The Sixth (2000) ACCP Guidelines for Antithrombotic Therapy for Prevention and Treatment of Thrombosis

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Abbreviations: ACCP = American College of Chest Physicians; RCT = randomized clinical trial

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Thrombosis, an important complication of atherosclerosis and of various medical and surgical conditions, can be prevented or treated effectively by a variety of pharmacologic agents. Three classes of agents are available: anticoagulants, antiplatelet agents, and thrombolytic drugs. The first two prevent the formation and growth of thrombi, whereas the third lyases existing thrombi.

The American College of Chest Physicians (ACCP) Task Force on Antithrombotic Therapy published the proceedings of their first consensus conference on antithrombotic therapy in 1986. The participants introduced a system of evidence that has served as a model for critically appraising the literature and has been adopted by many medical organizations. In the 14 years since the first conference, the field of antithrombotic therapy has witnessed enormous growth, due in part to the development of new and more powerful pharmacologic agents and in part to the evaluation of these agents in well-designed clinical trials. The proceedings of the sixth ACCP Consensus Conference provide an extensive critical review of the literature related to management of thromboembolic disorders, including venous thromboembolism, arterial thrombosis, and systemic arterial embolism. As in past reports, each section concludes with a detailed summary that documents the therapeutic recommendations, assigns a grade for each recommendation (1 or 2), and profiles the strength of the evidence on which the recommendations are based (A,B,C, or C+).

Major developments since the last conference, in 1998, include the following: the unequivocal demonstration that low doses of aspirin (80 to 325 mg) are at least as effective as higher doses (500 to 1000 mg) in cerebrovascular disease; confirmation of the new oral antiplatelet agent clopidogrel and of IV glycoprotein IIIb-IIIa antagonists as important antithrombotic agents; the lack of success of oral GPIIb/IIIa antagonists in large clinical trials in myocardial ischemia; the demonstration that the synergistic effect between aspirin and ticlopidine, in patients with coronary stents, also holds for aspirin and clopidogrel; confirmation of low-molecular-weight heparin preparations as replacements for unfractionated heparin in acute coronary ischemic syndromes and venous thromboembolism; consolidation of the evidence that the lower limit of the therapeutic range for oral anticoagulants in atrial fibrillation is an international normalized ratio of 2.0; and failure to demonstrate a benefit of the combination of low-intensity warfarin (either fixed low dose or INR <2.0) and aspirin in patients with atrial fibrillation.

Grades of Recommendation for Antithrombotic Drugs

Since the 1998 publication, the grading system has been refined further. In past publications, the recommendations were graded by considering the methodologic quality (A, B, or C) of the studies that provide the estimate of the treatment effect and then considering the panelists’ judgment about the balance between benefits and risks of treatment. In this report, the recommendation to use or not use a treatment is more clearly separated from the methodologic quality of the studies on which the estimate of the treatment effect is made.

Recommendation To Use or Not Use a Treatment

The recommendation to use (or not use) a particular treatment is based on the trade-off between benefits on the one hand and risks and/or costs on the other. If, after weighing all of the evidence, the experts conclude that benefits outweigh risks and/or costs, then treatment will be recommended; if the benefits do not outweigh risks and/or costs, treatment will not be recommended. If experts are very certain that benefits do, or do not, outweigh risks, a grade 1 recommendation is made. If they are less certain of the trade-off between benefits and risks, a weaker recommendation of grade 2 is made.

Methodologic Quality

There are four methodologic grades; grade A, B, C, and C+. Grade A recommendations are based on randomized trials with consistent results; grade B recommendations are made when randomized trials have inconsistent results or have substantial methodologic weaknesses; and grade C recommendations are based on observational studies or from generalization from randomized trials from one group of patients to a different group. When experts consider that the generalization from randomized trials is secure, or that the data from observational studies are overwhelming, then the grade C recommendation is upgraded to grade C+.

In an ideal world, all our recommendations would be grade 1A, that is, a very strong recommendation based on the results of well-designed, randomized, clinical trials (RCTs) with consistent results. However, since warfarin, heparin, and aspirin were introduced to clinical use prior to the advent of the RCT, many of the indications for these agents are based on clinical observations without RCTs. Less than half of the recommendations in this sixth report of the ACCP Consensus Conference are based on the results of RCTs (A or B evidence). It is clear that recommendations based on B evidence and grade 2 recommendations need further trials or further evaluations of cost benefit. The C recommendations are fertile ground for further RCTs. Nearly all the recommendations for antithrombotic treatment in children are grade C, and as a result, many important RCTs in children have
been initiated. Grade C+ recommendations may or may not require new RCTs. In most cases, grade C+ recommendations are based on compelling observational studies or secure generalizations from other RCTs, as in the case of warfarin treatment for patients with rheumatic mitral valve disease complicated by atrial fibrillation.

The evolution of the recommendations of the ACCP Task Force on Antithrombotic Therapy from 1986 to 2000 illustrates the importance of RCTs on the emergence of evidence-based medical practice.

It is the hope of the participants of the ACCP Task Force on Antithrombotic Therapy that these guidelines will assist clinicians to prevent or effectively treat thrombotic disorders in their patients.

REFERENCES