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Clinical Research Article

Lack of Bone Mineral Density Testing in Men With Hypogonadism: A Clinical Conundrum

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Abstract

Context: The 2012 Endocrine Society Clinical Practice Guidelines recommend that men aged 50 years or older with a diagnosis of hypogonadism undergo bone mineral density (BMD) testing.

Objective: The objective of this study was to determine the frequency at which men aged 50 years or older with a diagnosis of hypogonadism undergo BMD testing, and if found to have low BMD, are subsequently treated with an osteoporosis medication.

Methods: A retrospective chart review was conducted at a large academic medical center. Inclusion requirements were an International Classification of Diseases (ICD)-9 or -10 code for hypogonadism at any time between July 1, 2012 and September 30, 2020. Patients were followed until the date of BMD assessment or censoring (September 30, 2021). BMD results and treatment with osteoporosis medication were recorded.

Results: A total of 10 169 men with hypogonadism were identified, of whom the mean age was 63.4 (± 9.2), 86.3% White, mean body mass index 31.3 with prevalence of chronic kidney disease, type 2 diabetes, and hypertension of 20.6%, 36.9%, and 68.2%, respectively. The percentage that underwent BMD testing was 7.2%, of which 352 (48.4%) and 87 (12.0%) had osteopenia and osteoporosis, respectively. Among the 87 patients with osteoporosis, 57.5% were treated with an osteoporosis medication.

Conclusion: Only 7.2% of hypogonadal men underwent BMD testing, and among them, 12.0% were found to have osteoporosis. Among those with osteoporosis, 57.5% underwent treatment with osteoporosis medication. Further studies are needed to determine why so few men with hypogonadism undergo BMD assessment and what systems can be put in place to overcome this clinical conundrum.

Key Words: hypogonadism, bone mineral density, low testosterone, osteopenia, osteoporosis

Abbreviations: BMD, bone mineral density; BMI, body mass index; CKD, chronic kidney disease; DXA, dual-energy x-ray absorptiometry; HTN, hypertension; ICD, International Classification of Diseases; T2D, type 2 diabetes; TRT, testosterone replacement therapy; USPSTF, US Preventive Services Task Force.

Previous studies have reported that osteoporosis in men is underdiagnosed [1-7]. Hypogonadism is a known risk factor for decreased bone mineral density (BMD) and increased risk of fractures in men [8-11]. In June 2012, the Endocrine Society issued clinical practice guidelines recommending that men aged 50 years or older with a diagnosis of hypogonadism undergo BMD testing [12]. To the authors' knowledge, since the publication of these guidelines, no studies have been performed investigating the rate at which older men with hypogonadism undergo screening with BMD testing.

In addition to the recommendation to screen for decreased BMD in men with hypogonadism, the Endocrine Society also provides guidelines for treatment. Current guidelines recommend that all men at high risk of fracture, regardless of whether they have hypogonadism, be treated with an agent with proven antifracture efficacy [12]. Guidelines suggest that hypogonadal men at high risk of fracture, who lack standard indications for testosterone replacement but who have contraindications to approved standard osteoporosis medications, be treated with testosterone therapy [12]. Moreover, in men with hypogonadism at borderline high risk of fracture, testosterone therapy is suggested in lieu of a "bone drug" if there are signs or symptoms of hypogonadism [12].

While no studies have been performed looking specifically at the frequency of treatment in hypogonadal men with osteoporosis, previous studies have reported the undertreatment of men diagnosed with osteoporosis, even in those who have suffered a previous fracture [3, 4, 6].

In this report, men aged 50 years or older with a diagnosis of hypogonadism that underwent BMD testing (dual-energy x-ray absorptiometry [DXA]) at a large integrated delivery system in the United States were identified. Among those men who underwent testing, the percentage of patients that were diagnosed with osteopenia or osteoporosis, and were subsequently treated with an osteoporosis medication, was recorded. The frequency of treatment with testosterone replacement therapy (TRT) during the study period was also recorded. Furthermore, the frequency of BMD testing between patients seen by providers from different specialties was also collected.

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Materials and Methods

A retrospective chart review was conducted using the enterprise-wide electronic health record system at Cleveland Clinic. This study was approved by the institutional review board. Inclusion requirements were an International Classification of Diseases (ICD)-9 or -10 code for hypogonadism at any time between July 1, 2012 and September 30, 2020, and at least 2 subsequent visits with providers from primary care, endocrinology, or urology. Patients with a diagnosis of osteoporosis and those who had undergone treatment with an osteoporosis medication before the diagnosis of hypogonadism were excluded. Baseline variables including age, race, body mass index (BMI), history of smoking, and the comorbidities of hypertension (HTN), chronic kidney disease (CKD), and type 2 diabetes (T2D) at the time of hypogonadism diagnosis were recorded. Comorbidities were determined by ICD code. Patients were followed until the date of BMD assessment or censoring (September 30, 2021), whichever came first. BMD testing results, prescriptions of testosterone therapy, and documentation of treatment with an osteoporosis medication were recorded.

Categorical factors were summarized using frequencies and percentages and compared using Pearson chi-square tests or Fisher exact tests if nominal. Comparisons of ordered factors used Wilcoxon rank sum tests with 2 groups, and Kruskal-Wallis tests followed by pairwise Wilcoxon rank sum tests with a Bonferroni correction, if overall tests were statistically significant for 3 group comparisons. Continuous measures were summarized with means and SD and compared between 2 groups with 2-sample *t* tests, using tests for equal variance or Satterthwaite adjustment for unequal variances, as needed. Comparisons of the 3-level BMD outcome on continuous measures used analysis of variance models, followed by pairwise *t* tests with a Bonferroni correction, if overall tests were statistically significant. The distribution of visits across specialties was compared using a chi-square goodness of fit test. Analysis was performed using SAS software.

Results

A total of 10 169 men with an ICD-9 or -10 code for hypogonadism in their medical record between July 1, 2012 and September 30, 2020 were identified. General characteristics included mean age of 63.4 years (± 9.2), mean BMI of 31.3 (±6.0), 86.3% White, 53.5% with history of smoking, 68.2% with hypertension, 20.6% with CKD, and 36.9% with T2D. Of 728 (7.2%) patients that underwent BMD testing, 352 (48.4%) had osteopenia (*T* score = –1.0 to –2.5) and 87 (12.0%) had osteoporosis (*T* score ≤ –2.5). Of the 87 patients identified as having osteoporosis, 50 (57.5%) were treated with an osteoporosis medication.

Patients that underwent BMD testing were older, more likely to be former smokers, and had higher rates of HTN, CKD, and T2D (Table 1). Patients with low BMD (osteopenia or osteoporosis) were older, had lower BMI, were more likely to be former smokers, and had higher rates of CKD than those with normal BMD (Table 2). Three-level results (normal BMD vs osteopenia vs osteoporosis) also demonstrated those with osteopenia or osteoporosis were older and had lower BMI than those with normal BMD (Table 3). When comparing patients with osteoporosis that were treated with an osteoporosis medication vs those that were not, there were no statistically significant differences in baseline variables between the groups (Table 4).

After excluding patients with history of prostate cancer, 8463 men from the primary collection remained. Of these patients, 4996 (59.0%) received a prescription for TRT during the study period. Patients who underwent TRT were younger, had higher BMI, were more likely to be White, and were more likely to have HTN than those who did not receive TRT (Table 5). Patients that underwent BMD testing were more likely to receive TRT vs those who did not undergo testing, but there was no statistically significant difference in frequency of TRT in those with low BMD vs those with normal BMD (see Table 1 and 2).

Following the initial diagnosis of hypogonadism, 2661 patients had office visits with primary care, 2572 had office visits with endocrinology, and 4936 had office visits with urology. The percentage of patients in each group that underwent BMD testing include 9.6% (256) of those seen by primary care, 9.0% (232) of those seen by endocrinology, and 4.9% (240) seen by urology ($P < .001$). The frequency of low BMD vs normal BMD was not significantly different between patients seen by different specialty providers (Table 6).

Discussion

Despite a recommendation from the Endocrine Society for men aged 50 years or older with hypogonadism to undergo BMD testing, the rate at which this testing is performed in

Table 1. Bone mineral density testing comparison

Factor	Overall (N = 10 169)	No BMD testing (N = 9441)	BMD testing (N = 728)	*P*
Age at diagnosis, y	63.4 ± 9.2	63.2 ± 9.2	66.4 ± 9.0	< .001[b]
Race				.56[c]
White	8667 (86.3)	8036 (86.3)	631 (87.4)	
Black	1086 (10.8)	1014 (10.9)	72 (10.0)	
Other	285 (2.8)	266 (2.9)	19 (2.6)	
Missing	131 (1.3)	125 (1.3)	6 (0.8)	
BMI at diagnosis	31.3 ± 6.0	31.3 ± 6.0	30.7 ± 5.8	.003[b]
Missing	342	329	13	
Smoking				< .001[c]
Never smoker	4708 (46.5)	4394 (46.7)	314 (43.1)	
Former smoker	4665 (46.1)	4285 (45.6)	380 (52.2)	
Current smoker	754 (7.4)	720 (7.7)	34 (4.7)	
Missing	42 (0.4)	42 (0.4)	0 (0.0)	
Type 2 diabetes	3756 (36.9)	3449 (36.5)	307 (42.2)	.002[c]
Hypertension	6937 (68.2)	6335 (67.1)	602 (82.7)	< .001[c]
CKD	2094 (20.6)	1848 (19.6)	246 (33.8)	< .001[c]
Treatment with osteoporosis medication	212 (2.1)	88 (0.93)	124 (17.0)	< .001[c]
Treatment with TRT[a]	4996 (59.0)	4624 (58.4)	372 (68.3)	< .001[c]

Statistics presented as mean ± SD, N (column %).
Abbreviations: BMD, bone mineral density; BMI, body mass index; CKD, chronic kidney disease; TRT, testosterone replacement therapy.
[a]Among patients with no prior diagnosis of prostate cancer (overall N = 8463; no BMD testing N = 7918, BMD testing N = 545).
P values: [b]*t* test; [c]Pearson chi-square test.

Table 2. Bone mineral density result comparison (2-level)

Factor	Overall (N = 728)	Normal BMD (N = 289)	Low BMD[a] (N = 439)	*P*
Age at diagnosis, y	66.4 ± 9.0	63.8 ± 8.8	68.1 ± 8.7	**< .001**[c]
Race				.080[e]
White	631 (87.4)	241 (84.6)	390 (89.2)	
Black	72 (10.0)	37 (13.0)	35 (8.0)	
Other	19 (2.6)	7 (2.5)	12 (2.7)	
Missing	6 (0.8)	4 (1.4)	2 (0.5)	
BMI at diagnosis	30.7 ± 5.8	32.4 ± 6.1	29.5 ± 5.3	**< .001**[d]
Missing	13	4	9	
Smoking				**.034**[e]
Never smoker	314 (43.1)	133 (46.0)	181 (41.2)	
Former smoker	380 (52.2)	137 (47.4)	243 (55.4)	
Current smoker	34 (4.7)	19 (6.6)	15 (3.4)	
Type 2 diabetes	307 (42.2)	124 (42.9)	183 (41.7)	.74[e]
Hypertension	602 (82.7)	233 (80.6)	369 (84.1)	.23[e]
CKD	246 (33.8)	82 (28.4)	164 (37.4)	**.012**[e]
Treatment with osteoporosis medication	124 (17.0)	17 (5.9)	107 (24.4)	**< .001**[e]
Treatment with TRT[b]	372 (68.3)	156 (70.0)	216 (67.1)	.48[e]

Statistics presented as mean ± SD, N (column %).
Abbreviations: BMD, body mineral density; BMI, body mass index; CKD, chronic kidney disease; TRT, testosterone replacement therapy.
[a]Low BMD: *T* score ≤ −1.0.
[b]Among patients with no prior diagnosis of prostate cancer (overall N = 545; normal BMD N = 223; low BMD N = 322).
P values: [c]*t* test; [d]Satterthwaite *t* test, [e]Pearson chi-square test.

Table 3. Bone mineral density result comparison (3-level)

Factor	Normal (N = 289)	Osteopenia (N = 352)	Osteoporosis (N = 87)	*P*
Age at diagnosis, y	63.8 ± 8.8[b,c]	67.9 ± 8.6[a]	69.0 ± 9.3[a]	**< .001**[e]
Race				.21[f]
White	241 (84.6)	315 (90.0)	75 (86.2)	
Black	37 (13.0)	27 (7.7)	8 (9.2)	
Other	7 (2.5)	8 (2.3)	4 (4.6)	
Missing	4 (1.4)	2 (0.6)	0	
BMI at diagnosis	32.4 ± 6.1[b,c]	29.8 ± 5.1[a]	28.5 ± 5.6[a]	**< .001**[e]
Missing	4	7	2	
Smoking				.13[f]
Never smoker	133 (46.0)	145 (41.2)	36 (41.4)	
Former smoker	137 (47.4)	196 (55.7)	47 (54.0)	
Current smoker	19 (6.6)	11 (3.1)	4 (4.6)	
Type 2 diabetes	124 (42.9)	148 (42.0)	35 (40.2)	.90[f]
Hypertension	233 (80.6)	294 (83.5)	75 (86.2)	.41[f]
CKD	82 (28.4)	130 (36.9)	34 (39.1)	**.040**[f]
Treatment with osteoporosis medicine	17 (5.9)[b,c]	57 (16.2)[a,c]	50 (57.5)[a,b]	**< .001**[f]
Treatment with TRT[d]	156 (70.0)	176 (67.7)	40 (64.5)	.69[f]

Statistics presented as mean ± SD, N (column %).
Post hoc pairwise comparisons were conducted using Bonferroni adjustment.
Abbreviations: BMI, body mass index; CKD, chronic kidney disease; TRT, testosterone replacement therapy.
[a]Significantly different from normal.
[b]Significantly different from osteopenia.
[c]Significantly different from osteoporosis.
[d]Among patients with no prior diagnosis of prostate cancer (normal N = 223; osteopenia N = 260; osteoporosis N = 62).
P values: [e]analysis of variance; [f]Pearson chi-square test.

real-world practice is quite low, with only 7.2% of men in this report undergoing screening via DXA. Rates of screening were similar in patients seen by primary care and endocrinology providers, 9.6% and 9.0%, respectively, but were lower in those seen by urology providers (4.9%; *P* = < .001). While alarming, similarly low rates of screening have been observed in other studies involving men with other indications for undergoing BMD testing, including those who had previous fractures [1-7].

The reason why screening rates are so low is unclear, but there are likely multiple factors. Although the Endocrine Society, National Osteoporosis Foundation, and International Society for Clinical Densitometry all recommend screening for low BMD in men with risk factors (including hypogonadism) for men aged 50 to 70 years and for all men age 70 years or older, the US Preventive Services Task Force (USPSTF) concluded in their last recommendation statement in 2018 that "the current evidence is insufficient to assess the balance of benefits and harms of screening for osteoporosis to prevent osteoporotic fractures in men." [12-15] Although the USPSTF recommendations are in the process of being updated and may change, the current discrepancy in screening guidelines likely creates confusion among providers. A second major reason for underscreening is that third-party payers, including Medicare, vary in their coverage of BMD testing in men. Currently, Medicare will cover BMD screening in men only if they have been diagnosed with primary hyperparathyroidism, are on treatment with steroids, or have an x-ray suggestive of low BMD or vertebral fractures [16].

Table 4. Osteoporosis treatment

	Overall (N = 87)	Treated (N = 37)	Not treated (N = 50)	*P*
Age at diagnosis, y	69.0 ± 9.3	68.5 ± 9.5	69.3 ± 9.2	.66[a]
Race				.058[c]
White	75 (86.2)	29 (78.4)	46 (92.0)	
Black	8 (9.2)	4 (10.8)	4 (8.0)	
Other	4 (4.6)	4 (10.8)	0 (0.00)	
BMI at diagnosis	28.5 ± 5.6	29.5 ± 5.9	27.8 ± 5.4	.16[a]
Missing	2	0	2	
Smoking				.76[c]
Never smoker	36 (41.4)	15 (40.5)	21 (42.0)	
Former smoker	47 (54.0)	21 (56.8)	26 (52.0)	
Current smoker	4 (4.6)	1 (2.7)	3 (6.0)	
Type 2 diabetes	35 (40.2)	17 (45.9)	18 (36.0)	.35[b]
Hypertension	75 (86.2)	33 (89.2)	42 (84.0)	.49[b]
CKD	34 (39.1)	15 (40.5)	19 (38.0)	.81[b]

Statistics presented as mean ± SD, N (column %).
Abbreviations: BMI, body mass index; CKD, chronic kidney disease.
P values: [a]*t* test; [b]Pearson chi-square test; [c]Fisher exact test.

Table 5. Testosterone replacement treatment

	Overall (N = 8463)	No TRT (N = 3467)	TRT (N = 4996)	*P*
Age at diagnosis, y	62.5 ± 8.9	64.1 ± 9.0	61.3 ± 8.6	**< .001**[b]
Race				**< .001**[c]
White	7282 (87.2)	2900 (84.6)	4382 (89.0)	
Black	824 (9.9)	402 (11.7)	422 (8.6)	
Other	245 (2.9)	125 (3.6)	120 (2.4)	
Missing	112 (1.3)	40 (1.2)	72 (1.4)	
BMI at diagnosis	31.5 ± 6.1	30.6 ± 6.0	32.1 ± 6.2	**< .001**[a]
Missing	279	111	168	
Smoking				.11[c]
Never smoker	3955 (46.9)	1606 (46.6)	2349 (47.2)	
Former smoker	3834 (45.5)	1562 (45.3)	2272 (45.6)	
Current smoker	639 (7.6)	279 (8.1)	360 (7.2)	
Missing	35 (0.4)	20 (0.6)	15 (0.3)	
Type 2 diabetes	3191 (37.7)	1286 (37.1)	1905 (38.1)	.33[c]
Hypertension	5725 (67.6)	2,214 (63.9)	3511 (70.3)	**< .001**[c]
CKD	1694 (20.0)	710 (20.5)	984 (19.7)	.38[c]
Treatment with osteoporosis medication	142 (1.7)	46 (1.3)	96 (1.9)	**.036**[c]

Statistics presented as mean ± SD, N (column %).
Abbreviations: BMI, body mass index; CKD, chronic kidney disease; TRT, testosterone replacement therapy.
P values: [a]*t* test; [b]Satterthwaite *t* test, [c]Pearson chi-square test.

Table 6. Bone mineral density testing and result comparison by provider specialty

	Primary care (N = 2661)	Endocrinology (N = 2572)	Urology (N = 4936)	*P*
Provider type	2,661 (26.2)	2,572 (25.3)	4,936 (48.5)	**< .001**[g]
BMD performed	256 (9.6)[c]	232 (9.0)[c]	240 (4.9)[a,b]	**< .001**[f]
BMD result[d]				.96[e]
Normal	102 (39.8)	93 (40.1)	94 (39.2)	
Osteopenia	125 (48.8)	111 (47.8)	116 (48.3)	
Osteoporosis[d]	29 (11.3)	28 (12.1)	30 (12.5)	

Statistics presented as N (column %).
Post hoc pairwise comparisons were conducted using Bonferroni adjustment.
Abbreviation: BMD, bone mineral density.
[a]Significantly different from primary care.
[b]Significantly different from endocrinology.
[c]Significantly different from urology.
[d]Statistics % based on total BMD performed by provider type: primary care N = 256; endocrinology N = 232; urology N = 240.
P values: [e]Kruskal-Wallis test; [f]Pearson chi-square test; [g]chi-square goodness of fit test.

It is naturally expected that low rates of screening for low BMD in men with hypogonadism will result in lower rates of diagnosis as well. In this report, 60.3% (439) of men who underwent screening were found to have low BMD, including 48.4% (352) with osteopenia and 12.0% (87) with osteoporosis. These results can be compared to data from the National Health and Nutrition Examination Survey (2017-2018), which demonstrated that of men aged 50 and older, 33.5% had osteopenia and 4.4% had osteoporosis [17]. While it is unknown what other characteristics other than hypogonadism differed between the men in our study and those in the national survey, the comparison supports previous evidence showing that men with hypogonadism are at increased risk of low BMD.

Previous studies have shown that even in men with a clear indication for therapy with an osteoporosis medication, such as in those who have had a fragility fracture, treatment rates are quite low [3, 4, 6]. In our study, 16.1% (57) of patients with osteopenia and 57.5% (50) of patients with osteoporosis were treated with an osteoporotic medication (most commonly a bisphosphonate). While these rates of treatment are generally higher than found in prior studies, there remains opportunity for improvement. It is also interesting to note that the prescribing of TRT, after excluding those with a history of prostate cancer, was similar among those with low BMD and those with normal BMD (see Table 2).

Strengths of this study include the large number of patients identified and the robust amount of clinical data collected, which allowed for an extensive depiction of the patients. Furthermore, the average duration of follow-up was 6.6 years, and all patients were afforded at least 1 year from the diagnosis of hypogonadism to have the guideline-recommended testing.

A limitation of the study is its retrospective, descriptive nature. It is likely residual confounders are present. In addition, the diagnoses of hypogonadism were based only on ICD codes; testosterone values were not used to confirm diagnoses. Furthermore, while all patients with hypogonadism were included, it is likely that patients with certain underlying conditions, such as those with prostate cancer currently undergoing androgen-deprivation therapy, have higher rates of low BMD than men with age-related decreases in testosterone levels. Differences in etiology (ie, primary vs secondary hypogonadism) and severity of hypogonadism were not differentiated in this study.

An additional limitation is the lack of data on fractures. Also, patients may have had BMD testing performed outside our hospital system, and these results would not have been available to include in this study. Furthermore, it is possible some patients who did not have a DXA recorded may have undergone assessment of BMD via other means (eg, computed tomography, ultrasound) or were diagnosed with osteoporosis based on the presence of fragility fractures alone. These patients were not identified in this study. Additionally, patients with contraindications to TRT and/or osteoporosis medications were not identified or excluded from our study, which may limit what conclusions can be drawn.

While this study reviewed the rate of BMD testing in all men aged 50 years or older with a diagnosis of hypogonadism, further study is needed to investigate the differential effects of overt hypogonadism with the more subtle age-related decline in testosterone levels on BMD and fracture risk. It is possible that different screening recommendations may be needed for each group to best address the risk for low BMD. Further studies are also needed to determine the reasons for the low screening rate and what can be changed to improve the rate of BMD screening and subsequent treatment when low BMD is identified.

Conclusion

Despite guideline recommendations, this report revealed the low rate at which BMD testing is performed in hypogonadal

men in real-world practice. The high rate (60.3%) at which low BMD was discovered in hypogonadal men who did undergo testing, and further observation of a low rate of treatment with osteoporosis medication when indicated, is alarming and necessitates a call to action for more hypogonadal men to undergo testing and receive appropriate treatment. Further studies are needed to determine the reasons why so few men with hypogonadism undergo BMD assessment and what systems can be put in place to overcome this clinical conundrum.

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Disclosures

The authors have nothing to disclose.

Data Availability

Some or all data sets generated during and/or analyzed during the present study are not publicly available but are available from the corresponding author on reasonable request.

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