The dilemmas of breast cancer treatment and increased fracture risk

In *Annals of Oncology*, Bouvard et al. [1] reported fracture incidence and bone mineral density (BMD) evolution of 497 postmenopausal women with early-stage breast cancer who were treated with aromatase inhibitor (AI). Patients entering this prospective, longitudinal study were on AI for breast cancer treatment and increased fracture risk with or without evidence of osteoporosis at baseline. Patients with osteoporosis at baseline also received weekly oral bisphosphonate treatment. Women without bisphosphonates had a significant decrease in BMD over the 3 years with a fracture rate of 5.6%, while women treated with bisphosphonates for pre-existing osteoporosis maintained BMD at 3 years with a fracture rate of 9.8%. Bouvard et al. concluded that the treatment with AIs induced moderate bone loss and low fracture incidence in postmenopausal women without initial osteoporosis. Elderly women with pre-existing osteoporosis (and on oral bisphosphonates) maintained BMD but had a persistent fracture risk.

The findings of this study should be interpreted with caution because of several reasons. The proportion of patients who were eligible for the study and was offered participation remains unclear. Almost 21.7% patients (*N* = 108) did not undergo third-year evaluation i.e. nearly one-quarter of the initial study population which could bias the results. Currently, it is recommended that the optimal duration of adjuvant endocrine therapy is 5 years minimal [2]; therefore, the results at 3 years are very early and rather premature. Hence, what appears to be moderate bone loss because of a short follow-up duration is expected to increase with an increase in treatment duration. The incidence of symptomatic fracture rate is unclear as some asymptomatic fracture could be detected on screening imaging in elderly women. In fact, a substantial number of vertebral fractures in elderly are asymptomatic [3]. It will be interesting to know if the BMD loss varied depending upon the agent used as observed in some studies previously [4]. Furthermore, the compliance or adherence with oral bisphosphonate therapy was not looked at in this study. Poor compliance with bisphosphonates has been reported in other studies in the past [5]. It is important to recognize that a number of other conditions may equally contribute to loss of bone density in the study population including menopausal status, restricted mobility and diabetes mellitus.

Nonetheless, the authors should be commended for their efforts in exploring this important area of breast cancer management. Vertebral fractures and other osteoporotic fractures have important clinical implications. These fractures are associated with increased risks of new osteoporotic fractures and mortality, especially in older women. Women with vertebral fractures can also experience decreased quality of life due to physical limitations and psychosocial disabilities. Future research that involves (i) randomized design, (ii) health-related quality of life and differentiate between symptomatic versus asymptomatic fracture (iii) adjustment for other co-morbidities, (iv) a minimum of 5-year follow-up and (v) is adequately powered will further elucidate the symptomatic fracture incidence in women with or without osteoporosis receiving AI therapy.

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‘The dilemmas of breast cancer treatment and increased fracture risk’ by Malik

We read with interest the letter ‘the dilemmas of breast cancer treatment and increased fracture risk’ by Malik [1] and thank him to his attention to our article [2].