Review Article

Hip Structural Analysis and Bone Strain Index in Clinical Practice: Their Utility Beyond BMD

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Abstract

Previous studies have demonstrated that in certain medical conditions, fragility fractures tend to occur even at bone mineral density (BMD) levels that are in the nonosteoporotic range. This warrants the assessment of other factors beyond BMD that might confer an increased propensity to fracture. Hip structural analysis (HSA) is also performed by the DXA scanner and evaluates different variables pertaining to proximal hip geometry. Bone Strain Index (BSI) is another novel DXA-based tool that was recently developed to further assess bone health. This has been based on a finite element analysis of grey scale images of density distribution of the femoral and lumbar spine scans obtained from a DXA scanner. Preliminary studies assessing the utility of BSI in predicting fragility fractures have been promising. This review will focus on the technical details and utility of the HSA and BSI beyond conventional BMD assessment.

Keywords: Bone Strain Index, DXA, fragility fractures, hip structural analysis, osteoporosis

Introduction

The increase in life expectancy of the Indian population at large has witnessed a parallel increase in the prevalence of noncommunicable diseases such as cardiovascular disease, cancer, obesity, diabetes and osteoporosis. Among the noncommunicable diseases, osteoporosis continues to be underdiagnosed and undertreated, although its prevalence is about 40–50% among Indian postmenopausal women. This is further compounded by the presence of nutritional calcium and vitamin D deficiency.[1,2]

The gold standard in the diagnosis of osteoporosis is the assessment of bone mineral density (BMD) by DXA (Dual Energy X-ray Absorptiometry) scan.[3] DXA makes use of the principle of differential attenuation of two X-ray beams of differing energies to provide an image in which only the mineral content is present. However, the organic collagen which binds the mineral together is subtracted out. Besides bone mineral density, bone strength is also determined by the direction and magnitude of the force applied as well as the bone geometry. It is also dependent on the spatial distribution of bone mineral with respect to loading forces that may be encountered.

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Lacunae in Current Literature

Previous studies have also shown that both postmenopausal women and physicians at the level of primary care have a suboptimal understanding of the burden and treatment of osteoporosis.[4,5] The prevalence of fragility fractures at the thoracolumbar spine, as demonstrated by the vertebral fracture assessment (VFA) tool of the DXA in this age group, was about 65%.[6,7] Moreover, the mortality associated with a fracture of the proximal femur was about 20% in the first year after the fracture.[8] Thus, the high prevalence of osteoporosis, vertebral fractures and the morbidity and mortality associated with hip fractures, compounded by the high societal and out-of-pocket costs mandate that postmenopausal women be screened for the adequacy of their bone health.

Currently, the evaluation of bone health in postmenopausal women consists of assessment of bone mineral density by DXA

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scan, at least 5 years after menopause. There is no consensus on diagnosing osteoporosis based on non-BMD measures such as trabecular bone score (TBS), hip structural analysis or the bone strain index. Intriguingly, in a study done by Wainwright *et al*.,[9] it was found that among 243 women with incident hip fractures, a staggering 54% of them did not have osteoporosis. Moreover, there are medical conditions such as chronic kidney disease, diabetes, obesity and the spondyloarthropathies that may result in fragility fractures even at a subnormal, nonosteoporotic BMD.[10]

The assessment of BMD at the PA-lumbar spine may be further confounded by the presence of degenerative changes such as osteophytes, ligamental calcification and calcification of the anteriorly disposed abdominal aorta. These artefacts may cause a spurious increase in lumbar spine BMD and may not be reflective of optimal bone strength in this site. In a recently published study, it was reported that in postmenopausal women with and without type 2 diabetes mellitus, the bone mineral density at the femoral neck and lumbar spine did not differ significantly. However, there was significant impairment of the trabecular bone score and parameters of proximal hip geometry in subjects with diabetes, as compared to those without diabetes.[11] These conditions do therefore warrant the search for other predictive indices beyond BMD and additional evaluation using other measures such as HSA, VFA, TBS and BSI in these instances.

Hip Structural Analysis and its Components

The hip structural analysis (HSA) program was introduced to extract geometric strength information of the hip from archived DXA images.[12] HSA is also performed by the DXA scanner and evaluates different variables pertaining to proximal hip geometry such as the cross-sectional area (CSA), cross-sectional moment of inertia (CSMI), section modulus (Z) and the buckling ratio (BR) [Table 1]. These geometric indices are measured at each of three sites, namely, the narrow neck (NN), which is the narrowest region of the neck, the inter-trochanteric area (IT) along the bisector of the angle between the femoral shaft and neck and the femoral shaft (FS), along an axis perpendicular to the femoral shaft, 2 cm distal to the midpoint of the lesser trochanter [Figure 1].

Table 1: Components of the hip structural analysis programme with definitions

Component of HSA	Definition
Cross-sectional area (CSA) (cm^2)	Excludes soft spaces in the marrow and pores and is an index of resistance to axial forces
Cross-sectional moment of inertia (CSMI) (cm^4)	Provides an estimate of resistance to bending forces in a cross-section.
Sub-periosteal width (cm)	Outer diameter of the bone computed as the blur-corrected width of the mass profile.
Endocortical diameter (ED) (cm)	Estimate of inside diameter of cortex
Mean cortical thickness (cm)	Estimate of mean cortical thickness, calculated as (width-ED)/2
Section modulus(Z) (cm^3)	Index of strength calculated as the CSMI ÷ the distance from the bone edge to the centroid (assumed here to be half the subperiosteal width)
Buckling ratio (BR)	Index of susceptibility to local cortical buckling under compressive loads. A buckling ratio (NN) of >10 was considered to be deleterious[12]
Hip Axis Length (HAL) (mm)	Distance from the pelvic rim to the outer margin of greater trochanter along the neck axis
Neck Shaft Angle (NSA)	Angle between derived axis of neck and shaft

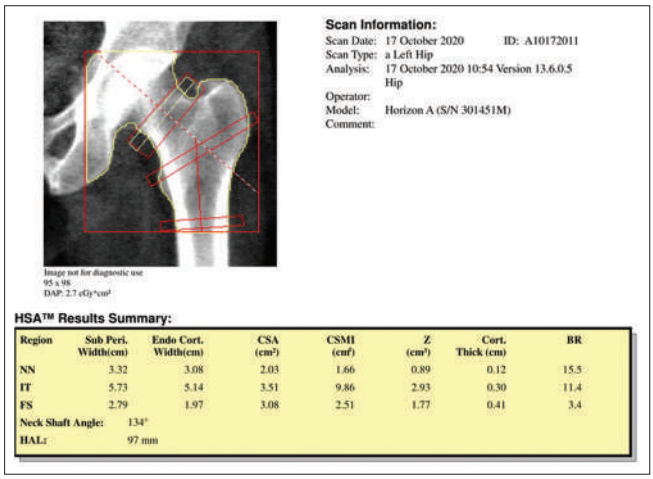

Figure 1: HSA report of a 78-year-old woman. The buckling ratio at the narrow neck is 15.5

Importance of Hip Geometry

A few previous studies have assessed the utility of HSA in various subjects, and this is shown in Table 2.[13-17] As mentioned above, the hip structural analysis may help to characterize finer details of bone strength in individuals with type 2 diabetes mellitus.[11] It has also been shown that the parameters of proximal hip geometry were significantly impaired in postmenopausal women with hip fractures (n = 90) as compared to control subjects without a fracture.[18] In a prospective study assessing changes in BMD, TBS and HSA following teriparatide therapy in postmenopausal women with severe osteoporosis or prevalent vertebral fractures (n = 43), it was demonstrated that the improvements in hip structural analysis were more robust than increments in bone mineral density.[19]

Parameters of hip structural analysis have also been studied in diseased cohorts such as cirrhosis and Parkinson's disease. In a study on 30 men with cryptogenic cirrhosis, it was found that affected individuals had a lower bone mineral density, trabecular bone score and impaired parameters of proximal hip geometry.[20] In a similar cohort of men with Parkinson's disease (PD), it was found that the bone mineral density was not significantly different between cases and controls, although the hip structural analysis was worse in those with PD as compared to age- and BMI-matched controls.[21]

Table 2: Data from previous studies

Previous studies	Findings
Khoo BC *et al*.[13]	Using a cohort of 1159 women with mean baseline age of 75 years, who sustained 139 hip fractures over 15 years, it was found that TR_σ*, total hip aBMD and age and provided improved utility for hip fracture prediction compared to total hip aBMD and age alone (C-statistic 0.73 vs. 0.69, *P*=0.009) *TR - Inter-trochanteric region, σ - standard deviation of normalised mineral-mass projection profile distribution. σ^2 is defined as CSMI/CSA at the region
La Croix AZ *et al*.[14]	10,290 postmenopausal women from the Women's Health Initiative were studied. Eight thousand eight hundred forty-three remained fracture free during follow-up to 11 years of follow-up, while 147 fractured their hip, and 1,300 had other clinical fractures. After adjustment for age, body size, clinical risk factors, and aBMD, intertrochanter and shaft outer diameter measurements remained independent predictors of hip fracture with hazard ratios for a one standard deviation increase of 1.61 (95% confidence interval (CI), 1.25-2.08) for the intertrochanter and 1.36 (95% CI, 1.06-1.76) for the shaft. Average buckling ratios also independently predicted incident hip fracture with hazard ratios of 1.43 (95% CI, 1.10-1.87) at the intertrochanter and 1.24 (95% CI, 1.00-1.55) at the shaft.
Naseri A, *et al*.[15]	Among ambulatory type 2 diabetic postmenopausal women and 539 healthy controls, TBS and BMD at the distal radius and total forearm were significantly lower in cases compared to controls after age and body mass index (BMI) adjustment. A number of geometric indices of the proximal hip were significantly lower in the controls than in those with diabetes.
Sone T, *et al*.[16]	Hip DXA scans from postmenopausal women and men (ABL, *n*=128; placebo, *n*=65) at baseline and up to week 78 were analysed. ABL treatment showed increased mean percent change from baseline to week 78 in cortical thickness at the NN (5.3%), IT (5.3%), and FS (2.9%); cross-sectional area at the NN (5.0%), IT (5.0%), and FS (2.6%); cross-sectional moment of inertia at the NN (7.6%), IT (5.1%), and FS (2.5%); section modulus at the NN (7.4%), IT (5.4%), and FS (2.4%); and decreased mean percent change in buckling ratio (BR) at the IT (- 5.0%).
Rathbun AM *et al*.[17]	The objective was to examine sex differences in proximal femur geometry following hip fracture (*N*=282) in both men and women. Women generally experienced nonsignificant increases in bone tissue and strength following hip fracture, while men had structural declines that were statistically greater at the NN region. Reductions in the mechanical strength of the proximal femur after hip fracture could put men at higher risk for subsequent fractures of the contralateral hip.

Bone Strain Index

Another paradigm in the comprehensive assessment of bone health is the development of the novel DXA-based tool, namely, the BSI. While BMD, TBS and the HSA do provide information on bone strength and susceptibility to fracture, the BSI is designed to assess the resistance of the bone to loading forces. It is measured at the femoral neck and lumbar spine.

Principle

It is indeed a novel tool that works on the principle of 'Finite Element Analysis (FEA)' on a greyscale of density distribution measured on the spine and femoral scans. Bone segmentation is initially performed using the DXA software. Following this, the FEA is done automatically by placing forces and constraints on a triangular mesh obtained through the bone segmentation. At the lumbar spine, each vertebra is loaded on the upper surface and constraints are placed on the lower surface.[22] At the femur, the algorithm for computing BSI is based on a potential lateral fall with constraints placed on the head and lower shaft. The force which is subject specific impact and linked to the weight of the individual is applied to the greater trochanter.[23] As the BSI value is related to its resilience of the bone to withstand an applied load, it reflects bone strength. A BSI value of ≤ 1.68 indicates normal strain and ≥ 2.40 [Figure 2] indicates increased a higher strain and a reduced resistance to fractures.[24]

Experimental Evidence

Experimental evidence concerning the usefulness of the bone strain index has been gathered from preclinical porcine studies and studies involving groups of individuals with osteoporosis.

A study done by Columbo *et al*.,[22] validated this procedure in 33 trabeculated porcine vertebrae under static compressive loading. These were then compared with numerically simulated values following which it was concluded that mechanical parameters of the bone had a better correlation with the Strain Index of Bone as compared to the bone mineral density and trabecular bone score. Buccino *et al*.[25] also showed how strain values increased with accumulated bone damage.

Precision

As any densitometric parameter is subjected to the error limits that govern precision and reproducibility, both *in vitro* and *in vivo* studies were undertaken in keeping with the ISCD guidelines. Messina *et al*.[26] reported that the reproducibility of the BSI at the hip was lower than that of BMD. The total femur reproducibility *in vivo* (CoV = 3.89%, reproducibility = 89.22%) was better as compared to that of the femoral neck (CoV = 4.17%, reproducibility = 88.46%).

Similarly, in the case of lumbar spine, BSI reproducibility was significantly lower than that of BMD and decreased proportionally with increasing BMI and waist circumference. This reduction of BSI reproducibility was more pronounced in patients with BMI ≥ 30 kg/m^2 and WC > 88 cm, as BSI is a parameter that is sensitive to weight.[27]

Clinical Studies

Fragility fractures

In a study by Sornay-Rendu *et al*.,[28] it was shown that BSI was positively associated with a significant increase in the risk of fragility fractures with an age-adjusted HR of 1.23 for neck BSI

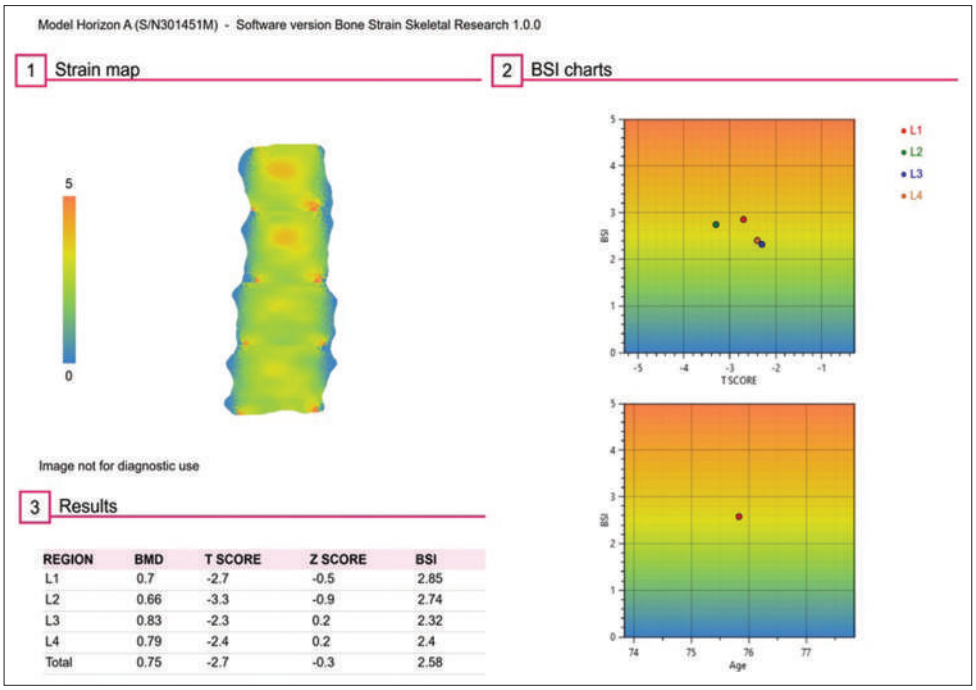

Figure 2: BSI report of the same woman. The BSI at the lumbar spine is 2.58, indicating reduced resistance to fracture or increased bone strain

($P = 0.02$); 1.27 for total hip BSI ($P = 0.004$) and 1.35 for the lumbar spine BSI ($P < 0.001$). Following adjustment for FRAX®, the association remained statistically significant for total hip BSI (HR 1.24, $P = 0.02$ for all fragility fractures 1.31, $P = 0.01$ for MOF) and spine BSI (HR 1.33, $P < 0.001$ for all fragility fractures; 1.33, $P = 0.005$ for MOF; 1.67, $P = 0.002$ for clinical VFx). In a multicentric retrospective study on the prediction of refracture, it was found that the BSI hazard ratio of incident refracture 95% CI was 1.372 (1.038-1.813), $P = 0.02$.[29]

Primary hyperparathyroidism

Tabacco G *et al*.[30] evaluated the utility of BSI in secondary osteoporosis caused by primary hyperparathyroidism. It was found that BSI was significantly higher at the lumbar spine LS (2.28 ± 0.59 vs 2.02 ± 0.43, $P = 0.009$), femoral neck (1.72 ± 0.41 vs 1.49 ± 0.35, $P = 0.001$) and total hip (1.51 ± 0.33 vs 1.36 ± 0.25, $P = 0.002$) in PHPT (N = 50) when compared to matched controls (N = 100). LS-BSI showed moderate accuracy for discriminating VFs (AUC 0.667; 95% CI, 0.513-0.820). LS-BSI ≥2.2 was a statistically significant independent predictor of VFs, with an adjusted odds ratio ranging from 5.7 to 15.1.

Utility in monitoring response to therapy

Messina *et al*.[31] studied the response of DXA-derived parameters to teriparatide therapy in 40 individuals. He reported that in the entire population, the improvements posttherapy were seen in the lumbar BSI (−13.9%), TBS (5.08%) and BMD (8.36%).

Conclusion and Future Direction

Although there is no consensus on the routine use of these tools in clinical practice, these are being used in the setting of research to try and identify additional parameters of bone strength not routinely captured by BMD assessment. As far as cost effectiveness is concerned, hip structural analysis and bone strain index make use of additional software and the results may be obtained from archived densitometric images of the proximal hip and lumbar spine. These may be performed at an additional cost of INR 300–500. As these are performed on the same DXA scanner, access to DXA ensures access to these facilities as well. Based on our literature review, these adjuncts may be used in the following circumstances:

a. The presence of fragility fractures in the absence of osteoporosis.
b. Conditions leading to a paradoxically high BMD such as type 2 diabetes mellitus and obesity.
c. Other conditions leading to spuriously high BMD such as spondyloarthropathies, degenerative changes and abdominal aortic calcification.

Presently, data with regards to proximal hip geometry and bone strain index in Indian women are limited. Current DXA scanners incorporate reference database on hip geometry based on the NHANES data in Caucasian women. A study done by Zengin A *et al*.[32] has shown that ethnic differences do exist in areal bone mineral density as well as bone geometry. Data on bone strain index are limited. Deriving ethnicity-specific reference ranges for these parameters is thus imperative and may be the way forward in the advancement of bone health assessment in the Indian population.

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Author Contribution

This review was conceptualized by KEC. The literature search was done by KEC and TVP. Both authors contributed equally to the manuscript preparation and approved the final version.

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Conflicts of interest

There are no conflicts of interest.

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