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# Predictors of significant coronary artery disease in atrial fibrillation: Are cardiac troponins a useful measure

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ABSTRACT

*Background:* Cardiac Troponin I (cTnI) is frequently measured in patients presenting with symptomatic atrial fibrillation (AF). The significance of elevated cTnI levels in this patient cohort is unclear. We investigated the value of cTnI elevation in this setting and whether it is predictive for significant coronary artery disease (sCAD).
*Methods:* We conducted a retrospective, single-center, case–control study of 231 patients who presented with symptomatic AF to The Prince Charles Hospital emergency department, Brisbane, Australia between 2006 and 2014. Patients who underwent serial cTnI testing and assessment for CAD were included. Clinical variables that are known to predict CAD and could potentially predict cTnI elevation were collected. Binary logistic regression was performed to identify predictors of sCAD and cTnI elevation.
*Results:* Cardiac Troponin I elevation above standard cut off was not predictive for sCAD after adjustment for other predictors (OR 1.62, 95% CI 0.79–3.32. p = 0.19). However, the highest cTnI concentration value (cTnI peak) was predictive for sCAD (OR 2.02, 95% CI 1.02–3.97, p = 0.04).
Dyspnea on presentation (OR 4.52, 95% CI 1.87–10.91, p = 0.001), known coronary artery disease (OR 3.44, 95% CI 1.42–8.32, p = 0.006), and ST depression on the initial electrocardiogram (OR 2.57, 95% CI 1.11–5.97, p = 0.028) predicted sCAD in our cohort, while heart rate on initial presentation was inversely correlated with sCAD (OR 0.99, 95% CI 0.971–1.00, p = 0.034).
*Conclusion:* Troponin elevation is common in patients presenting to hospital with acute symptomatic AF and it is not a reliable indicator for underlying sCAD in this patient cohort. However, cTnI peak was a predictor of significant coronary artery disease.



## 1. Introduction

AF is the most common cardiac arrhythmia requiring hospital care with a prevalence that rises with age. It has an estimated prevalence of approximately 4% among patients 60 years or older and approximately 9% among patients 80 years or older [1]. AF is frequently associated with cardiovascular diseases such as hypertension (HTN), valvular and congenital heart disease, cardiomyopathies and coronary artery disease [1–3].

Patients with AF can present with symptoms suggestive of myocardial ischemia such as chest pain and dyspnea. Their electrocardiogram (ECG) often demonstrates ST depression in association with rapid ventricular rate, which has been termed a stress test equivalent [4,5]. Hence, it is not surprising that looking for CAD or ruling out an acute coronary syndrome (ACS) is a significant part of the clinical burden of managing this patient cohort [5,6].

Cardiac troponins, including cTnI, are the most sensitive and specific biomarkers of myocardial injury, whereby troponin elevation is part of the universal definition of myocardial infarction [7,8]. Cardiac troponins can be elevated in a wide variety of clinical settings including AF, even in the absence of sCAD [9–14]. This has been attributed to myocardial oxygen supply and demand mismatch (type two myocardial infarction) [15]. However, troponin elevation in these settings translates into poorer prognosis and increased mortality [16–19].

Although major society guidelines do not include troponin measurement as a part of the diagnostic workup for AF, approximately 86% of patients presenting with AF will have their cardiac biomarkers tested with approximately 4% of patients with elevated troponin diagnosed with ACS [20–22]. The challenge for physicians treating patients presenting

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with symptomatic AF and an elevated troponin concentration is to astutely judge which patient should be aggressively investigated and treated for ACS caused by significant CAD.

The aim of this study is to determine the reliability of cardiac troponin elevation in diagnosing significant coronary artery stenosis in patients presenting with symptomatic atrial fibrillation. We also aim to investigate other possible predictors of sCAD and cardiac troponin elevation in these patients.

## 2. Methods

### 2.1. Patient selection

We conducted a retrospective case–control study of patients who presented to the emergency department of The Prince Charles Hospital, Brisbane, Australia between January 2006 and January 2014 with a primary diagnosis of AF. This hospital is a 630-bed quaternary, university-affiliated teaching center.

Patients were included if they were ≥18 years of age, presented with cardiac symptoms (chest pain, dyspnea or palpitations), had serial cardiac troponin measurements taken, with an admission twelve-lead ECG result showing AF. Patients required an invasive or non-invasive coronary artery assessment during or within six months of the index hospital admission to be included.

We excluded patients with ST-Elevation Myocardial Infarction (STEMI), AF due to concomitant predisposing illness or asymptomatic AF. Patients with prior cardiac surgery including coronary bypass surgery, underlying complex congenital heart disease, or valvular AF were also excluded.

The sample was identified using the coding system utilized for hospital reimbursement. During the study period, 3548 patients presented with AF. Of these, 2627 did not satisfy the inclusion criteria on review of the patient's imaging results, laboratory data and discharge summaries. After medical charts review, a further 690 patients were excluded due to the absence of cardiac symptoms, and/or no coronary artery testing on or within six months from the index hospital admission. Subsequently, 231 were included in the final study set. Of these 231 patients, 107 had cTnI elevation, and 124 had negative cTnI on serial measurements (Fig. 1).

### 2.2. Data collection

Data was collected through a careful review of patient records using a standardized data collection template. We recorded patient demographics, their presenting symptoms, risk factors for CAD and the CHADS2 stroke risk model scores. Heart rate and degree of ST segment depression were measured from a 12 lead ECG. Left ventricular ejection fraction (EF) and presence of valvular AF were determined from echocardiography results. Laboratory data including two serial troponin measurements on admission and within 6 to 9 h from the initial measurement were collected. We examined the results of coronary angiography or non-invasive cardiac imaging to determine the presence of sCAD.

### 2.3. Definitions

Significant CAD was defined as one or more of the following coronary artery stenosis:

1- ≥70% diameter

2- 50% to 70% diameter stenosis with Fractional Flow Reserve (FFR) confirmed hemodynamic significance

3- 50% to 70% Left Main Coronary Artery (LMCA) disease confirmed by Intravascular Ultrasound (IVUS) to be significant.

This definition is in keeping with The American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines and the Society for Cardiovascular Angiography and Interventions for percutaneous coronary intervention (ACCF/AHA/SCAI) 2011 guidelines [23]. Non-invasive coronary artery disease test results were interpreted by a cardiologist or a radiologist specialized in cardiac imaging. Any reported positive test with a high probability of CAD was followed by gold standard invasive coronary angiography.

AF was classified into the categories of first diagnosed AF, paroxysmal AF, persistent AF, long-standing persistent AF and permanent AF. These categories are in accordance with the 2014 American College of Cardiology/American Heart Association/Heart Rhythm Society (AHA/ACC/HRS) task force on practice guidelines, and the 2010 European Society of Cardiology (ESC) Guidelines [24,25].

Known CAD was defined as prior angiography showing non-significant disease or previous percutaneous coronary intervention. ST-segment depression was defined as ≥1.0-mm horizontal or downsloping depression 0.08 s after the J-point on a 12-lead electrocardiogram [10].

### 2.4. Troponin assay

cTnI testing was performed on Beckman Coulter AccuTnI analyzers (Beckman Coulter, Brea, CA, USA) with 99th percentile cut-off value of 0.040 μg/L.

### 2.5. Statistical analysis

Descriptive statistics were reported as mean (standard deviation (SD)), median (interquartile range (IQR)) or frequency (percent). Univariable analyses were performed to assess the relationship between potential predictors against sCAD and cTnI elevation. Chi-square tests were used for categorical predictors (Fisher's exact test was used when the assumptions of the chi-square test were not met) and one-way ANOVAs for parametric continuous variables (Mann–Whitney U test was used in place of ANOVA for non-parametric data). Those with a p-value less than 0.15 were considered for modeling via binary logistic regression. Backwards elimination was used to obtain the final model.

ROC curve analyses were performed, and Youden Indices calculated to determine a suitable cut-off point of cTnI peak to predict sCAD. Youden Index was defined as the sensitivity + specificity − 1. This ROC analysis was repeated stratified by model covariates. Data analyses were performed using IBM SPSS Statistics for Windows (2013, IBM Corp., Armonk, NY, USA).

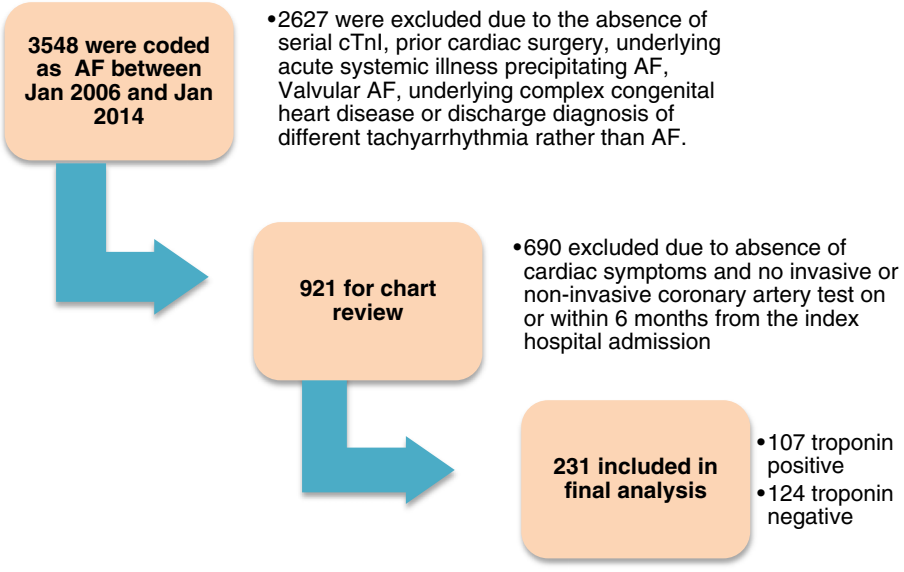


**Fig. 1.** Flow chart for final cohort.