Emerging Trends in Dual Energy X-ray Absorptiometry

By Kevin E. Wilson, PhD

New developments in dual energy x-ray absorptiometry (DXA) technology are leading to major improvements in diagnosing osteoporosis, more accurately determining future fracture risk, and most recently, diagnosing cardiovascular disease.

Newer fan-beam DXA systems can detect vertebral fractures with fast, low dose lateral scans of the vertebra from T4 to L4 in as little as 10s. Vertebral fractures are the most common fracture in osteoporosis and an indication for treatment irrespective of BMD.[1-3] However, without a diagnostic test such as that available on fan-beam DXA systems, as many as 75% of vertebral fractures would never come to clinical attention.[4]

Some DXA systems can measure bone structure and strength using conventional DXA scans. And coming down the road are three-dimensional (3-D) DXA scans taking advantage of the rotating C-arms found on some of the newer DXA systems.

Recently, a DXA manufacturer received FDA clearance to assess an important risk factor for heart attacks and stroke: abdominal aortic calcifications (AAC). Using the same scan used to identify vertebral fractures, the ability to assess the risk of two highly prevalent diseases, osteoporosis and cardiovascular disease, greatly increases the economic utility of DXA systems.

Osteoporosis Overview

Osteoporosis is a serious, but not fully appreciated disease. The statistics are staggering:

- An estimated 10 million American women suffer from osteoporosis,[5] 200 million suffer worldwide.[1]
- Osteoporosis causes 1.5 million fractures per year in the US alone.[6]
- Osteoporotic fractures create a heavy economic burden in the US at costs of $13.8 billion annually. In comparison, the direct cost of cardiovascular disease is $20.3 billion and asthma, $7.5 billion.[1]
- In the US, osteoporosis is the direct cause of more than 500,000 hospital admissions, 2.6 million physician visits, and nearly 180,000 nursing home admissions.[5]

Osteoporosis is a "silent" disease. In the US, 4 times as many men and nearly 3 times as many women have osteoporosis than report having the condition. One of the most dangerous myths about osteoporosis is that only women need to worry about bone health. Four out of every 10 white women age 50 or older in the US will experience a hip, spine, or wrist fracture during the remainder of her life. Thirteen percent of white men in the US will suffer a similar fate.[7]

Tomographic 3-D representation of the hip

Fracture shown in vertebral assessment puts women at increased risk of more fractures

Image showing severe abdominal aortic calcification

Figure 1. New directions in DXA imaging

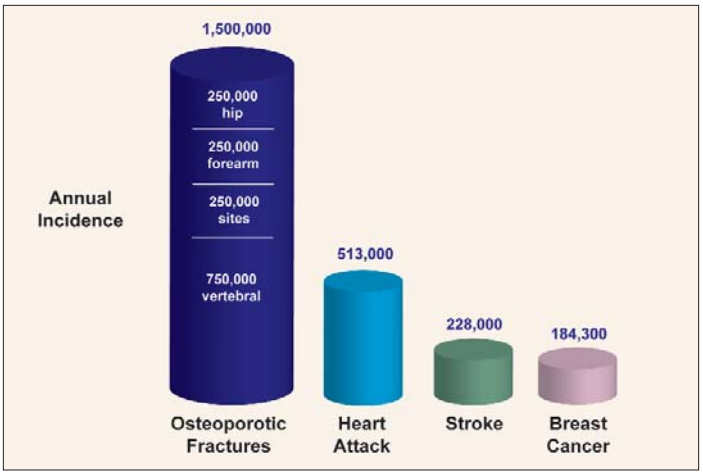

Figure 2. The incidence of osteoporotic fractures in the US females versus other diseases. [6]

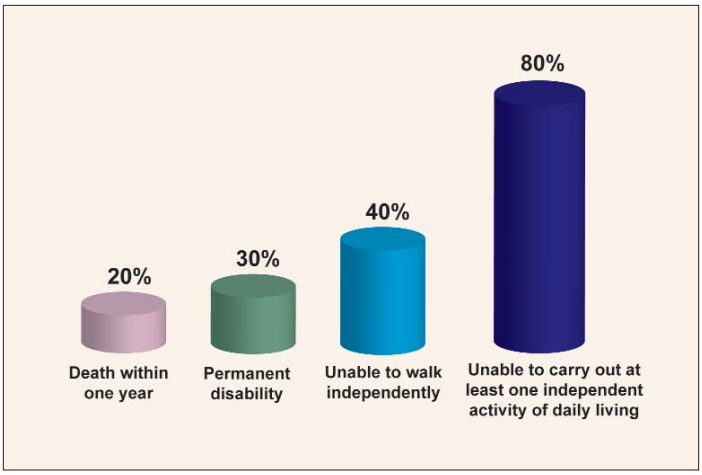

Figure 3. Impact of a hip fracture on the US female population.[8]

All fractures are associated with significant morbidity and mortality, but hip fractures are particularly traumatic. Twenty percent of the women who suffer a hip fracture die within the first year (Figure 3). Because of the aging population, it is estimated that the number of hip fractures could double or even triple in the US by 2020.[5]

Measuring Bone Mineral Density (BMD)

Fragility fracture and BMD at the spine or hip measured with DXA are the 2 primary methods for diagnosing osteoporosis in an individual. While non-DXA measurements or risk factors can be used to better refine a patients future fracture risk, BMD with DXA is the only recognized diagnostic test for osteoporosis other than radiographic evidence of a fracture.[2, 9] In conventional (DXA) systems, 2 energies of x-rays are used to calculate a 2-D measurement of areal BMD.

The indications and reimbursement for BMD vary from country to country. The International Society of Clinical Densitometry[2] has identified those patients most likely to benefit from BMD screenings as:

- Women age 65 and older
- Postmenopausal women under age 65 with risk factors
- Men age 70 and older
- Adults with a fragility fracture
- Adults with a disease associated with low bone mass or bone loss
- Adults taking medications associated with low bone mass or bone loss

Additionally, BMD testing is indicated to monitor patient treatments, or if a patient is being considered for pharmacologic therapy.

The International Osteoporosis Foundation prefers a case finding strategy where, in addition to age, clinical risk factors such as paternal history of hip fracture, smoking, corticosteroids use, etc, are used to select those who should be tested.[9]

Vertebral Fracture Assessment (VFA)

Vertebral fractures, which are associated with increased disability and morbidity, are the most common osteoporotic fracture; however, only about one-quarter of vertebral fractures come to clinical attention.[4] Nevertheless, women with vertebral fractures have been shown to have a 5-fold increase in their risks for a subsequent vertebral fracture, and a 2-fold increase in the likelihood of a hip fracture. One out of every 5 women who have an incident of vertebral fractures will suffer a subsequent fracture within the following 12 months.[10] The importance of low-trauma vertebral fractures is such that both the International Osteoporosis Foundation and the National Osteoporosis Foundation, based in the US, agree that its presence is an indication for the need for osteoporosis treatment irrespective of BMD.

Modern fan-beam DXA devices can perform VFA of the T4 to L4 vertabrae in as little as 10s. This is done without film and with one-fiftieth of the radiation dose of a conventional x-ray.[4] For those DXA devices with a rotating C-arm, the lateral exam can even be done without moving the patient from the supine position. By combining VFA with BMD, the two strongest risk factors for future fracture can be obtained on the same device with little additional exam time.

The American Medical Association has established a Current Procedural Terminology (CPT®) code for DXA bone densitometers that provides imaging of the spine for assessing the presence of vertebral fractures. The identification of the CPT code represents a major milestone in recognition of the clinical and economic value of combined bone density and VFA testing. Some Medicare regional payors reimburse for VFA thanks to the efforts of the major medical societies and associations including the ISCD, AACE (Endocrine), ACR (Rheumatology), and the NOF. As with other new procedures, it may be several years before the majority of insurers are on board.

VFA has the potential to improve the diagnostic accuracy

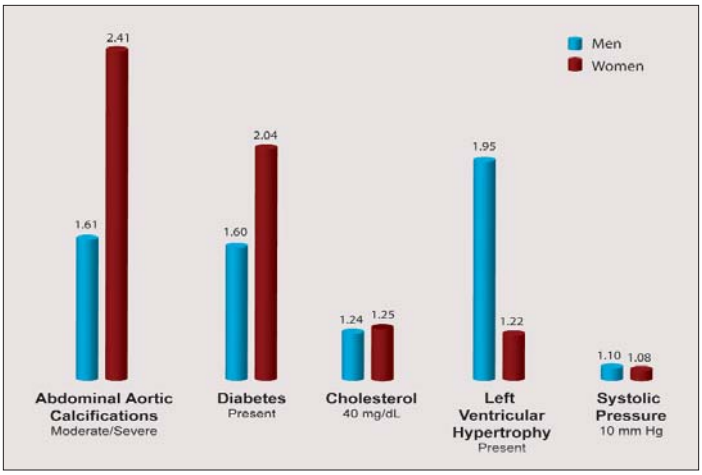

Figure 4. Cardiovascular heart disease multivariate adjusted relative risk.[14]

in identifying women who are eligible for treatment. In fact, several studies have shown that for women over the age of 65, 20-25% have vertebral fractures that would not qualify for treatment based on BMD alone.[11, 12] These are women who are at a very high risk of fracture and should be treated, but they would have been missed if VFA testing had not been done.

Hip Structural Analysis

Hip Structural Analysis (HSA) is a program for computing the structural properties of various cross sections of the proximal femur, using 2-D DXA scans. HSA algorithms are able to calculate bone strength in the two dimensions projected by the DXA scan.[13] Dr. Thomas Beck and his colleagues in the School of Medicine at The Johns Hopkins University are widely recognized for their work in the development of biomechanical parameters of hip structure derived from densitometric information. HSA is the leading bone structure analysis method for DXA scans used in research and pharmaceutical studies and has been included in over 30 peer-reviewed articles.

3-D Bone Imaging

The natural extension of HSA is to consider the femur as the 3-D object that it is, and calculate its strength in 3-D. The next generation of DXA imaging for the diagnosis of osteoporosis will use the rotating C-arm feature found on some DXA devices to take multiple projections of the femur. These multiple projections will be combined to form a tomographic 3-D representation of the hip. This low-dose tomographic assessment is expected to become the ultimate clinical tool for diagnosis of osteoporosis; not only will it give a more accurate picture of bone density, but also the geometry and underlying strength of a bone.

DXA as a Predictor of Heart Disease and Stroke

The US Food and Drug Administration recently cleared one manufacturer's DXA system for the visualization of abdominal aortic calcification, which is strongly associated with cardiovascular disease.[14-16] This new indication targets the number one cause of morbidity and mortality in older women and men: heart disease and stroke.

The risk of heart disease and stroke increases with age. Cardiovascular disease is the leading cause of death of women in the US and most developed countries, with nearly 39% of all female deaths in the US occurring from CVD.

AAC is a particularly valuable measurement since it contributes independently of traditional clinical risk factors such as cholesterol, blood pressure, diabetes, and age to the prediction of heart attack risk.

As shown in Figure 4, a woman suffering from moderate to severe AAC is at 2.4 times increased risk of cardiovascular heart disease, even after adjusting for age, cigarettes, diabetes mellitus, systolic pressure, left ventricular hypertrophy, bone mass index, and cholesterol. Detection of moderate to severe AAC is equivalent to the risk incurred if the patient had an additional 160 mg/dL of total cholesterol.[14]

AAC also has a strong and graded association with coronary calcium score as measured by electron beam CT. There was a 10-fold increase and 20-fold increase in coronary calcium score in the presence of severe AAC in men and women, respectively.[17]

With proper patient positioning, which is automatically accomplished with the rotating C-arm featured on some DXA systems, AAC can be seen in the same scans used for VFA. Fortuitously, AAC seems to be a particularly strong risk factor in postmenopausal women, which is the population that is also in greatest need of VFA scans.

DXA as a Measure of Body Composition

Obesity is now classified as a disease by Medicare, and is increasingly a worldwide problem. Body Mass Index (BMI) formulas and waist circumference measurements are not adequate to accurately define obesity. DXA has long been considered the gold standard in the precise measurement of a person's percent body fat. However, there has been a lack of accurate reference data from which to define healthful levels of percent body fat (% fat) and muscle mass (% lean).

The US Center for Disease Control's "National Health and Nutrition Examination Survey" has taken on the task of collecting accurate body composition (% fat and % lean) in the US. This reference data, collected from whole body DXA exams on a single manufacturer's equipment, should provide information for the accurate diagnosis of obesity with DXA.

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Evaluating DXA Devices

Two manufacturers sell a variety of central DXA systems in the U.S. market. Each has a number of different features and capabilities. Central DXA systems use either fan-beam or pencil-beam technology. Millennium Research Group, a research and consulting group, notes that fan-beam systems have shorter scan times and better image quality than pencil beam systems. Only fan-beam systems are capable of vertebral and 3-D imaging, abdominal aortic calcification detection and body composition analysis. Millennium says that fan-beam systems are quickly replacing the older pencil-beam systems.[18]

While methods of evaluating DXA devices are not yet fully developed, traditional phantoms for evaluating radiological devices are still relevant. This includes line pair phantoms for measuring the resolution and contrast/detail phantoms. Resolution, while not critical for BMD measurements, is important for VFA, AAC detection, and measurements of bone structure and strength.

In addition to image quality, long-term stability of the BMD measurements should be provided for since it is required to detect very small changes. It is recommended by the ISCD that a quality control phantom (different than a calibration phantom) be scanned at least weekly to monitor stability of the BMD of the device.[2]

Conclusion

DXA systems have advanced beyond BMD measurements. The new DXA devices could change the way doctors and scientists look at osteoporosis and how hospital administrators think about the utility of DXA devices. VFA assessment allows for early detection of fractures and fracture risks. HSA and 3-D imaging promises to provide information on bone strength and structure. AAC detection and body composition measurements are extending DXAs' utility outside of the osteoporosis field and addressing the important preventive health fields of cardiovascular disease and physical fitness.

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