Osteoporosis in men treated with androgen deprivation therapy for prostate cancer

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Background
Thousands of patients diagnosed with prostate cancer will be treated with androgen ablation therapy as part of their cancer treatment. These patients include those with advanced disease (T3-4 or node positive) or high Gleason Score (8-10). In addition, long-term androgen ablation (> 2 years) has been proven to be more efficacious than shorter durations. Hence, investigators are exploring the multiple side effects of this therapy, one of the most notable of which is osteoporosis. This review article surveys the existing literature on osteoporosis secondary to androgen ablation (AA).

Methods
- Pertinent studies of male osteoporosis and complications arising from osteoporosis were reviewed.
- Bone mineral density loss and the osteoporotic fracture rates were reviewed.
- Possible therapeutic approaches for osteoporosis caused by AA were also examined.

Results
- Dual energy x-ray absorptiometry, quantitated CT scan and several biochemical tests (alkaline phosphatase, osteocalcin, deoxypyridinoline, etc.) are used to evaluate bone mineral density.
- In some reviews, long-standing testosterone deficiency (such as caused by AA) was responsible for up to 30% of cases of male osteoporosis.
- Bone mineral density decreases with AA almost immediately with total loss of 1.2%-17%, or 2-4% per year.
- Osteoporotic fracture rates were increased to an incidence of 5% at 22 months to 28% at 7 years. Other estimates place the relative risk of osteoporotic fractures with AA at 2.1.
- It is not known whether combined blockade, antiandrogens, or LHRH agonists contribute more to the development of osteoporosis.
- The mechanism by which lack of testosterone leads to osteoporosis is unknown.
- Treatment possibilities for male osteoporosis include calcitonin, calcium and vitamin D, exercise, and bisphosphonate therapy.
- Oral bisphosphonate therapy with calcium supplementation has been shown to increase bone density. In a randomized trial, bisphosphonate therapy (pamidronate) was proven to be statistically better than placebo.

Authors’ Conclusions
- Osteoporosis is an important toxicity of androgen ablation therapy and patients undergoing AA should be tested for bone mineral density loss.
- It is prudent for all men undergoing AA to receive calcium and vitamin D supplementation and maintain a moderate exercise regimen.
- Bisphosphonate therapy should be investigated as a possible therapy for AA induced osteoporosis.

Discussion
AA has been proven to add to the efficacy of treatment of prostate cancer in a large patient population. However, osteoporosis should be recognized as an expected toxicity. This will likely be more pronounced when long-term AA is used or if it results in permanent gonadal failure. This report shows a decrease in bone mineral density in several studies. In addition, this loss of bone density has led to an increase in osteoporotic fracture rates in those treated with AA therapy. However, in patients with prostate cancer, it is often difficult to determine the etiology behind fractures, whether they are caused by osteoporosis or
metastatic disease. There is no standard treatment of AA induced osteoporosis, though several are offered in this paper. Perhaps the most promising is bisphosphonate therapy. Pamidronate has been shown in recent NEJM articles to be an efficacious treatment in men, specifically decreasing bone loss in those patients receiving AA therapy as compared to those given no bisphosphonate therapy. Whether this difference in bone mineral density is clinically significant remains to be seen. This report gives evidence that osteoporosis is a definite toxicity of AA therapy in patients with prostate cancer. Prospective trials are needed to quantify this problem and to investigate therapies to treat it; namely, bisphosphonate therapy.