Time Course of Inflammation, Myocardial Injury, and Prothrombotic Response After Radiofrequency Catheter Ablation for Atrial Fibrillation

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Background—Inflammation has been linked to the genesis of stroke in atrial fibrillation (AF) and is implicated in early recurrent arrhythmia after AF ablation. We aimed to define the time course of inflammation, myocardial injury, and prothrombotic markers after radiofrequency ablation for AF and its relation to AF recurrence.

Methods and Results—Ninety consecutive AF patients (53% paroxysmal) undergoing radiofrequency ablation were recruited. High-sensitivity C-reactive protein (hs-CRP), Troponin-T, creatine kinase-MB, fibrinogen, and D-Dimer concentrations were measured at baseline, at 1, 2, 3, 7 days, and at 1 month after ablation. AF recurrence was documented at 3 days and at 1, 3, and 6 months follow-up. Troponin-T and creatine kinase-MB peaked at day 1 after procedure (both P<0.05). Hs-CRP peaked at day 3 after procedure (P<0.05). Fibrinogen (P<0.05) and D-Dimer (P<0.05) concentrations were significantly elevated at 1 week after procedure. Ln hs-CRP elevation correlated with Ln Troponin-T and fibrinogen elevation. The extent of Ln hs-CRP, Ln Troponin-T, and fibrinogen elevation predicted early AF recurrence within 3 days after procedure (P<0.05, respectively), but not at 3 and 6 months.

Conclusions—Patients undergoing radiofrequency ablation for AF exhibit an inflammatory response within 3 days. The extent of inflammatory response predicts early AF recurrence but not late recurrence. Prothrombotic markers are elevated at 1 week after ablation and may contribute to increased risk of early thrombotic events after AF ablation. (Circ Arrhythm Electrophysiol. 2014;7:83-89.)

Key Words: atrial fibrillation ▪ catheter ablation ▪ inflammation ▪ thrombosis

Inflammation is increasingly recognized to play a significant role in the genesis and perpetuation of atrial fibrillation (AF).1,2 Markers of inflammation such as C-reactive protein (CRP) are found to be predictive of increased risk for future development of AF.2 Inflammation as a cause of AF has also been suggested on the grounds of the time course of postoperative AF after cardiac surgery, when the inflammatory cascade is most activated.1 Furthermore, patients with AF undergoing catheter ablation are at increased risk of thromboembolic events, particularly in the first 2 weeks after the procedure, although the exact mechanisms are not known.3

Radiofrequency (RF) ablation for atrial arrhythmias is known to cause an increase in various markers of inflammation and myocardial injury.4,5 Moreover, biomarker detection of myocardial injury is a key component in the third universal definition of myocardial infarction, and ablation is known to be a confounder.6 A protracted elevation of CRP is seen after AF ablation and, after successful ablation of long-lasting persistent AF, a decline in CRP at 3 months is observed.7,8 Studies linking inflammation levels at baseline and after ablation with early and late AF recurrences after ablation have yielded varying results.9-11

To date, the specific time course of inflammation, myocardial injury, and prothrombotic markers after RF ablation for AF has not been well defined. We aimed to investigate the inflammatory response after ablation and its relation to AF recurrence and to examine the relationship between inflammation and prothrombotic risk after ablation.

Methods

Patient Selection
Ninety consecutive patients undergoing elective RF catheter ablation for AF were prospectively studied. All patients >18 years old, with a...
history of AF, were included. Exclusion criteria were the following: previous myocardial infarction (≤3 months), unstable angina, surgery or ablation procedure within the preceding 3 months, congenital heart disease, history of connective tissue disease or chronic inflammatory condition, acute or chronic infection, chronic renal or liver failure. Type of AF was defined according to the Heart Rhythm Society (HRS) expert consensus statement.12 All patients provided written informed consent to the study protocol, which was approved by the Clinical Research Ethics Committee of the Royal Adelaide Hospital, Adelaide, Australia.

Patient Preparation
All patients underwent anticoagulation with warfarin to maintain their international normalized ratio (INR) between 2 to 3 for ≥26 weeks before the procedure. Warfarin was stopped 7 days before the procedure and substituted with enoxaparin at a dose of 1 mg/kg twice a day until ≥12 hours before the procedure. Transesophageal echocardiography was performed to exclude left atrial thrombus. Transthoracic echocardiography was performed at baseline and at postprocedure. All anti-arrhythmic agents, with the exception of amiodarone, were ceased 5 half-lives before the procedure. Details of the ablation procedure are in the Data Supplement.

Blood Collection
Blood samples were taken peripherally for total white cell count (WCC), neutrophil count, high-sensitivity CRP (hs-CRP), Troponin-T, creatine kinase (CK), creatine kinase-MB (CKMB), fibrinogen, and D-Dimer measurements at the start of the procedure, and at 1, 2, and 3 days, at 1 week, and at 1 month after procedure. Samples were analyzed immediately.

Markers of Inflammation, Myocardial Injury, and Thrombosis
Hs-CRP was analyzed with an immunoturbidimetric latex CRP assay (Olympus Diagnostics, Melville, NY). Total WCC and neutrophil count was analyzed using the Sysmex XE2100 (Sysmex, Kobe, Japan). Cardiac troponin-T was analyzed with the Elecsys Troponin-T immunoassay (Roche Diagnostics, Indianapolis, IN). CK was analyzed using a kinetic UV serum test (Olympus, Ireland). CKMB was analyzed with the Elecsys CKMB immunoassay (Roche Diagnostics, Indianapolis, IN). Fibrinogen and D-Dimer were analyzed using the STAR coagulation analyzer (Diagnostica Stago, Parsippany, NJ). Normal reference ranges were the following: WCC, 4.0 to 11.0 (×10³/L); neutrophils, 1.8 to 7.5 (×10³/L); hs-CRP, lower limit of detection (LLD) 0.08 mg/L; Troponin-T, 0 to 0.1 µg/L (LLD 0.01 µg/L); CK, <150 U/L (LLD 3 U/L); CKMB, <7.0 µg/L (LLD 0.1 µg/L); Fibrinogen, 1.5 to 4.0 g/L; and D-Dimer, <0.5 fibrinogen equivalent units. The extent of biomarker elevation was defined as the maximum recorded value (from day 1 to day 30) minus the baseline value (day 0).

Patient Follow-Up
Continuous monitoring was performed for 3 days after the procedure. Body temperature was measured at baseline before the procedure and 6 hourly during the first 3 days after procedure. Outpatient follow-ups were scheduled at 7 days and at 1, 3, and 6 months after procedure. At all visits ≥1 month after ablation, a clinical review, an ECG, and a 7-day Holter monitoring were undertaken to determine the presence of recurrent arrhythmias. Recurrent arrhythmia was defined as per the HRS expert consensus as any atrial arrhythmia ≥30 seconds. For the purposes of this study, early recurrences were defined as any atrial arrhythmia ≥30 seconds within the first 3 days after procedure while continuous monitoring was undertaken.

Warfarin was continued for a minimum of 3 months. In patients with a CHADS² score ≥1, anticoagulants were ceased at this point in the absence of recurrent arrhythmia. In all other patients, anticoagulation was continued for 12 months, at which point its cessation was discussed on an individual basis.

Statistical Analysis
Continuous variables were expressed as means±SD, and categorical data were expressed as counts and percentages. Data were tested for normality and log transformed as appropriate. Continuous variables between 2 groups were compared using Student t tests. Categorical variables were compared using Fisher exact or Pearson χ² tests as appropriate. Correlations between the extents of elevation of the biomarkers were analyzed using Spearman correlation coefficient. Linear mixed effects models were created to examine the temporal changes in biochemical markers after AF ablation; in which, time was included as a fixed effect and where a compound symmetry correlation structure allowed for correlation within patients because of repeated measurements. If the time main effect was significant, post hoc testing was used to reveal where the significant differences lied.

Univariate and multivariate linear regression analyses were used to determine the predictors for the extent of elevation of each biomarker. All univariate predictors with P<0.10 were then added to a multivariate model. For outcomes that were log transformed, coefficient estimates and confidence intervals were presented in the exponentiated form to describe the effect of a 1-unit increase in the predictor on the geometric mean of the outcome. To predict AF recurrence at 3 days and at 1, 3, and 6 months from the extent of each biochemical marker elevation, univariate logistic regression models were developed. Multivariate logistic regression models were developed to identify predictors of early AF recurrence and AF recurrence at 6 months. P values <0.05 were considered statistically significant. Statistical analyses were performed using PASW Statistics 18 (version 18.0.0).

Results
Patient and Procedural Characteristics
Patient demographics and procedural characteristics are shown in the Table. These patients had paroxysmal (44%), persistent (43%), and long-standing persistent AF (12%). Mean CHADS² score was 0.9±0.9. The RF ablation times for pulmonary vein isolation, complex fractionated atrial electrogram ablation, and linear ablation were 65.8±34.8, 32.3±21.6, and 20.6±16.0 minutes, respectively. Total procedural time was 210.3±55.7 minutes.

Time Course of Inflammation, Myocardial Injury, and Prothrombotic Markers
All measured markers increased significantly with time after RF ablation for AF (P<0.001 for all markers). Hs-CRP peaked at days 2 to 3 and was significantly elevated at 1 day to 1 week after RF ablation (Figure 1A). Total WCC and neutrophil count were significantly elevated days 1 to 3 after procedure (Figure 1B and 1C).

Troponin-T peaked at day 1 after procedure and was significantly elevated up to day 3 after procedure (Figure 2A). CKMB peaked similarly at day 1 after procedure (Figure 2B). CK levels were significantly elevated days 1 to 3 after procedure (Figure 2C).

Prothrombotic markers seemed to peak slightly later at ≥3 days and at 1 week after procedure. Fibrinogen levels were significantly elevated at days 2 to 3 and at 1 week after procedure (Figure 3A). D-Dimer levels were significantly elevated and peaked at 1 week after procedure (Figure 3B).

Correlation Between Inflammation, Myocardial Injury, and Prothrombotic Markers
The extent of Ln hs-CRP elevation correlated with the extent of Ln Troponin-T elevation (r=0.35, P<0.02), Ln CKMB elevation (r=0.51, P<0.01), and fibrinogen elevation (r=0.59, P<0.01).
There was a significant correlation seen between the extent of WCC elevation and neutrophil elevation ($r_s=0.93$, $P<0.01$), whereas there was no significant correlation between these 2 markers and Ln hs-CRP. The extent of Ln CKMB elevation correlated with the extent of Ln CK elevation ($r_s=0.55$, $P<0.01$).

### Predictors of Elevation for Inflammation, Myocardial Injury, and Prothrombotic Markers

Univariate and multivariate linear regression analyses were used to determine the predictors of the extent of elevation in each biomarker. Variables used were age, male sex, BMI (body mass index), hypertension, diabetes mellitus, congestive heart failure, history of stroke/transient ischemic attack, left atrial diameter, statin therapy, type of AF, baseline hs-CRP, ablation approach, RF ablation time, total procedural time, fluoroscopy time, and dose. Univariate predictors of the extent of elevation of each specific biomarker with $P$ values <0.10 were the following. hs-CRP elevation (mg/L): total procedural time (5 minute units; coefficient=1.03, 95% confidence interval [CI]; $1.01–1.06$; $P<0.01$); Troponin-T elevation ($\mu$g/L): RF ablation time (5 minute units; coefficient=1.06, 95% CI $[1.03–1.08]$, $P<0.01$), total procedural time (5 minute units; coefficient=1.02, 95% CI $[1.00–1.04]$; $P=0.02$), nonparoxysmal AF (coefficient=1.53, 95% CI $[1.02–2.28]$; $P=0.04$); CK elevation (U/L): RF ablation time (5 minute units; coefficient=1.05, 95% CI $[1.00–1.11]$; $P=0.06$); and CKMB elevation ($\mu$g/L): RF ablation time (5 minute units; coefficient=1.05, 95% CI $[1.00–1.11]$, $P=0.06$) and CKMB elevation (U/L): RF ablation time (5 minute units; coefficient=1.05, 95% CI $[1.00–1.10]$, $P=0.06$).

There was a significantly higher Troponin-T elevation in patients with persistent AF compared with paroxysmal AF (Ln Troponin-T $0.49±0.55$ versus $0.06±0.76$; $P=0.038$). Multivariate analysis revealed RF ablation time as the only significant multivariate predictor for Troponin-T elevation ($\mu$g/L); RF ablation time, 5 minute units, coefficient=1.04, 95% CI $[1.01–1.08]$; $P<0.05$). There was no significant difference in baseline Ln hs-CRP between patients with paroxysmal and persistent AF in this cohort ($P=0.4$), and baseline Ln hs-CRP level was not a predictor of the extent of Ln hs-CRP elevation ($P=0.2$) or Ln Troponin-T elevation ($P=0.7$) after ablation.

### Follow-Up and AF Recurrence

A total of 19 patients (21.1%) had early atrial arrhythmia within 3 days; 22 patients had AF recurrence between 4 and 30 days; 9 patients had AF between 30 and 90 days; 40 patients sustained no AF; and 14 patients had multiple AF recurrences during this period.
Patients with early AF recurrence after procedure had a significantly higher elevation in hs-CRP, Troponin-T, CKMB, fibrinogen levels, and maximum body temperature compared with patients without early AF recurrence (Figure 4A–F). Patients with AF recurrence at 1 month also had a higher level of fibrinogen elevation (Figure 4E). The extent of Ln hs-CRP elevation (OR, 2.8; CI [1.3–6.0]; P<0.01) and Ln Troponin-T elevation (OR, 3.2; CI [1.1–9.7]; P<0.05) significantly predicted AF recurrence at 3 days, but not at 1, 3 and 6 months after procedure. The extent of fibrinogen elevation significantly predicted AF recurrences within 3 days after ablation was significantly associated with early AF recurrence (OR, 11.1; CI [1.2–102.4]; P=0.03).

At 6 months with a 3-month blanking period, 35 patients (39.8%) had AF recurrence. Of these 35 patients, 30 patients also sustained recurrence during the 3-month blanking period. There was a nonsignificant trend toward higher 6-month AF recurrence in patients with persistent AF compared with paroxysmal AF (46% versus 30%; P=0.1). Of interest, only about half the patients who sustained initial AF recurrence within the first 3 days after ablation was significantly associated with early AF recurrence (OR, 11.1; CI [1.2–102.4]; P=0.03).

Patients undergoing RF catheter ablation for AF exhibited an inflammatory response and myocardial injury within the first 3 days after ablation. The major findings were the following:

1. Patients undergoing RF catheter ablation for AF exhibited an inflammatory response and myocardial injury within the first 3 days after ablation.
2. The extent of inflammatory response predicts early recurrence of AF.

**Discussion**

**Main Findings**

This study presents new information on the specific time course of inflammation, myocardial injury, and prothrombotic response after ablation for AF. The major findings were the following:

1. Patients undergoing RF catheter ablation for AF exhibited an inflammatory response and myocardial injury within the first 3 days after ablation.
2. The extent of inflammatory response predicts early recurrence of AF.
3. Prothrombotic markers are elevated at 1 week after AF ablation and correlate with the inflammatory response. This may explain the increased risk of early thromboembolic events after ablation.

**Inflammation and Myocardial Injury**

Results of the current study demonstrate a consistent inflammatory response after RF ablation for AF within the first 3 days after ablation. In the current study, markers of myocardial injury were elevated early (1 day) after RF ablation. The pattern of elevation for these markers was consistently earlier compared with the inflammatory markers (peak 3 days). Other studies on mixed cohorts of patients undergoing RF ablation have found a peak in markers of myocardial injury within the first few hours after ablation. The findings of RF ablation time being an independent predictor of Troponin-T elevation, consistent with previous studies, and higher extent of Troponin-T elevation in patients with persistent AF suggest that markers for myocardial injury relate to the extent of ablation, with more extensive ablation performed in patients with persistent forms of AF.

Our study demonstrated a correlation between markers of myocardial injury and hs-CRP elevation after ablation. This is in accordance with the cardiac surgical setting, where a significant correlation was shown between postoperative troponin-I levels and clinical inflammation–associated parameters. With the positive correlation between hs-CRP elevation and markers of myocardial injury, this inflammatory response could partly be explained by local myocardial injury. However, the elevation in peripheral WCC, neutrophil count, hs-CRP, prothrombotic markers, and body temperature suggest a systemic inflammatory process in addition to local inflammation after RF ablation.

**Inflammation and Thrombotic Risk**

Inflammation and thrombogenesis in AF are increasingly identified as being intimately linked. CRP levels are positively correlated with clinical risk factors of stroke. We have previously reported increased thrombogenesis and inflammatory mediators within the human atrium with the onset of AF. Furthermore, D-dimer levels have been shown to predict thromboembolic events even in patients with anticoagulated AF.

Results of the current study document an elevation in the prothrombotic markers fibrinogen (Figure 3A) and D-dimer (Figure 3B). Fibrinogen elevation positively correlated with

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**Figure 3.** Time course of prothrombotic markers after RF ablation for AF. A, Fibrinogen. *P*<0.05 (compared with baseline); *P*<0.001 (change with time). B, D-dimer. *P*<0.05 (compared with baseline); *P*<0.001 (change with time).

**Figure 4.** Extent of elevation in biomarkers and early AF recurrence. A, Hs-CRP. *P*<0.01 AF recurrence vs no recurrence. B, Troponin-T. *P*<0.05 AF recurrence vs no recurrence. C, CKMB. *P*<0.01 AF recurrence vs no recurrence. D, Fibrinogen and early AF recurrence within 3 days. *P*<0.01 AF recurrence vs no recurrence. E, Fibrinogen and AF recurrence at 1 month. *P*<0.01 AF recurrence vs no recurrence. F, Body temperature and AF recurrence within 3 days. *P*<0.01 AF recurrence vs no recurrence.
remains debatable. In a study by Richter et al,6 AF recurrences for immediate AF recurrence. Acute inflammatory changes after ablation may be responsible for delayed prothrombotic timeframe coincides with the finding that the majority of thromboembolic complications after AF ablation occur within the first 2 weeks after procedure.3 These findings suggest that inflammation could be an important contributing factor to the increased prothrombotic state in AF early after ablation.

**Inflammation and AF Recurrence**

Previous studies have shown that baseline preprocedural hs-CRP levels were independently predictive of AF recurrence after RF ablation for AF.11 In this study, we did not find a significant relationship between the baseline inflammatory state and the extent of elevation in the markers of inflammation and myocardial injury, and AF recurrence at 6 months. However, our study found that the degree of inflammatory response after ablation (extent of hs-CRP elevation) was significantly associated with early AF recurrence within 3 days after procedure. This finding is consistent with Koyama et al6 who found that acute inflammatory changes after ablation may be responsible for immediate AF recurrence.

The impact of early AF recurrence on long-term outcome remains debatable. In a study by Richter et al.6 AF recurrence within 48 hours of ablation was a predictor of poorer clinical outcome on follow-up. However, in another study, the patient cohort that experienced immediate AF recurrence within 3 days subsequently had a higher AF-free rate at 6 months compared with those with later recurrences between 4 and 30 days.6 In our study, we found that about half of the patients with initial early AF recurrence continued to have AF recurrence at 6 months, whereas all patients with recurrence in the 30-day to 3-month period continued to have recurrence at 6 months. Our results suggest that in about half of the early AF recurrences, the effect is transient and may not have a negative impact on long-term outcome, whereas recurrences between 30 days and 3 months may be because of a different pathophysiology, such as pulmonary vein reconnection, and confers poorer long-term outcome.9

Several studies have found that ameliorating the postablation inflammatory response by steroids and anti-inflammatories reduces the incidence of early arrhythmic recurrences.12,22 Colchicine administered for 3 months was found to decrease early AF recurrences after AF ablation.22 Transient administration of steroids for 3 days after ablation reduced not only immediate AF recurrence but also AF recurrence at midterm follow-up.22 However, in an experimental porcine study, the use of prophylactic steroids in pigs that underwent atrial ablation was not shown to alter the systemic inflammatory response or the healing of the lesions.23

**Clinical Implications**

This study demonstrated a consistent increased inflammatory response exhibited within 3 days after RF ablation for AF. The extent of inflammatory response was associated with early AF recurrence. There is emerging evidence that early AF recurrence has a different underlying mechanism but may still influence long-term recurrence. Understanding the time course of inflammation could help direct the timing and regimen of future potential interventions aimed at ameliorating the inflammatory response after AF ablation.21,22

In our study, increased prothrombotic tendency was documented at 1 week after AF ablation. This may explain the increased thromboembolic rates within the first 2 weeks after catheter ablation for AF.2 Strategic antithrombotic measures targeting this specific time frame may further decrease postprocedural thromboembolic events.

**Study Limitations**

First, the lack of further significant predictors for the elevation in the various inflammatory, myocardial injury, and prothrombotic markers in our study could be because of limited numbers in the study. Alternatively, this could be because of the mechanism of the documented inflammatory response being multifactorial. Second, the earliest blood sample measurement made after ablation was at postprocedural day 1, which may have missed the exact peak for myocardial injury.

**Conclusions**

Patients undergoing catheter ablation for AF exhibit an inflammatory response and myocardial injury within the first few days after ablation. The extent of inflammatory response predicts early AF recurrence but not late recurrence. Prothrombotic markers are elevated 1 week after catheter ablation, associated with inflammation and may contribute to the increased risk of early thrombotic events after AF ablation.

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References

CLINICAL PERSPECTIVE
Inflammation has been linked to the genesis of stroke in atrial fibrillation (AF) and is implicated in early recurrent arrhythmia after AF ablation. This study examined the specific time course of inflammation, myocardial injury, and prothrombotic markers after radiofrequency ablation for AF. A consistent increased inflammatory response was demonstrated within 3 days after radiofrequency ablation for AF. The extent of inflammatory response was associated with early AF recurrence. The impact of early AF recurrence on long-term outcome remains debatable. There is emerging evidence that early AF recurrence has a different underlying mechanism but may still affect long-term recurrence. Understanding the time course of inflammation could help direct the timing and regimen of future potential interventions aimed at ameliorating the inflammatory response after AF ablation. Increased prothrombotic tendency was documented at 1 week after AF ablation in the present study. This may explain the increased thromboembolic rates detected within the first 2 weeks after catheter ablation for AF. Strategic antithrombotic measures targeting this particular time frame may further decrease postprocedural thromboembolic events.
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Ablation Procedure

Electrophysiological study and ablation was performed with sedation utilizing midazolam and fentanyl. The left atrium (LA) was accessed using a single transeptal puncture. All patients underwent wide encircling pulmonary vein ablation with an end point of isolation confirmed by circumferential mapping (PVI; Lasso, Biosense-Webster, Diamond Bar, California) with either elimination or dissociation of pulmonary venous potentials. Ablation of the pulmonary veins was performed using a 3.5mm-tip externally irrigated catheter (Thermocool, Biosense-Webster) delivering 25-30W of power with irrigation rates of 17-30ml/min. Additional substrate modification (linear ablation along the LA roof and/or mitral isthmus and/or ablation of complex fractionated atrial electrograms (CFAE)) was performed in patients with an episode of AF ≥48hours, evidence of structural heart disease or with the largest atrial diameter ≥57mm. Linear ablation and CFAE ablation was performed with a delivered power of 25-35W with irrigation rates of 30-60-ml/min.

After LA access was achieved, repeated bolus unfractionated heparin was utilized to maintain the activated clotting time between 300-350s. After ablation, sheaths were removed without reversal of heparin and warfarin commenced the night of the procedure. Patients were administered enoxaparin 0.5mg/kg twice a day until the INR≥2.
**Supplementary Table 1**: Inflammatory, myocardial injury and prothrombotic markers following RF ablation for AF

<table>
<thead>
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<th></th>
<th>Baseline</th>
<th>Day 1</th>
<th>Day 2</th>
<th>Day 3</th>
<th>Day 7</th>
<th>Day 30</th>
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<tr>
<td>Hs-CRP (mg/L)</td>
<td>2.57 ± 2.16</td>
<td>12.14 ± 12.09*</td>
<td>36.89 ± 34.87*</td>
<td>44.29 ± 37.37*</td>
<td>11.65 ± 16.39*</td>
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<td>WCC (x10⁹/L)</td>
<td>6.14 ± 1.98</td>
<td>8.91 ± 2.37*</td>
<td>7.37 ± 2.18*</td>
<td>7.42 ± 2.11*</td>
<td>7.01 ± 2.14*</td>
<td>6.71 ± 1.85</td>
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<td>Neutrophil (x10⁹/L)</td>
<td>3.95 ± 1.76</td>
<td>6.78 ± 2.10*</td>
<td>5.13 ± 1.85*</td>
<td>5.14 ± 1.82*</td>
<td>4.66 ± 1.70</td>
<td>3.97 ± 1.20</td>
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<tr>
<td>Troponin-T (µg/L)</td>
<td>0.05 ± 0.08</td>
<td>1.61 ± 1.07*</td>
<td>1.01 ± 0.75*</td>
<td>0.54 ± 0.46*</td>
<td>0.11 ± 0.13</td>
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<td>CK (U/L)</td>
<td>101.25 ± 53.91</td>
<td>216.31 ± 141.03*</td>
<td>182.59 ± 190.57*</td>
<td>207.25 ± 275.46*</td>
<td>105.75 ± 60.55</td>
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<td>CKMB (µg/L)</td>
<td>3.21 ± 1.20</td>
<td>10.65 ± 5.10*</td>
<td>4.95 ± 2.27*</td>
<td>3.54 ± 1.10</td>
<td>2.66 ± 0.72</td>
<td>2.27 ± 0.29</td>
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<tr>
<td>Fibrinogen (g/L)</td>
<td>3.11 ± 0.61</td>
<td>3.21 ± 0.55</td>
<td>4.12 ± 0.76*</td>
<td>4.71 ± 0.86*</td>
<td>4.71 ± 1.42*</td>
<td>3.10 ± 0.75</td>
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<tr>
<td>D-Dimer (FEU)</td>
<td>0.28 ± 0.13</td>
<td>0.32 ± 0.24</td>
<td>0.32 ± 0.29</td>
<td>0.44 ± 0.30*</td>
<td>0.58 ± 0.46*</td>
<td>0.41 ± 0.24*</td>
</tr>
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</table>

Data presented as mean ± SD. All markers demonstrated a significant increase over time (p<0.001). *p<0.05 compared to baseline values. Note: Statistical analyses performed using mixed effects models on logged data as appropriate, in which statistical significance was achieved.
**Supplementary Table 2:** Extent of elevation in biomarkers and early AF recurrence

<table>
<thead>
<tr>
<th>Biomarker</th>
<th>AF recurrence</th>
<th>No AF recurrence</th>
<th>p-value</th>
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<tr>
<td>Ln Hs-CRP elevation (mg/L)</td>
<td>3.75 ± 0.80</td>
<td>2.79 ± 1.07</td>
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<td>Ln Troponin-T elevation (µg/L)</td>
<td>0.59 ± 0.62</td>
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<td>Ln CKMB elevation (µg/L)</td>
<td>2.35 ± 0.57</td>
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<td>Fibrinogen elevation (g/L)</td>
<td>2.23 ± 1.39</td>
<td>1.14 ± 0.70</td>
<td>&lt;0.005</td>
</tr>
<tr>
<td>Fibrinogen elevation (g/L) (recurrence at 1-month)</td>
<td>1.96 ± 1.25</td>
<td>1.13 ± 0.63</td>
<td>0.005</td>
</tr>
<tr>
<td>Body temperature (°C)</td>
<td>37.6 ± 0.6</td>
<td>37.2 ± 0.3</td>
<td>0.011</td>
</tr>
</tbody>
</table>

Data presented as mean ± SD.