# Clinical Utility and Prognostic Significance of Measuring Troponin I Levels in Patients Presenting to the Emergency Room With Atrial Fibrillation

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ABSTRACT

*Background:* The clinical significance of mildly elevated troponins in patients presenting to the emergency room (ER) with atrial fibrillation (AF) is not well understood.

*Hypothesis:* We hypothesized that mildly elevated troponin in these patients is associated with adverse cardiovascular outcomes.

*Methods:* In a multi-center, retrospective study, 662 patients with AF were divided into 3 groups based on troponin levels: group 1, mildly elevated; group 2, normal; and group 3, troponin not measured. Primary outcome was the combined endpoint of all-cause mortality and myocardial infarction (MI) at one year.

*Results:* Levels of TnI were measured in 503 (76%) patients. They were elevated in 220 patients (33%, group 1; mean, 0.56 ng/mL), normal in 283 patients (43%, group 2), and not measured in 159 patients (24%, group 3). Significantly more cardiac testing was done at index hospitalization in group 1 (50%) compared with groups 2 and 3 (28% and 29%, $P \leq 0.001$) and in the following year (29%, vs 20% and 17%, $P = 0.02$). Group 1 had more positive tests (62%) compared with groups 2 and 3 (25% and 43%, $P \leq 0.001$). Group 1 had a significantly higher occurrence of the primary endpoint (22%, vs 10% and 15%, $P = 0.002$), driven primarily by a higher incidence of MI in group 1 (7%, vs 1% and 2%, $P = 0.001$).

*Conclusions:* Troponin levels are routinely checked in a majority of patients presenting to the emergency department with AF. Even mildly elevated TnI is associated with a greater incidence of coronary artery disease on diagnostic testing and a higher 1-year incidence of MI.

## Introduction

Elevation in troponin levels in settings other than myocardial infarction (MI) have been reported in diverse disease states, such as pulmonary embolism, sepsis, shock, critical illness, and decompensated heart failure.[1,2] Mild troponin elevation associated with atrial fibrillation (AF) and rapid ventricular response (RVR) in the absence of MI or manifest coronary artery disease (CAD) has been less well studied.[3–6] The incidence and the prognostic significance of mild troponin elevation in patients presenting with AF as the primary diagnosis also is not well established.

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Atrial fibrillation is a worldwide problem, affecting 2.2 million people in the United States and 4.5 million in the European Union, with an estimated economic burden of $15.7 billion in the European Union.[7–9] Atrial fibrillation is the most common reason for hospital admissions for cardiac-rhythm disturbances. Hospital admissions for AF from 1993 to 2004 have risen by 66%.[10,11] In the setting of MI, AF occurs in about 7% to 18% of cases.[12] When complicated with AF, MI is associated with increased in-hospital and 1-year mortality.[13]

Although the incidence of AF occurring as a complication of MI has been well studied, the incidence and significance of cardiac-enzyme elevation in patients presenting with primary AF without clinical and electrocardiographic (ECG) evidence of MI has not been well studied. It is a common practice to check troponin levels in patients presenting to the

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emergency department (ED) with AF and RVR, irrespective of the presence or absence of symptoms and features of MI. However, currently there are no guidelines that recommend routine troponin testing in patients presenting with AF and without clinical or ECG evidence of MI. The utility of this practice of routinely measuring troponin remains unclear.

Current guidelines indicate that any amount of troponin elevation represents an MI and is associated with adverse prognosis.[14] Whether mild troponin elevation in the setting of AF is also associated with adverse cardiovascular (CV) outcomes is not clear.

The primary objective of this study was to assess the prognostic significance of mild troponin elevation for major adverse CV events (MI, all-cause mortality, and composite endpoint of all-cause mortality and MI at 1 year) in patients presenting to the ED with AF as the primary diagnosis. The secondary objectives were: (1) to determine the clinical factors that prompt physicians to measure troponins; (2) to identify clinical predictors of elevated troponins; and (3) to evaluate the impact of elevated troponins on further CV testing in these patients.

## Methods

We conducted a multicenter retrospective study of patients admitted through the ED with a primary diagnosis of AF between January 2000 and December 2005 at 3 medical centers (1 large academic medical center and 2 US Department of Veterans Affairs [VA] hospitals). All patients admitted through the ED with a primary diagnosis of AF were considered for the study. Prior institutional review board approval was obtained from each institution, and the study was conducted in accordance with the regulations.

### Study Population

All patients age >18 years presenting to ED with a primary diagnosis of AF or atrial flutter were included, irrespective of the duration (new as well as with history of AF/flutter). Exclusion criteria included (1) patients with a primary diagnosis of ST-elevation myocardial infarction (STEMI) based on the clinical presentation; (2) patients with a troponin I (TnI) elevation >5 ng/mL, as these were considered more likely to have a non–ST-segment elevation MI (NSTEMI), or if the patient was treated as primary diagnosis of NSTEMI even when TnI was <5 ng/mL based on chart review; (3) other causes of troponin elevation, including end-stage renal disease, decompensated heart failure, sepsis, pulmonary embolism, myocarditis, pericarditis, or acute stroke; (4) advanced malignancy or severe comorbidity with life expectancy <1 year; and (5) patients in whom AF was not the primary diagnosis or those who developed AF during hospitalization. The entire study cohort was divided into 3 groups: group 1, patients whose TnI was measured and elevated; group 2, patients whose TnI was measured and not elevated; and group 3, patients whose TnI was not measured.

### Data Collection

Appropriate *International Classification of Diseases, Ninth Edition* (ICD-9) codes were used to identify patients with a primary diagnosis of AF/flutter. Patients not admitted through the ED were excluded. Presenting ECGs of the patients taken in the ED were reviewed by an attending cardiologist in a blinded manner to confirm AF/flutter and to document other abnormalities, such as ST changes and other arrhythmias. Electronic medical records were reviewed, and trained research personnel collected demographic and clinical information on admission and at follow-up. Presenting symptoms, admission heart rate, and cardiac markers (if checked) were noted.

### Troponin I Measurement

Of all the available TnI measurements done at the time of the primary admission, the highest value was used for study analysis. As per the manufacturer's recommendations and the hospital laboratory standards, TnI was considered elevated if it measured ≥0.05 ng/mL at the university hospital (DxI 800 immunoassay system; Beckman Coulter, Brea, CA). The lower detection zone for troponin at the 2 veterans hospitals was 0.022 ng/mL (DPC Immulite 2500 immunoassay analyzer; Siemens, Erlangen, Germany). Because the study aimed to investigate the significance of only mild TnI elevation, and to exclude possible primary acute cardiac syndrome patients, we excluded all patients with TnI >5 ng/mL. Thus, in the elevated TnI group, levels ranged between 0.05 and 5 ng/mL at the university hospital and from 0.023 to 5 ng/mL at the VA hospitals. The hospitalization records were reviewed for any cardiac ischemia workup (stress echocardiograms, nuclear myocardial perfusion imaging, or coronary angiography).

### Cardiac Diagnostic Testing

The presence of myocardial ischemia on stress echocardiogram, reversible or fixed defects on nuclear stress test that were considered significant for ischemia or prior infarction, or >50% luminal stenosis on cardiac catheterization were considered as positive tests. Positive tests were used to identify patients as having CAD.

### Outcomes

The impact of troponin elevation on further cardiac testing was evaluated by checking the number of diagnostic cardiac procedures performed during that index admission, as well as procedures performed in the following 1 year. Primary outcome was major adverse cardiovascular events, which included rate of (1) MI, (2) all-cause mortality, and (3) combined endpoint of MI and mortality. Secondary outcomes included (1) number of diagnostic tests (for CAD detection) done during the index admission, (2) number of positive diagnostic tests, (3) number of diagnostic tests in the following 1 year, and (4) number of positive diagnostic tests at 1 year. We also assessed the predictors of TnI testing and those of elevated troponin levels.

### Follow-up

Records of all patients were reviewed until 1 year from the date of index admission. Information on subsequent diagnostic tests, results of the tests, and cardiac catheterization was obtained. Any incidence of MI in the subsequent year


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was also noted. This was done by manual chart review of individual charts and review of each event. An MI was recorded if a diagnosis of MI was made by the treating physician based on clinical presentation and if treated accordingly. All-cause mortality was obtained from the Social Security Death Index as well as from chart review when available. Cause of death could not be ascertained in all patients.

### Statistical Analysis

All continuous data were expressed as mean ± standard deviation, and categorical data as percentages. The analysis of variance was used for comparison of continuous data with post hoc multiple comparison testing done using the Bonferroni statistic. The $\chi^2$ test or Fisher exact test (as appropriate) was used for categorical data analysis. Between-group comparisons were made by examining the standardized residuals in each cell and by further stratified $\chi^2$ testing.[15] A $P$ value $<0.05$ was considered statistically significant. Forward stepwise logistic regression analysis was used to identify predictors of troponin testing and positive troponin values. Survival analysis and the Tarone-Ware statistic were used to compare event rates at 1 year between cohorts. SAS version 9.1.3 (SAS Institute, Inc., Cary, NC) was used for all statistical analyses.

## Results

A total of 662 patients who presented to the EDs of the 3 institutions with AF between January 2000 and December 2005, and who met the inclusion and exclusion criteria, were included in the study.

### Troponin I Levels

Levels of TnI were measured in 76% of the patients (503/662). Troponin I was found to be elevated in 44% (n = 220) of these patients (group 1) and was negative in 56.3% (n = 283) of these patients (group 2). Of the 662 total subjects, 159 patients (24%) did not have TnI measured, and these were categorized into group 3 (Figure 1).

The baseline clinical characteristics are summarized in Table 1. Ventricular rate and mean creatinine were higher in group 1. There was no significant difference in the baseline prevalence of CAD or diabetes mellitus between groups. The mean TnI level in group 1 was 0.56 ng/mL (range, 0.05–4.17 ng/mL).

### Clinical Symptoms at Presentation

The study evaluated the presence of symptoms of chest pain, palpitations, dyspnea, lightheadedness, and fatigue at presentation. The distribution of symptoms among the 3 groups is summarized in Table 2.

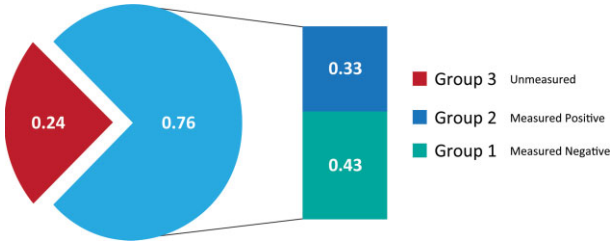


Figure 1. Percentage of patients in each group.

### Predictors of Troponin I Measurement and Elevation

The patient characteristics that prompted physicians to check troponin levels in these patients were female sex, obstructive sleep apnea, renal insufficiency, palpitations, fatigue, and chest pain on univariate analysis ($P$ <0.1). Symptoms of dyspnea, lightheadedness, and dizziness did not predict troponin measurement. On multivariate analysis, patients in whom troponin was measured were more likely to be women (odds ratio [OR]: 3.3, 95% confidence interval [CI]: 1.4-10, $P = 0.003$) and were more likely to have symptoms of palpitations (OR: 1.6, 95% CI: 1.1-2.5, $P = 0.03$), fatigue (OR: 2.0, 95% CI: 1.1-3.3, $P = 0.02$), or chest pain (OR: 2.0, 95% CI: 1.2-3.3, $P = 0.005$). The mean troponin level in group 1 was 0.56 ng/mL (range, 0.05–4.17 ng/mL). Among those in whom troponin was measured, univariate and multivariate predictors of troponin elevation were analyzed. Univariate predictors are summarized in Table 3. Multivariate analysis showed that an elevated troponin was significantly associated with older age (OR: 1.004, 95% CI: 1.0-1.04, $P = 0.017$), male sex (OR: 3.33, 95% CI: 2.0-10, $P \leq 0.001$), and presence of hypertension (OR: 3.3, 95% CI: 2.0-10, $P \leq 0.001$). Also, patients without any palpitations (OR: 2.1, 95% CI: 1.4-3.2, $P \leq 0.001$), fatigue (OR: 2.3, 95% CI: 1.4-3.7, $P \leq 0.001$), or valvular lesions (OR: 2.3, 95% CI: 1.4-3.7, $P \leq 0.001$) were found to have elevated troponin.

### Diagnostic Testing for Coronary Artery Disease

The frequency of diagnostic testing for CAD during index hospitalization was significantly greater in group 1 (50%, 112/220 patients) compared with group 2 (28%, 79/283 patients) and group 3 (29%, 47/159 patients; $P < 0.001$ for both). These tests were positive for presence of CAD in 36% (41/112 patients) in group 1, 31.6% (25/79 patients) in group 2, and 23.4% (11/47 patients) in group 3, although the differences were not statistically significant (Table 4). Thus, for the overall groups, the percentages of tests positive for CAD were as follows: 18% (n = 41/220) of the patients in group 1, 8.8% (n = 25/283) in group 2, and 7% (n = 11/159) in group 3. Thus, the finding of a positive troponin resulted in physicians ordering significantly more diagnostic testing for the detection of CAD during the index admission. However, the diagnostic yield from this testing was not significantly different among the 3 groups. During index hospitalization of the patients who did undergo diagnostic testing, 19% (21/112) of patients in group 1, 11% (9/79) in group 2, and 6% (3/47) in group 3 underwent coronary angiography ($p = 0.09$).

Diagnostic procedures performed for the detection of CAD in the year following the index hospitalization are also presented in Table 4. Group 1 had significantly more cardiac testing performed in the year following the index admission (29%) compared with groups 2 (20%) and 3 (17%, $P = 0.02$). Among those who underwent diagnostic testing, group 1 had a higher rate of positive tests (62.5%, n = 40/64) compared with groups 2 (25%, n = 15/59) and 3 (42.8%, n = 12/28), with $P < 0.001$ (Table 3). Looking at each of the 3 groups overall, group 1 had higher incidence of positive tests (18%,


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Table 1. Baseline Characteristics of Study Patients

| Clinical Variable | Group 1: Tn Positive, N = 220 | Group 2: Tn Negative, N = 283 | Group 3: Tn Not Measured, N = 159 | *P* Value |
|---|---|---|---|---|
| Age, y (range) | 69.2 ± 11.1 (35–92)[a] | 65.0 ± 14.9 (23–95)[a] | 67.4 ± 12.8 (26–95) | 0.002 |
| Male sex | 85 | 72[a] | 85 | <0.001 |
| BMI, kg/m² | 29.6 ± 7.3 | 31.1 ± 24.5 | 29.4 ± 6.6 | 0.545 |
| Prior history of AF | 43 | 53[a] | 35[a] | 0.001 |
| DM | 27.1 | 31.8 | 31.3 | 0.493 |
| Hypertension | 84.4[a] | 67.2[a] | 74.0 | <0.001 |
| CAD | 46.3 | 39.7 | 35.9 | 0.126 |
| Revascularization | 25.0 | 17.0 | 21.4 | 0.096 |
| Stroke | 12.0 | 12.9 | 9.1 | 0.358 |
| PVD | 12.4 | 13.5 | 11.5 | 0.841 |
| CRF | 20.6 | 19.2 | 13.0 | 0.181 |
| OSA | 8.7 | 16.2[a] | 6.1 | 0.004 |
| Pacemaker | 4.6 | 9.2 | 5.3 | 0.109 |
| ICD | 3.2 | 7.6[a] | 3.1 | 0.048 |
| LVH | 15.5 | 20.1 | 8.9 | 0.008 |
| TSH, μIU/mL | 2.77 ± 4.15 | 2.20 ± 2.37 | 2.34 ± 2.73 | 0.335 |
| Hg, g/dL | 13.5 ± 2.0 | 14.1 ± 5.5 | 13.4 ± 2.1 | 0.150 |
| Cr, mg/dL | 1.68 ± 1.95[a] | 1.34 ± 1.39 | 1.23 ± 0.58 | 0.012 |
| Ventricular rate, bpm | 131.2 ± 42.8[a] | 121.6 ± 32.9 | 125.3 ± 28.9 | 0.020 |
| LVEF, % | 50.4 ± 16.7 | 52.9 ± 15.4 | 50.0 ± 14.2 | 0.261 |

Abbreviations: AF, atrial fibrillation; BMI, body mass index; Cr, creatinine; CRF, chronic renal failure; DM, diabetes mellitus; Hg, hemoglobin; ICD, implantable cardioverter-defibrillator; LVEF, left ventricular ejection fraction; LVH, left ventricular hypertrophy; OSA, obstructive sleep apnea; PVD, peripheral vascular disease; SD, standard deviation; Tn, troponin; TSH, thyroid-stimulating hormone.
Data are presented as % or mean ± SD.
[a]Denotes between-group differences.

Table 2. Symptoms at Presentation

| Symptoms | Group 1: Tn Positive, N = 220 | Group 2: Tn Negative, N = 283 | Group 3: Tn Not Measured, N = 159 | *P* Value |
|---|---|---|---|---|
| Palpitations | 40.6 | 63.6[a] | 40.6 | <0.001 |
| Dyspnea | 51.4 | 44.3 | 46.9 | 0.297 |
| Fatigue | 21.2 | 36.5[a] | 18.0 | <0.001 |
| Chest Pain | 40.9 | 37.1 | 20.3[a] | <0.001 |
| Dizziness | 20.8 | 28.3 | 24.2 | 0.162 |
| Lightheadedness | 23.1 | 29.2 | 20.3 | 0.114 |

Abbreviations: Tn, troponin.
Data are presented as %.
[a]Denotes between-group differences.

n = 40/220) compared with group 2 (5%, n = 15/283) and group 3 (7%, n = 12/159, $P < 0.0001$).

We also looked at patients who had a normal test at index admission and had new disease or progressive disease that was detected over the next year. Patients in group 1 had significantly more new disease detected (20%, n = 16/73) compared with groups 2 and 3 (5% and 5%, n = 3/54 and n = 2/36, respectively, $P = 0.03$).

## Major Cardiovascular Outcomes

During the 1-year period following the index admission, the composite endpoint of death and MI was significantly higher in group 1 as compared with groups 2 and 3 (22% vs 10% and 15%, respectively, $P = 0.002$). This was driven primarily by the incidence of MI, which was significantly higher in patients in group 1 (7%) compared with the other 2 groups (1% and 2% in groups 2 and 3, respectively, $P = 0.001$; Figure 2). There was no statistically significant difference in all-cause mortality at 1 year among the 3 groups (Figure 3). However, patients in group 1 had a trend toward a higher all-cause mortality at 1 year when compared with the group with negative troponins (group 2, $P = 0.16$; Table 5).


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Table 3. Univariate Predictors of Positive Troponin

| Variable | OR | CI | *P* Value |
|---|---|---|---|
| Age | 1.02 | 1.01-1.03 | <0.001 |
| Male sex | 2.09 | 1.3-3.4 | 0.002 |
| Hypertension | 2.64 | 1.7-4.1 | <0.001 |
| OSA | 0.50 | 0.3-0.9 | 0.01 |
| Valvular heart disease | 0.42 | 0.2-0.6 | <0.001 |
| Pacemaker | 0.50 | 0.2-1.1 | 0.05 |
| ICD | 0.42 | 0.17-1.0 | 0.04 |
| Palpitations | 0.40 | 0.2-0.6 | <0.001 |
| Fatigue | 0.48 | 0.3-0.7 | <0.001 |
| Dizziness | 0.67 | 0.45-1.1 | 0.059 |
| Heart rate | 1.01 | 1.0-1.14 | 0.003 |
| Cr | 1.10 | 1.0-1.2 | 0.03 |
| LVEF | 1.01 | 1.0-1.02 | <0.001 |
| CAD | 3.33 | 1.6-5.0 | <0.001 |

Abbreviations: CAD, coronary artery disease; CI, confidence interval; Cr, creatinine; ICD, implantable cardioverter-defibrillator; LVEF, left ventricular ejection fraction; OR, odds ratio; OSA, obstructive sleep apnea.

Table 4. Secondary Outcomes

| Outcome | Group 1: Tn Positive | Group 2: Tn Negative | Group 3: Tn Not Measured | *P* Value |
|---|---|---|---|---|
| Diagnostic procedures at index admission | 112/220 (50.0)[a] | 79/283 (28.0) | 47/159 (29.0) | <0.001 |
| Positive diagnostic tests at index admission | 41/112 (36.6) | 25/79 (31.6) | 11/47 (23.4) | 0.264 |
| Diagnostic procedures in 1 year | 64/220 (29.0)[a] | 59/283 (20.0) | 28/159 (17.0) | 0.02 |
| Positive tests in 1 year | 40/64 (62.5)[a] | 15/59 (25.0) | 12/28 (42.8) | 0.001 |

Abbreviations: Tn, troponin.
Data presented as n (%).
[a]Denotes between-group differences.

## Discussion

The main finding of this study is that even a mild elevation in TnI levels is associated with higher 1-year risk of MI in patients presenting to the ED with AF as the primary diagnosis. This study shows that cardiac enzymes are frequently checked in patients presenting with AF to the ED; despite absence of prior evidence supporting this practice,

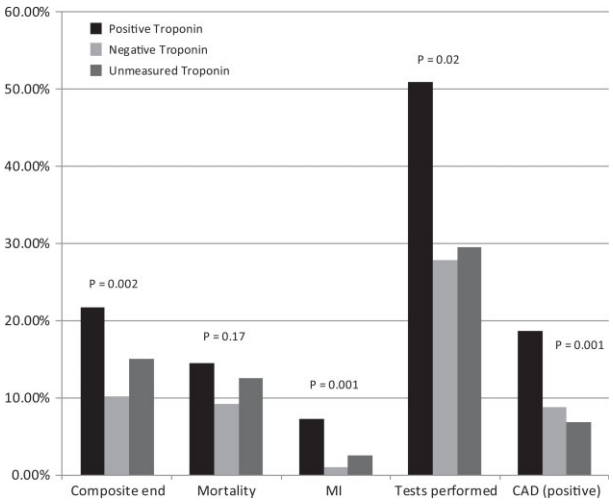


Figure 2. One-year outcomes in the 3 groups. Abbreviations: CAD, coronary artery disease; MI, myocardial infarction.

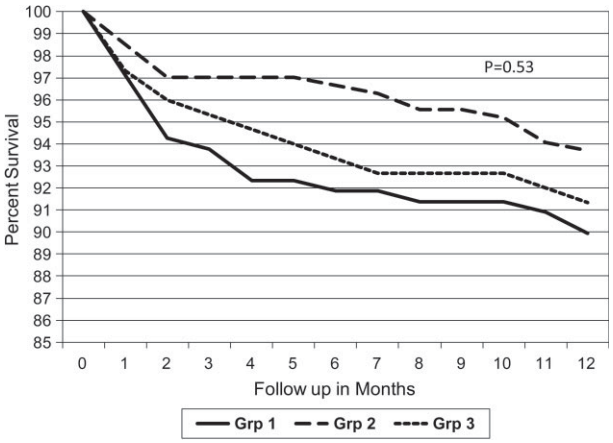


Figure 3. Kaplan-Meier estimates of mortality. Abbreviations: Grp, group.

troponins were checked in >75% of patients presenting with AF. However, the results of our study do lend some justification to this practice and may help in identifying patients with a higher CV risk, as even a mild elevation of troponin in these patients was associated with adverse CV events.

This study attempted to identify factors that prompt physicians to check troponins in patients with AF presenting to the ED. Results show that patients who are most likely to be tested are those presenting with chest pain, palpitations, and fatigue, and they are more likely to be women. Next, the study shows that those with troponin elevation had significantly more diagnostic testing for detection of CAD, both at index hospitalization and over the next 1 year. Patients with troponin elevation, in fact, had a higher cardiovascular disease (CVD) burden, as reflected by a higher rate of abnormal diagnostic test for CAD at 1 year and a higher 1-year incidence of MI compared with patients with a negative troponin. Thus, the study suggests that even mildly elevated TnI in patients presenting with AF is


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Table 5. Major Adverse Cardiovascular Outcomes

| Primary Outcome | Group 1: Tn Positive, N = 220 | Group 2: Tn Negative, N = 283 | Group 3: Tn Not Measured, N = 159 | *P* Value |
|---|---|---|---|---|
| Composite endpoint of MI and mortality | 48 (22)[a] | 29 (10) | 24 (15) | 0.002 |
| Mortality | 32 (14) | 26 (9) | 20 (12) | 0.169 |
| MI at 1 year | 16 (7)[a] | 3 (1) | 4 (2) | 0.001 |

Abbreviations: MI, myocardial infarction; Tn, troponin.
Data presented as n (%).
[a]Denotes between-group differences.

associated with a higher likelihood for the presence of CAD and with future MI risk.

The European Society of Cardiology/American College of Cardiology guidelines[14] indicate that any amount of troponin elevation is associated with adverse clinical outcomes and that there is no discernible threshold below which an elevated troponin level is deemed harmless. However, this is in the setting of acute coronary syndromes (ACS), with atherothrombosis as the etiology of underlying myocardial necrosis.

The significance of mild troponin elevation in non-ACS settings is less well defined. A report on 50 patients with elevated troponins in clinical settings other than ACS suggested that in a non-ACS setting, troponin elevation does not predict adverse outcomes for up to 1 year.[16] The study included patients admitted with diagnoses of heart failure, gastrointestinal bleed, end-stage renal disease, malignancy, and others; only 2 patients with AF were included in this study. However, other studies have shown increased mortality with troponin elevation in patients with end-stage renal disease, chronic pulmonary hypertension, and other disease states.[17,18]

Our study demonstrated higher rates of MI in AF patients with mild elevations of troponin but no difference in mortality. In a recent study from the Netherlands, Van den Bos et al evaluated the prognostic significance of minor and mild elevation of troponins in patients with AF.[3] In a total of 407 patients, they reported an elevated troponin in 39%. They also found increased incidence of cardiac testing in these patients compared with the negative-troponin group. They also found that the positive-troponin group had a higher 3-year mortality and MI. Our study did not find the association with mortality. This may have been because their study group was significantly older overall, and the positive-troponin group was also significantly older, with more CAD and diabetes mellitus compared with the negative-troponin group. The overall mortality in their study population was also significantly higher (25%).

## Troponin Elevation and Atrial Fibrillation

Prior case reports that reviewed patients with AF with mild troponin elevation have reported absence of significant coronary artery stenosis.[4–6,19,20] The mechanism of troponin elevation in AF with RVR is not well defined, but several hypotheses have been proposed.[1] Troponin elevation in AF patients with RVR has been attributed not to coronary atherothrombosis, but to ischemia related to (1) increased myocardial demand and (2) decreased coronary perfusion due to reduced diastolic filling time secondary to increased heart rate. The reduced diastolic time could cause supply–demand mismatch and possible subendocardial ischemia. Increased myocardial stretch has also been implicated, and it has been demonstrated that brain natriuretic peptide values increase, as do troponin levels, with an increase in heart rate.[21,22] However, it is also likely that patients with underlying CAD may be more prone to troponin leak, as they are more prone to demand ischemia at increased heart rates than those with normal coronaries.

Our study results indicate that TnI elevation is associated with higher rates of adverse outcomes at 1 year. It is noteworthy that the positive troponins prompted a more detailed CV workup and identification of more CVD at the index admission and continues to be associated with higher MI rates. The beneficial effect, if any, of this diagnostic testing on these CV endpoints cannot be ascertained from this study. For instance, it is unknown if the MI rates could have been even higher had the diagnostic testing and interventions not been performed.

Ours is the first large study in the United States that describes the incidence and prognostic significance of troponin elevation in non-MI patients presenting to the ED with AF and RVR. One previous study measured creatine kinase MB (CK-MB) in 255 patients admitted to the ED with AF; of the patients in whom CK-MB was checked, only 5.5% had elevated creatine kinase, and most of these patients could be identified by other clinical and ECG parameters.[23] The authors thus recommended against such routine practice of measuring CK-MB. This report did not look at troponins and did not look at the prognostic value of such an asymptomatic elevation of CK-MB in the setting of AF. Another study, by Meshkat et al, reported the incidence of troponin testing in patients presenting to the ED with AF to be 86%. However, that study included all patients with positive troponins, including those with MI and ACS, and did evaluate the prognostic significance of troponin elevation.[24]

Another unique finding of this current study is that we looked at the group of patients who did not have any troponins measured despite presenting with AF (group 3). The study found that this group had similar MI and mortality rates as the group with negative troponins. This may indicate that physicians were in fact able to correctly identify the low-risk groups and chose not to measure troponins in these patients. To our knowledge, this group has not been investigated in the prior studies.

## Study Limitations

This study has several limitations. First, this is a retrospective study, with those inherent limitations. However, the wide heterogeneity that the 3 participating institutions offer provides a good real-life value of the observations made in this study. Second, although we looked at several clinical variables that we thought may be predictors of measurement of troponins in these patients, we could have missed several other factors that may prompt physicians to check


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troponin elevation in patients who do not have clinical presentation suggestive of MI. Third, follow-up was obtained by review of electronic medical records. If the patients had follow-up at any other hospital, that could have been missed, although the results of such admissions and testing would have been detailed in the electronic medical records on subsequent clinic or hospital visits. Fourth, we measured 1-year all-cause mortality and not CV mortality. Fifth, the clinical endpoint of MI was based on the diagnosis and treatment of MI documented in the chart by the treating physician. Sixth, true prevalence of CVD in the 3 groups is probably underestimated, as diagnostic testing was not performed in all patients.

## Conclusion

Serum troponin levels are routinely checked in a majority of patients who present to the ED with AF, and >50% are found to have mild troponin elevations. Mild troponin elevation in the setting of AF is associated with a higher incidence of MI and new CAD detected over the next year. There is however, no difference in 1-year mortality. Measuring troponins in patients presenting with AF, even without a clinical picture suggestive of MI, may be reasonable, as it does identify a subset that has a higher risk of cardiac events.

## References


1. Jeremias A, Gibson CM. Narrative review: alternative causes for elevated cardiac troponin levels when acute coronary syndromes are excluded. *Ann Intern Med.* 2005;142:786–791.
2. Newby LK, Jesse RL, Babb JD, et al. ACCF 2012 Expert Consensus Document on Practical Clinical Considerations in the Interpretation of Troponin Elevations: a Report of the American College of Cardiology Foundation Task Force on Clinical Expert Consensus Documents. *J Am Coll Cardiol.* 2012;60:2427–2463.
3. Van den Bos EJ, Constantinescu AA, van Domburg RT, et al. Minor elevations in troponin I are associated with mortality and adverse cardiac events in patients with atrial fibrillation. *Eur Heart J.* 2011;32:611–617.
4. Zellweger MJ, Schaer BA, Cron TA, et al. Elevated troponin levels in absence of coronary artery disease after supraventricular tachycardia. *Swiss Med Wkly.* 2003;133:439–441.
5. Bakshi TK Choo MK, Edwards CC, et al. Causes of elevated troponin I with a normal coronary angiogram. *Intern Med J.* 2002;32:520–525.
6. Nunes JP, Silva JC, Maciel MJ. Troponin I in atrial fibrillation with no coronary atherosclerosis. *Acta Cardiol.* 2004;59:345–346.
7. Fuster V, Rydén L, Cannom DS, et al. ACC/AHA/ESC 2006 Guidelines for the Management of Patients With Atrial Fibrillation. A Report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines and the European Society of Cardiology Committee for Practice Guidelines (Writing Committee to Revise the 2001 Guidelines for the Management of Patients With Atrial Fibrillation). *Circulation.* 2006;114:e257–e354.
8. Friberg J, Buch P, Scharling H, et al. Rising rates of hospital admissions for atrial fibrillation. *Epidemiology.* 2003;14:666–672.
9. Stewart S, Murphy N, Walker A, et al. Cost of an emerging epidemic: an economic analysis of atrial fibrillation in the UK. *Heart.* 2004;90:286–292.
10. Wattigney WA, Mensah GA, Croft JB. Increasing trends in hospitalization for atrial fibrillation in the United States, 1985 through 1999: implications for primary prevention. *Circulation.* 2003;108:711–716.
11. McDonald AJ, Pelletier AJ, Ellinor PT, et al. Increasing US emergency department visit rates and subsequent hospital admissions for atrial fibrillation from 1993 to 2004. *Ann Emerg Med.* 2008;51:58–65.
12. Sugiura T, Iwasaka T, Ogawa A, et al. Atrial fibrillation in acute myocardial infarction. *Am J Cardiol.* 1985;56:27–29.
13. Wong CK, White HD, Wilcox RG, et al. New atrial fibrillation after acute myocardial infarction independently predicts death: the GUSTO-III experience. *Am Heart J.* 2000;140:878–885.
14. Alpert JS, Thygesen K, Antman E, et al. Myocardial infarction redefined—a consensus document of The Joint European Society of Cardiology/American College of Cardiology Committee for the redefinition of myocardial infarction [published correction appears in *J Am Coll Cardiol*. 2001;37:973]. *J Am Coll Cardiol.* 2000;36:959–969.
15. Snedecor GW, Cochran WG. Statistical Methods. 6th ed. Ames, Iowa: Iowa State University Press; 1967:251–253.
16. Barasch E, Kaushik V, Gupta R, et al. Elevated cardiac troponin levels do not predict adverse outcomes in hospitalized patients without clinical manifestations of acute coronary syndromes. *Cardiology.* 2000;93:1–6.
17. Apple FS, Murakami MM, Pearce LA, et al. Predictive value of cardiac troponin I and T for subsequent death in end-stage renal disease. *Circulation.* 2002;106:2941–2945.
18. Torbicki A, Kurzyna M, Kuca P, et al. Detectable serum cardiac troponin T as a marker of poor prognosis among patients with chronic precapillary pulmonary hypertension. *Circulation.* 2003;108:844–848.
19. Kanjwal K, Imran N, Grubb B, et al. Troponin elevation in patients with various tachycardias and normal epicardial coronaries. *Indian Pacing Electrophysiol J.* 2008;8:172–174.
20. Redfearn DP, Ratib K, Marshall HJ, et al. Supraventricular tachycardia promotes release of troponin I in patients with normal coronary arteries. *Int J Cardiol.* 2005;102:521–522.
21. Higgins JP, Higgins JA. Elevation of cardiac troponin I indicates more than myocardial ischemia. *Clin Invest Med.* 2003;26:133–147.
22. Qi WF, Kjekshus HF, Klinge RF, et al. Cardiac natriuretic peptides and continuously monitored atrial pressures during chronic rapid pacing in pigs. *Acta Physiol Scand.* 2000;169:95–102.
23. Zimetbaum PJ, Josephson ME, McDonald MJ, et al. Incidence and predictors of myocardial infarction among patients with atrial fibrillation. *J Am Coll Cardiol.* 2000;36:1223–1227.
24. Meshkat N, Austin E, Moineddin R, et al. Troponin utilization in patients presenting with atrial fibrillation/flutter to the emergency department: retrospective chart review. *Int J Emerg Med*. 2011;8;4:25.




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