Underdiagnosis of osteoporosis in different ethnic groups when bone mineral density is measured in a single area

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Summary

The aim of the present review was to assess the difference in osteoporosis (OP) prevalence, when measuring the DXA bone mineral density (BMD) of the lumbar spine (LS) or the femoral neck (FN). To reach it, 15 reports on the simultaneous determination of both areas were reviewed, including results obtained as of the age of 50, periodically assessed every 5 to 10 years and at least up to 79 years of age. The WHO definition of osteoporosis (T-score ≤ -2.5) was used in all studies. Results from men and women were included in six studies; only women values were reported in eight of them, and only men, in one.
***Results*. The prevalence of OP in women measuring only the LS rose from 12.1% in the 6th decade to 39.7% in the 8th decade, while as regards the FN, it rose from 3.0% to 30.2% among the same age groups. In all studies on the 6th and 7th decades, OP prevalence was greater in the LS compared to the FN. In the 8th decade (70-79 y.o), only in 3 out of 14 studies, prevalence was greater in the FN compared to the LS. Failure to diagnose OP when measuring only the FN was 9.1% in the 6th, 16.2% in the 7th and 9.5% in the 8th decade.**
In six studies, the Authors reported not only the OP prevalence of each area but also the prevalence at any site, allowing to determine underdiagnosis when measuring only the LS or the FN. Underdiagnosis was significantly greater when measuring only the FN than when measuring only the LS. The results in women were: 6th decade: 76.4 ± 8.3% *vs* 11.3 ± 9.1% p<0.001; 7th decade: 65.0 ± 6.3% *vs* 15.9 ± 6.9% p <0.001 and 8th decade: 37.2 ± 13.1% *vs* 20.1 ± 5.8% p <0.02. As expected, OP prevalence in men is lower than its prevalence in women. There is a failure to diagnose OP in men when measuring only the FN ranging from 3.2% in the 6th decade to 1.3% in the 8th. There was a great dispersion of the results, and no clear predominance from one area to the other was observed. The underdiagnosis of OP, evaluating only the FN, or the LS calculated in four studies showed no significant differences in any of the three decades reported.
***Conclusion*. The present review confirms that, especially in women from different ethnic groups or regions neglecting the measurement of the BMD of the LS, leads to a significant underdiagnosis of osteoporosis. This result reinforces the guidelines of the ISCD about measuring both the lumbar spine and the upper femur for a more accurate assessment of osteoporosis prevalence.**

KEY WORDS: osteoporosis prevalence; lumbar spine; femoral neck; underdiagnosis of osteoporosis.

Introduction

Osteoporosis (OP) is a highly prevalent disease causing bone fractures, decreased quality of life, disability, increased mortality and a heavy economic burden on health care systems (1).
In spite of the availability of safe and efficacious treatments to reduce the risk of bone fractures, a decline in the number of patients receiving preventive treatment has been observed in the United States of America (USA) (2). In order to address this regrettable situation, physicians grouped in the National Bone Health Alliance (USA) have expanded the criteria for diagnosing osteoporosis of men and women aged 50 or above, adding other factors to the bone mineral density (BMD) measurement of the lumbar spine (LS) and femoral neck (FN) (3).
Despite these laudable efforts to expand the prevention of osteoporosis, on a global basis (and even by the newly proposed criteria), the BMD assessment continues to be the most important item for diagnosis.
Some discrepancy on which skeletal areas should be assessed to diagnose osteoporosis has been observed. While the International Society for Clinical Densitometry (ISCD) advises to include measurements of the lumbar spine, femoral neck and total femur (4), the European Guidance, whose last version was released in 2013, included only the evaluation of the femoral neck (5).
The purpose of the present review is to contribute to the clarification of the above mentioned discrepancy. We have revised a group of studies carried out in different countries and ethnic groups that have determined the prevalence of osteoporosis measuring both skeletal areas: the lumbar spine and the femoral neck, reporting results separately.

Methods

Bibliography search in PubMed was performed using the following key words: "Bone mineral Density (BMD), prevalence, osteoporosis, Lumbar spine (LS) and femoral neck (FN)". Out of 915 articles listed, 23 reports published in the English language from year 2000 to 2017 were found suitable for review (6-28). Eight were excluded for different reasons: reporting only one area (21-23), the combined prevalence of both (24), two meta-analysis (25, 26), estimated results (27) or results included in one of the selected articles (28).
In total, 15 cross-sectional studies were included in the review (6-20) with the following characteristics:
a) BMD measurement of the LS and FN, with the results of each area reported separately
b) results provided from 50 to 80+ years of age, periodically assessed every 5 or 10 years including at least the 70-79 age period
c) diagnosis of OP following the WHO definition: T- score ≤ -2.5 SD compared to normal young values obtained from the same or similar population.

Statistical analysis

The results of the studies included are expressed as average ± SD. In all studies, failure to diagnose OP when measuring only the FN was estimated by the simple subtraction: LS prevalence - FN prevalence.
In 6 studies on women and 4 on men: prevalence at any site (LS or FN or total femur) was also reported, allowing to calculate the "true" underdiagnosis, as follows:

$$\frac{\text{Prevalence of LS or FN} - \text{Prevalence at any site}}{\text{Prevalence at any site}} \times 100$$

A t test was used to compare the underdiagnosis of the LS versus the FN. The age group 80+ years was not included in this analysis due to the small number of observations.

Results

Table 1 shows the year of publication, country, region or city, and the number of individuals included in each study. The results concerning men and women were included in six studies; results reporting only women values were informed in eight studies, and one study reported only men values. In three studies (7, 10, 15), the results were obtained from figures.

Women

Table 2 shows the average ± SD of OP prevalence in women per decade of age as regards the LS and FN.
Prevalence of OP measuring only the LS rose from 12.1% in the 6th decade to 39.7% in the 8th decade, while in the FN rose from 3.0% to 30.2% during the same age periods. In all studies of the 6th and 7th decades, osteoporosis prevalence was greater in the LS compared to the FN. In the 8th decade (70-79 y.o.) only in 3 out of 14 studies, prevalence was greater in the FN compared to the LS. Failure to diagnose OP when measuring only the FN was 9.1% in the 6th, 16.2% in the 7th and 9.5% in the 8th decade (Figure 1).
In six studies (11, 13, 15, 17-19), the Authors reported not only OP prevalence in each area but also prevalence at any site. OP prevalence at the LS, FN, and at any site, and un-

Table 1 - Author (reference), year of publication, country, region, number of subjects and age of the 15 studies included.

Author	Publication (years)	Country	City/Region	Women		Men	
				n	Age	n	Age
Henry et al.(6)	2000	Australia	Geelong	1494 (20-80+)	50-80+	-	-
Tenenhouse et al.(7)	2000	Canada	Various	4761	50-80+	-	-
Ikeda et al.(8)	2002	Japan	Sangawa	366	50-70+	-	-
Yang et al.(9)	2004	Taiwan	Taipe	3591	50-80+	-	-
Wu et al.(10)	2004	China	Hunan (Mid-South)	1166	50-90	-	-
Cheng et al. (11)	2007	China	6 Regions	5083	50-89	-	-
Cui et al.(12)	2008	Korea	Namwon	1806	50-79	1424	50-79
Sanfelix et al.(13)	2010	Spain	Valencia	824	50-75+	-	-
Shin et al.(14)	2010	Korea	Aunsung	1991	50-79	1547	50-79
Lee et al.(15)	2014	Korea	National	5787	50-70+	5355	50-70+
Park et al. (16)	2014	Korea	National	4011	50-70+	3414	50-70+
Lu et al. (17)	2016	Taiwan	Taipe	1712	50-70+	2028	50-70+
Mautalen et al.(18)	2016	Argentina	Buenos Aires	5448	50-80+	-	-
Lim et al. (19)	2017	Korea	Chungju	3484	50-80+	2198	50-80+
Liu et al. (20)	2017	China	Han (Ethnicity)	-	-	1489	50-80+

Table 2 - Osteoporosis prevalence at the lumbar spine (LS) or femoral neck (FN) per decade of age in all studies in woman and failure to diagnose osteoporosis when measuring only the femoral neck (LS-FN) (n=14).

	Lumbar Spine				Femoral Neck				Failure: LS-FN		
Author (Reference)	**50-59**	**60-69**	**70-79**	**>80**	**50-59**	**60-69**	**70-79**	**>80**	**50-59**	**60-69**	**70-79**
Henry et al. (6)	6.3	18.0	31.6	36.5	3.9	12.8	28.8	48.8	2.4	5.2	2.8
Tenenhouse et al.(7)	5.0	15.0	19.0	21.0	2.0	9.0	14.0	31.0	3.0	6.0	5.0
Ikeda et al. (8)	18.3	34.5	45.7	ND	1.5	9.2	26.7	ND	16.8	25.3	19.0
Yang et al. (9)	8.6	14.1	14.2	16.0	5.3	11.2	17.3	24.0	3.3	2.9	-3.1
Wu et al. (10)	17.0	40.0	48.0	59.0	4.0	17.0	39.0	61.0	13.0	23.0	7.0
Cheng et al. (11)	14.2	36.7	50.1	65.5	3.9	15.2	33.9	63.6	4.3	21.5	16.2
Cui et al. (12)	21.5	51.3	60.2	ND	1.7	11.4	36.7	ND	19.8	39.9	23.5
Sanfélix et al. (13)	15.5	23.3	38.4	ND	3.8	8.5	25.1	ND	11.7	14.8	13.3
Shin et al. (14)	9.3	28.5	47.5	ND	0.7	4.8	17.8	ND	8.6	23.7	29.7
Lee et al. (15)	11.0	21.0	45.0	ND	2.0	10.0	46.0	ND	9.0	11.0	-1.0
Park et al. (16)	12.9	30.9	53.4	ND	5.1	17.0	54.3	ND	7.8	13.9	-0.9
Lu et al. (17)	3.8	12.6	22.9	ND	2.1	5.3	19.8	ND	1.7	7.3	3.1
Mautalen et al. (18)	6.8	17.0	22.7	21.4	1.1	5.5	11.5	28.6	5.7	11.5	11.2
Lim et al. (19)	19.9	42.4	57.7	75.7	4.9	21.9	51.7	73.5	15.0	20.5	5.4
Average	12.50	27.52	39.70	42.17	3.00	11.34	30.19	47.21	8.72	16.18	9.37
±1SD	5.75	12.12	15.01	24.30	1.57	5.01	13.89	19.58	5.79	10.12	9.86

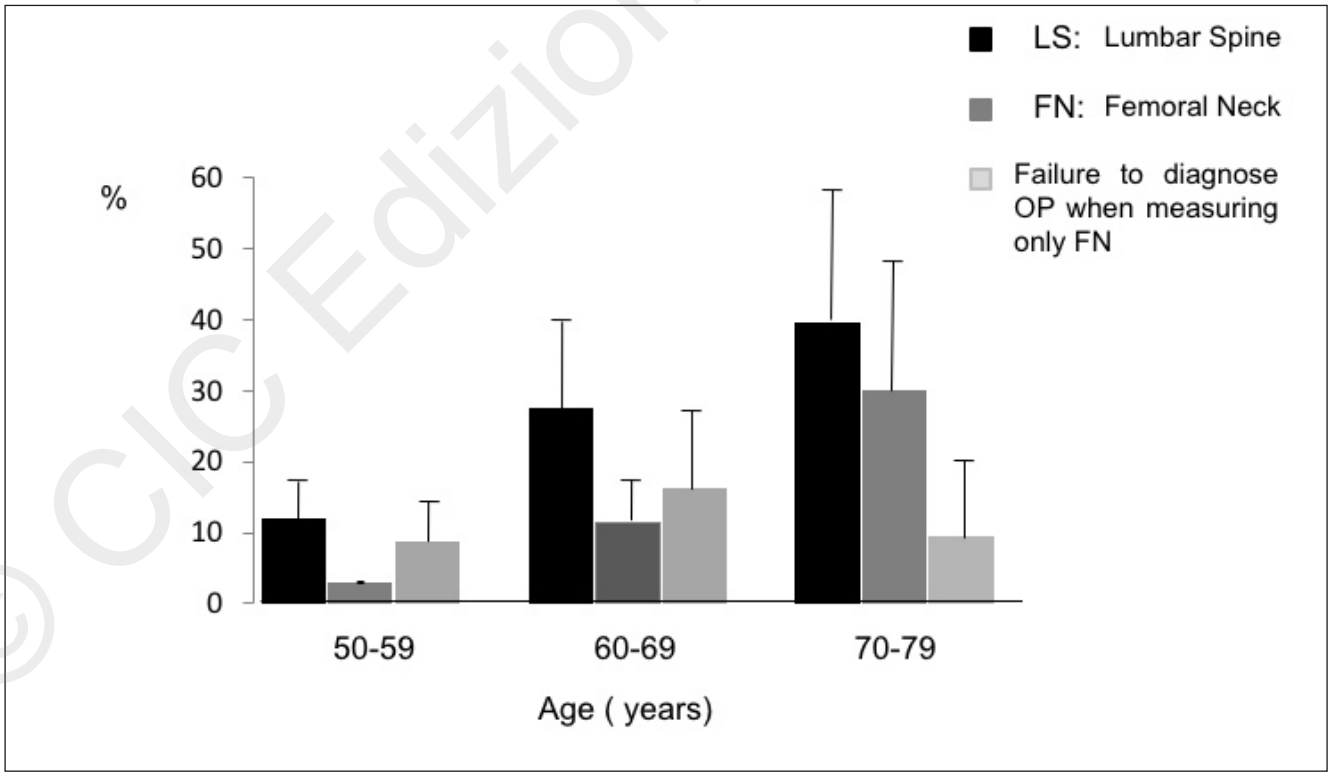

Figure 1 - Average prevalence of osteoporosis at lumbar spine (LS), femoral neck (FN) and failure (LS-FN) to diagnose osteoporosis when only the femoral neck is measured in women (n=14 studies).

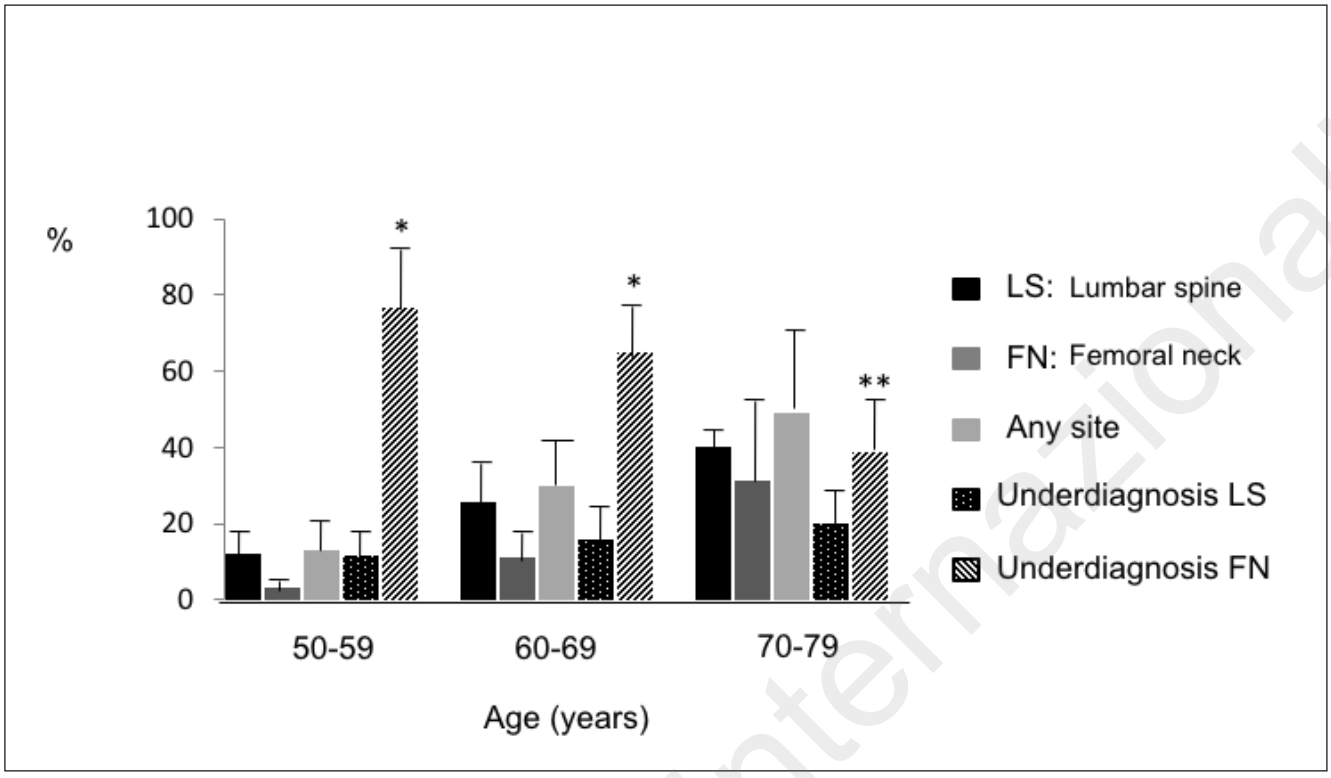

Figure 2 - Average prevalence of osteoporosis at lumbar spine (LS), femoral neck (FN) or any site and underdiagnosis when measuring only the lumbar spine or the femoral neck in women (n=6 studies). *p<0.001 *vs* LS; p<0.02 *vs* LS (Underdiagnosis: Prevalence of LS or FN –Prevalence any site x 100 / Prevalence any site).

derdiagnosis when measuring only the LS or FN per decades of age in these studies are shown in Figure 2. Underdiagnosis was significantly greater when measuring only the FN than when measuring only the LS. The results were: 6th decade 76.4 ± 8.3% *vs* 11.3 ± 9.1% p<0.001; 7th decade 65.0 ± 6.3% *vs* 15.9 ± 6.9% p <0.001 and 8th decade 37.2 ± 13.1% *vs* 20.1 ± 5.8% p <0.02.

Men

Table 3 shows the osteoporotic prevalence in seven studies in men (all Asiatic individuals). As expected, OP prevalence in men is lower than OP in women. Failure to diagnose OP when measuring only the FN ranged from 3.2% in the 6th decade to 1.3% in the 8th (Figure 3). There was a great dispersion of the results and no clear predominance from one area to the other was observed. OP underdiagnosis, evaluating only the FN or the LS was calculated in four studies. No significant differences were found in any of the three decades reported.

Discussion

The determination of osteoporotic prevalence in different re-

Table 3 - Osteoporosis prevalence at the lumbar spine (LS) or femoral neck (FN) per decade of age in all studies in men and failure to diagnose osteoporosis when measuring only the femoral neck (LS-FN) (n=7).

	Lumbar Spine			Femoral Neck			Failure:LS-FN		
	50-59	**60-69**	**70-79**	**50-59**	**60-69**	**70-79**	**50-59**	**60-69**	**70-79**
Cui et al. (12)	3.3	8.7	12.8	2.3	7.3	15.2	1.0	1.4	-2.4
Shin et al. (14)	9.3	13.7	22.4	0	1.2	5.6	9.3	12.5	16.8
Lee et al. (15)	4.0	6.0	12.0	2.0	7.0	26.0	2.0	-1.0	-14.0
Park et al. (18)	3.5	5.9	11.7	0.3	2.7	11.0	3.2	3.2	0.7
Lu et al. (17)	1.5	1.6	5.6	1.7	2.3	7.7	-0.2	-0.7	-2.1
Lim et al. (19)	8.2	13.6	19.5	0.5	2.3	6.1	7.7	11.3	13.4
Average	4.26	7.19	12.09	0.97	3.57	10.73	3.29	3.61	1.36
±1SD	3.37	5.18	7.48	0.99	2.49	7.77	3.77	5.89	10.52

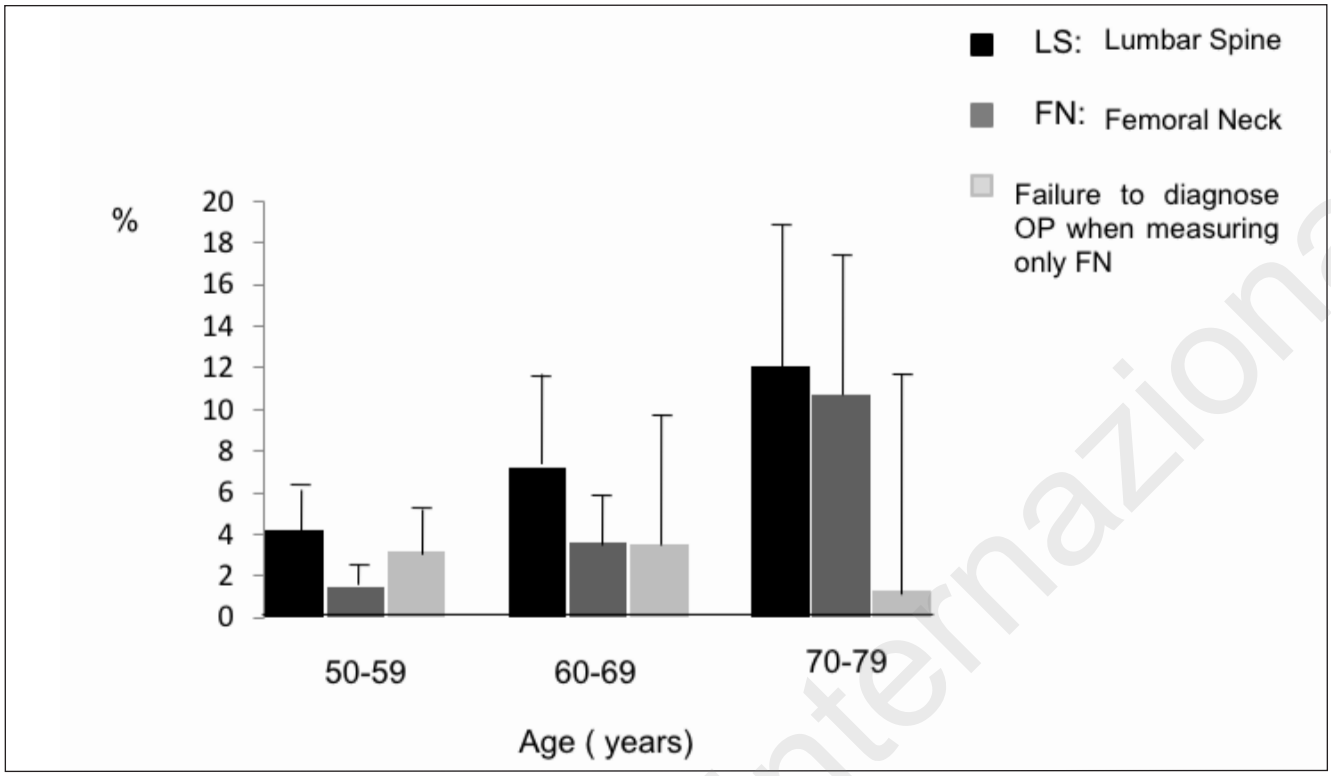

Figure 3 - Average prevalence of osteoporosis at lumbar spine (LS), femoral neck (FN) and failure (LS-FN) to diagnose osteoporosis when only the femoral neck is measured in men (n=7 studies).

gions and ethnic groups is crucially important for the development of strategies to prevent it and to foresee the economic burden to be assumed (29). A thorough review of risk factors contributing to osteoporotic fractures has been recently reported (30). The addition of clinical factors, previous history of fragility fractures, family history of OP, habits, other medications taken or concomitant diseases (3) increases the diagnostic scope of the disease (31). Furthermore, a recent article emphasizes that bone fractures are the consequence of a dysmobility syndrome that includes at least osteoporosis, sarcopenia, previous fall, diabetes and obesity (32). However, the DXA BMD evaluation of skeletal sites still continues to be the main determinant in diagnosing osteoporosis on a global basis.

In order to address the discrepancy between measuring only the FN (5) or both the LS and FN (4), we have reviewed published studies from different regions and ethnic groups that reported separately the prevalence of osteoporosis based on the results obtained in both areas.

Considering all studies in women, the results clearly show a failure to diagnose OP when measuring only the FN, ranging from 9.1% in the sixth decade, 16.2% in the seventh decade and 9.5% in the eighth decade.

More importantly an accurate "true underdiagnosis" obtained in six studies revealed that there was a failure to detect all cases of osteoporosis when measuring only one area but the deficit was significantly greater when measuring only the FN. In spite of the reduced number of observations along the three decades under study, a surprisingly high underdiagnosis with the FN measurement was observed from 50-69 years of age. Even at the 70-79 age range, the respective underdiagnosis was 37.2% measuring only the FN *versus* 20.1% measuring only the LS ($p<0.02$). These findings agree with previous reports concerning an increased OP prevalence at LS compared with FN (33) and an overall underdiagnosis in the 50 to 89 age range of 53% and 54% from two studies when only the FN is measured (18 and 24 respectively).

Finally, the most relevant issue is whether the measurement of BMD in both areas improves the estimation of future bone fracture. Leslie et al. (34) reported that, considering all ages, the BMD assessment of the LS did not improve the prediction of bone fractures. However, in women 50-65 years old the measurement of LS and FN significantly improved the prediction of vertebral fractures, compared to evaluation of only the FN ($p<0.001$). In addition to the clinical relevance, vertebral fractures establish by themselves the diagnosis of osteoporosis and help to predict future fractures on other skeletal areas.

Osteoporosis underdiagnosis, when only the BMD of the FN is evaluated in women, could be due to the different remodeling rate of the trabecular and cortical bone. In early menopause (50-65 years of age), the rate of bone loss is greater in the trabecular bone of the vertebral bodies compared to the trabecular bone of other areas and the cortical bone. An annual bone loss of ~ 1.0 -1.4%, that could amount a total of ~ 21% 15 years after the onset of menopause, occurs in the vertebral bodies. In addition, the rate of loss could be greater in the trabecular bone adjacent to the red bone marrow (in vertebral bodies) compared to the trabecular bone adjacent to the yellow bone marrow (i.e. ulna) due to the hematopoietic role of the former (35). Therefore, the bone remodeling process explains the very high rate of osteoporosis underdiagnosis during the 6th decade (~ 70%) and

7th decade (~50%) when the DXA measurement of the LS is neglected.

Frequent changes occur in women's spine with age: soft tissue and aortic calcifications, osteophytes, osteoarthritis has been observed in ~61% of the radiological studies of the lumbar spine in older women (36), leading to a reduction of the sensitivity and specificity the LS is taken as the only skeletal site to estimate osteoporosis prevalence.

The present review did not find any study in Caucasian men with simultaneous measurement of LS and FN. The results from Asiatic men reveal a great dispersion of the results from the seven available studies. A slightly greater prevalence of osteoporosis at the LS compared with the FN was observed only in the 6th decade, that was no longer significant in the 7th decade and subsequently. While the underdiagnosis of osteoporosis, measuring only the FN, was significant in women from 50 to 79 years of age, the same results were not observed in Asiatic men.

Conclusion

The present review confirms that, especially in women of different ethnic groups from 50 to 79 years old neglecting the BMD measurement of the LS, leads to a significant underdiagnosis of osteoporosis. Woman with OP only at the spine may have a fracture risk to warrant preventive treatment. These results reinforce the guidelines of the ISCD on measuring both the lumbar spine and the upper femur.

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