

Clinical profile and angiographic findings among patients with atrial fibrillation presenting for selective coronary angiography

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ABSTRACT

Background: Coronary artery disease is the most common form of cardiovascular disease while Atrial fibrillation is the most common sustained arrhythmia. We set out to investigate the prevalence and clinical profile of patients with atrial fibrillation who present for selective coronary angiography and whether this has an effect on the angiogram findings and the treatment options offered to them. **Methods and Results:** This was a retrospectively collected database of 494 patients presenting for SCAG from 01.11.2010 to 30.11.2010 and 01.04.2010 to 30.04.2010. We collected and analyzed clinical characteristics of patients, their SCAG finding and modes of treatment offered up to discharge. 24.6% of patients had AF. They tended to be older, more commonly women, current or ex-smokers; presented with symptoms of atypical chest pain and were more likely to have a history of congestive heart failure or valvular heart disease. They had a longer hospital stay. Using CHADS-Vasc score, 83.6% were moderate to high risk for CVA. At SCAG, they were more likely to have non-significant coronary artery disease, and hence were more likely to be treated conservatively. **Conclusion:** AF patients presenting for SCAG constitute a unique subset of patients who despite having a higher likelihood of non-significant coronary stenosis are still prone to suffering from poorly-understood and under-appreciated myo-

cardial ischemia.

KEYWORDS

Atrial Fibrillation; Selective Coronary Angiography

1. INTRODUCTION

Each year, cardiovascular disease (CVD) causes over 4.3 million deaths in Europe overall including 1.9 million deaths inside the European Union (EU) [1]. Coronary artery disease is the most common form of cardiovascular disease with a prevalence of 6.9% and 6% among men and women [2]. Each year, two million Europeans die of CAD [3]. Selective coronary angiography is considered the golden standard for detection of coronary artery disease, especially among patients with acute coronary syndromes [4,5]. Atrial fibrillation (AF) is the most common sustained arrhythmia in humans affecting 1% - 2% of the population worldwide. Inside Europe and the United States, this translates to 3 and 6 million people respectively [6-9]. In the Renfrew survey [10], at a 20-year follow-up, 89% of women and 66% of men who had atrial fibrillation also developed a cardiovascular event. Atrial fibrillation was an independent predictor of cardiovascular events among women (rate ratio [RR] = 3.0; 95% confidence interval [CI]: 2.1 - 4.2), and men (1.8; 95% CI: 1.3 - 2.5).

We set out to investigate the prevalence of atrial fibrillation among patients presenting for SCAG at present days. We looked at their clinical profile and investigate

whether atrial fibrillation was associated with their outcome of SCAG and how this affected the mode of treatment.

2. METHODS

This is a retrospectively collected database of patients presenting for SCAG to the National Institute for heart and vascular disease in Bratislava, Slovak Republic in the month of November, 2010 (01.11.2010-30.11.2010). To avoid random bias we randomly chose to collect data from another month of April (01.04.2010-30.04.2010). In November, 231 patients had SCAG and were included. In April, 263 patients presented for SCAG were enrolled.

Medical records of the patients was accessed and data about past medical and surgical history, baseline characteristics, indication for SCAG, results of SCAG, and the resulting form of therapy offered (Optimal Medical Therapy, Percutaneous Coronary Intervention, Coronary Artery Bypass and/or Valve replacement) were collected. Data about medications on discharge were also collected.

Atrial fibrillation (AF) was considered present by history, or if documented on Holter study or if it was present on ECG during hospital stay. Indications for SCAG were divided into seven categories: SCAG for a patient with established Acute Coronary Syndrome; SCAG for a patient with typical symptoms of angina; SCAG for a patient with atypical chest pain or shortness of breath or palpitations; SCAG for a patient with a Positive stress test; SCAG done for purposes of preoperative evaluation and possible treatment; SCAG done in context of workup of documented ventricular tachycardia or unexplained syncope.

Results from SCAG were recorded as “non-significant coronary disease”, “single vessel disease”, “two vessel disease”, and triple vessel disease, triple vessel disease with involvement of left main.

Mode of treatment was summarized into Optimized medical treatment (OMT), Coronary artery bypass grafting and valve replacement or repair, percutaneous coronary intervention treatment (PCI). Medications upon discharge were recorded into groups (ACE inhibitors, beta blockers, calcium channel blockers, statins, etc).

3. STATISTICAL ANALYSIS

All continuous variables are expressed as means \pm SD. The mean differences for continuous variables were compared using the Student *t* test (two-tailed) or analysis of variance (in case of multiple comparisons). Categorical variables were compared using a chi-square statistic. A *p* value 0.05 was considered significant; where appropriate, 95% confidence intervals were employed. Cox proportional hazards analysis was applied to determine

the independent prognostic value of clinical, historical, and lab parameters. Selection of variables for consideration for entry was based on both univariate statistical significance and clinical judgment. The threshold for entry of variables into the final model was $p = 0.05$.

4. RESULTS

4.1. Patient Characteristics

One hundred and twenty two patients fulfilled our criteria for atrial fibrillation. This constituted 24.6% of study population. AF patients tended to be older, more commonly women, current or ex-smokers (**Table 1**); presented with symptoms of atypical chest pain or shortness of breath or palpitation; but also syncope or other documented arrhythmia (**Figure 1**). They were more likely to have history of congestive heart failure and valvular heart disease. They had a longer hospital stay. AF patients tended to have a higher prevalence of valvular heart disease and less wall motion abnormality (**Figure 2**). Using the CHADS-Vasc score, only 3.3% were at low risk for stroke, 13.1% were at intermediate risk, and 83.6% were at moderate to high risk. At SCAG, they were more likely to have non-significant coronary disease (**Figure 3**), and more likely to be treated conservatively (OMT) (**Figure 4**). They were less often to be prescribed clopidogrel upon discharge; more often had warfarin, digoxin, calcium channel blockers and amiodarone prescribed.

There were no significant differences between the laboratory values or the hemodynamic parameters between the 2 groups.

4.2. Univariate and Multivariate Analysis

For all the patients, factors significantly associated with a finding of non-significant coronary disease at univariate analysis were: presence or history of atrial fibrillation, female gender, history of congestive heart failure, indication for SCAG as part of preoperative evaluation for valve surgery (**Table 2**).

At multivariate analysis; SCAG for preoperative evaluation, atrial fibrillation, female gender; were all positively associated with non-significant coronary artery disease findings at SCAG. On the other hand, the presence of diabetes, history of CAD, presenting with acute coronary syndrome; all were negatively associated with a finding of non-significant CAD (**Table 3**).

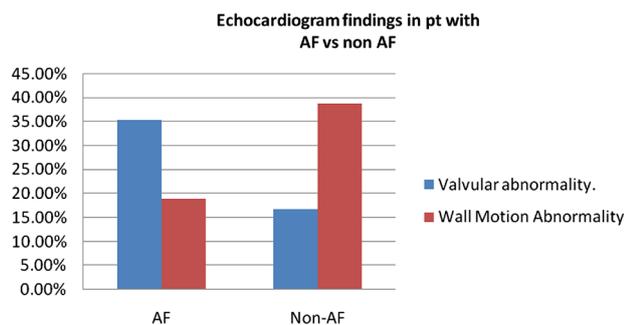
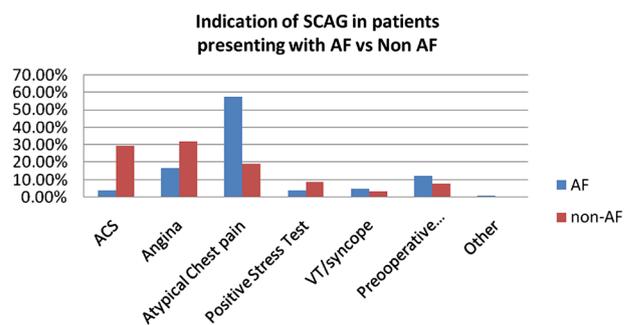
5. DISCUSSION

5.1. Prevalence of AF

Atrial fibrillation commonly accompanies other heart diseases [11]. Frequently, it presents as nonspecific complaints and symptoms. In a previous registry [12], the sensitivity and positive predictive value of patient-re-

Table 1. Baseline characteristics of patients enrolled in this analysis by presence or absence of atrial fibrillation.

	AF (122)	n-AF (372)	p value
	Mean (95%CI)	Mean (95%CI)	
Age	65.5 (62 - 68.8)	60 (58 - 61.8)	0.041
Males	72 (59%)	266 (71.5%)	0.013
Females	50 (41%)	106 (28.5%)	
Length of hospitalization	5.2 (4.1 - 6.4)	4.5 (3.9 - 4.1)	0.006
BMI	28.5 (26.1 - 30.8)	29.1 (28.1 - 30.1)	0.921
HTN	99 (81%)	294 (79%)	0.698
DM	36 (29.5%)	105 (28.2%)	0.818
Metabolic syndrome	18 (14.8%)	48 (12.9%)	0.646
Dyslipidemia	82 (67.2%)	255 (68.5%)	0.823
Known IHD	36 (29.5%)	131 (35.2%)	0.271
Previous PCI	7 (5.7%)	52 (14%)	0.015
Previous CABG/valve	7 (5.7%)	27 (7.3%)	0.827
Previous vascular surgery	1 (0.8%)	8 (2.2%)	0.516
Family history CAD	1 (0.8%)	3 (0.8%)	1.000
HOCM	1 (0.3%)	1 (0.8%)	0.433
Valvular heart disease	32 (26.2%)	52 (14%)	0.003
Other congenital heart disease	2 (1.6%)	7 (1.9%)	1.000
CHF	47 (38.5%)	64 (17.2%)	0.001
Rheumatic heart disease	11 (9%)	7 (1.9%)	0.001
Old PTMCA	6 (4.9%)	1 (0.3%)	0.001
CVA	3 (2.5%)	9 (2.4%)	1.000
Chronic renal Failure	11 (9%)	24 (6.5%)	0.318
Anemia	10 (8.2%)	25 (6.7%)	0.548
COPD	19 (15.6%)	83 (22.3%)	0.546
Current or previous smoker	37 (30.3%)	147 (39.6%)	0.013
Cancer	3 (2.5%)	14 (3.8%)	0.775
Other co-morbidities	14 (11.5%)	44 (11.8%)	1.000
Echo performed	118 (96.7%)	364 (97.8%)	0.502
Stress testing/CT angio	6 (4.7%)	35 (9.1%)	0.093
LV Ejection Fraction	49.5 (43.1 - 55.8)	52.1 (49.5 - 54.6)	0.660
Moderate/severe diastolic dysfunction	26 (21.3%)	54 (14.5%)	0.287
Moderate/severe valvular abnormality	43 (35.2%)	62 (16.7%)	0.001
Wall motion abnormality	23 (18.9%)	144 (38.7%)	0.001

**Figure 1.** Indications of SCAG in patients presenting with AF vs non AF.**Figure 2.** Echocardiographic findings in AF vs. non AF presenting for CAG.

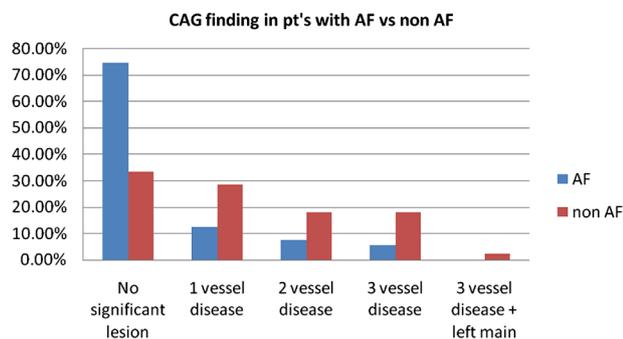


Figure 3. CAG findings in patients with AF vs. non AF.

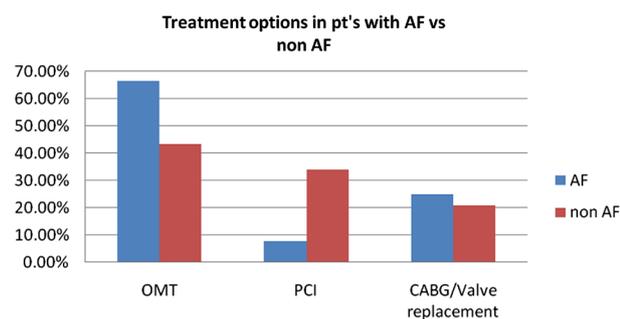


Figure 4. Treatment options offered to patients with AF vs non AF.

Table 2. Predictors for non-significant SCAG findings in univariate analysis in patients enrolled in this analysis by presence or absence of atrial fibrillation. CAD = coronary artery disease. CHF = congestive heart failure.

	AF	n-AF	p value
Atrial fibrillation	73.8%	33.1%	0.001
Previously known CAD	16%	46.8%	0.001
Preoperative evaluation for			
Valve surgery	70%	36%	0.001
Female gender	57%	43%	0.001
Multiple other			
Co-morbid conditions	60%	40%	0.004
Diabetes Mellitus	33%	47%	0.004
CHF	43%	61%	0.001
Presentation with ACS/Angina			

Table 3. Multivariate regression analysis for predictors of non-significant SCAG in patients enrolled in this analysis by presence or absence of atrial fibrillation.

	Odds ratio	p value
Preoperative evaluation for Valve surgery	4.1 (2.6 - 6.5)	0.005
Atrial fibrillation	2.5 (1.81 - 3.46)	0.001
Female gender	2.1 (1.85 - 3.93)	0.001
Multiple other co-morbid conditions	2.2 (1.3 - 3.9)	0.009
Diabetes Mellitus	0.6 (0.38 - 0.85)	0.012
Previously known CAD	0.2 (0.14 - 0.34)	0.011
Presentation with ACS/angina	0.2 (0.15 - 0.31)	0.001

ported symptoms for atrial fibrillation was merely 19% and 21%, while 74% of patients who had episodes of paroxysmal AF documented by their pacemakers, yet had no complaints. Hence the real prevalence of AF is likely to be under appreciated [13]. The prevalence of atrial fibrillation among patients with proven coronary artery is thought to be low; 0.2% - 5% [14-19]. AF Patients may present with chest pain, which can be accompanied by transient ischemic-type ST-segment changes with marginally elevated cardiac markers, thus mimicking symptoms of coronary artery disease [20]. Little is known about the prevalence of atrial fibrillation among specific subset of patients presenting for selective coronary angiography in modern era. In 1976, among 841 patients presenting for SCAG, AF was present in 5.3% [15]. It was mostly associated with valvular heart disease and cardiomyopathy; while only 1 patient showed significant coronary artery disease. More recently in another survey in 1993, among 703 patients presenting for SCAG, 10.2% had concomitant AF. Again these patients had more often valvular heart disease and cardiomyopathy, with non-significant CAD [18]. By far the largest group presenting for SCAG and investigated for AF was reported in 1999; out of 3220 patients, AF was present in 2.3% [19]. They were more likely to have history of heart failure, triple vessel coronary artery disease and mitral valve insufficiency. In the AFFIRM Study [21], 38% of their study population had Coronary artery disease. Another trial by Kravec *et al.* reported an overall incidence of coronary artery disease in patients presenting with AF to be 34% [22]. For the sake of comparison, we could not locate any previously published data documenting prevalence of AF among Slovakian patients presenting for SCAG. However, in this study we note a high prevalence of AF among SCAG patients (24.5%). This may be attributed to a high prevalence of CHF and valvular heart disease among our patient population. Twenty percent of patients were indicated for SCAG as preoperative evaluation for valve surgery; 22.5% have a history of CHF, and 28.5% were indicated for SCAG due to symptoms that could be related to congestive heart failure such as atypical chest pain, worsening exercise tolerance and increased shortness of breath.

5.2. Factors Associated with AF

Atrial Fibrillation patients were older ($p = 0.041$) and more likely female (41% vs. 28.5% non-atrial fibrillation patients). This is contrast with the study group of Lokshyn *et al* [19], who were mostly men (71%). The mean age of our AF patients was 65.5 years; which is in concordance with the findings from this other groups [19]. Generally it has been well described that the prevalence of AF doubles with each advancing decade of age, from

0.5% at age 50 - 59 years to almost 9% at age 80 - 89 years [23]. AF patients had more often history of congestive heart failure and valvular heart disease, this is in agreement with most earlier reports [19,24,25]. Heart failure may contribute to the pathogenesis of atrial fibrillation, with electromechanical feedback and neurohumoral activation playing an important mediating role [26]. Only 51% of all patients presented with documented acute coronary syndrome and angina.

5.3. AF and Coronary Ischemia

It is conceivable that AF patients are over indicated for SCAG due to their nonspecific symptoms and the similar pool of risk factors to those with CAD (e.g. hypertension is a risk factor for both) [27]. The other possibility is that these patients suffer from ischemia despite the negative findings on SCAG [28,29]. Previous animal studies have documented a positive association between AF and myocardial ischemia. In dogs, artificially induced AF causes abnormal myocardial blood flow due to coronary vasoconstriction that is mediated by sympathetic activation of coronary alpha receptors [30]. In humans, AF has been known to reduce resting and hyperemic Myocardial Blood Flow (MBF), while coronary vascular resistance (CVR) increases [28]. Other studies indicated that acute AF causes a decline in diastolic coronary flow and promotes sub-endocardial ischemia [31]. Similar changes have been shown among AF patients with hypertrophic cardiomyopathy [32], and dilated cardiomyopathy [33], proving that AF may be a causative factor and not merely a bystander. AF patients are more likely to have positive SPECT finding for ischemia, yet have a lower yield of significant CAD by SCAG (15% for AF patients vs. 67% in n-AF; $p = 0.006$) [34].

This begs the question as to which is it the correct strategy for identifying Coronary Artery Disease in AF patients?

Furthermore; knowing that AF patients with false positive findings on scintigraphy still suffer a higher prevalence of cardiac death [35], should physicians become more aggressive at diagnosing and treating intermediate lesions found in AF patients (50% - 70% stenosis lesions)?

6. CONCLUSION

AF patients presenting for SCAG constitute a unique subset of patients who despite having a higher likelihood of non-significant coronary stenosis are still prone to suffering from poorly explained and under-appreciated myocardial ischemia. Newer pathways are needed for further risk stratification and treatment of this growing subset of patients.

STUDY LIMITATIONS

There are numerous sources of bias. First this is a retrospectively collected database of patients who elected for SCAG in only one tertiary institution in Europe. The definition of atrial fibrillation has been collected from chart documentations and it has not been possible to verify it for these patients. Furthermore AF could not be stratified into various types (e.g. paroxysmal, persistent, and permanent). It is possible that the effect of AF is gradual *i.e.* more so for permanent AF patients versus patient with paroxysmal AF. This also needs further studying in prospectively collected data. Any conclusions drawn are clinical hypothesis generating and need further examination in a randomized trial setting; involving multiple centers. To date, scarce data have been published about this subject.

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APPENDIX

What's New?

1) Prevalence of AF in patients presenting for Selective Coronary angiogram was 24.6%.

2) AF was more prevalent among patients presenting for coronary angiogram with a history of congestive heart disease and valvular heart disease.

3) Majority of patients with AF had non-clinically significant coronary artery disease on coronary angiogram and required conservative medical management only.

4) Echocardiogram studies showed patients with AF to have more valvular heart disease and less regional wall motion abnormalities.

5) It is feasible that AF patients have myocardial ischemia; though not solely related to coronary stenosis but to previously documented, accentuated sympathetic tone causing enhanced coronary vasoconstriction and altered autonomic function; among other issues. This requires further prospective studying.

ABBREVIATIONS

CVD: Cardiovascular Disease

EU: European Union

AF: Atrial Fibrillation

RR: Rate Ratio

CI: Confidence Interval

SCAG: Selective Coronary Angiography

OMT: Optimized Medical Treatment

PCI: Percutaneous Coronary Intervention

CAD: Coronary Artery Disease

MBF: Myocardial Blood Flow