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Prophylaxis of Deep Vein Thrombosis in Total Hip Replacement: Which Heparin and What Duration?

When deep vein thrombosis is above or in a popliteal vein it is defined as a proximal deep vein thrombosis. Such thrombi have a high tendency to migrate toward the pulmonary circulation and generate an acute pulmonary embolism. Subsequently, these two entities, deep vein thrombosis and pulmonary embolism, should be considered part of the same disease, called venous thromboembolism. This pathological process is an important public health concern. The incidence has been estimated at 1/1,000 per year in a 25-year population-based study recently published [1]. Deep vein thrombosis is frequently clinically silent, symptoms of pulmonary embolism are not specific and there is no simple test with a high sensitivity and specificity to affirm the diagnosis of pulmonary embolism. Therefore sophisticated and/or invasive tests are necessary for the diagnosis. Even when the diagnosis of acute pulmonary embolism is accurately made and adequate therapies are initiated, the mortality related to this pulmonary vascular disease remains relatively high at about 10% [2]. For all these reasons the prevention of deep vein thrombosis is of paramount importance.

One of the major risks of venous thromboembolism is orthopedic surgery. Clearly such surgery generates at least two factors of the classical Virchow triad. It produces stasis of blood and trauma to the vessel wall. Furthermore, when the endothelium is injured there is a local hypercoagulability which is the third component of the Virchow triad. These are probably the reasons why the incidence of deep vein thrombosis in the absence of prophylactic anticoagulation approaches 50% in the perioperative period of total hip replacement [3]. Thus, there is no controversy

about the need for prophylaxis of deep vein thrombosis with that procedure. The means used are mechanical and/or pharmaceutical. The mechanical approach evaluated for total hip replacement is intermittent pneumatic leg compression [4] which significantly reduced the prevalence of proximal deep vein thrombosis from 27 to 14% after total hip replacement in a randomized trial involving 310 patients. The pharmaceutical approach includes unfractionated heparin [5] which was the prophylaxis considered in the report of *Manganelli et al.* [6], warfarin [3], low-molecular-weight heparin [7] and a more recent drug, recombinant hirudin [8].

Low-dose unfractionated heparin is known as an effective and safe prophylaxis of deep vein thrombosis since the publication in 1975 of an international multicenter trial [5] involving more than 4,000 patients. In addition to its efficacy and safety, the advantages of such a prophylaxis are that first, it does not require laboratory monitoring and second, as pointed out by *Manganelli et al.* [6], its cost is low. Although low-molecular-weight heparin tends to be the standard regimen of prophylaxis of deep vein thrombosis in patients undergoing total hip replacement, low-dose unfractionated heparin is still widely used in Europe.

Important questions concern the time points for starting and stopping the prophylaxis. In Europe it is recommended to start injection of unfractionated heparin or low-molecular-weight heparin from 2 to 4 h before the surgical procedure [8] whereas in North America the prophylaxis is initiated postoperatively. Concerning the cessation of the prophylaxis, there is now evidence that stop-

ping anticoagulant therapy 2 weeks after the total hip replacement or sooner if the patient is ready for discharge leaves patients at high risk of deep vein thrombosis for 45–90 days after the surgical procedure. Unfortunately, at present many orthopedic surgeons stop prophylaxis too early. Two recent studies [9, 10] demonstrated that the continuation of prophylactic anticoagulation with low-molecular-weight heparin after total hip replacement during 1 full month postoperatively significantly reduced the prevalence of deep vein thrombosis. Importantly *Manganelli et al.* [6] observed in their study that this was also true for unfractionated heparin and that such prolonged anticoagulant therapy did not increase hemorrhagic complications.

Finally, the regimen tested by *Manganelli et al.* [6], 15,000 IU/day of unfractionated heparin, costs approximately one third of the regimen of low-molecular-weight heparin. This latter prophylaxis is frequently preferred by orthopedic surgeons although its superiority in terms of efficacy has never been demonstrated in the prophylaxis of deep vein thrombosis after total hip replacement. Therefore as proposed by *Manganelli et al.* [6] a large prospective randomized trial comparing efficacy and cost-effectiveness of prolonged prophylaxis of these two regimens would be of great interest.

References

- 1 Silverstein MD, Heit JA, Mohr DN, Petterson TM, O'Fallon WM, Melton LJ III: Trends in the incidence of deep vein thrombosis and pulmonary embolism: A 25-year population based study. *Arch Intern Med* 1998;158: 585–593.
- 2 Carson JL, Kelley MA, Duff A, et al: The clinical course of pulmonary embolism. *N Engl J Med* 1992;326:1240–1245.
- 3 Clagett GP, Anderson FA Jr, Heit J, Levine MN, Wheeler HB: Prevention of venous thromboembolism. *Chest* 1995;108(suppl):312–334.
- 4 Hull RD, Raskob GE, Gent M, et al: Effectiveness of intermittent pneumatic leg compression for preventing deep vein thrombosis after total hip replacement. *JAMA* 1990;263:2313–2317.
- 5 Prevention of fatal postoperative pulmonary embolism by low doses of heparin. An international multicentre trial. *Lancet* 1975;ii:45–51.
- 6 Manganelli D, Pazzagli M, Mazzantini D, et al: Prolonged prophylaxis with unfractionated heparin is effective to reduce delayed deep vein thrombosis in total hip replacement. *Respiration* 1998;65:369–374.
- 7 Levine MN, Hirsch J, Gent M, et al: Prevention of deep vein thrombosis after elective hip surgery: A randomized trial comparing low molecular weight heparin with standard unfractionated heparin. *Ann Intern Med* 1991;114:545–551.
- 8 Eriksson BI, Wille-Jørgensen P, Kålebo P, et al: A comparison of recombinant hirudin with a low-molecular-weight heparin to prevent thromboembolic complications after total hip replacement. *N Engl J Med* 1997;337: 1329–1335.
- 9 Planes A, Vochelle N, Darmon JY, Fagolla M, Bellaud M, Huet Y: Risk of deep venous thrombosis after hospital discharge in patients having undergone total hip replacement: Double blind randomized comparison of enoxaparin versus placebo. *Lancet* 1996;348:224–228.
- 10 Bergqvist D, Benoni G, Björnell O, Fredin H, Hedlund U, Nicolas S, et al: Low molecular weight heparin (enoxaparin) as prophylaxis against venous thromboembolism after total hip replacement. *N Engl J Med* 1996;335: 696–700.