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ORIGINAL ARTICLE

Does hip structural analysis confer additional benefit to routine BMD assessment in postmenopausal women with hip fracture? A study from a tertiary center in southern India

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Abstract

Summary This study from southern India showed that proximal hip geometry was significantly impaired in postmenopausal women with femoral neck fracture. The trabecular bone score (TBS), which is reflective of bone microarchitecture, was also significantly impaired in patients with fracture.

Introduction There is limited information with regard to comprehensive bone health in Indian postmenopausal women with neck of femur fracture. We studied the bone mineral density (BMD), trabecular bone score (TBS), proximal hip geometry, and bone mineral biochemistry in postmenopausal women with and without femoral neck fractures.

Methods This was a cross-sectional study conducted at a tertiary care center in South India. BMD, TBS, and hip structural analysis (HSA) were assessed using a dual-energy X-ray absorptiometry (DXA) scanner. Bone mineral biochemical profiles were also studied.

Results A total of 90 postmenopausal women with acute femoral neck fracture with mean (SD) age of 63.2 (6.1) years and 90 age-matched controls were included. The prevalence of osteoporosis was higher among cases as compared to controls (83.3% vs 47.8%; $P < 0.001$). Degraded bone microarchitecture (TBS value < 1.200) was more frequent among women with hip fracture as compared to controls (46.7% vs 31.1%; $P = 0.032$). Cross-sectional moment of inertia (CSMI) was significantly lower at the narrow neck (NN) and inter-trochanteric (IT) region in cases ($P < 0.05$) and buckling ratio (BR) was significantly higher at all three sites in postmenopausal women with femoral neck fracture as compared controls. Multivariate logistic regression analysis showed that femoral neck osteoporosis, low CSMI at NN and high BR at NN and femoral shaft emerged as factors significantly associated with femoral neck fractures.

Conclusion This study highlights that impaired parameters of proximal hip geometry and a low trabecular bone score may be significantly associated with femoral neck fractures in postmenopausal women.

Keywords Hip structural analysis · India · Postmenopausal osteoporosis · Trabecular bone score · Neck of femur fracture · Proximal hip geometry

Introduction

In India, about 30–50% of ambulatory postmenopausal women are affected with osteoporosis [1]. Fragility fracture is the most serious complication of osteoporosis and hip fractures account for about 20% of all osteoporotic fractures [2]. Osteoporotic hip fractures are a major concern due to multiple reasons. Firstly, it contributes to significant morbidity and mortality, with about 30% of people with hip fracture dying in the following year and the rest experiencing significant functional loss [3]. Secondly, it is the most costly

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type of fracture for health care services [4]. Also, increased risk of recurrent fractures is a recognized consequence and accounts for about 15% in 4 years [5].

Low bone mineral density (BMD) is a major risk factor for fragility fractures. However, the predictive capacity of BMD alone is not adequate to capture all fracture risks [6]. Microarchitectural alterations and geometric changes can also contribute significantly to fracture risk. Trabecular bone score (TBS) is a densitometric tool that evaluates pixel gray level variations in the lumbar spine DXA image, providing an indirect measure of bone microarchitecture [7]. TBS improves fracture risk prediction beyond that is provided by BMD and clinical risk factors, and can be incorporated to the Fracture Risk Assessment tool (FRAX®) to enhance fracture prediction [8].

Hip structural analysis (HSA) is also performed by the DXA and evaluates variables pertaining to proximal hip geometry such as the cross-sectional area (CSA), cross-sectional moment of inertia (CSMI), section modulus (Z), and buckling ratio (BR) [9, 10]. Each of these geometric indices is measured at three sites, namely the narrow neck (NN), the inter-trochanteric area (IT), and the femoral shaft (FS). Previous studies have shown that ethnic differences do exist in macroscopic parameters of proximal hip geometry [11, 12].

There is limited literature on HSA and TBS in postmenopausal women with neck of femur fracture. In this study, we aimed to assess DXA-derived parameters including BMD, TBS, and HSA as well as bone biochemistry in South Indian postmenopausal women with neck of femur fracture and compare them with age- and BMI-matched controls without fracture, recruited from the community.

Methodology

This was a cross-sectional study conducted over 2 years in which consecutive postmenopausal women aged 55 years or more with fragility fractures of the neck of femur admitted in a teaching hospital in southern India were recruited. Age- and BMI-matched healthy control subjects without fracture were recruited from the community.

This study was approved by the Institutional Review Board (IRB Min no. 6282). All subjects provided a written informed consent at the time of recruitment in the study. Postmenopausal women who were on treatment for osteoporosis, those with chronic kidney disease stages 4 and 5, those with secondary osteoporosis such as hyperthyroidism, chronic liver disease, those with a known malignancy, immobilization, malabsorption, and exogenous steroid use were excluded. Also, those taking medications (except calcium and vitamin D supplements) known to affect bone health were excluded from the study in both the case and control groups.

All patients were confirmed to have neck of femur fracture with plain radiograph of the hip. Fractures involving other sites of the proximal hip were excluded to ensure homogeneity.

Biochemical parameters

Fasting (overnight for 8 h) venous blood samples were collected for the measurement of serum calcium (N 8.3–10.4 mg/dL), phosphate (N 2.5–4.5 mg/dL), alkaline phosphatase (N 40–125 U/L), albumin (N 3.5–5.0 g/dL), creatinine (N 0.6–1.4 mg/dL), 25-hydroxy vitamin D (N 30–75 ng/mL), and intact parathormone (N 8–76 pg/mL). Serum calcium, phosphate, albumin, creatinine, and alkaline phosphatase were measured using colorimetric method with Beckman Coulter (Beckman Coulter AU 5800). An iced sample for intact parathormone (iPTH) was collected and estimated by chemiluminescence assay (Advia Centaur XPT immunoassay system), and 25-hydroxyvitamin D (vitamin D) was measured using electrochemiluminescence assay (Roche Cobas 6000—Immunoassay system). Vitamin D deficiency was defined as a 25-hydroxy vitamin D level that was less than 20 ng/mL.

Dual-energy X-ray absorptiometry scan parameters

Subjects underwent DXA scanning in the Hologic Horizon A (S/N 301,451 M) with APEX software Version 13.6.0.5:3 for BMD measurements at the lumbar spine and femoral neck, hip structural analysis, vertebral fracture assessment using the VFA tool in the same machine, and Trabecular Bone Score at the lumbar spine using TBS iNsight version 3.0.2.0. The reference for *T*-scores used was of Caucasian women from the NHANES database based on a previous study from our center which showed that the Indian database underperformed when compared to the Hologic database of Caucasian women from NHANES database in predicting osteoporosis in subjects with hip fracture [13].

Bone mineral density

Areal BMD (g/cm^2) at the non-fractured femoral neck, total hip, and lumbar spine (L1-L4) were assessed using DXA scanner Hologic machine Discovery A series. The categorization of BMD into normal, osteopenia, and osteoporosis was done based on *T*-scores, as defined by the ISCD (International Society for Clinical Densitometry) guidelines [14]. The reference database used was of Caucasian women, as provided by the manufacturer. The CV of BMD assessment at the femoral neck was 2–3% and at the lumbar spine was < 1%.

Trabecular bone score

TBS is a non-invasive method that evaluates pixel gray level variations in the lumbar spine DXA image and helps in assessing the microarchitecture of the bone [15]. TBS was assessed using iNsight Software version 3 (Med-Imaps, Bordeaux, France). A TBS value of more than 1.350 indicates normal microarchitecture. TBS value between 1.200 and 1.350 indicates partially degraded microarchitecture and a TBS < 1.200 indicates degraded bone microarchitecture [16, 17]. Moreover, in this study, the BMI ranged from 15 to 33 kg/m^2, and this was within the range of BMI allowed for TBS measurements [18].

Hip structural analysis

Hip structural analysis (HSA) is a simple tool to determine bone strength at the proximal femur by geometric assessment [19]. The HSA program performs its analysis at 3 femoral sites using averages from 5 parallel lines 1 pixel apart across the cross-section of three sites: (1) Narrow neck (NN), which is the narrowest point of the femoral neck. (2) Inter-trochanteric region (IT), along the bisector of the angle of the axes of the neck and femoral shaft. (3) Femoral shaft (FS), a site across the shaft at a distance of 2 cm distal to the midpoint of the lesser trochanter. The following four parameters of HSA were assessed in all the three sites: (a) Cross-sectional area (CSA) excluding soft spaces in the marrow and pores—an index of resistance to axial forces (cm^2). (b) Cross-sectional moment of inertia (CSMI)—estimate of resistance to bending forces in a cross-section (cm^4). (c) Section modulus (Z)—an index of strength calculated as the CSMI ÷ the distance from the bone edge to the centroid (assumed here to be half the subperiosteal width) (cm^3). (d) Buckling ratio (BR)—index of susceptibility to local cortical buckling under compressive loads [20]. Other parameters which can be analyzed in HSA include the Hip Axis Length (HAL) which is the distance from the pelvic rim to the outer margin of the greater trochanter along the axis of the femoral neck and the Neck Shaft Angle (NSA) which is the angle between the derived axes of the femoral neck and shaft.

The reproducibility as assessed by short-term precision was < 1% for measurements of TBS of the lumbar spine. Similarly, for HSA measurements the CV was about 2% [21].

The Fracture Risk Assessment Tool (FRAX®) was utilized to assess the 10 years risk of major osteoporotic fracture (MOF) and hip fracture (HF) in two categories (FRAX® with BMD, and FRAX® with BMD and TBS).

Sample size estimation Based on a previous study by Ming et al. [22], on 196 subjects with hip fracture, the mean difference in cross-sectional area at the femoral neck was found to be 0.23 cm^2. With a desired confidence interval of 95% and power of 80%, the sample size was estimated to be 93 subjects in each group.

Statistical methods Data were analyzed using SPSS v 24.0 (SPSS IBM Corp, USA). Continuous variables were expressed as mean and SD, and categorical variables were expressed as frequencies and percentages. The differences in means of continuous variables in the two groups were compared using Student's *t* test for normally distributed parameters, and the Mann–Whitney test was used to compare the parameters that were not normally distributed. The differences in proportions were compared using Pearson's chi-square test or the Fisher exact test as appropriate. The relationship between two quantitative variables was assessed using Pearson's correlation coefficient. Covariates predictive of femoral neck fractures were assessed using a logistic regression analysis. For all comparisons, a two-tailed *P* value of < 0.05 was considered statistically significant.

Results

A total of 90 postmenopausal women with femoral neck fractures, and 90 age- and BMI-matched control women were included in this study. Baseline characteristics of the study subjects are shown in Table 1. The mean (SD) age of cases and controls were 63.2 (6.1) years and 62.1 (6.0) years respectively. Type 2 diabetes mellitus was present in 15/90 (16.7%) of cases while none of the control subjects had diabetes. The FRAX® (Fracture Risk Assessment Tool) risk scores among cases were significantly higher ($P \leq 0.001$) as compared to controls.

Among the bone biochemical parameters, the mean (SD) 25-hydroxyvitamin D [18.8 (7.8) vs 25.8 (10.2) ng/mL; $P < 0.001$] was significantly lower and the PTH [75.8 (33.4) vs 65.5 (25.1) pg/mL; $P = 0.021$] higher among cases as compared to controls.

Among the densitometric parameters, it was found that the bone mineral density at the femoral neck, total hip, lumbar spine, and the trabecular bone score was significantly lower among cases as compared to controls ($P < 0.01$). The prevalence of osteoporosis at any site was significantly higher among cases as compared to controls (83.3% vs 47.8%; $P < 0.001$) (Table 2). Degraded bone microarchitecture as defined by a TBS value < 1.200 was encountered more frequently among postmenopausal women with hip fracture as compared to matched controls (46.7% vs 31.1%; $P = 0.032$).

Furthermore, the parameters of the hip structural analysis were also compared between cases and controls (Table 3). It was found that the cross-sectional moment of inertia (CSMI) was significantly lower at the narrow neck and the inter-trochanteric region in cases as compared to

Table 1 Demographics and bone biochemistry in postmenopausal women with hip fractures (cases) versus age- and BMI-matched controls

Variable	Cases ($N=90$) Mean (SD)	Controls ($N=90$) Mean (SD)	P value
Age (in years)	63.2 (6.2)	62.1 (6.1)	0.202
Height (cm)	149.9(5.4)	154.9(3.7)	< 0.001
Weight (kg)	51.1(9.4)	56.3(9.4)	< 0.001
BMI (kg/m^2)	22.7 (3.9)	23.3 (3.4)	0.166
Age of menopause (years)	46.7 (4.4)	45.7(4.8)	0.202
FRAX® (hip fracture)	3.2 (2.4)	1.9 (1.7)	0.001
FRAX® (major osteoporotic fracture)	7.9 (3.6)	5.7 (4.4)	< 0.001
TBS adjusted FRAX® (hip fracture)	3.9 (2.7)	2.1 (1.4)	< 0.001
TBS adjusted FRAX® (major osteoporotic fracture)	9.5 (4.0)	6.7 (4.0)	< 0.001
Calcium (mg/dL) *N*: 8.3–10.4 mg/dL	9.6(0.4)	9.5(0.4)	0.292
Phosphate (mg/dL) *N*: 2.5–4.5 mg/dL	4.1(0.5)	3.9(0.5)	NS
Creatinine (mg/dL) *N*: 0.6–1.1 mg/dL	0.8(0.2)	0.7(0.1)	NS
Alk. Phos (U/L) *N*: 40–125 U/L	98.7(22.2)	91.8(21.1)	0.035
25(OH) vitamin D (ng/mL) *N*: 30–75 ng/mL	18.8(7.8)	25.8(10.2)	< 0.001
PTH (pg/mL) *N*: 8–76 pg/mL	75.8(33.4)	65.5(25.1)	0.021

Table 2 Bone mineral density and trabecular bone score in cases and controls

Variable	Cases ($N=90$) Mean (SD)	Controls ($N=90$) Mean (SD)	P value
Lumbar spine BMD (g/cm^2)	0.696 (0.123)	0.787 (0.147)	< 0.001
Femoral neck BMD (g/cm^2)	0.545 (0.051)	0.642 (0.125)	< 0.001
Hip BMD (g/cm^2)	0.682 (0.083)	0.761 (0.142)	< 0.001
TBS score	1.204 (0.078)	1.235 (0.091)	0.017
Prevalence of vitamin D deficiency, osteoporosis, and low TBS			
Variable	Cases ($N=90$)		
N (%)	Controls ($N=90$)		
N (%)	P value		
Vitamin D deficiency	53 (58.9)	28 (31.1)	< 0.001
Osteoporosis	75 (83.3)	43 (47.8)	< 0.001
TBS < 1.200	42 (46.7)	28 (31.1)	0.032

controls ($P<0.05$). Moreover, the buckling ration, which indicates cortical instability, was significantly higher at all three sites, namely the NN [13.2(3.3) vs 11.2(2.9); $P<0.001$], IT [10.5(3.5) vs 9.4(2.3); $P=0.013$], and FS [3.6(1.2) vs 2.9(0.7) $P<0.001$], in postmenopausal women with hip fracture as compared to age- and BMI-matched controls.

Among the 90 women with femoral neck fractures, 41 (45.6%) had BMD at the femoral neck that was in the non-osteoporotic range. Similarly, among 90 women without fractures, 65 (72.2%) had BMD that was in the non-osteoporotic range. Comparisons in HSA were made between these two groups—i.e., 41/90 (cases with fracture and no osteoporosis) and 65/90 (controls with no fracture and no osteoporosis). Between these two groups, it was found that the buckling ratio at the NN [12.4 (2.9) vs 10.6 (2.7); $P=0.001$] and FS [3.3 (2.7) vs 2.9 (0.6) $P=0.001$] was significantly higher among women with fracture as compared to matched controls.

On doing a chi-square analysis, we found that the number of individuals who had a fracture was significantly higher among those with osteoporosis (63.6% vs 36.4% $P<0.001$) as compared to those without osteoporosis, those with a low TBS (< 1.200) (60% vs 40% $P=0.032$) and those with a high buckling ratio as compared those with a BR < 10 (55.2% vs 44.8% $P=0.013$).

In the exploratory multivariate analysis, the presence of femoral neck osteoporosis, low CSMI at the narrow neck and high BR of the narrow neck and femoral shaft emerged as factors significantly associated with femoral neck fractures (Table 4). The combined risk factor of a low CSMI, presence of femoral neck osteoporosis, presence of high buckling ratio at the narrow neck and femoral shaft was computed by utilizing the OR from the multivariate analysis. The performance

Table 3 Parameters of hip structural analysis compared between cases and controls

HSA variable	Cases ($N=90$) Mean (SD)	Controls ($N=90$) Mean (SD)	P value
NN (CSA) cm^2	2.19 (0.57)	2.26 (0.30)	0.335
NN (CSMI) cm^4	1.44 (0.27)	1.60 (0.38)	0.001
NN (Z) cm^3	0.96 (0.19)	0.94 (0.18)	0.669
NN (BR)	13.2 (3.3)	11.2 (2.9)	< 0.001
IT (CSA) cm^2	3.84 (0.95)	4.00 (0.84)	0.234
IT (CSMI) cm^4	8.73 (2.52)	9.51 (2.29)	0.032
IT (Z) cm^3	3.11 (0.83)	3.08 (0.69)	0.867
IT (BR)	10.5 (3.5)	9.4 (2.3)	0.013
FS (CSA) cm^2	3.33 (0.63)	3.42 (0.51)	0.285
FS (CSMI) cm^4	2.53 (0.66)	2.59 (0.60)	0.521
FS (Z) cm^3	1.77 (0.33)	1.77 (0.34)	0.909
FS (BR)	3.6 (1.2)	2.9 (0.7)	< 0.001
Hip Axis Length (HAL) (mm)	95.2(6.2)	94.9(5.8)	0.748

CSA cross-sectional area, *CSMI* cross-sectional moment inertia, *Z* section modulus, *BR* buckling ratio, *NN* narrow neck, *IT* inter-trochanteric, *FS* femoral shaft

Table 4 Multivariate logistic regression analysis to predict hip fractures

Clinical covariate	Adjusted OR	95% CI	P value
NN CSMI	0.15	0.04–0.52	0.003
NN BR	1.24	1.06–1.45	0.006
IT CSMI	1.09	0.92–1.31	0.308
IT BR	0.86	0.73–1.02	0.104
FS BR	2.46	1.43–4.52	0.001
FN osteoporosis	2.50	1.16–5.37	0.019
TBS	0.02	0.002–1.12	0.056

Table 5 Performance of individual and combination of risk factors in predicting hip fractures (ROC)

Variable	AUC	95% CI	P value
TBS	0.599	0.517–0.682	0.021
Femoral neck T-score	0.768	0.693–0.842	< 0.001
NN CSMI	0.613	0.532–0.695	0.009
NN BR	0.688	0.611–0.733	< 0.001
FS BR	0.686	0.610–0.763	< 0.001
Combined (presence of femoral neck osteoporosis, CSMI, NN BR, and FS BR)	0.754	0.681–0.826	< 0.001

of this composite risk factor in predicting hip fracture was assessed by a ROC curve and was found to have an AUC of 0.754 (95% CI 0.681–0.826; $P < 0.001$). This is shown in Table 5 and Fig. 1.

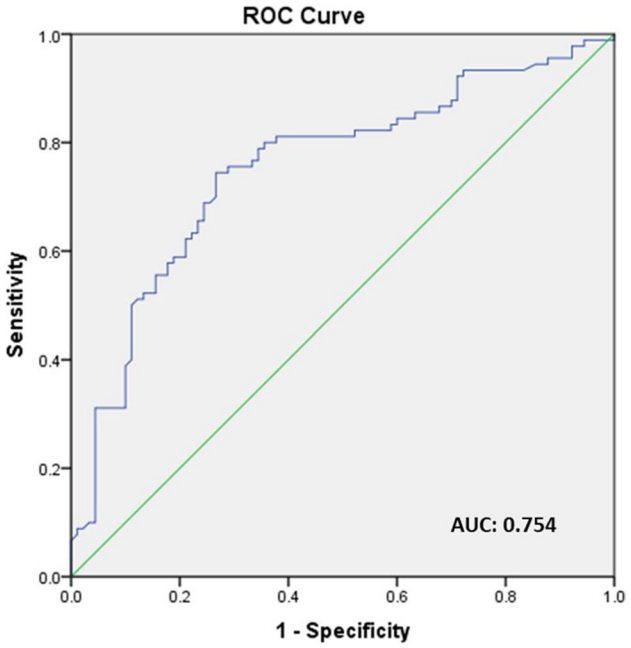

Fig. 1 Performance of combined risk factors of CSMI, NN BR, FS BR and presence of femoral neck osteoporosis in predicting hip fracture

Discussion

This is the first study from India assessing comprehensive bone health including bone mineral density (BMD), hip structural analysis (HSA), and trabecular bone score (TBS) in postmenopausal women with neck of femur fracture compared with age- and BMI-matched controls. Beyond BMD, the factors that were found to be significantly associated with hip fractures were CSMI at the narrow neck and buckling ratio at the narrow neck and femoral shaft. The prevalence of osteoporosis was significantly higher among women with femoral neck fractures as compared to those without fractures. Degraded bone microarchitecture was encountered more frequently among postmenopausal women with femoral neck fracture as compared to matched controls although it was not significantly associated in the multivariate analysis.

With regard to osteoporosis and hip fractures, our findings were in keeping with what has been described in the literature [23, 24]. Hip structural analysis (HSA) refers to the methodology used to assess bone strength based on the measurement of geometric characteristics in the proximal femur [25]. Low values of CSA, CSMI, and Z and a high BR denote poor hip strength and a higher tendency to fracture [26]. In the present study, it was observed that most indices of proximal hip geometry were significantly worse in subjects with femoral neck fracture as compared to controls. Majority of available data pertaining to proximal hip geometry are from a heterogenous sample of proximal

femoral fractures. In a study by Gnudi et al. comparing 429 women with hip fracture, 273 with femoral neck (FN) and 156 with trochanter (TR) fractures and 1646 women without fracture individuals with hip fracture had lower BMD, cross-sectional area, and section modulus with higher buckling ratio (BR), than controls [27]. Both femoral neck BMD and buckling ratio predicted trochanteric fracture significantly better than they did femoral neck fracture. Ming et al. [22] studied consecutive series of 196 patients with hip fracture aged over 50 years [109 cases of neck of femur fractures (36 males and 73 females) and 87 cases of trochanteric fractures (34 males and 53 females)]. Cross-sectional moment of inertia at the femoral neck and buckling ratio in the trochanteric region were significant risk factors for trochanteric fractures compared with cervical fractures.

In this study, among the subjects with femoral neck fractures, 45.6% had bone mineral density at the femoral neck that was reported to be in the non-osteoporotic range. Among women without osteoporosis at the femoral neck, buckling ratio at the NN and FS was significantly higher among women with fracture as compared to matched controls. Among the participants of the women's health initiative (WHI), among 10,291 women who were followed up for 11 years, 147 had hip fractures. It was found that after adjusting for clinical risk factors and areal BMD, intertrochanteric outer diameter and buckling ratio significantly predicted incident hip fractures [26].

It was also found that the presence of femoral neck osteoporosis, low CSMI at the narrow neck, and high buckling ratio at the NN and FS were significantly associated with fracture risk. This may implicate the utility of hip structural analysis as an adjunct to BMD in fragility fractures involving the proximal femur. Degraded bone microarchitecture was encountered more frequently among postmenopausal women with femoral neck fracture as compared to matched controls in the current study. Data available in published literature have also shown that bone microarchitecture predicts fracture risk [28]. Individuals with fracture had higher prevalence of vitamin D deficiency and elevated PTH values. A high prevalence of vitamin D deficiency was similarly reported by other studies in subjects with hip fracture [29–31].

The key strength of this research work is that it is the first study from the Indian subcontinent comparing bone mineral parameters, bone mineral density, trabecular bone score, and hip structural analysis in postmenopausal women with and without neck of femur fracture. Also, the study population was homogenous as it included only subjects with neck of femur fracture. This study highlights the utility of the trabecular bone score and hip structural analysis in predicting fracture risk, even in subjects with non-osteoporotic BMD at femoral neck. This study, however, is limited by its inherent cross-sectional design and inclusion of only postmenopausal women from southern India. Also, the HSA parameters of the fractured hip were not available prior to the event.

Conclusion

This study highlights that impaired parameters of proximal hip geometry and a low trabecular bone score may be significantly associated with osteoporotic fractures of the femoral neck in postmenopausal women. However, the utility of these additional densitometric tools beyond routine BMD assessment in adequately predicting femoral neck fracture risk needs to be further validated in prospective studies.

Declarations

Conflicts of interest None.

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