Published in final edited form as:

J Clin Densitom. 2018 ; 21(3): 355–359. doi:10.1016/j.jocd.2018.02.004.

TBS in Mexican American Women with Type 2 diabetes

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Introduction

Dual energy x-ray absorptiometry (DXA) acquired bone mineral density (BMD) remains the gold standard for diagnosing osteoporosis and assessing risk of fragility fractures (1).

However, a paradoxical presence of fragility fractures with high or normal (non-osteoporotic) BMD in patients with type 2 diabetes (T2D) suggests that DXA may not be reliable for assessing fracture risk in subjects with T2D. (2). An altered state of bone quality - caused by underlying metabolic changes of T2D - has been hypothesized to cause reduced strength and bone turnover leading to increased fracture risk in T2D patients (2–3).

Trabecular bone score (TBS), an indirect measure of trabecular microarchitecture derived from lumbar-spine DXA images, provides information on bone quality based on pixel grey-level variations in the DXA image (4–5). Previous studies reported lumbar spine TBS (LS-TBS) was decreased in T2D patients compared to those without diabetes (6–7). However, TBS was also reported to be affected by demographic patterns and body size, and thus may be different in people from various ethnic/racial backgrounds (8). One study reported that LS-TBS may not be a better indicator of fracture in African Americans with T2D, as described for their Caucasian counterparts (5). Thus, it is important to understanding associations between T2D and LS-TBS for each ethnic/racial group separately. Specifically, data are lacking in the literature concerning associations of TBS with T2D in older Mexican Americans (MAs). In order to evaluate the utility of LS-TBS for assessing fracture risk in MAs with T2D, it is important to first determine if lower LS-TBS is associated with T2D in older MAs men and women.

The Cameron County Hispanic Cohort (CCHC) is a two-stage randomly selected ‘Framingham-like’ cohort of MAs on the US Mexico border with severe health disparities. Prevalence of T2D in this cohort is much higher than the national average (9–10). Here, we report associations between LS-TBS and T2D in the older MAs who are CCHC participants.

Materials and Methods

Study Participants

A bone health protocol (approved by UTHealth Committee for the Protection of Human Subjects) was developed in 2013 to understand epidemiology of skeletal health risk factors in relation to age-related bone loss and fracture risk in this population. Under this protocol, participants receive annual dual energy x-ray absorptiometry (DXA) acquired bone mineral density (BMD) of the hip and spine regions by Hologic QDR 4500. A total of 171 men and women (72 with T2D and 99 without diabetes) from the CCHC who were 50 years or older were identified as having a LS-DXA scans performed between August 2014 and June 2017. After excluding men and women with body mass index (BMI) <15 and >37 (based on working BMI ranges for LS-TBS (5,8), a total of 153 LS-BMD scans were reanalyzed with the TBS software. Thus, 42 men and 59 women without diabetes and 14 men and 38 women with T2D were included in the final analysis.

Measurements

Areal bone mineral density (BMD) of the hip (femoral neck) and spine regions (L1-L4) were measured using Hologic Discovery W (Hologic Inc., Marlborough, MA). The lumbar spine anterior-posterior DXA images from these participants were used to calculate LS-TBS using TBS iNsite v2.1 (Medimpas, Merignac France) in accordance with the manufacturer recommendations to generate the LS-TBS parameters of the lumbar spine (L1-L4). The percent coefficient of variation (CV%) for lumbar spine scans in the particular DXA machine used in our study is 0.97%.

Height in centimeters was measured using a stadiometer after participants removed their shoes, standing on the floor. Weight in kilograms was measured to the nearest 10th on a digital scale after participants removed their shoes and personal items from pockets. Body mass index (BMI) was calculated as weight in kilograms divided by height squared in meters (kg/m²). T2D status was based on self-reported physician diagnosed of diabetes and/or on the American Diabetes Association guidelines based on fasting plasma glucose and HbA1c results.

Statistical analysis

To account for known differences in BMD between men and women, data analysis for men and women were done separately in the current study. Data such as age, weight, height, and HbA1c were collected as part of the CCHC protocol.

For descriptive purposes, we also reported percent distribution of LS-TBS and LS-BMD in 3 different categories. We used the following ranges for categorizing the LS-TBS values (4): LS-TBS ≤ 1.200 was categorized as degraded microarchitecture; LS-TBS between 1.200 and 1.350 was classed as partially degraded microarchitecture; and LS-TBS ≥ 1.350 was classed as normal microarchitecture. LS-BMD was categorized based on T-scores according to the WHO criterion: osteoporotic (t-score ≤ -2.5); osteopenia (t-score between -2.5 and -1.0); and or normal (t-score ≥ -1.0).

Linear regression analysis determined if low LS-TBS was associated with T2D in older MA men and women. For the regression analysis, LS-TBS was the outcome (continuous form) variable for this study and status of diabetes (a diagnosis of T2D or no diabetes) was the independent (categorical) variable for our analysis. The regression model was adjusted for age, BMI, hemoglobin A1c (HbA1c) and LS-BMD.

Results

Descriptive data for included subjects is shown in Table 1. Mean ($\pm$ standard deviation) age for men and women were 64 (8) and 63 (8) years. Mean ($\pm$ SD) BMI for men and women were 29 (4) and 30 (4) kg/m². Men with T2D had a statistically significant higher mean LS-BMD than men without diabetes, but there was no difference in LS-BMD for women. While there was no differences of TBS between men with T2D and without diabetes, women without diabetes had a significantly higher mean TBS (Table 1).

Regardless of gender or diabetes status, the categorical breakdown was significantly different depending on whether LS-TBS or LS-BMD was used for classification (Figure 1): more subjects were classified as having degraded architecture by LS-TBS than as osteoporotic by LS-BMD. However, when comparing subjects with T2D to subjects without diabetes, the results were dependent on gender. For MA men, LS-BMD was significantly different with more T2D subjects classified as having normal bone density, but LS-TBS did not result in different classifications. For MA women, LS-TBS was significantly different with more T2D subjects classified as having degraded architecture, but LS-BMD classifications were similar.

Having a diagnosis of T2D was not associated with LS-TBS in men but, for women, having T2D was significantly associated with lower LS-TBS (Table 2). Higher age and BMI and lower LS-BMD were associated with lower LS-TBS for both men and women in our study (Table 2). There was no significant interaction ($p>0.05$) between T2D and BMI or T2D and age.

Discussion

It has been shown that fracture risk is higher in both men and women with T2D (11–12) and that BMD assessment using DXA is paradoxically either normal or higher in subjects with diabetes. It has been proposed that LS-TBS may be a better indicator for fracture risk than BMD in T2D, but most studies investigating LS-TBS in individuals with have not included ethnicity as a variable. Here we present an investigation of LS-BMD and LS-TBS in a population that has been understudied: older MA men and women with T2D. Our data show that the relationship between BMD and TBS is similar in this population of MA to that published in other studies and suggest that the relationship may be gender dependent (7,13–14).

In our study, T2D was associated with an increase in BMD for MA men but no change for MA women compared to subjects without diabetes. MA men and women also showed different relationships between T2D and LS-TBS in our study: for MA men in the CCHC, T2D did not show any significant association with LS-TBS but, for women, T2D was associated with lower LS-TBS scores. For both genders, LS-TBS decreased with increasing age or BMI, and had a significant positive relationship with LS-BMD. Regardless of diabetes status, there were less MA men and women categorized as having normal LS-TBS than normal LS-BMD. Percent distribution of LS-TBS vs. LS-BMD categories in our study indicates that LS-TBS does discriminate between T2D and non-diabetic groups of older MA women, but not men.

The relationship between T2D and BMD that we found has been demonstrated in other populations in the United States, Korea and Japan (7,13–14). Further, our results are consistent with findings reported in a previous study that discussed relationship of lower LS-TBS with older age regardless of gender or ethnicity. (8). The same study reported a higher mean LS-TBS in older MA men (>65 years old) than MA women of same age group (8) which is also consistent with our results. Distribution of the LS-TBS and LS-BMD categories are consistent with previous reports of LS-TBS distribution using same categories (poor to normal) among men and women from other ethnic/racial backgrounds, mainly Caucasians from Houston, TX (15).

The gender difference that we have found in terms of the relationship between BMD, TBS and T2D may be due to the small number of men with diabetes in our sample or it may indicate that there is a real difference in terms of the ability of LS-TBS to assess fracture risk in men versus women with T2D. Previous research has shown conflicting data concerning LS-TBS in men with T2D compared to those without diabetes (7,13). In a large study of American men and women, T2D resulted in an increased BMD and increased nontraumatic

fracture risk for both genders (11). In contrast, in an analysis of men with diabetes from the MrOS study, diabetes was not found to result in an increased risk of vertebral fracture (14).

To our knowledge, this is the first study reporting associations between LS-TBS and T2D in older MA men and women with poor glycemic control and high prevalence of obesity. Cross-sectional nature with a small N are limitations in our study. A small number of men in the T2D group in our study may have influenced the results from the regression study. Use of health disparate group of MA participants from CCHC in our study warrants caution when interpreting results and may not be generalized to other Hispanic populations. In general, our subjects were older and had higher BMI and HbA1c than populations analyzed in other studies. Thus, there could be additional metabolic derangement contributing to worsening bone quality in our subjects. This is a cross-sectional analysis of a prospective cohort study and results from longitudinal follow up may help confirm our results in the future analysis, including an assessment of the association between LS-TBS and fracture.

Conclusions

LS-TBS may be a valuable addition to DXA BMD in identifying older MA women with T2D who are at risk of fracture due to poor regardless of non-osteoporotic BMD. Relationships between T2D and LS-TBS remains unclear for MA men and further studies are recommended to confirm our findings.

Acknowledgments

We thank our cohort team, particularly, Neryeda Buenorostro and Rocio Uribe and their team, who recruited and documented the participants. We also thank Marcela Morris and other laboratory staff for their contributions, and Christina Villarreal for administrative support. We thank Valley Baptist Medical Center, Brownsville, Texas for providing us space for our Center for Clinical and Translational Science Clinical Research Unit. We also thank the community of Brownsville, Laredo and Harlingen and the participants who so willingly participated in this study in their city.

This work was supported by MD000170 P20 funded from the National Center on Minority Health and Health disparities (NCMHD), and the Centers for Clinical and Translational Science Award UL1 TR000371 from the National Center for Research Resources (NCRR).

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Figure 1.

Percentages of subjects in the LS-BMD and LS-TBS categories, by gender and diabetes status. Category 1 represents degraded architecture by TBS or osteoporosis by BMD, category 2 represents partially degraded architecture by TBS or osteopenic by BMD, and category 3 is normal by either measure.

Table 1

Participants' characteristics described in groups with type 2 diabetes (T2D) and no diabetes

Variables	Men		Women		p-value
	Without any diabetes N = 42 (75%)	With T2D N=14 (25%)	Without any diabetes N= 59 (61%)	With T2D N = 38 (39%)	
	N(%) or mean±SD		N(%) or mean±SD		
Age (years)	63±8	67±8	62±7	65±8	0.01
BMI (kg/m ²)	28.91±3.88	28.86±3.33	29.67±4.12	29.49±4.44	0.84
HbA1c	5.78±0.30	8.25±2.53	5.74±0.39	7.64±2.08	<0.01
FN-BMD (g/cm ²)	0.76±0.14	0.78±0.13	0.70±0.11	0.66±0.10	0.07
LS-BMD (g/cm ²)	0.97±0.16	1.16±0.17	0.89±0.16	0.86±0.15	0.49
LS- TBS	1.27±0.11	1.33±0.11	1.24±0.11	1.17±0.09	<0.01

Note: BMI = body mass index; HbA1c: Hemoglobin A1c; FN-BMD = femoral neck bone mineral density; LS-BMD = lumbar spine BMD; LS-TBS = Lumbar spine trabecular bone score

Table 2

Associations between TBS and diabetes in men and women in CCHC: results from multivariable regression analysis

Variables	Men (N=54)	Women (N=94)
Outcome variable TBS (continuous)	Regression co-efficient (95% Confidence Interval)	
Diabetes (no diabetes = control)	0.016 (– 0.051 to 0.083)	–0.050 (–0.093 to –0.007) *
Age (years)	–0.004 (–0.006 to –0.001) *	–0.002 (–0.005 to –0.000) *
BMI (kg/m ²)	–0.018 (–0.025 to –0.012) *	–0.007 (–0.011 to –0.003) *
HbA1c (%)	–0.013 (–0.030 to 0.004)	0.000 (–0.013 to 0.013)
LS-BMD (g/cm ²)	0.466 (0.332 to 0.600) *	0.343 (0.233 to 0.452) *

Note: TBS = Trabecular Bone Score; BMI = body mass index; LS-BMD – lumbar spine BMD;

*
p<0.05