Oral Anticoagulation for Atrial Fibrillation After ST-Elevation Myocardial Infarction
New Evidence to Guide Clinical Practice

Frederick G. Kushner, MD; Elliott M. Antman, MD

Atrial fibrillation (AF) in the setting of ST-segment elevation myocardial infarction (STEMI) is estimated to occur in up to 20% of patients, depending on the population studied.1-3 The development of AF during hospitalization for STEMI is associated with a significant increase in both in-hospital and short-term mortality (odds ratio, 1.4 to 1.98).3 Predictors of developing AF include increased age, magnitude of creatine kinase elevation, Killip class, anterior location of infarction, left ventricular dysfunction, and both hypertension and hypotension. Those patients who develop AF during their hospitalization have a worse prognosis than those who present with AF on admission.1 Even in the fibrinolytic era, stroke rates are increased in STEMI patients with AF.4

Clinical trials have addressed the efficacy of oral anticoagulation (OAC) in patients with AF but without STEMI,3 and other studies have addressed the efficacy of OAC in post-STEMI patients. There are, however, no randomized controlled trials of OAC with or without antiplatelet therapy specifically in the cohort that includes patients with both STEMI and AF. In the Warfarin, Aspirin, Reinfarction Study (WARIS II) of 3630 MI patients, high-intensity warfarin (international normalized ratio [INR], 2.8 to 4.2) was compared with medium-intensity warfarin (INR, 2 to 2.5) plus aspirin (ASA) 75 mg and with ASA 160 mg alone in patients <75 years of age.6 There was a 29% reduction in the rate of the composite end point of death, nonfatal reinfarction, or thromboembolic stroke in the combined group and a 19% reduction in the high-intensity group versus ASA alone group. The benefit, however, resulted from a reduction in nonfatal myocardial infarction (MI) and nonfatal stroke. The WARIS II investigators did not report data specifically on patients with AF alone.6

The ACC/AHA Guidelines on the Management of STEMI published recommendations on OAC with AF and other strong indications for anticoagulation.3 Formulation of the recommendations had to account for whether a patient underwent percutaneous coronary intervention and had a stent implanted, as well as for the possibility that the patient may have had a history of ASA allergy (Figure).3 On the basis of available data, warfarin (INR, 2.0 to 3.0) was recommended for post-STEMI patients with persistent AF (Class I, level of evidence A). A Class I, level of evidence B recommendation was given for warfarin (INR 2.5 to 3.5) or warfarin (INR 2 to 3) used in combination with ASA (75 to 162 mg), with no stent implanted, and with indications that include AF for anticoagulation. A Class IIa, level B recommendation was given for use of warfarin in paroxysmal AF. A Class IIb, level C recommendation was given for warfarin (INR 2.0 to 3.0) in combination with ASA (75 to 162 mg) and clopidogrel (75 mg) in patients with a stent implanted and concomitant indications that include AF for anticoagulation. The consensus of the STEMI Writing Committee was that clopidogrel be discontinued 1 month after implantation of a bare metal stent or several months after a drug-eluting stent (3 months for sirolimus and 6 months for paclitaxel) because of the potential increased risk of bleeding. ASA and warfarin could then be continued long term in patients with AF. It was noted by the STEMI Writing Committee that the indications for OAC were controversial and evolving. The ACC/AHA/ESC Guidelines for the Management of Patients With Atrial Fibrillation recommended OAC with optional low-dose ASA in patients with AF who are ≥60 years of age and who have either coronary artery disease or diabetes mellitus.7 The ESC, however, stated in its guidelines for STEMI that although patients with AF might benefit from OAC, definitive studies were lacking; therefore, no firm recommendations were made.8 To address these issues, Stenestrand et al9 performed a prospective cohort study that used data from the Register of Information and Knowledge about Swedish Heart Intensive care Admission (RIKS-HIA) on patients who were admitted to Swedish coronary care units in 72 hospitals from 1995 to 2002. The study tracked 6182 patients who were discharged alive with diagnoses of AF and MI and followed up short- and long-term (1 year) outcomes for those patients. The registry tracked 100 variables, and no patients were excluded on the basis of inclusion or exclusion criteria. Although the study was nonrandomized, advanced statistical methods and a robust database were used to minimize potential sources of bias. Only 29% of the patients (1848) discharged alive with AF and MI received OAC; 60% were given ASA and/or thienopyridines, and 11% received neither treatment. ASA and/or other antiplatelet therapy was given concomitantly to
26% of the OAC group. The AF group that received OAC was significantly younger; had less chronic obstructive pulmonary disease, cancer, or dementia; but more frequently had prior stroke and coronary revascularization. Reperfusion therapy was given to 20% of each group, and percutaneous coronary intervention occurred in only 5% of each group. Angiotensin-converting enzyme inhibitors, β-blockers, digitals, and lipid-lowering drugs were given to significantly more patients discharged with OAC. The 11% that received no therapy were removed from the analysis. Using statistical regression analysis and adjusting for propensity scores, 1-year survival was significantly better in the OAC group, with a relative risk of 0.73 (95% confidence interval, 0.62 to 0.86; \(P \leq 0.01\)) and an adjusted absolute risk reduction of 7%.

The bulk of the difference was accounted for increased new MI or stroke (ischemic and hemorrhagic) in the antiplatelet group. Bleeding complications were similarly low in both groups. The combination of OAC and ASA appeared to have a benefit similar to that of the OAC group over the antiplatelet group.

This study appears to support the recommendations of the ACC/AHA STEMI Guidelines in that AF in the setting of STEMI should be treated with OAC. It is gratifying that not only was OAC with or without antiplatelet therapy superior to antiplatelet therapy alone but also the risk of fatal and nonfatal bleeding (a major concern for the STEMI Guidelines Writing Committee) was surprisingly low in the OAC groups (see Table 4 of Stenestrand et al). It is also recommended that clinicians prescribe proton pump inhibitors for patients who have a history of gastrointestinal bleeding.

Even after this excellent report from the RIKS-HIA registry, many unanswered questions remain. Given the results of Clopidogrel as Adjunctive Reperfusion Therapy (CLARITY)-TIMI 28, 11 what role will clopidogrel play in antithrombotic therapy for patients who receive fibrinolytic therapy for STEMI and who are in AF? How should we treat patients who have received drug-eluting stents for STEMI and have persistent or transient AF? Should the treatment algorithm be the same for NSTEMI and STEMI patients? In a routine practice outside the setting of a well-organized registry, what will be the discontinuation rate of OAC and the hemorrhagic complication rate when patients are potentially on warfarin, aspirin, and clopidogrel simultaneously and may have been treated with glycoprotein IIb/IIIa inhibitors and drug-eluting stents? What, if any, will be the role of the new oral antithrombin inhibitors?

Although clinicians confront on a daily basis the questions posed above, it is important to be responsive to evolving data on the importance of OAC in AF. The RIKS-HIA report lends support to the practice recommendations from the ACC/AHA STEMI Guidelines (Figure), but it can be argued that the level of evidence has now moved beyond consensus opinion alone.

**Long-term antithrombotic therapy at hospital discharge after STEMI.** Clopidogrel is preferred over warfarin because of increased risk of bleeding and low patient compliance in warfarin trials. †For 12 months. ‡Discontinue clopidogrel 1 month after implantation of a bare metal stent or several months after implantation of a drug-eluting stent (3 months after sirolimus and 6 months after paclitaxel) because of the potential increased risk of bleeding with warfarin and 2 antiplatelet agents. Continue aspirin and warfarin long term if warfarin is indicated for other reasons such as AF, left ventricular thrombus, cerebral emboli, or extensive regional wall motion abnormality. §An INR of 2.0 to 3.0 is acceptable with tight control, but the lower end of this range is preferable. The combination of antiplatelet therapy and warfarin may be considered in patients <75 years of age with low bleeding risk who can be monitored reliably. LOE indicates level of evidence. Reproduced with permission from the ACC/AHA STEMI Guidelines. 3

**References**


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