Usefulness of Trabecular Bone Score (TBS) to Identify Bone Quality and Bone Fragility in Primary Hyperparathyroidism compared with Secondary Hyperparathyroidism——hypercortisolism patients

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Research Article

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Abstract

Purpose: This study was designed to evaluates the effects of TBS, bone mineral density (BMD), and fracture risk in PHPT patients.

Methods: The study group comprised 82 PHPT patients, and sex-, age-matched 50 hypercortisolism patients. The BMD and TBS were measured using DXA and TBS iNsight software. A receiver operating curve and logistic analysis were used to evaluate TBS. The FRAX index was calculated with and without the adjustment of TBS to evaluate the sensitivity and specificity of fracture risk.

Results: Sixty-two per cent of PHPT patients exhibited degraded bone microstructure, thirty-nine per cent were diagnosed with osteoporosis by DXA. TBS had a moderately positive correlation with the lumbar spine, femoral neck, and total hip BMD. For PHPT patients, the BMD of the fracture group was lower compared to that of the non-fracture group, and the FRAX indexes were higher than that of the non-fracture group. There was no statistical difference in TBS between the fracture group and the non-fracture group. In hypercortisolism patients, there was no statistical difference in BMD and TBS between the fracture group and the non-fracture group. In PHPT patients, TBS was a predictor of osteoporosis even after adjusting for age, gender, and BMI (P = 0.001, OR = 0.120, 95% CI [0.033-0.435]); In contrast, TBS was not a predictor in hypercortisolism patients, regardless of whether adjusting confounding factors or not. The sensitivity of FRAX in the prediction of fracture risk in PHPT and hypercortisolism is higher than TBS alone.

Conclusions: TBS combined with BMD can increase the diagnostic accuracy of PHPT patients. Moreover, FRAX is more sensitive to fracture prediction than TBS in patients with PHPT or hypercortisolism.

Introduction

Primary Hyperparathyroidism (PHPT) is a common endocrine disease that leads to secondary osteoporosis. It affects the bone quality and results in fractures. Recent developments in medical monitoring technology have shown that PHPT patients in China have turned to be asymptomatic[1]. Typically, the application of Dual-energy X-ray absorptiometry (DXA) is useful for monitoring the bone mineral density (BMD) of PHPT patients. In most cases, the DXA shows that the BMD of cortical bone sites (such as the distal third of radius) is reduced. Meanwhile, the lumbar spine is relatively preserved[2, 3]. However, the incidence of vertebral and nonvertebral fractures in PHPT patients has increased, indicating that DXA is insufficient to make a comprehensive assessment of bone quality in PHPT patients. Therefore, a newer assessment method, called trabecular bone score (TBS), provides a novel method to evaluate the bone microstructure in PHPT patients[4]. However, studies evaluating the association between TBS and fracture risk in PHPT patients are inconsistent. Two European studies have shown that TBS is associated with vertebral fractures in PHPT patients[5, 6]. Another research[7] compared a group of patients with fractures and a non-fracture group of PHPT patients. However, the authors did not find any statistical difference in TBS. So, the present study attempts to assess the role of TBS in

predicting bone quality and fracture risk to provide comprehensive evidence regarding the usage of TBS in PHPT patients.

Hypercortisolism can cause secondary osteoporosis. Cortisol damages the resorption of intestinal calcium and promotes renal calcium excretion, both stimulating PTH secretion[8]. Besides, cortisol can also improve recruitment of basic multicellular units in bone and then procuring the stimulation of bone turnover with the catabolic processes involved trabecular bone[8, 9]. As a result, patients with hypercortisolism are prone to fracture despite normal or slightly lower BMD[10]. PHPT and hypercortisolism can directly or indirectly affect the PTH, which will also affect bone metabolism and bone quality, therefore, sex-, age-matched hypercortisolism patients were selected as a control group compared with PHPT patients.

This study aims to compare TBS, BMD, and fracture risk in PHPT patients to hypercortisolism and investigate the association of TBS with fracture risk.

Materials And Methods

Study Participants and Recruitment

The study involved eighty-two PHPT patients and 50 age-sex matched hypercortisolism patients in the Endocrinology and Metabolism Disease Department of Tianjin Medical University General Hospital from January 2014 to December 2019. All participants satisfy the inclusion criteria. The inclusion criteria and exclusion criteria of the patients were as follows:

Inclusion criteria:

Patients aged > 20 years old;

$15kg/m^2 \leq BMI \leq 37kg/m^2$;

Complete clinical data;

PHPT patients should satisfy with the following criteria[11]: 1) Increased serum calcium above the upper limit of the normal range of 2.55mmol/L, excluding other causes of hypercalcemia; 2) Increased PTH above the upper limit of the normal range of 7.63pmol/L; 3) Decreased serum phosphorus, and 4) A combination of clinical symptom and characteristic radiographic features;

Hyperparathyroidism patients should meet the standards[12]: 1) Typical symptoms and signs of hyperparathyroidism; 2) Increased serum cortisol above the upper limit of the normal range of 25ug/dl and abnormal rhythm; 3) Increased free urinary cortisol in 24 hours, two times above the upper limit of the normal range of 110ug/24h; 4) After a low dose dexamethasone suppression test, the serum cortisol > 50 nmol/L (1.8ug/dl) at 8:00 am the next day after the suppression.

Exclusion criteria were as following:

1. Patients with multiple endocrine adenomas, secondary or tertiary hyperparathyroidism;
2. Cancer patients or those with poor physical conditions;
3. Patients who use or have used drugs that significantly affect the cortisol levels in the past three months (including oral glucocorticoids, contraceptive drugs, central nervous system drugs, dopaminergic drugs, etc.);
4. Patients with a history of other diseases causing secondary osteoporosis or use of drugs that affect bone metabolism at present or within two years[13];
5. Incomplete clinical data.

Laboratory measurements and clinical information

The following clinical information was collected from the participants: disease course, history of fractures, history of parents' fractures, history of rheumatoid arthritis, smoking and drinking status. Moreover, this study also determined the blood and 24-hour urine electrolytes, kidney and liver function, parathyroid hormone, 25OHD and bone turnover indices. Patients considering hypercortisolism underwent a comprehensive adrenal function assessment, including plasma renin activity, serum aldosterone levels, blood cortisol and adrenocorticotropic hormone levels, cortisol circadian rhythm, and low dose dexamethasone suppression test followed by at least two 24h urine cortisol tests. PTH, 25OHD and bone turnover indices were detected using an electrochemiluminescence assay in the hospital's central laboratory. All patients underwent abdominal and parathyroid ultrasonography. Confirmation of parathyroid lesions was established using enhanced computed tomography (CT) and radionuclide examination. X-ray examinations of the vertebrae, pelvis, skull, and hands were performed in almost all participants. The radiologist reviewed the X-rays to issue the reports. The diagnosis of fragile fractures was based on the X-rays reports and medical history. Body mass index (BMI, $kg/^2$) was calculated based on height and weight.

Bone mineral density assessment

A bone densitometer (Lunar Prodigy; GE Healthcare, Waukesha, WI, USA) was used to measure the BMD at the lumbar spine, femoral neck, and total hip parts. The BMD results were expressed in grams per square centimetre (g/cm^2) and as T-score.

Trabecular bone score assessment

Spine TBS values were measured using the TBS software installed on the bone densitometer (TBS iNsight® v2.1, Med-Imaps, France). The spine TBS was calculated based on the raw data acquired in our DXA scan to assess the same vertebrae part on which the lumbar spine BMD was measured. The bone microstructure was diagnosed using the TBS level[14]: normal bone microstructure (TBS $\geq$ 1.310), partially reduced bone microstructure (1.23<TBS<1.31), and severely reduced bone microstructure (TBS $\leq$ 1.23).

FRAX tool assessment

The FRAX tool was based on individual patients that integrate the risks associated with clinical risk factors and BMD at the femoral neck. The FRAX tool was used to assess the risk of major osteoporotic fractures (clinical spine, forearm, hip or shoulder fracture) and hip fracture in the next ten years[15].

Data analysis

Data analysis was performed using SPSS 25.0 (SPSS, Chicago, IL, USA). The results are presented as the mean ± SD. Categorical variable analysis was performed using $\chi 2$ or Fisher's test, and comparative analysis between the two groups was performed using an independent- sample t-test. The continuous variables of non-normal distribution were expressed by M (P25, P75), and the non-parametric test was used for comparisons between the groups. Correlation analysis is expressed using Pearson or Spearman. Logistic regression analysis was used to access the risk factor of the fracture. The receiver operating curve (ROC curve) and the area under the curve (AUC area) were used to compare the sensitivity. In all analyses, $P<0.05$ was considered statistically significant.

Results

Three PHPT and 5 hypercortisolism patients were excluded because of their BMI>37kg/m^2. In total, 82 PHPT patients (aged 25–68 years) and 50 age-sex matched hypercortisolism patients (aged 31-71years) were included in the present study. Out of which, 13 patients with fractures were found in the PHPT group (3 males, 10 females), including 2 thoracolumbar fractures, 2 rib fractures, 5 hand and foot fractures, 2 long bone fractures, 1 combined fracture of more than 2 locations, and 1 unknown case; 7 patients with fractures were found in the hypercortisolism group (1 male and 6 females), including 1 thoracolumbar fracture, 2 hand and foot fractures, 2 rib fractures, and 2 long bone fractures. Table 1 lists the demographic, clinical, biochemical, and densitometric characteristics of the patients.

Table 1
Comparison of clinical data of the PHPT patients and hypercortisolism patients

Variable	PHPT(82)	Hypercortisolism (50)	P
Sex (male/female)	17/65	8/42	0.501
Age, y	54(47,59)	49(38,57)	0.095
BMI, kg/m2	24.55 ± 3.53	25.44 ± 4.22	0.196
Medical history(y)	1(0.16,4.25)	2(0.77,5.75)	0.018
Thoracolumbar fractures(N)	2	1	
Rib fractures(N)	2	2	
Hand/foot fracture(N)	5	2	
Long bone fracture(N)	2	2	
≥ 2 fractures(N)	1	0	
Fractures of unknown location(N)	1	0	
With fracture /without fracture (N)	13/69	7/43	0.773
Albumin, g/L	41.68 ± 3.64	38.92 ± 4.61	0.000
Albumin-corrected serum calcium, mmol/L	2.67 ± 0.32	2.23 ± 0.10	0.000
Serum phosphate,mmol/L	0.85 ± 0.22	1.01 ± 0.16	0.000
AkP(U/L)	90(68,135)	70(55.5,81.5)	0.000
Serum creatinine, umol/L	56(47.75,66.25)	53(45,61)	0.115
PTH (pmol/L)	22(14.02,58.10)	7.75(5.44,12.2)	0.000
25OHD (nmol/L)	27.77(21.32,39.54)	30.32(20.6,38.99)	0.744
Serum cortisol (ug/dL)	21.00(16.95,25.87)	31.2(24.25,39.7)	0.000
OC(ng/ml)	39.95(25.89,83.94)	9.17(3.88,23.13)	0.000
CTX(ng/ml)	0.95(0.59,1.54)	0.55(0.45,0.87)	0.044
PINP(ng/ml)	64.18(40.48,121.4)	29.08(12.06,68.67)	0.022
Urinary calcium, (mmol/24h)	8.69(5.88,9.86)	6.67(4.21,8.74)	0.007
Urinary phosphate, (mmol/24h)	19.65(14.37, 24.97)	18.98(14.47,24.83)	0.980
Serum cortisol (ug/24h)	40(29,69)	382.2(153.5,564.05)	0.000
L1-L4(g/cm2)	0.932 ± 0.197	1.020 ± 0.179	0.012
Femoral neck (g/cm2)	0.741 ± 0.146	0.822 ± 0.134	0.002

Variable	PHPT(82)	Hypercortisolism (50)	P
Total hip (g/cm2)	0.781 ± 0.167	0.891 ± 0.153	0.000
TBS	1.271 ± 0.130	1.233 ± 0.126	0.102
PMOF(%)	3.3(2.2,6.3)	3.05(2.1,4.2)	0.291
PHF (%)	0.9(0.4,2.4)	0.65(0.3,1.5)	0.169
TBS adjusted PMOF(%)	4.8(2.7,9.2)	4.4(2.6,6.2)	0.412
TBS adjusted PHF(%)	1(0.3,4.0)	1.2(0.2,2.1)	0.588

As shown in **Fig. 1**, sixty-two per cent of PHPT patients exhibited severe or partial degradation of bone microstructure (TBS ≤ 1.310). However, thirty-nine per cent of the patients were diagnosed with osteoporosis by DXA, and the fracture rate was 15.8%. Similarly, seventy per cent of hypercortisolism patients had a TBS level ≤ 1.310, twenty-two per cent of the patients were diagnosed with osteoporosis, and the fracture rate was 14%. There was no statistical difference in the fracture rate between the two groups (P>0.05).

Correlation analysis was found that TBS was negatively related to medical history time, alkaline phosphatase ($P = 0.000$,R= -0.369), and serum osteocalcin. Meanwhile, it was positively correlated with creatinine levels, lumbar spine ($P = 0.000$,R = 0.587), femoral neck ($P = 0.000$,R = 0.497), and total hip BMD ($P = 0.000$,R = 0.506). TBS had no correlation with age, BMI, blood calcium and phosphorus, and urine calcium and phosphorus.

As described in Table 2, all 132 patients were divided into two groups: fracture group and non-fracture group. CTX, FRAX indexes (PMOF, PHF, TBS adjusted PMOF, TBS adjusted PHF) were statistical different (P < 0.05) in the two groups. However, there was no difference between BMD and TBS.

Table 2
Comparison of data between all patients with fractures and without fractures

Variable	With farcture (20)	Without farcture (112)	P
Sex (male/female)	4/16	21/91	0.895
Age, y	56.5(45.5,63)	52(43,58)	0.081
BMI, kg/m^2	25.12(22.69,31.44)	23.9(22.22,26.8)	0.263
OC(ng/ml)	25.12(18.89,49.17)	38.78(24.49,82.6)	0.094
CTX(ng/ml)	0.56(0.46,1.02)	0.96(0.62,1.65)	0.035
PINP(ng/ml)	43.59(23.79,80.14)	64.18(38.59,117.35)	0.149
L1-L4(g/cm^2)	0.917 ± 0.255	0.974 ± 0.182	0.235
Femoral neck (g/cm^2)	0.735 ± 0.165	0.778 ± 0.143	0.226
Total hip (g/cm^2)	0.783 ± 0.211	0.830 ± 0.162	0.254
TBS	1.234 ± 0.142	1.261 ± 0.127	0.388
PMOF(%)	6.95(4.6,9.75)	2.9(2.1,4.6)	0.000
PHF (%)	2.05(0.8,6.92)	0.7(0.3,2.2)	0.012
TBS adjusted PMOF(%)	49.4(6.35,17.5)	3.7(2.4,6.2)	0.000
TBS adjusted PHF(%)	3.6(1.15,9.65)	0.7(0.2,2.2)	0.002

As shown in Table 3, the lumbar spine, femoral neck, and total hip BMD in PHPT patients with fractures were lower compared to the non-fracture group. Moreover, the PMOF, PHF, TBS adjusted PMOF, and TBS adjusted PHF were higher (both $P<0.05$). However, there was no statistical difference in TBS.

Table 3
Comparison of data between PHPT patients with fractures and without fractures

Variable	With farcture (13)	Without farcture (69)	P
Sex (male/female)	3/10	14/55	1.000
Age, y	57.08 ± 8.81	51.43 ± 9.57	0.052
BMI, kg/m^2	24.61 ± 4.58	24.54 ± 3.33	0.945
OC(ng/ml)	25.83(19.15,51.69)	41.86(29.77,86.68)	0.025
CTX(ng/ml)	0.59(0.37,1.01)	1.11(0.71,1.75)	0.018
PINP(ng/ml)	40.48(26.04,67.48)	69.88(44.35,143.65)	0.025
L1-L4(g/cm^2)	0.798 ± 0.162	0.957 ± 0.194	0.007
Femoral neck (g/cm^2)	0.662 ± 0.151	0.756 ± 0.141	0.033
Total hip (g/cm^2)	0.684 ± 0.175	0.780 ± 0.161	0.021
TBS	1.229 ± 0.169	1.279 ± 0.121	0.201
PMOF(%)	8.1(5.2,15)	3(2.2,5.7)	0.000
PHF (%)	3.1(1.65,7.8)	0.75(0.3,2.27)	0.002
TBS adjusted PMOF(%)	10(6.8,21.5)	3.5(2.45,6.7)	0.001
TBS adjusted PHF(%)	5.3(1.4,12.5)	0.65(0.2,2.35)	0.003

Compared with the non-fracture group, there was no significant difference in BMD and TBS in the fracture group in hypercortisolism patients. Only PMOF had a statistical difference.

TBS was a predictor of osteoporosis even after adjusting for age, gender, and BMI (P = 0.001, OR = 0.120, 95% CI [0.033–0.435]). Regardless of whether confounding factors are excluded, TBS is meaningless in hypercortisolism patients.

As displayed in Fig. 2 and Fig. 3, the figures respectively describe the sensitivity of FRAX alone, TBS alone, and TBS combined with FRAX in predicting the risk of fracture in patients with PHPT and hypercortisolism in the next ten years. Among them, the sensitivity of FRAX alone for predicting the fracture risk of patients in the next ten years is higher than that of TBS alone, and the sensitivity of TBS adjusted FRAX in prediction is a little different from that of FRAX alone.

Discussion

Previous studies have shown that TBS can assess the bone quality of secondary osteoporosis and predict fracture risk independently of BMD and FRAX scores. When combined with any method, it can increase the accuracy of fracture prediction. However, there is a lack of research on TBS about PHPT in China. Therefore, the present study studied the role of TBS in assessing bone quality in PHPT patients.

In the present study, it was found that sixty-two per cent of PHPT patients exhibited bone microstructural deterioration. Moreover, thirty-nine per cent of patients were diagnosed with osteoporosis by DXA. Similarly, seventy per cent of hypercortisolism patients had bone microstructural deterioration, and only twenty-two per cent were diagnosed with osteoporosis by DXA. A retrospective study involving 72 PHPT patients by Manuel et al. obtained similar findings. Accordingly, 73.6% of PHPT patients had a decrease in TBS, and 37.5% of patients were diagnosed with osteoporosis based on BMD[16]. Silva and colleagues [17]and Vinolas et al. also obtained similar findings in PHPT patients and hypercortisolism patients, respectively.[18] In combination with the results of the current study, there is sufficient evidence to claim that a difference between TBS and BMD exists when assessing patients' bone health. Moreover, studies have suggested that the combined application of TBS and BMD increases the sensitivity of bone strength assessment in patients with secondary osteoporosis[19]. So, the aim is to draw conclusions which index has higher sensitivity or specificity for the occurrence of fragility fractures of clinical concern.

In this study, it was found that the BMD of the lumbar spine, femoral neck, and total hip of PHPT patients were significantly lower than that of the patients in the hypercortisolism group. However, there was no statistical difference in the TBS and fracture rate between the two groups. Hypercortisolism patients have higher BMD than PHPT patients. However, the incidence of fractures was similar in the two groups, suggesting that hypercortisolism patients are more prone to fractures and BMD is less sensitive to predict fracture occurrence in these patients.

Furthermore, a logistics regression analysis was conducted on the occurrence of osteoporosis and it was found that TBS is a predictive factor for osteoporosis in PHPT patients. After adjusting for confounding factors such as age, gender, and BMI, TBS still had a similar predictive effect. On the contrary, for patients with hypercortisolism, TBS is meaningless, even after adjusting for confounding factors. The reason could be that hypercortisolism patients may have a longer medical history than those in the PHPT group. Reportedly, TBS is an early predictor in hypercortisolism patients[20]. Considering that some of the participating patients had hypercortisolism with a longer medical history, it could be considered as the reason why TBS is a non-osteoporotic predictor for hypercortisolism patients.

The correlation between TBS and BMD is not consistent in different populations[21, 22, 23]. The difference could be related to the difference of the race. The findings indicate TBS was positively correlated with lumbar, femoral neck, and total hip BMD at moderate strength. Moreover, it was also observed that the correlation could lead to a reduction in the capacity of TBS to predict fractures. Therefore, it cannot be concluded that TBS is completely independent of bone density, and there is not sufficient evidence to consider supporting the replacement of BMD with TBS. On the contrary, the combined use of these two measurement methods may be more meaningful for the assessment of bone mass with underestimated

bone density. Similarly, the present analysis also found that TBS was negatively correlated with AKP and serum osteocalcin levels. Increased AKP and bone turnover indices[24] suggest that the high bone turnover is related to bone microstructure damage.

BMD is a crucial indicator in the assessment of future fracture risk, and FRAX scores are used for people with reduced bone mass. A study examining the fracture risk of patients with hypercortisolism and TBS involved 182 patients with Cushing's syndrome and found that TBS was not associated with fractures, and the 24-hour urine cortisol level was a predictor of fracture[25]. Similar results were obtained from the present study. Among patients with hypercortisolism, there was no statistically significant difference in TBS between the fracture group and the non-fracture group. Two European studies have shown that TBS is associated with vertebral fractures commonly found in PHPT[5, 6]. When compared with PHPT patients in the non-fracture group, there was no statistical difference in TBS in the fracture group of the present study, which conform with the results of Liu MH, et al.[7]. Analysis of the fracture sites of the PHPT patients in this study showed that only 2 patients had vertebral fractures, and whether the prediction of fracture by TBS is related to the fracture site is still inconclusive. Therefore, it is unknown whether the different fracture sites will affect the results of the present analysis.

In order to explore the sensitivity of FRAX and TBS in predicting future fractures, the current analysis employed a ROC curve on the sensitivity of FRAX, TBS, and TBS adjusted FRAX for fracture prediction. Accordingly, it was found that the sensitivity of FRAX for predicting fracture risk in patients with PHPT and hypercortisolism in the next ten years is higher than that of TBS alone, and the sensitivity of TBS and FRAX combined prediction is not significantly different from FRAX alone. The result indicates that TBS is not as effective as FRAX in assessing fracture risk in patients with PHPT and hypercortisolism.

Several limitations of this study should be acknowledged. Firstly, the sample size is relatively small, which might restrict the wide applicability of the findings. It may require further validation in a larger cohort. Nevertheless, the fracture sites of fracture patients are not typical enough, and more prospective studies of patients with vertebral fractures are needed in the future.

In summary, TBS and BMD have differences in evaluating bone quality. TBS appears to be associated with bone microarchitecture, and when combined with BMD, the combination increases the diagnostic accuracy of secondary osteoporosis, including primary hyperparathyroidism and hypercortisolism. Moreover, in patients with PHPT or hypercortisolism, FRAX is more sensitive to fracture prediction than TBS. Nevertheless, extensive longitudinal studies are required to recommend this tool in clinical practice guidelines for this population.

Abbreviations

PHPT Primary hyperparathyroidism

DXA Dual energy X-ray absorptiometry

BMD Bone Mineral Density

TBS Trabecular Bone Score

BMI Body Mass Index

CTX Cross Linked C-Telopeptide of Type Collagen

OC osteocalcin

PINP procollagen type 1 N-terminal propeptide

ALKP Alkaline phosphatase

25(OH)VD 25 hydroxy vitamin D

PTH parathyroid hormone

L1-L4 Lumbar 1-4

FDA Food and Drug Administration

FRAX Fracture Risk Assessment Tool

PMOF probability of a major osteoporotic fracture

PHF probability of hip fracture

ROC Curve Receiver Operating Characteristic Curve

AUC Area Under Curve ROC

Declarations

ETHICS STATEMENT

Ethics approval and consent to praticipate

This is a retrospective study based on data collected from the Endocrinology and Metabolism Disease Department of TJMUG Hospital. The paper was reported after the approval of Institutional Review Board (IRB)/Ethical Committee of TJMUG Hospital.

COMPETING INTERESTS

WNT, HWJ, BPW, YC, TL, HW and CLD declare that they have no competing interests.

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None.

AUTHOR CONTRIBUTIONS

HWJ, BPW, and CLD conceived and devised the study. WNT, YC, TL and HW collected the data and WNT analyzed the data. All authors contributed to the interpretation of the data. WNT drafted the article, and all authors reviewed and edited the manuscript, approved the version to be published and agreed to be accountable for all aspects of the work. WNT and CLD accept full responsibility for the work and the conduct of the study, had access to the data, and controlled the decision to publish it.

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DATA AVAILABILITY STATEMENT

The datasets used and/or analysed during the current study available from the corresponding author on reasonable request.

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Figures

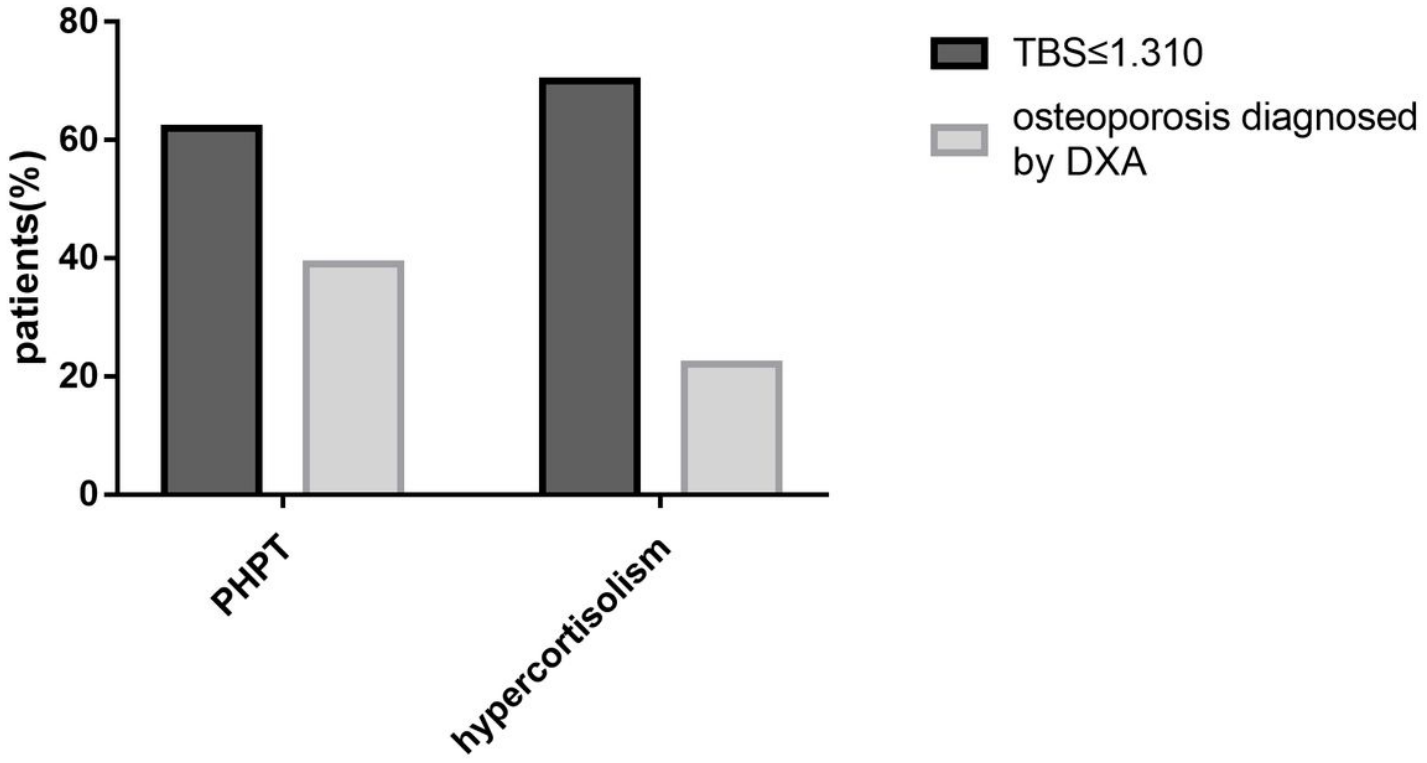

Figure 1

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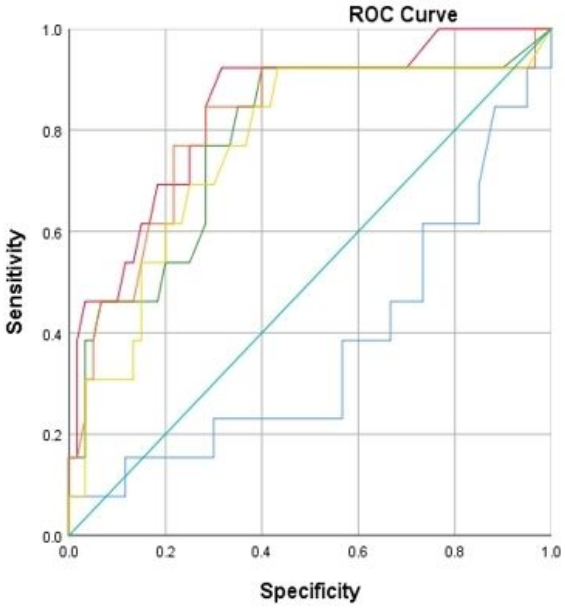

Variable	AUC	P	95%CI	
TBS	0.368	0.138	0.189	0.547
FRAX(PMOF)	0.841	0.000	0.722	0.960
FRAX(PHF)	0.779	0.002	0.631	0.928
FRAX adjusted PMOF	0.804	0.001	0.657	0.951
FRAX adjusted PHF	0.764	0.003	0.614	0.914

Figure 2

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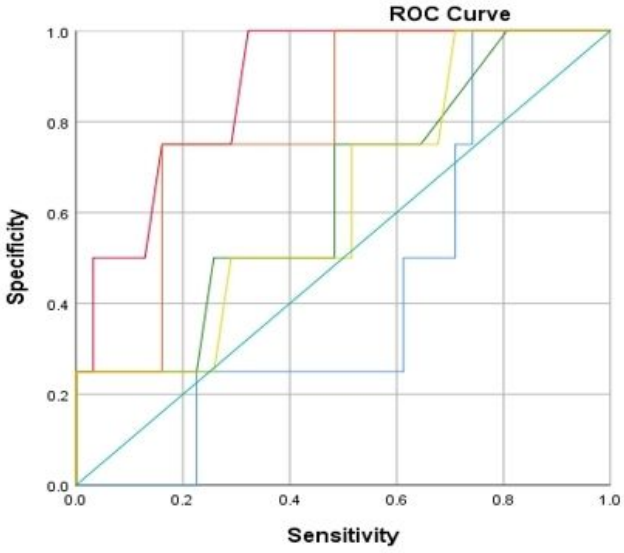

Variable	AUC	P	95%CI	
TBS	0.427	0.641	0.182	0.673
FRAX(PMOF)	0.879	0.015	0.736	1.000
FRAX(PHF)	0.637	0.378	0.349	0.925
FRAX adjusted PMOF	0.798	0.055	0.598	0.999
FRAX adjusted PHF	0.629	0.407	0.349	0.909

Figure 3

Legend not included with this version.