

Even Fractures Missed as Osteoporosis Sign in Men

BY TIMOTHY F. KIRN

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SEATTLE — Even after older men fracture their bones, osteoporosis is rarely diagnosed and rarely treated, according to the findings of a Kaiser Permanente study of 1,171 men.

Of men over the age of 65 years with a fracture, only 3.3% had a diagnosis of primary osteoporosis and only 7% received

treatment with a bisphosphonate or calcitonin before or after their fractures, Adrienne C. Feldstein, M.D., reported at the annual meeting of the American Society for Bone and Mineral Research.

Another 15% either had a diagnosis of secondary osteoporosis or received treatment for secondary osteoporosis, said Dr. Feldstein, a clinical investigator for Kaiser Permanente Northwest, Portland, Ore.

Only 1% of the men had a bone mineral

density test. The study included all men in the system who had at least one fracture over a 3.5-year period that ended in 2001. The investigation excluded any patient with a fracture that was unlikely to be associated with brittle bones, such as skull, face, finger, or ankle fractures. The mean age of the men included was 76 years.

The rates at which treatments were prescribed varied, depending on the type of fracture. Among men who fractured their

vertebrae, 30% had or were given a prescription for a bisphosphonate, but only 1% of those with an upper extremity fracture received a bisphosphonate. Only 2.2% of those with a hip fracture had or were given a prescription.

During the course of the study, there appeared to be a slight increase in awareness. Of men who had a fracture in the last year of the study, 10% either had or were given bisphosphonate or calcitonin treatment. ■

DRUG UPDATE

DVT Prophylaxis Following Orthopedic Surgery

No antithrombotic agent can completely eliminate a patient's risk of deep vein thrombosis following knee or hip replacement surgery.

Venographic studies have shown that the incidence of thrombosis in patients who undergo orthopedic surgery and receive no prophylaxis is 50%-70%. Total knee replacement surgery imparts the highest risk, followed by total hip replacement surgery and surgery for a fractured hip. Optimal use of the prophylactic agents currently cuts the risk of deep vein thrombosis (DVT) to about 10%-20%. Over the past 20 years, orthopedic surgeons have gradually embraced the notion of prophylaxis, and more than 90% of patients who undergo orthopedic

surgery today receive some form of prophylaxis.

Oral warfarin (Coumadin) or subcutaneous injections of a low-molecular-weight heparin (LMWH) are the current mainstays for prophylaxis. Aspirin therapy alone following orthopedic surgery is insufficient, but some physicians use it in conjunction with other agents or with vigorous physical therapy. The introduction of fondaparinux (Arixtra) to the market in 2003 brought mixed news. Results from clinical trials suggested that this subcutaneous agent was more effective than the LMWH enoxaparin (Lovenox) for preventing blood clots, but this benefit was offset by a 1% higher risk of bleeding, compared with enoxaparin.

Clinical trial results for a new, oral antithrombotic, ximelagatran (Exanta) generated a lot of anticipation, but the Food and Drug Administration rejected its licensing application last October due to safety concerns.

All of the drugs listed here can be safely used in patients aged 70 and older with normal renal function. All are given for 7-10 days postoperatively or until the patient is fully ambulatory. High-risk patients may require intermittent pneumatic compression devices plus graded elastic stockings to better protect against DVT.

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Drug	Cost/Day*	Dosage	Comment**
enoxaparin [Lovenox]	no generic available [\$40.84]	30 mg b.i.d.	Available in trade formulation only. Given subcutaneously. Most widely used LMWH in the United States because it was the first approved, plus it's backed by results from several clinical trials, and marketing has been aggressive. LMWHs are preferred by some over warfarin because they're used at a fixed dosage, and close monitoring of serum levels isn't needed; the downside is higher cost. More effective than unfractionated heparin. Reaches peak antithrombotic activity in 2-4 hours and has a half-life of 3.5-4.5 hours. Usually started 12-24 hours after surgery. Results from almost all clinical studies showed fewer bleeding episodes in patients on LMWH, compared with those on unfractionated heparin, but differences were not statistically significant. Risk of thrombocytopenia is less than 1%. Use cautiously in patients with renal insufficiency because enoxaparin is excreted largely by the kidney, as are all LMWHs. Dosage of 40 mg once daily may be best for extended prophylaxis following hospital discharge. Safe during pregnancy, but switch to standard heparin at least 12 hours before delivery. Safe during lactation.
dalteparin [Fragmin]	no generic available [\$27.95]	5,000 IU/day	Available in trade formulation only. Given subcutaneously. Other LMWH on the U.S. market, but use lags way behind enoxaparin due to familiarity and marketing. Pharmacokinetics and efficacy comparable with enoxaparin's. Another dosing option is 2,500 IU 6-8 hours postoperatively, then 5,000 IU the next day. Same pregnancy precautions and lactation recommendations as for enoxaparin.
fondaparinux [Arixtra]	no generic available [\$43.50]	2.5 mg/day	Available in trade formulation only. Newest agent approved for this indication. Synthetic, specific inhibitor of activated factor X; does not directly affect thrombin or platelets. Given at fixed dosage, subcutaneously, for all patients. Trial results showed it was more effective than enoxaparin for preventing blood clots, but the bleeding rate—particularly at the surgical site—is about 1% higher with fondaparinux, compared with enoxaparin, due mainly to its long half-life. This safety concern plus high cost has kept it from sweeping the market for this indication, although cost is very similar to b.i.d. enoxaparin. A plus is that it has an extremely low risk of causing thrombocytopenia. Started 6-12 hours after surgery. Safe during pregnancy but must stop days before delivery to fully clear because of long half-life.
warfarin [Coumadin]	\$0.66 (5 mg/day) [\$0.86]	5-7.5 mg/day	Available in both generic and trade formulations. Decades of clinical experience with this drug provide some reassurance, but safety and efficacy have not been thoroughly compared with LMWHs'. Oral administration is convenient but takes 5 or more days to exert its anticoagulant effect and requires careful, ongoing laboratory monitoring to maintain correct dosage. Even in carefully monitored trials, patients are often outside their target anticoagulant range for a substantial period of time. A typical starting dosage is 5-10 mg/day for 3 days, with subsequent dosages adjusted to maintain the international normalized ratio at between 2 and 3. Smaller dosages often needed in patients aged 70 and older. Study results suggest it's less effective following total knee, compared with total hip, replacement surgery. Contraindicated during pregnancy; safe during lactation.
heparin, unfractionated	\$2.12 (5,000 U b.i.d.)	5,000 U b.i.d. or t.i.d.	Infrequent choice for preventing DVT following orthopedic surgery, but better than nothing. Inexpensive, but some clinicians consider it less effective than LMWH or warfarin. Requires subcutaneous administration. Prophylactic doses of unfractionated heparin do not require laboratory monitoring. Carries a 1%-3% risk of heparin-induced thrombocytopenia and thrombosis syndrome. Safe during pregnancy or lactation.

*Cost/day is based on the average wholesale price for the generic or trade formulations in the 2004 Red Book.

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