Transient ST-Segment Depression During Paroxysms of Atrial Fibrillation in Otherwise Normal Individuals: Relation With Underlying Coronary Artery Disease

To the Editor: Ischemic ST-segment changes during atrial fibrillation (AF) are a common electrocardiographic finding in patients with acute coronary syndromes (1) or structural heart disease. However, not uncommonly, subjects free of apparent heart disease present with ischemic ST-segment depression during an episode of AF, out of the setting of an acute cardiopulmonary syndrome. Although clinicians often consider this clinical presentation to be a "positive stress-test equivalent," its relationship with occult coronary artery disease (CAD) is currently unknown. In this prospective study we estimated, by coronary angiography, the prevalence of CAD in otherwise "healthy" individuals who exhibit ischemic changes during paroxysms of AF but not during sinus rhythm (SR). Furthermore, we evaluated the accuracy of 3 commonly used myocardial stress tests (treadmill electrocardiographic stress-test [TST], thallium-201 myocardial perfusion scintigraphy [MPS], and myocardial contrast dobutamine stress echocardiography [MCDSE]) to diagnose CAD in these patients.

Between January 2001 and July 2005, we screened more than 2,500 patients older than 40 years who presented to the emergency department with AF of recent onset (paroxysmal AF or persistent AF with duration <30 days) and concomitant ischemic ST-segment depression. Ischemic ST-segment changes were defined according to exercise testing standards (2). Patients with a history of CAD, other cardiac disorders, or severe comorbidities were excluded from the study. Those who had biochemical and/or echocardiographic findings indicating an acute cardiopulmonary event or structural heart disorder were also excluded (Fig. 1). Hospital admission was suggested to the remaining 407 patients who comprised the target group of our study. Conversion to SR was attempted in all admitted patients, either pharmaceutically or by synchronized transthoracic cardioversion, unless AF terminated spontaneously. Cardioverted patients with persistent ST-segment depression of more than 48 h and patients in whom cardioversion was unsuccessful were excluded (Fig. 1).

Patients who fulfilled all entry criteria and consented to the study protocol were evaluated both by coronary angiography and by all 3 stress tests (TST, MPS, and MCDSE) in a random order. Obstructive CAD was defined as a stenosis ≥70% in at least 1 epicardial coronary artery. All stress tests were performed according to standard protocols (2–4), within a period of 2 weeks to 3 months after SR had been restored. Patients unable to exercise underwent only dipyridamole MPS and MCDSE. The physicians who performed the diagnostic tests were blinded to the findings of other examinations. The study protocol was approved by our institutional research ethics committee.

Obstructive CAD was documented by angiography in 27 (15 men, 12 women) of the 83 patients who completed the study (Fig. 1), corresponding to a prevalence of 32.5%. Nineteen of these patients had 1-vessel disease (9 patients had stenosis of the right coronary artery, 6 of the circumflex, and 4 of the left anterior descending artery), 5 patients had 2-vessel disease, and 3 patients had 3-vessel disease. One patient with 2-vessel disease also had a 70% stenosis of the left main coronary artery.

Patients with CAD were marginally older (67.4 ± 7.6 years vs. 63.8 ± 8.5 years, p = 0.06 by Student t test) and had a higher prevalence of smoking (59% vs. 23%, p = 0.001 by chi-square test) compared to patients without CAD. The male/female ratio (15/12 vs. 27/29), the prevalence of other classical risk factors, and the mean heart rate at presentation (131 ± 17 beats/min vs. 129 ± 19 beats/min) did not differ between the 2 groups (all p = NS).

Among the 24 patients with CAD who underwent all 3 stress tests (3 patients with CAD were unable to exercise), 15 patients had positive results on all 3 tests, 7 patients had 2 positive tests, and in 1 patient, only MCDSE was positive. Interestingly, all 3 tests were negative in 1 patient with a stenosis of the marginal branch of the circumflex artery.

Overall, TST had low sensitivity and specificity for CAD diagnosis. Myocardial perfusion scintigraphy and MCDSE had a higher sensitivity that corresponded to a relatively high negative predictive value (Table 1). Myocardial perfusion scintigraphy and MCDSE misdiagnosed 4 and 3 patients with CAD, respectively. All these patients had 1-vessel disease confined to relatively small branches (branch of the right coronary artery, 6 of the circumflex, and 4 of the left anterior descending artery), 5 patients had 2-vessel disease, and 3 patients had 3-vessel disease. One patient with 2-vessel disease also had a 70% stenosis of the left main coronary artery.

This is the first prospective study to investigate the prevalence of occult CAD in “apparently healthy” individuals who present with ischemic type ST-segment depression during an episode of AF that is not related to an acute cardiopulmonary event. In clinical practice, it is common for such patients to proceed to coronary arteriography, because: 1) this presentation is considered to be a “positive stress test equivalent,” and 2) there are no data on the diagnostic accuracy of the available noninvasive diagnostic tests in this population. Current guidelines recommend that patients with
AF and suspected myocardial ischemia should undergo TST (5). However, there are no specific recommendations for patients with characteristics similar to our study subjects. These patients are not uncommon in everyday practice, and their proper management is often a challenge. Our findings shed some light on this issue and indicate that, in this setting, ST-segment changes are not consistently associated with the presence of obstructive CAD, given that approximately only 1 of 3 patients had angiographically significant coronary lesions. Also, multivessel disease was not frequent in those patients with CAD. In contrast, MPS had a high rate of false positive defects and thus a low specificity for CAD diagnosis. Atrial fibrillation might alter membrane function in vascular endothelial cells and cardiomyocytes, and this might have accounted, at least partly, for the high rate of false positive MPS tests in our population. Accordingly, it seems reasonable for patients with the aforementioned specific clinical presentation to be risk stratified by a noninvasive stress test, preferably MCDSE, rather than proceeding directly to coronary angiography.

We should acknowledge a limitation of this study. Most patients visited the hospital because of AF-related symptoms (palpitations, chest discomfort, dyspnea). Among the eligible patients, only 1 of 5 (83 of 407) completed the study. So, it is possible that the prevalence of CAD in our population has been overestimated, because of inclusion bias (i.e., patients with more severe symptoms might have had a higher probability to accept enrolment in the study).

In conclusion, in a population of patients without a history of cardiovascular disease, we found that there is no strong association between transient ischemic type ST-segment depression during paroxysms of AF and underlying occult CAD.

*Aristides Androulakis, MD, FESC
Cardiology Department
Hippokration Hospital
30 Dodekanisou Str., Vrilissia, 152 35
Athens
Greece
E-mail: antaris@otenet.gr

Konstantinos A. Aznaouridis, MD
Constantina J. Aggeli, MD, FESC
Georgios N. Roussakis, MD
Andreas P. Michaelides, MD, FESC, FACC
Athanasis N. Kartalis, MD
Pavlos N. Stougianos, MD
Polychronis E. Dilaveris, MD, FESC
Platon I. Misovoulous, MD
Christodoulos I. Stefanadis, MD, FESC, FACC
Ioannis E. Kalikazaros, MD, FESC, FACC

doi:10.1016/j.jacc.2007.08.005

REFERENCES

<table>
<thead>
<tr>
<th>Table 1</th>
<th>Diagnostic Performance of Noninvasive Stress Tests for Predicting CAD</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Treadmill Stress Test*</td>
</tr>
<tr>
<td>Patients with CAD (+/- for ischemia) (n = 27)</td>
<td>18/6</td>
</tr>
<tr>
<td>Patients without CAD (+/- for ischemia) (n = 56)</td>
<td>21/27</td>
</tr>
<tr>
<td>Sensitivity, % (95% CI)</td>
<td>75.0 (53.3–90.2)</td>
</tr>
<tr>
<td>Specificity, % (95% CI)</td>
<td>56.3 (41.2–70.5)</td>
</tr>
<tr>
<td>PPV, % (95% CI)</td>
<td>46.2 (30.1–62.8)</td>
</tr>
<tr>
<td>NPV, % (95% CI)</td>
<td>81.8 (65.4–93.0)</td>
</tr>
</tbody>
</table>

The 95% confidence intervals (CIs) were calculated from the binomial distribution. *For treadmill stress test, total n = 72 (11 patients were unable to exercise). CAD = coronary artery disease; NPV = negative predictive value; PPV = positive predictive value.


---

**Letters to the Editor**

**Coenzyme Q10 in Statin-Associated Myopathy**

The excellent review by Macroff and Thompson titled “The role of coenzyme Q10 on statin-associated myopathy” (1) concludes that insufficient evidence exists for supplementation to treat or prevent myopathy.

However, the authors recommend its use “if only via placebo effect.” Should we not first be certain that statin-induced inhibition of the farnesyl (and dolichol) pathways does not contribute to the many pleiotropic benefits of statins before we attempt to “correct” them?

*Harvey Wolinsky, MD, PhD, FACC
*Clinical Professor of Medicine
Mt. Sinai Medical Center
Department of Medicine
49 East 96th Street, Suite 1A
New York, New York 10128
E-mail: HWolinskymd@aol.com

REFERENCE


---

**Reply**

Dr. Wolinsky raises an interesting issue. Statins block the rate-limiting enzyme in the mevalonate pathway reducing cholesterol production, but also reduce production of farnesyl and geranylgeranyl pyrophosphate. These molecules participate in post-translational modification or prenylation of the Ras superfamily guanosine triphosphatases or small G proteins. Small G proteins are involved in cell signaling and proliferation. Statin inhibition of these G proteins decreases vascular smooth muscle hypertrophy and proliferation, improves endothelial function, and reduces angiotensin I receptor expression (1). It may also explain the statin antiarrhythmic effect in atrial fibrillation (2).

Coenzyme Q10 (Q10) supplementation should not affect small G protein production since Q10 is not involved in the G protein prenylation process. Furthermore, we recommended that Q10 supplementation be “tested” or “trialed” (3) only in statin myalgic patients to allow ongoing statin treatment.

Leo Marcoff, MD
*Paul D. Thompson, MD, FACC
*Hartford Hospital
Cardiology
80 Seymour Street
P.O. Box 5037
Hartford, Connecticut 06102-8000
Email: pthomps@harthosp.org

doi:10.1016/j.jacc.2007.08.009

REFERENCES


---

**Can Critically Short Telomeres Cause Functional Exhaustion of Progenitor Cells in Postinfarction Heart Failure?**

With great interest we read the article of Kissel et al. (1) on the selective functional exhaustion of progenitor cells in patients with ischemic cardiomyopathy (ICM) compared with nonischemic dilated cardiomyopathy. As stated by the authors, obviously this clinical study cannot disclose the potential mechanisms underlying the functional impairment of progenitor cells. However, circumstantial evidence for a very reasonable explanation for the selective exhaustion of (progenitor) cells in ICM could have been easily obtained. Cells with telomeres reaching a critical length become genomically unstable, become apoptotic, or enter replicative senes-

---