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Clinical Guide - Post MI (Reviewed 2006)

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Background

Thrombosis plays a major role in ischemic heart disease. Patients who have sustained an acute myocardial infarction are at increased risk of developing vascular events such as sudden death, recurrence of infarction and thromboembolic stroke. The results of recent clinical studies indicate that antithrombotic therapy significantly reduces the number of vascular events in these patients. The time course of anticoagulation or antiplatelet therapy varies whether the patient has received thrombolysis or not. The antithrombotic therapy during the hospital phase of MI is beyond the scope of this guideline.

Epidemiology

Following the recovery of an acute MI, patients remain at increased risk of sustaining subsequent thromboembolic complications or death for many years.

The risk of having a recurrent MI is approximately 15-20 % in the 2 to 3 years following a myocardial infarction.

The risk of stroke ranges generally from 1% to 3% but in some patients may be as high as 6% per year. The risk increases mainly with the extent of left ventricular dysfunction and with presence of atrial fibrillation.

Rationale for Antithrombotic Therapy

Thrombogenesis ⇒ Treatment	
Vascular injury ⇒	Reduce risk factors
Platelet activation ⇒	Platelet inhibition: ASA and/or Clopidogrel
Thrombin generation ⇒	Anticoagulation: heparin/warfarin Direct thrombin inhibitors
Fibrin formation ⇒	Thrombolysis: IV Fibrinolytic drugs

Anticoagulants vs Placebo post-MI (without risk stratification)

Three trials (Sixty Plus reinfarction studies, WARIS and ASPECT) comparing placebo with oral anticoagulants have yielded greater risk reductions of stroke and reinfarction but the mortality reduction was similar. These studies targeted an INR between 2.7 to 4.5 (Sixty +) or between 2.8 to 4.8 (WARIS and ASPECT): risk stratification in those two last trials was not detailed.

Antiplatelets or Oral anticoagulants (without risk stratification)

A comprehensive meta-analysis published in 1999 by Dr Anand and Yusuf reviewed the available data up to 1998 concerning patients after an acute MI (STEMI and non-STEMI) or after CABG. Since that time, 4 major studies

have added to the gathered evidence and have led to a joint 2003 AHA/ACC Scientific Statement on Warfarin therapy under the guidance of Doctors Hirsh, Fuster, Ansell and Halperin. The recommendations pertaining to myocardial infarction can be summarized as follows:

* High-intensity oral anticoagulation (INR 3.0 to 4.0) is more effective than aspirin but is associated with more bleeding
* The combination of aspirin and moderate-intensity warfarin (INR 2.0 to 3.0) is more effective than aspirin but is associated with a greater risk of bleeding
* The combination of aspirin and moderate intensity warfarin (INR 2.0 to 3.0) is as effective as high intensity warfarin and is associated with a similar risk of bleeding
* The contemporary trials have not addressed the effectiveness of moderate-intensity warfarin (INR 2.0 to 3.0) and in the absence of direct evidence, it cannot be assumed that moderate-intensity warfarin is any more effective than aspirin in preventing death or reinfarction
* There is no evidence that the combination of aspirin and low-intensity warfarin (INR 2.0) is more effective than aspirin alone despite the fact that the combination produces more bleeding

Risk Stratification and Treatment Strategy

Highest risk of embolization:

* Persistent atrial fibrillation
* LV thrombus
* Previous systemic or pulmonary embolism

Warfarin therapy at INR 2.0-3.0 (target 2.5) for at least 3 months or long term (AF) Class I AHA recommendation

High risk of embolization:

* Extensive wall motion abnormalities (Class IIa AHA recommendation)
* Paroxysmal AF (Class IIa AHA recommendation)
* Severe LV systolic dysfunction with or without CHF: evidence less well established (Class IIb AHA recommendation)

Warfarin therapy at INR 2.0-3.0 (target 2.5) for at least 3 months or long term (AF)

ST-elevation MI with otherwise Low risk of embolization:

* Long-term aspirin therapy (75-162 mg/d)
* Consider clopidogrel for patients allergic or intolerant to ASA: Clopidogrel, more expensive than ASA, has been shown to be 8.7% better than ASA in reducing the combined incidence of MI, stroke and vascular mortality, mainly by reducing MI, in patients having suffered from a stroke or a MI or presenting peripheral arterial disease.
* Combined clopidogrel and aspirin.Two recent trials have demonstrated a reduced rate of vascular events in ST-elevation MI with combined clopidogrel and ASA. No consensus yet has been reached concerning the implementation and especially the duration of such a combined therapy, which is in the range of 8 to 12 months in the setting if non ST-elevation acute coronary events.

Non ST-elevation MI with otherwise Low risk of embolization:

* Combination of Clopidogrel with low dose ASA for 8 to 12 months, then ASA long term

Target INR with Warfarin

In general, the 2004 ACCP guidelines suggest a target INR of 2.5 (2.0 to 3.0) for most situations where warfarin is indicated whereas the 2004 ACC/AHA guidelines suggest such an INR target for situations where another antiplatelet agent is prescribed but a higher target of 3.0 (2.5-3.5) when no antiplatelet drug is prescribed.

Antithrombotic therapy post-MI with stenting

Clopidogrel, along with ASA 80mg for long term therapy, should be prescribed at least 1 month following bare stent implantation, 3 months following sirolimus coated stents and 6 months following paclitaxel coated stents. If anticoagulation is also indicated during this period of combined antiplatelet therapy, a target INR of 2.5 is recommended

Risk Versus Benefits

Major bleeding occurs in less than 2% of the patients treated with oral anticoagulants or Antiplatelet drugs per year. The risk of bleeding is associated with the intensity of anticoagulation, ASA dosage, combined use of aspirin and oral anticoagulants and underlying disorders.

The clinical benefits of chronic antithrombotic therapy in post-MI patients outweigh potential side-effects. Therefore, as a general rule, when a patient presents with an MI, one must consider anticoagulation or antiplatelet therapy, based on the clinical risk of thromboembolism and the scientific information available to date.

Contraindications to Aspirin

* Active gastrointestinal blood loss
* Peptic ulcer disease: consider clopidogrel once treated
* Ulcer bleeding: once treated, consider ASA 80 mg with esomeprazole 20mg BID rather then Clopidogrel alone. A reasonable alternative could be Clopidogrel with esomeprazole
* Hypersensitivity: consider clopidogrel
* Bleeding disorders
* Gastrointestinal intolerance to ASA:consider clopidogrel

Contraindications to Warfarin

* Pregnancy, especially 6th to 10th first weeks
* Hemorrhagic tendencies
* Recent surgery to CNS, eyes, large surfaces, especially within a week
* Inadequate monitoring facilities
* Unreliable patient or circumstances
* Malignant hypertension (Refer to CPS for more information)

Safety of Warfarin Therapy

Bleeding is the most important complication of anticoagulant therapy. The intensity of anticoagulation, the concomitant use of ASA, non COX-2 NSAIDs and the underlying clinical disorder are major factors influencing the risk of bleeding.

Drug interactions are the commonest cause of significant change in the INR value. Patients should be informed not to change any medication without a physician's or pharmacist's advice. Adequate monitoring is the key to a successful and safe warfarin therapy. Please refer to the TIGC guideline on warfarin therapy.

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