths and limitations

The strengths of our study include the use of a large and socioeconomically diverse study population, including both patients who did and did not undergo CABG surgery for their ACS. On the other hand, we did not collect information on duration and type of AF and WBCC differentials (e.g., neutrophils, lymphocytes). Importantly, we did not collect data on the timing of the rise in WBCC relative to the time of onset of AF. The observational nature of this longitudinal study could not rule out the influence of additional potentially confounding or contributory factors that were not assessed or were able to be adequately measured. Thus, the potential predictive value of short-term increases in the WBCC in relation to the onset and duration of AF needs to be elucidated in future studies.

5. Conclusions

We found an association between an increase in the WBCC, but not the WBCC at the time of hospital admission, and the risk of developing AF in patients discharged from the hospital after an ACS. Our data suggest that future longitudinal studies should evaluate whether an increase in the WBCC during hospitalization for an ACS may be used as a simple, readily-available, and cost-effective tool to predict the occurrence of AF after an acute coronary event. Further studies remain needed to examine the association between WBCC, including patterns of WBCC progression, and different forms of AF, as well as the involvement of atrial fibrosis in the development of AF in the setting of an ACS.

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