Hip Fracture Repair Tied to High MI Risk in Elderly

BY BRUCE JANCIN
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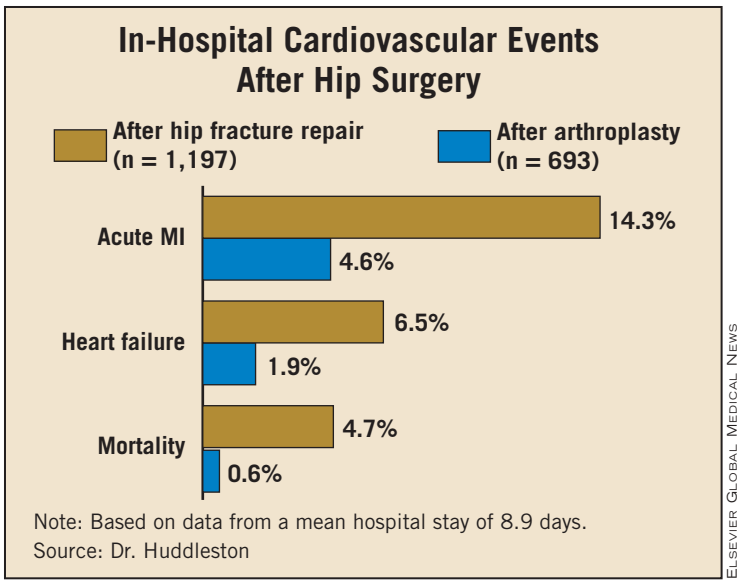
DALLAS — Surgical repair of hip fracture in the elderly is linked to a high risk of postoperative MI or death—a reality not reflected in current American College of Cardiology/American Heart Association preoperative cardiovascular evaluation guidelines, Dr. Jeanne Huddleston said at the annual meeting of the Society of Hospital Medicine.

The guidelines lump all orthopedic surgical procedures in an intermediate-risk category, meaning their combined risk of postoperative MI or death is expected to be less than 5%. That's true of elective total hip arthroplasty, but hip fracture repair is different, said Dr. Huddleston, a hospitalist at the Mayo Clinic, Rochester, Minn., and former society president.

She presented a population-based retrospective study of 1,197 patients who underwent repair of a fractured hip and 693 who had hip replacement. During a mean hospital stay of 8.9 days, the incidence rates of postoperative MI, heart failure, and mortality were markedly lower in the elective hip arthroplasty group (see chart). Moreover, the combined 1-year rate of MI and all-cause mortality was 34.2% in patients undergoing fracture repair, versus 7.5% in the arthroplasty group. Adjusting for age, gender, and American Society of Anesthesiologists physical status classification, racture repair patients were 3.6-fold more likely to have an MI or die within a year postsurgery.

Hip fracture repair is typically done on an urgent basis, but doesn't fall within the definition of "emergency" surgery in guidelines. Since it's considered nonemergent, physicians can take up to 48 hours postfracture to optimize cardiac status—a sound strategy given the high CV risk, according to Dr. Huddleston. ■



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Jaw Osteonecrosis Risk Increases With More Bisphosphonate Infusions

BY KERRI WACHTER
Senior Writer

CHICAGO — The risk of jaw osteonecrosis increases with the number of bisphosphonate infusions, according to studies presented at the annual meeting of the American Society of Clinical Oncology.

Osteonecrosis of the jaw (ONJ) is a rare but serious side effect of bisphosphonates that has popped up in a number of case reports in the literature. Three groups of researchers conducted retrospective analyses to understand the natural history, incidence, and risk factors of this side effect.

In one study, Dr. Tracey L. O'Connor of Roswell Park Cancer Institute in Buffalo, N.Y., and colleagues identified 354 patients with metastatic cancer involving bones on intravenous bisphosphonates between 2002 and 2006 at the Institute. Using dental records, they identified 25 patients (7%) with ONJ. Most (80%) had breast cancer, and 27% had a medical comorbidity such as diabetes mellitus, hypertension, or chronic anticoagulation therapy for deep vein thrombosis or pulmonary embolism. In general, patients who developed ONJ had more bisphosphonate infusions—an average of 11—versus patients without ONJ (an average of 7 infusions). Most ONJ patients (52%) had stage 1 disease (exposed necrotic cortical bone); 36% had stage 2 (localized involvement of the mandible); and 12% had stage 3 (diffuse involvement of the mandible). Most (84%) were managed with antibiotics; 16% had debridement and alveoplasty. "If detected early, ONJ can be conservatively managed," the authors wrote.

To see if scintigraphy could predict ONJ, planar whole body scans were performed 3 hours after injection of Tc-99m methylene diphosphonate using anterior and posterior perspectives. Jaw uptake was graded relative to normal posterior uptake within the ileum (grade 1), sacrum (grade 2), and sacroiliac joints (grade 3). In ONJ patients, 14 had bone scans, and 13 showed grade 3 uptake. In comparison, 183 controls had bone scans; of these, 128 (70%) had grade 3 uptake. "Uptake on bone scans is not a reliable predictor of ONJ," the authors wrote.

In another study, Dr. Matthew R. Stumpe, an otolaryngology resident at the University of Tennessee, Memphis, and colleagues performed a retrospective review of 638 patients treated with intravenous bisphosphonate therapy for cancer. The most common malignancies were prostate, lung, breast, and multiple myeloma. Most patients were treated with pamidronate (53%), followed by zoledronic acid (26%). The rest were treated with both drugs.

"Patients who developed osteonecrosis underwent a greater number of bisphosphonate infusions and greater total infusion hours, suggesting a positive correlation between osteonecrosis and drug dose," the authors wrote. In all, six patients had ONJ, or 0.94%. Patients with ONJ had a significantly greater number of infusions (21), versus controls (11) and a significantly greater mean number of hours of infusion time (43 vs. 18). All ONJ patients presented with exposed bone. In four, ONJ occurred after dental treatment. The mandible was affected in five patients; the maxilla in one. Bisphosphonates were discontinued in five patients after ONJ diagnosis. The patient who did not stop had a small area of exposed bone covered surgically using viable mucosa. Another patient recovered from ONJ and resumed bisphosphonates.

Dr. Mimi I. Hu of the department of endocrine neoplasia and hormonal disorders at the University of Texas M.D. Anderson Cancer Center in Houston, and colleagues performed a retrospective analysis of patients treated with intravenous bisphosphonates between 1996 and 2004. They identified 4,025 patients; 35 had ONJ. Fourteen were followed for over 6 months at a dental clinic. Patients were evenly split between having breast cancer or multiple myeloma. The average length of exposed bone at the initial evaluation was 11 mm. Most (10) were treated with pamidronate followed by zoledronic acid. Four were treated with zoledronic acid alone. The median cumulative dose was 1,710 mg for pamidronate and 72 mg for zoledronic acid. The median duration of follow-up from initial diagnosis was 17 months.

The researchers focused on the natural course of ONJ. ONJ resolved in 21% of long-term follow-up patients. On the basis of the change in the lesion from baseline to last noted size, seven patients had progression. Two were stable, one regressed, one had recurrences at different sites over 67 months, and three had resolution for over a year. Modification of therapy doesn't appear linked to resolution, the researchers noted. In some patients, persistent ONJ was seen whether therapy was discontinued, decreased in frequency, or continued at the same dose and frequency. In others, resolution occurred if intravenous bisphosphonate therapy was discontinued, decreased in frequency, and replaced by weekly oral alendronate. ■

Continued Bisphosphonate Use Remains Gray Area

WASHINGTON — Physicians and patients need to work together to decide for or against long-term bisphosphonate treatment for osteoporosis, said Dr. Sundeep Khosla at an international symposium sponsored by the National Osteoporosis Foundation

Alendronate is the longest-available bisphosphonate, with 10 years of follow-up data. In one analysis of 10 years of data for postmenopausal women on varying regimens of alendronate, those on 10 mg daily of alendronate had increased BMD for the spine and hip (N. Engl. J. Med. 2004;350:1189-99). Spine BMD increased by 14% from baseline over that period, and total hip BMD increased by 7%.

Smaller gains in BMD were noted for women on 5 mg daily of alendronate: 9% and 3% for the spine and total hip, respectively.

For women in the discontinuation group, spinal BMD leveled off (an increase of 0.3% from years 6-10) and total hip BMD declined slightly (a decrease of 1% from years 6-10).

This study "told us that alendronate did in fact have sustained effects over 10 years on bone density and bone turnover markers," said Dr. Khosla, research chair of the division of endocrinology at the Mayo Clinic in Rochester, Minn. However, the fracture data were inconclusive.

In the FLEX (Fracture Intervention Trial [FIT] Long-Term Extension) study, published late last year, researchers assessed the effects of continuing or stopping alendronate after 5 years of treatment (JAMA 2006;296:2927-38).

For women on placebo for years 5-10, total hip BMD returned to baseline levels. Women on 5 mg/day or 10 mg/day of alendronate gained and maintained a 4% increase in hip BMD over baseline during the same period.

Women on placebo during years 5-10 had a slight increase in spine BMD, and women on alendronate had a steeper increase. Women who continued on alendronate for 10 years had an almost 50% reduction in clinical vertebral fractures, compared with those who stopped treatment after 5 years. There was no difference between the groups in terms of nonvertebral or morphometric vertebral fractures.

"Continuation of alendronate for 10 years maintains bone mass and reduces bone remodeling, compared with discontinuation after 5 years," said Dr. Khosla.

Discontinuation did not increase the risk of nonvertebral fractures or x-ray–detected vertebral fractures, but the risk of clinically detected vertebral fractures was significantly increased in those who discontinued therapy after 5 years.

"For many women, stopping alendronate after 5 years for up to 5 more years does not significantly increase fracture risk, but women at high risk of vertebral fractures—such as those who already have a vertebral fracture or those [who might have] very low bone density—may benefit by continuing beyond 5 years."

—Kerri Wachter