We invite you to submit questions on specific clinical problems

Preventing DVT: Is short-duration prophylaxis effective?

What are the benefits and risks of short-duration (7 to 10 days) anticoagulant prophylaxis against deep venous thrombosis (DVT) after hip or knee replacement surgery?

In patients who have had total hip or knee replacement, there is a 40% to 70% risk of DVT, which can result in fatal pulmonary embolism (PE), the most common preventable cause of postoperative death. Consequently, it currently is recommended that these patients receive at least 7 to 10 days of anticoagulant prophylaxis with fixed-dose low molecular weight heparin (LMWH) or adjusted-dose warfarin, administered to achieve a target international normalized ratio of 2.0 to 3.0.[1,2] In patients who are at increased risk for bleeding complications, usually because of excessive intraoperative bleeding, active mechanical thromboprophylaxis with an intermittent pneumatic compression device is an acceptable option.[1,2]

Short-duration anticoagulant prophylaxis reduces the risk of postoperative venous thromboembolism (VTE) by 50% to 70%.[1,2] However, there is concern about a high prevalence of residual DVT in patients who receive the therapy. For example, in patients who undergo hip replacement and receive 7 to 10 days of LMWH therapy, the rate of residual asymptomatic DVT, as detected by venography, is 16%.[1] Therefore, some authorities advocate extended-duration anticoagulant prophylaxis for 4 to 5 weeks after hip or knee replacement.[3,4] The argument against this approach is that most asymptomatic DVT detected by venography is not clinically important and will resolve spontaneously.[5,6]

We recently investigated the risk of symptomatic VTE in patients who had received 7 to 10 days of LWMH or warfarin therapy after hip or knee replacement; the results are summarized in the Table.[7] In this pooled analysis of 6089 patients, symptomatic, nonfatal VTE occurred in 1 of 33 patients, and fatal PE was rare, occurring in 1 of 1000 patients within 12 weeks after surgery. Among patients who completed 7 to 10 days of anticoagulant prophylaxis without any thromboembolic events and who did not receive additional anticoagulant prophylaxis, symptomatic VTE occurred in 1 of 45 patients, and fatal PE occurred in 1 of 2000 patients during the next 3 months.

The duration of anticoagulant thromboprophylaxis after hip or knee replacement depends on individual patient risks. Patients at high risk for postoperative VTE include those who are not fully weight-bearing after surgery,[8] those who previously had VTE or cancer, and those who are obese.[9] Also at high risk are patients with concomitant cardiorespiratory insufficiency, who may be more susceptible to the adverse effects of VTE.[10] Because of the costs and inconvenience of administering extended-duration anticoagulant prophylaxis to all patients who undergo hip or knee replacement, it may be reasonable to limit extended-duration prophylaxis to high-risk groups.

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Table – Incidence of symptomatic nonfatal VTE and fatal PE in 6089 patients after total hip or knee replacement

Event	During prophylaxis* (95% CI)	Post-prophylaxis† (95% CI)	During prophylaxis and post-prophylaxis (95% CI)
Nonfatal VTE	1.1% (0.03 - 1.9)	2.2% (1.4 - 3.0)	3.2% (2.0 - 4.4)
Fatal PE	0.04% (0 - 0.10)	0.06% (0 - 0.12)	0.10% (0.02 - 0.20)
Fatal PE (including possible episodes)	0.05% (0 - 0.12)	0.07% (0 - 0.14)	0.13% (0.04 - 0.24)

VTE, venous thromboembolism; PE, pulmonary embolism; CI, confidence interval.
*Initial 7 to 10 days after surgery while patients are receiving antithrombotic treatment.
†Period from completion of antithrombotic treatment until 3 months after surgery.
Adapted from Douketis JD et al. *Arch Intern Med.* 2002.[7]

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Post-MI lipid levels: Smoking cessation for an improved profile

To what extent can smoking cessation affect lipid levels in patients who have had an acute myocardial infarction (MI)?

Cigarette smoking has consistently been linked to higher rates of cardiovascular morbidity and mortality in large-scale epidemiologic studies.[1-5] An estimated 17% to 30% of all annual cardiovascular deaths are related to smoking,[6] and MI rates are directly related to amount and duration of cigarette use.[2,7] Smoking cessation results in a gradual reduction of cardiovascular risk over several months to years.[6-10] Eventually, the risk for ex-smokers approaches that for nonsmokers.

Despite this strong association between smoking and cardiovascular disease, the underlying pathophysiology has not been fully elucidated. Experimental laboratory and animal investigations have suggested an enhancement of atherothrombotic mechanisms in response to smoking; these findings have been supported in numerous clinical observational studies. Both smoking[11-13] and atherothrombotic factors[14-19] have been independently associated with death and reinfarction in patients with a prior MI, and mortality rates are higher in post-MI patients who continue to smoke than in nonsmokers.[20-22] Few data exist, however, on the effects of cigarettes and smoking cessation on postinfarction lipid levels or inflammatory mediators.

In the early 1990s, the Diet and Reinfarction Trial (DART) evaluated smoking status and hematologic variables in 1755 men recovering from a recent MI.[13] A statistically significant association between tobacco use and all-cause mortality was observed over the 18 months after a coronary event. Among smokers, those who gave up cigarettes reduced their mortality by almost half (4.1% vs 7.9%) during the follow-up period. Plasma fibrinogen levels also were highly correlated with both mortality and ongoing cigarette use, and reductions in fibrinogen levels correlated with improved outcomes among the former smokers.

Recently, the more comprehensive Thrombogenic Factors and Recurrent Coronary Events (THROMBO) study prospectively enrolled 1045 stable post-MI patients whose lipid levels and various inflammatory markers were measured 2 months after the index coronary event.[23] Tobacco use was categorized as nonsmoking, past smoking, or active smoking. The primary end point was coronary death or nonfatal MI, and patients were followed for an average of 26 months. High levels of D-dimer and apolipoprotein B and low levels of apolipoprotein A-I were independently associated with recurrent coronary events in a Cox survivorship model after adjustment for relevant clinical covariates.

A subgroup analysis was performed to assess the interaction between smoking and the measured atherothrombotic factors.[24] After adjustment for clinical variables, active smokers were found to have higher levels of total cholesterol and apolipoprotein B, and both active and past smokers had higher fibrinogen levels than nonsmokers. Of note, smokers who refrained from using cigarettes for 24 hours before blood sampling had lower apolipoprotein B, total cholesterol, and fibrinogen levels than patients who smoked just before the clinic visit. Levels of high-density lipoprotein cholesterol and apolipoprotein A were similar in all 3 groups.

These studies have several clinical implications. While higher average lipid levels are found in all MI patients than in matched controls, active smoking is associated with even further increases in lipid levels among such patients. Cessation of smoking after MI reduced atherogenic lipid levels to those found in nonsmokers, even by 2 months post-MI. While past and present smokers had elevated fibrinogen levels after MI, suggesting a higher tendency toward procoagulant activity and recurrent coronary events, this prothrombotic milieu was favorably modified after as

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