Prostate cancer treated with androgen deprivation therapy has consequences for bone

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From the meta-analysis by Lassemillante et al. [1] in this issue of the Journal, it is clear that there is a high prevalence of osteoporosis and low bone mass (osteopenia) by dual energy x-ray absorptiometry (DXA) in men treated with androgen deprivation therapy (ADT) for prostate cancer. While the prevalence of osteoporosis varied among the cited studies, there is no doubt that the impact of ADT on bone mineral density, and therefore, fracture risk is underappreciated by patients and medical professionals. ADT may include analogs of gonadotropin releasing hormone (GnRH), androgen receptor blockers, or a combination of the two. In the past and rarely today, orchiectomy has been used to lead to a hypogonadal state. It is important to note that the dramatic decrease of testosterone by GnRH analogs or orchiectomy also leads to very low levels of estradiol, which is of particular import for bone in older men [2]. Prostate cancer patients treated with only androgen receptor blockade have less loss of bone than those treated with GnRH analogs or combined therapy [3].

Lassemillante et al. [1] also comment on the addition of forearm bone density, usually the distal 1/3 radius, as an important measure of bone density in men on ADT. In older men, degenerative changes in the spine commonly prevent interpretation of bone density. In some studies [4, 5], an additional 15 % or more of patients are diagnosed

with osteoporosis or low bone mass by the addition of radius bone density. This suggests that all older men on ADT should have forearm bone density done routinely. An additional method to identify ADT patients at risk for fracture would be to use the FRAX calculation. Saylor et al. [6] found that FRAX identified additional men at risk for fracture—beyond those found by DXA. In our own study [7] of 115 consecutive men on ADT, FRAX calculations with and without DXA produced different populations considered at risk for fracture. Finally, the International Society for Clinical Densitometry is now recommending that a white female database be used for calculating T-scores for men [8], which will lower the percentage of men with low bone mass and osteoporosis. The confusion from such varied results makes evaluation and treatment of men on ADT less likely.

As pointed out by Lassemillante et al. [1], men on ADT may have sexual dysfunction, gynecomastia, and body composition changes that may increase the risk of metabolic syndrome. In addition, hot flashes/flushes and fatigue are common complaints in men on ADT. Thus, even though the risk of osteoporosis may be as high as 50 % and the risk of fracture after 5 years of ADT may be as high as 20 % [9], it is doubtful that the man on ADT will be concerned about the silent disorder osteoporosis. This is particularly disturbing because bisphosphonates [10, 11] and more recently denosumab [12] have been shown to improve bone mineral density and in the case of denosumab [12] decrease morphometric vertebral fractures. Teriparatide [13], an estrogen agonist/antagonist has also been shown to decrease morphometric vertebral fractures in men on ADT.

Hence, as in other causes of secondary osteoporosis in men, such as glucocorticoid-induced osteoporosis [14], little attention is paid to the high fracture risk despite the

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availability of generally safe and effective therapy. In the United States, Medicare will not reimburse a DXA ordered for a man on ADT. Because ADT is a commonly used treatment of a common cancer in men, the meta-analysis of Lassemillante et al. [1] reminds us that we must find ways to translate a strong literature into the day-to-day practice of medicine. A recent study from Canada [15] demonstrated that much of bone loss from ADT occurs in the first year of therapy. Recognition of the high fracture risk of men on ADT should lead to treatment for those who need it, continued surveillance of those who are at lower risk, and practice of good bone health measures for all.

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