Association of Heart Rate With Troponin Levels Among Patients With Symptomatic Atrial Fibrillation

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Introduction

Cardiac troponins are routinely used to rule in or rule out acute coronary syndrome in the emergency department (ED). Among patients with symptomatic atrial fibrillation (AF), mildly elevated troponin levels are common but rarely caused by type 1 myocardial infarction. We aimed to investigate the association of heart rate with high-sensitivity cardiac troponin T (hs-cTn T) levels in patients admitted to the ED for AF.

Methods

The Ethics Committee of the Hospital District of Southwest Finland approved this cohort study and determined that written informed consent was not required because of the retrospective nature of the study. This study is reported following the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) guideline for the reporting of observational studies. The Tropo-AF study aimed to investigate the factors associated with minor hs-cTn T elevations (<0.1 ng/mL; to convert to micrograms per liter, multiply by 1) in 2911 patients with AF at the ED; 501 patients from the Tropo-AF study fulfilled the inclusion criteria for this cohort study: at least 2 hs-cTn T samples within 72 hours and principal discharge diagnosis of AF. The primary outcome measure was peak hs-cTn T serum level within 72 hours of ED admission. Categorical variables were compared using Fisher exact test or Mantel-Haenszel linear-by-linear association test for trend, and continuous variables were compared between groups using Mann-Whitney U test. P values were 2-sided, and significance was set at P < .05. Statistical evaluation was conducted from January 2020 to April 2020 using statistical software SPSS for Windows version 25.0 (IBM) and R version 3.6.1 (R Project for Statistical Computing) (eAppendix in the Supplement).

Results

A total of 501 patients (median [interquartile range] age, 75.6 [66.6-82.3] years; 262 [52.3%] women) were included in analysis (Table). In multiple linear regression analysis (Akaike information criterion, 4319.44), increase in peak hs-cTn T level was independently associated with a higher heart rate ($\beta = 0.194; P < .001$). Other factors independently associated with peak hs-cTn T levels were age ($\beta = 0.141; P = .004$), low hemoglobin levels ($\beta = 0.142; P = .001$), decreasing estimated glomerular filtration rate ($\beta = 0.130; P = .004$), diabetes ($\beta = 0.129; P = .001$), heart failure ($\beta = 0.124; P = .002$), new-onset AF ($\beta = 0.155; P < .001$), and absence of palpitation ($\beta = 0.152; P < .001$).

Multiple logistic regression revealed that the association of heart rate with elevated hs-cTn T level (>0.014 ng/mL) was limited to patients in the 2 groups with the highest heart rates (heart rate, 125-139 beats per minute [bpm]: adjusted odds ratio, 2.03; 95% CI, 1.05-3.90; $P = .03$; heart rate $\geq 140$ bpm: adjusted odds ratio, 4.05; 95% CI, 1.80-9.12; $P = .001$) compared with patients with admission heart rate less than 90 bpm. The generalized additive model confirmed a nonlinear association between peak hs-cTn T and admission heart rate (Figure A). While 68 of 85 patients with CHA$_2$DS$_2$-VASc score 4 or higher and heart rate 125 bpm or higher (80.0%) had elevated hs-cTn T levels, only 17 of 48 patients with CHA$_2$DS$_2$-VASc score at least 1 and heart rate less than 125 bpm (35.4%) had elevated hs-cTn T levels (P for overall trend < .001) (Figure B).
Patients with coronary artery disease had higher median (interquartile range) peak hs-cTnT levels (0.024 ng/mL [0.014-0.045]) compared with patients without known disease (0.019 [0.011-0.035] ng/mL; \( P = .001 \)). The peak hs-cTnT level was independently associated with higher heart rate in patients with known coronary artery disease (\( \beta = 0.168; \ P = .04 \)) and those without (\( \beta = 0.205; \ P < .001; \ P \) for interaction = .66).

Of 501 patients, 69 patients (13.8%) had a dynamic change of more than 50% in hs-cTnT level. Multiple logistic regression analysis showed that heart rate 140 bpm or greater was significantly associated with a change of more than 50% in hs-cTnT level (adjusted odds ratio, 4.61; 95% CI, 1.62-13.14; \( P = .004 \)).

### Table. Baseline Characteristics and Follow-up Data

| Characteristic | No. (%) | Heart rate, bpm | \( P \) value |
|---------------|---------|-----------------|--------------|
| Age, median (IQR), y | 75.6 (66.6-82.3) | 76.0 (66.7-82.4) | 75.0 (66.3-82.1) | .41 |
| Women | 262 (52.3) | 142 (47.5) | 120 (59.4) | .01 |
| CHA2DS2-VASc score, median (IQR) | 3 (2-4) | 3 (2-4) | 3 (2-4) | .43 |
| Congestive heart failure | 45 (9.0) | 29 (9.7) | 16 (7.9) | .53 |
| Hypertension | 318 (63.5) | 192 (64.2) | 126 (62.4) | .71 |
| Diabetes mellitus | 93 (18.6) | 60 (20.1) | 33 (16.3) | .35 |
| Prior stroke/TIA | 60 (12.0) | 37 (12.4) | 23 (11.4) | .78 |
| Coronary artery disease\(^a\) | 131 (26.1) | 85 (28.4) | 46 (22.8) | .18 |
| Prior myocardial infarction | 67 (13.4) | 42 (14.0) | 25 (12.4) | .69 |
| Prior PCI or CABG | 66 (13.2) | 37 (12.4) | 29 (14.4) | .59 |
| Hypercholesterolemia | 193 (38.5) | 119 (39.8) | 74 (36.6) | .51 |
| Current smoker | 28 (5.6) | 13 (4.3) | 15 (7.4) | .17 |
| Active malignancy | 26 (5.2) | 14 (4.7) | 12 (5.9) | .54 |
| Types of AF | | | |
| Permanent or persistent | 91 (18.2) | 69 (23.1) | 22 (10.9) | .001 |
| Paroxysmal | 280 (55.9) | 165 (55.2) | 115 (56.9) | .72 |
| New-onset | 130 (25.9) | 65 (21.7) | 65 (32.2) | .01 |
| Antithrombotic therapy | | | |
| Antiplatelet therapy | 120 (24.0) | 74 (24.7) | 46 (22.8) | .67 |
| Acetylsalicylic acid | 108 (21.6) | 70 (23.4) | 38 (18.8) | .23 |
| Clopidogrel | 14 (2.8) | 5 (1.7) | 9 (4.5) | .10 |
| Anticoagulation | 269 (53.7) | 173 (57.9) | 96 (47.5) | .03 |
| Antiarrhythmic agents | 341 (68.1) | 219 (73.2) | 122 (60.4) | .003 |
| \( \beta \) blockers | 332 (66.3) | 214 (71.6) | 118 (58.4) | .003 |
| Symptoms | | | |
| Chest pain | 99 (19.8) | 57 (19.1) | 42 (20.8) | .65 |
| Dyspnea | 133 (26.5) | 79 (26.4) | 54 (26.7) | >.99 |
| Palpitations | 250 (49.9) | 148 (49.5) | 102 (50.5) | .86 |
| Heart rate at admission, median (IQR), bpm\(^b\) | 116 (95-135) | 98 (83-113) | 138 (113-146) | <.001 |
| Laboratory variables, median (IQR) | | | |
| Peak hs-cTnT T at 72 h, ng/mL | 0.020 (0.012-0.038) | 0.018 (0.011-0.032) | 0.026 (0.014-0.045) | <.001 |
| Systolic blood pressure, mm Hg\(^c\) | 116 (120-150) | 136 (121-152) | 135 (118-149) | .29 |
| Hemoglobin, g/dL | 11.8 (12.5-14.8) | 13.8 (12.5-14.9) | 13.7 (12.6-14.7) | .68 |
| C-reactive protein, mg/dL\(^d\) | 0.3 (0.2-1.0) | 0.3 (0.2-0.8) | 0.4 (0.2-1.1) | .01 |
| eGFR, ml/min/1.73 m\(^2\) | 66.6 (51.3-82.4) | 66.1 (50.5-80.6) | 67.8 (53.7-84.1) | .24 |
| <60 | 186 (37.1) | 115 (38.5) | 71 (35.1) | .51 |
| End points at 1 y | | | |
| All-cause mortality | 41 (8.2) | 19 (6.4) | 22 (10.9) | .10 |
| Myocardial infarction | 4 (0.8) | 3 (1.0) | 1 (0.5) | .65 |
| Stroke | 4 (0.8) | 4 (1.3) | 0 (0) | .15 |

Abbreviations: AF, atrial fibrillation; bpm, beats per minute; CABG, coronary artery bypass graft; eGFR, estimated glomerular filtration rate; hs-cTnT, high-sensitivity cardiac troponin T; IQR, interquartile range; PCI, percutaneous coronary intervention; TIA, transient ischemic attack.

SI conversion factors: To convert hs-cTnT to micrograms per liter, multiply by 1; hemoglobin to grams per liter, multiply by 10; C-reactive protein to milligrams per liter, multiply by 10.

\( ^a \) Defined as a diagnosis of coronary disease, history of myocardial infarction, percutaneous coronary intervention, or coronary artery bypass graft surgery.

\( ^b \) Heart rate was determined from the first 12-lead electrocardiogram obtained during the emergency department visit.

\( ^c \) Missing data on systolic blood pressure in 60 patients (12%).

\( ^d \) Missing data on C-reactive protein in 85 patients (17%).

\( ^* \) Calculated using the Chronic Kidney Disease Epidemiology Collaboration equation.
Discussion

This cohort study found that high ventricular heart rate was significantly associated with troponin release in patients admitted to the ED primarily for symptomatic AF. The association of heart rate with hs-cTn T release was nonlinear and became evident above the heart rate threshold of 125 bpm.

Persistent mild elevation of troponin levels is a common finding in AF, but the underlying etiopathogenesis remains unclear. Old age and multiple comorbidities were associated with minor troponin elevations in patients with AF independent of heart rate. This study’s findings suggest that inadequate ventricular rate control in the acute setting was associated with increased troponin T levels. Patients with elevated troponin levels were not at increased cardiovascular risk, and the magnitude of troponin release was not associated with the presence of known coronary artery disease or chest pain. Similarly, elevated troponin levels can be observed after marathon racing, supraventricular tachycardia, or rapid atrial pacing in individuals with normal coronary arteries and even in individuals without biochemical evidence of myocardial ischemia.

Limitations of this study include its retrospective design, small sample size, and determination of heart rate from single admission electrocardiogram. Nevertheless, these results suggest that high ventricular heart rate at admission was independently associated with troponin release in patients with AF. The effect of ventricular heart rate should be taken into consideration in the differential diagnosis of patients with AF and increased troponin levels.

ARTICLE INFORMATION

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**Author Contributions:** Dr Airaksinen had full access to all of the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

**Concept and design:** Jaakkola, Biancari, Airaksinen.

**Acquisition, analysis, or interpretation of data:** All authors.

**Drafting of the manuscript:** Pouru, Jaakkola, Biancari, Airaksinen.

**Critical revision of the manuscript for important intellectual content:** All authors.

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**SUPPLEMENT.**

*eAppendix.* Supplementary Methods