

**This Week's Citation Classic®****Harris W H, Salzman E W, Athanasoulis C, Waltman A C, Baum S &****DeSanctis R W.** Comparison of warfarin, low-molecular-weight dextran, aspirin, and subcutaneous heparin in prevention of venous thromboembolism following total hip replacement. *J. Bone Joint Surg.—Amer.* Vol. 56-A:1552-62, 1974.

[Depts. Orthopaedic Surg., Radiol., and Med., Mass. Gen. Hosp.; Dept. Surg., Beth Israel Hosp.; and Depts. Orthopaedic Surg., Radiol., Surg., and Med., Harvard Medical Sch., Boston, MA]

Four agents were compared for their efficacy in preventing or reducing thromboembolism following total hip replacement in 187 patients without prior history of phlebitis. Warfarin (W), dextran (D), and aspirin (A) were equally effective and superior to heparin (H) with respect to the number of patients with fresh thrombi or the prevalence of thrombi in the thigh. W and D were superior in reducing the number of thrombi formed. Significantly fewer bleeding complications occurred with A than with W. Prophylactic use of W or A followed by W treatment if a thrombus was detected provided protection against pulmonary embolism. [The *SCI*® indicates that this paper has been cited in over 175 publications.]

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My commitment to attacking the problem of postoperative fatal pulmonary emboli grew out of a very disturbing experience that occurred when I was chief resident in Orthopaedic Surgery at the Massachusetts General Hospital in 1959. A marvelous man died in my arms from a fatal pulmonary embolus two weeks after a cup arthroplasty. The price he paid for an attempt at the surgical correction of a benign condition was far too high.

After joining forces with Ed Salzman and Roman DeSanctis, we embarked on a series of studies, which now includes 17 publications spanning the past 20 years. Compared with the circumstances 25 years ago, extraordinary progress has been made. At that time the concept of the disease was primitive, diagnosis was woefully inadequate, prophylaxis hardly existed, and treatment was inept and dangerous.

Major advances have been made in each of these features, but the problem remains with us. Sensitivity to this issue has improved dramatically, and the percentage of physicians and surgeons alerted to the problem is quite high. But accurate diagnosis remains unresolved following hip surgery in the absence of venography.

We now know that the incidence of postoperative deep vein thrombosis following total hip replacement surgery in the adult over 39 years is about 50 percent. Twenty percent of the patients have angiographically proven asymptomatic pulmonary emboli despite prophylaxis, and fatal pulmonary emboli remain a major threat to the adult patient undergoing reconstructive hip surgery. Effective prophylaxis has reduced the incidence of the disease from 50 percent to under 20 percent. The bleeding risk has been substantially reduced.

The two current prophylactic regimens with the greatest efficacy and greatest safety for total hip patients are low-dose warfarin and subcutaneous heparin combined with dihydroergotamine. Estimates of the cost-effectiveness of the use of low-dose warfarin plus routine venography indicate that, when compared with no prophylaxis and clinical surveillance of patients over the age of 39 undergoing elective total hip replacement, the incidence of fatal pulmonary embolization is reduced from 20 to 0.2 per 1,000. The total cost of management of 1,000 patients without prophylaxis followed by clinical surveillance is estimated to be \$550,000. The cost for low-dose warfarin prophylaxis with routine venography for diagnosis is estimated to be \$1,100,000.

We have recently proposed a hypothesis for the management of such patients with low-dose warfarin for three months without venography. The estimated reduction in fatal pulmonary embolization is the same as with the low-dose warfarin combined with routine venography, but the overall cost is estimated to be \$571,000. The bleeding risk during the first two weeks from low-dose warfarin is an overall figure of 4 percent and the major bleeding risk is only 1 percent. This hypothesis is under active investigation at this time.<sup>1</sup>

1. Paiement G D, Bell D, Wessinger S J & Harris W H. New advances in the prevention, diagnosis, and cost effectiveness of venous thromboembolic disease in patients with total hip replacement. (Brand R A, ed.) *The hip: proceedings of the 14th Open Scientific Meeting of the Hip Society*. St. Louis: Mosby, 1986. p. 94-119.