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Original Article

Low bone mineral density may be associated with long-term risk of cancer in the middle-aged population: A retrospective observational study from a single center

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Abstract *Background:* It is generally understood that cancer patients are at an increased risk for osteoporosis. Additionally, recent studies have suggested a shared pathophysiological mechanism between the development of cancer and osteoporosis. The purpose of this investigation was to investigate whether low bone mineral density is associated with cancer risk.
Methods: We enrolled 8780 subjects who underwent dual-energy X-ray absorptiometry (DXA) and cancer screening from January 1, 2008—December 31, 2012 from a cohort selected from Chang Gung Health Care Center in Taiwan. The study end point was a definite pathological diagnosis of cancer or admission for cancer treatment.
Results: During a mean follow-up of 6.6 ± 1.5 years, 110 incident cases of cancer occurred. The overall incidence of cancer was significantly higher in those patients with a low BMD (1.3%) than in those with a normal BMD (1.0%). Multivariate Cox regression analysis showed that older age, smoking, and low BMD (hazard ratio: 1.5; 95% confidence interval: 1.0—2.3) were significant independent risk factors for cancer.

Conflicts of interest: The authors have no conflicts of interest relevant to this article.

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Conclusion: Our investigation suggested that subjects with a low BMD may have a higher long-term risk of cancer compared with subjects with a normal BMD.

Introduction

Osteoporosis is a progressive systemic bone disease characterized by low bone mass and microarchitecture deterioration of bone tissue, leading to increased bone fragility and susceptibility to fracture. It is recognized as a major public health problem in many countries, as well as in Taiwan.[1,2] Cancer is a risk for bone loss due to the direct effects of cancer cells on the skeleton. In addition, cancer patients, independent of cancer type, had been reported to have a higher risk of osteoporosis than general population.[3–5] From a pathophysiological point of view, there may be a link between osteoporosis and the incidence of cancer. For example, bone morphogenetic proteins (BMPs) associated with osteoporosis[6] have been identified in the pathological pathways of cancer.[7–10] Although previously published studies had investigated the possible association between incidence of breast cancer and bone mineral density (BMD), some of them showed a significant association between higher BMD and higher incidence of breast cancer.[11] However, data arising from investigation of the association of long-term risk of cancer and BMD are still too scarce and weak to produce dependable conclusions. Thus, we conducted this cohort study using data from a healthcare center to investigate the association between the risk of cancer and low BMD.

Methods

Cohort definition

We identified 43,995 individuals who underwent dual-energy X-ray absorptiometry (DXA) to measure BMD and also cancer screening at the same time from January 1, 2008 to December 31, 2012 at the Chang Gung Health Care Center. Among them, 16,725 subjects were enrolled having regular health check-ups or outpatient follow-ups on the basis of a review of electronic medical records. Patients were excluded if they: 1) were aged <50 years old, because nearly normal BMD is typical in the young population; 2) had a previous history of cancer; 3) were diagnosed with cancer within 1 year after the index health check-up; or 4) subjects with incomplete electronic medical records for the data of cancer screening or the diagnosis of cancer (Fig. 1).

DXA technique

Central DXA for BMD assessment was performed using standard techniques according to International Society for Clinical Densitometry (ISCD) guidelines, and scans of the lumbar spine, and both femurs were performed to assess BMD by iDXA model from Lunar Co. (GE LUNAR, Madison, WI, USA). For lumbar spine BMD, at least two evaluated vertebrae from L1 through L4 without fractures or other abnormalities were measured.[12] DXA scans and subjects positioning were standardized with a long-term coefficient of variation of less than 1%. Quality controls for the DXA equipment were undertaken daily according to the manufacturer's guidelines to verify the stability of the system. For inclusion, at least one valid T-score report for the lumbar spine or hips was required. Osteoporosis was diagnosed if found to be 2.5 standard deviations below the mean of young by sex-matched reference populations or lower, where osteopenia was defined as a DXA T-score between −1.0 and −2.5; the reference BMD values were determined from young healthy adults in accordance with the recommendations of the World Health Organization and ISCD and the method chosen by the DXA manufacturer.

Cancer screening

The protocol of cancer screening included the following steps. First, physical examination and history were noted, where examination of the body was performed to check for general signs of health, including any signs of disease such as lumps or anything else that seemed unusual. A history of the patient's health and past illnesses and treatments was also recorded. Second, laboratory tests and blood tests were performed to check for specific substances that may indicate the presence of disease. The cancer screening blood tests included CA-125 (ovarian cancer), alpha-fetoprotein (liver cancer), CEA (colorectal cancer, lung cancer, etc), CA 19-9 (biliopancreatic cancer, malignancies of gastrointestinal tract), and prostate specific antigen (prostate cancer). Fecal occult blood tests were also performed to check for blood in patient stools to screen for colon cancer. Pap smears were also performed to check for abnormalities in cells collected from the cervix. Third, imaging studies, including chest X-rays (lung cancer), mammograms (breast cancer), abdominal echography (liver cancer), and kidney echography (renal cancer) were used for screening.

Confirmation of a cancer end-point

After a single baseline session of cancer screening, the assessment of cancer was derived from routine clinical follow-up including regular health check-ups or outpatient follow-ups. The end point of the study was defined as a definite pathological diagnosis of cancer or admission for cancer treatment. Follow-up was from the date of index health check-up until the date of the first cancer event or date of Dec. 31, 2015, whichever came first.

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