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TAKE-HOME POINTS FROM LECTURES BY CLEVELAND CLINIC AND VISITING FACULTY

Diagnosing primary osteoporosis: It's more than a T score

ABSTRACT

Although densitometry has contributed immensely to detecting primary osteoporosis, it is only a tool that generates some useful numbers to guide diagnosis. The T score, a leading diagnostic marker for primary osteoporosis, must be put in its proper context. It is but one measurement that is quite useful in one cohort of patients, namely, postmenopausal women older than 60, but it can be misleading in others. The *z* score is a more descriptive measurement of bone loss in younger patients. However, both the T score and *z* score are limited in their diagnostic potential and must be incorporated with other diagnostic aspects, such as family history, laboratory results, and genetic influences. In the end, physicians diagnose osteoporosis, not densitometry.

OVER THE PAST DECADE, the most important development in the field of osteoporosis is arguably the use of bone densitometry to improve diagnosis. With about 28 million people affected by osteoporosis in the United States annually,[1] improving early diagnosis is critical to preventing and alleviating the substantial morbidity, mortality, and economic toll associated with this disease.

But the key measure of densitometry—the T score—has taken on a "magical" aura that it does not deserve. Diagnosing osteoporosis is more difficult than getting a number back on a report. The T score must be viewed in the context of a variety of factors, most important of which is who is being tested and what are his or her risk factors.

Indeed, sole reliance on the T score to diagnose primary osteoporosis often leads to inaccurate diagnosis. This is because other factors remain integral to the accurate diagnosis of whether the patient has primary osteoporosis, secondary osteoporosis, or simply a lower bone mass but no medical abnormalities.

This article challenges some of the conceptions and misconceptions about the T score, shows that diagnosis of primary osteoporosis is more nuanced than sometimes presented, and outlines a strategy to diagnose primary osteoporosis.

Sole reliance on the T score often leads to inaccurate diagnosis

THE T SCORE IS NOT 'MAGICAL'

The T score is a person's bone mass at a particular site, expressed in standard deviations away from the mean of a reference population—people in the time of life when a person should have his or her peak bone mass. **TABLE 1** lists the four diagnostic categories established by the World Health Organization (WHO) based on the T score.[2]

This score, commonly used in clinical practice, provides a way to assess a person's risk of developing a fracture. Generally, the more the T score deviates from the mean, the greater the risk of fracture. As shown in **TABLE 1**, a T score of –2.5 generally indicates a high risk for fracture and thus is used to define osteoporosis.

However, this is not always the case. For instance, patients using glucocorticoids can have a fracture at a T score that is "normal," whereas patients with primary osteoporosis are more likely to have a fracture at a low T score.

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TABLE 1

Diagnostic categories based on T score established by the WHO

SCORE	DIAGNOSIS
0 to –0.99	Normal
–1 to –2.49	Osteopenia (low bone density)
≤ –2.5	Osteoporosis
≤ –2.5 with fracture	Severe or established osteoporosis

MISCONCEPTION ABOUT THE T SCORE

A main misconception about the T score is that it can be used to identify primary osteoporosis without consideration of other critical factors. What many clinicians do not recognize is that the T score was originally derived from a very select, limited cohort of patients, that is, postmenopausal Caucasian women over the age of 60. The T score was originally used as a surrogate for bone destruction in this cohort of patients, which then led to the diagnosis of primary osteoporosis.

T scores can be misleading in younger women, men, and nonwhites

Unfortunately, T scores are now often used outside the cohorts for which they were originally intended. For younger women, for men, and for people of other races, T scores are not as meaningful and, in fact, they can be misleading without taking into account other important diagnostic information such as age, sex, family history, genetic influences, poor growth problems in puberty, and other factors.

Another integral component of diagnosis is the *z* score, which is not as well recognized as the T score but is gaining importance in accurately diagnosing osteoporosis in patients other than older, postmenopausal women.

IMPORTANCE OF THE *z* SCORE

A *z* score, which is also generated by densitometry, is a way of comparing a person's bone mass with the mean of a similar population of a similar age. This score is generally used to determine whether the loss of bone density is secondary to another disease or condition, such as those listed in TABLE 2. That is, if a patient's bone mass is lower than expected for age (ie, low *z* score), then there must be something accelerating this loss beyond the normal process of aging.

The *z* score has been part of the analysis of bone density since the very beginning of densitometry. However, its utility is only now being appreciated. The *z* score is available for a variety of cohorts, such as younger women, middle-aged men, and men and women of different races, and it is increasingly used to analyze bone density in younger cohorts of patients.

For premenopausal or early postmenopausal women younger than 60 years, a low *z* score may indicate osteoporosis if risk factors are present or may indicate low bone density from prior influences such as family history. In people younger than 30 years, and in children, a *z* score of –2.0 may indicate low bone density for that age and may reflect some past illness that affected skeletal growth and attainment of low peak bone mass.

Whether a low *z* score reflects low density or osteoporosis rests upon clinical data. For example, a low *z* score with a history of a fragility fracture, or other risk factors, implies osteoporosis, but a low *z* score with nothing more than a family history of small stature implies low peak bone mass.

Although a cutoff score indicative of secondary osteoporosis has yet to be firmly determined, it is generally thought that secondary osteoporosis is suggested if a person's *z* score is –1.5 to –2.0 deviations below the mean of the patient's peers of the same age.

LIMITATIONS OF DENSITOMETRY

Although the ability to measure bone density has added an important tool to diagnosing primary osteoporosis, bone density is only one component of bone strength. Bone quality is the other component. It is operationally defined as all the characteristics of bone that allow its resistance to fracture. It includes such elements as bone microarchitecture, turnover, microscopic damage, mineralization, and the quality of collagen, to name but a few. Current densitometry techniques cannot measure bone quality very accurately.

The following cases illustrate the limitations of densitometry measurements used alone to accurately diagnose primary osteoporosis, and

highlight the need for clinicians to look beyond the T score as a sole indicator of diagnosis.

CASE STUDIES

Patient 1: A 55-year-old woman with unexplained rib fractures

A 55-year-old woman has had several unexplained rib fractures in the past 2 years. She has used hormone replacement therapy since reaching menopause 5 years ago. She says she had colitis when younger. She does not smoke or drink, she exercises daily, and she uses calcium and vitamin supplements. She has no family history of osteoporosis.

Densitometry measurements

- Spinal T score –2.8
- Hip T score –1.9
- Spinal *z* score –1.6
- Hip *z* score –1.6.

Laboratory results

- 25-vitamin D level 29 ng/mL (normal 10–60)
- Urine calcium excretion 20 mg/day (100–300)
- Serum parathyroid hormone (PTH) 75 pg/mL (10–60)
- Serum calcium 8.9 mg/dL (8.5–10.5).

Diagnosis and interpretation. Although the history and T score suggest that this woman may have primary osteoporosis, her laboratory results combined with her medical history suggest that she has osteomalacia.

The low serum and urine calcium, and the increased PTH, were unusual for someone using supplements of calcium. Although the serum vitamin D was not low, it seemed inappropriate for someone using daily supplements. All these findings were suspicious for some form of malabsorption. A workup for celiac disease confirmed the diagnosis.

Patient 2: A 36-year-old woman with a history of hysterectomy and hip pain

A 36-year-old woman is referred because of osteoporosis suspected because of an earlier hysterectomy. She is healthy and energetic and has been a jogger since age 25. She has had several stress fractures of the distal extremities over the years with complete resolution in each case. She has been on estrogen replacement therapy since a hysterectomy for fibroids 5 years ago.

Following a short run, she developed pain in her left hip that persisted despite conservative treatment. A bone scan showed a stress fracture of the femoral neck. One year later she developed pain in her right hip while working and was later diagnosed with a femoral neck fracture on the other side.

Densitometry measurements

- Spinal T score –2.5
- Spinal *z* score –2.0.

Laboratory results

- CO_2 34 mmol/L (normal 24–32)
- Serum potassium 3.0 mmol/L (3.5–5.0).

Diagnosis and interpretation. The T score of this patient and the history of fracturing would seem to be consistent with osteoporosis, but the ineffectiveness of estrogen therapy, the abnormal lab results, and the abnormal *z* score indicate that she had a secondary problem causing it.

TABLE 2

Causes of secondary bone loss

Endocrine disorders
- Cushing syndrome
- Hyperparathyroidism
- Hypogonadism

Gastrointestinal disorders
- Malabsorption
- Cirrhosis
- Gastric bypass surgery

Renal insufficiency and failure

Pulmonary diseases or treatment

Drug use
- Corticosteroids
- Antigonadotropins
- Anticonvulsants
- Aromatase inhibitors
- Antirejection drugs

Nutritional factors
- Alcohol
- Tobacco
- Eating disorders

Neurologic disease or treatment

Transplantation

Genetic metabolic disorder

Whether a low *z* score reflects low density or osteoporosis rests on clinical data

The patient had unexplained hypokalemic alkalosis. The common culprit for this finding is a diuretic drug, which she did not use. There was nothing in the history suggestive of any drug use.

In-depth questioning revealed subtle changes in facial hair and apparent weight gain, with distribution of fat centrally. Examination showed facial telangiectasia and fullness to the face and supraclavicular areas, but no striae. Subsequent testing of urine free cortisol showed values three times normal. With the medical history noted and a lack of steroid use, the workup focused on an evaluation for Cushing syndrome. Computed tomography (CT) showed that she had a left-sided adrenal tumor.

Patient 3: A 77-year-old woman with vertebral fracture

A 77-year-old woman is seen for back pain and presumed osteoporosis. She developed an L2 compression fracture while golfing in Hilton Head. She was treated with analgesics and calcium, but her back pain persisted for 1 to 2 months. Her medical history indicated tobacco and alcohol use, and she had undergone a cholecystectomy.

Densitometry measurements

- Spinal T score –2.8
- Spinal *z* score –0.9.

Laboratory results

- Serum calcium 8.9 mmol/L (normal 8.5–10.5)
- Alkaline phosphatase 86 U/L (20–120)
- Hemoglobin 10 g/dL (12.0–16.0)
- Sedimentation rate 110 mm/hour (0–30).

Diagnosis and interpretation. By all the usual criteria of bone density, this patient would appear to have primary osteoporosis. However, there were some abnormalities in her laboratory test results—anemia and a high sedimentation rate—that required further scrutiny. Review of her old radiograph showed a compression at L2, but it was a strange type of fracture, that is, it lacked the usual compression apprearance of a fracture in primary osteoporosis.

Rescanning with CT showed that this fracture was caused by a large mass eroding the vertebra. The mass was lymph tissue of malignant lymphoma. Hence, although she had osteoporosis, her fracture was due entirely to another disease.

PRIMARY OSTEOPOROSIS IS AN EXCLUSIONARY DIAGNOSIS

As we can see, relying solely on the T score would have led us astray in each of these cases. With a clearer understanding that the diagnosis of primary osteoporosis must be more nuanced than is currently perceived, we need a better strategy for making the diagnosis than simply focusing on T scores.

Instead of focusing on densitometry to generate a diagnosis, T scores and *z* scores should be used in conjunction with other diagnostic information to generate a full picture of the patient in order to exclude the possibility of other conditions that may be causing secondary bone loss or fractures.

Exclude other conditions that may be causing secondary bone loss or fractures

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SUGGESTED READING

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