Much lower prevalence and severity of osteoporotic vertebral facture in elderly Chinese women than in age-matched Italian women: a radiographic comparison study.

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Running title: Lower OVF severity in Chinese than Italian women

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Abstract

Introduction: Many studies reported that East Asian's prevalence of radiographic OVF is similar to that of Caucasian. Since elderly Chinese's osteoporotic hip fracture prevalence is half (or less than half) of that of their age-match Caucasians, we hypothesize that elderly Chinese's OVF prevalence could be only half, or even less than half, of that of their age-match Caucasians.

Materials: Age-matched elderly women's radiographs (T4–L5) were from two OVF population-based epidemiological studies conducted in Hong Kong (n=200) and in Rome (n=200). The study subjects had a mean age of 74.1 yrs (range: 65-87 yrs). All radiographs were double read by one reader in Hong Kong and one reader in Rome. Radiological osteoporotic vertebral deformity (ROVD) classification included no ROVD (grade 0), and ROVDs with <20%, 20~25%, ≥25%~1/3, ≥1/3~40%, ≥40%~2/3, and ≥2/3 height loss (grade 1~6). Spinal deformity index (SDI) was calculated with each vertebra assigned a score of 0, 0.5, 1, 1.5, 2, 2.5 and 3 for no ROVD or ROVDs grade 1~6.

Results: 77 (38.5%) Chinese subjects and 123 Italian subjects (61.5%) had ROVD respectively ($p<0.0001$). ROVDs in Italian subjects tended to be more severe (total and mean SDI: 454.5 and 3.71 for Italian, and 212 and 2.72 for Chinese, $p<0.05$), more likely to be multiple ($p<0.001$), more likely to have severe and collapsed grades ($p<0.001$). The slope of the relationship between age vs. SDI was steeper for the Italian subjects than for the Chinese subjects, suggesting aging Italian subjects developed faster for the prevalence of ROVD and their severity. A trend suggested earlier onset of ROVD among Italian.

Conclusion: Compared with elderly Italian women, elderly Chinese women have much lower prevalence of OVF. OVF in Chinese women tend to be less severe and less likely to have multiple fractures and less likely to collapse.

Keywords: osteoporotic vertebral fracture (OVF); vertebral deformities; Chinese; Italian; extended semi-quantitative (eSQ) method; Spine Deformity Index (SDI)

Osteoporotic fractures (i.e., fragility fractures) may occur in almost all skeletal segments, but the preferential locations are the vertebral column, the proximal ends of the femur and humerus, and the distal end of the radius (Colles fracture). Trauma due to a fall is by far the most frequent cause of osteoporotic fractures affecting long bones, while it is more difficult to determine the cause and the exact time of osteoporotic vertebral fracture (OVF) which often go undiagnosed. The detection of OVF in women suggests that the patient's bone strength is compromised, and the risk of future fracture is substantially increased, both for further OVF and non-vertebral fragility fracture [1].

It has been well noted that prevalence of clinical fractures is substantially lower among elderly East Asian compared to Caucasians, both for men and women [2-7]. Bow *et al* [4] reported that at the age of 65 or above, the hip fracture rates for Hong Kong Chinese and Japanese men and women were less than half of that in Caucasians. In the study of Shin *et al* [6], the prevalence of self-reported non-traumatic fracture was US Caucasians: 17.1%; US Asian: 10.5%; and Hong Kong Chinese: 5.6 %.

On the other hand, many earlier studies reported that, compared with Caucasian, East Asian's prevalence of radiographic OVF were similar or even higher [4, 8-12]. As majority of OVF are independent of falls and clinically silent, identification of true OVF on radiograph remains a challenge [1, 13]. Considering our own data and literature reports, we hypothesize that elderly Chinese's OVF prevalence could be only half, or even less than half, of that of their age-match Caucasians [14-20]. Aim of this study was to compare OVF prevalence in age-matched elderly women with population-based epidemiological study radiograph samples from Hong Kong, China, and from Rome, Italy.

Materials and Methods

The study protocols were approved by the Ethics Committees of the Chinese University of Hong Kong and Sapienza University of Rome, respectively. Written informed consent was obtained from all subjects. The radiographs were from two population-based OVF epidemiological studies conducted in Hong Kong, China, and in Rome, Italy, with in total 400 subjects included (200 in Hong Kong and 200 in Rome). In both studies, all participants

were community welling, and the recruitment plan was designed so that the participants would represent the general elderly population in age and gender proportion. Italian cases with targeted age range were firstly randomly selected, the radiographs without identification but with age information were sent to Hong Kong. Age matched Chinese cases' radiographs were primarily randomly selected from Ms(Hong Kong) year-4 follow-up study due to its better image quality than the baseline study [19]. As all cases from the year-4 follow-up were older than 69 yrs, for the 49 Italian cases aged 65-68 yrs, age matched Chinese cases' radiographs were randomly selected from Ms(Hong Kong) baseline study conducted during August 2001 to March 2003 [14].

All radiographs in digitalized format were first read by an experienced reader in Hong Kong (YXJW) and then by an experienced reader in Rome (Daniele D). Finally, consensus was achieved for all study cases. Nonfractural changes of the vertebrae shape were evaluated to exclude deformities such as developmental changes and degenerative remodeling (degenerative remodeling is also termed as 'morphometric vertebral deformity' in some publications) [21, 22]. Thoracic and lumbar vertebrae (T4–L5) were evaluated with an extended version of semi-quantitative (eSQ) method with the following criteria [23, 24]: (1), minimal grade refers to radiological osteoporotic vertebral deformities (ROVDs) with < 20% height loss, which would be theoretically equivalent to Genant SQ grade-0.5; (2), mild grade was the same as Genant SQ mild grade (≥20~25% height loss); (3), SQ moderate grade was divided into two subgrades: ≥25% ~1/3 height loss and ≥1/3~40% height loss; (4), SQ severe grade was divided into two subgrades: ≥40%~2/3 height loss and with ≥2/3 height loss (collapsed grade). As Genant's criteria emphasize a radiological diagnosis while do not require a conventional "fracture" sign, the term "ROVD" is used this study's method and results section; while the terms of both OVD (osteoporotic vertebral deformity) and OVF are used loosely in the discussion section.

Spinal deformity index (SDI) was calculated with each vertebra assigned a score of 0, 0.5, 1, 1.5, 2, 2.5 and 3 for no ROVD or ROVDs of <20%, 20~25%, ≥25% ~1/3, ≥1/3 ~40%, ≥40%~2/3, and ≥2/3 vertebral height loss, respectively. The SDI for each subject was calculated by summing the scores of all vertebrae (T4 to L5).

Results

The study subjects had a mean age of 74.1 yrs (SD: 6.14 yrs, range: 65-87 yrs). In total 77 (38.5%) Hong Kong Chinese subjects had ROVD, among them 27 subjects (i.e., 31.2% of the ROVD cases) had only minimal grade ROVD. 123 Italian subjects (61.5%) had ROVD, among them 31 subjects (i.e., 25.5% of the ROVD cases) had only minimal grade ROVD. A comparison of these age-matched women of two ethnic groups showed that Italian had higher prevalence of all-inclusive ROVDs (with all grades included, $p<0.0001$), and ROVDs in Italian tended to be more severe (total and mean SDI: 454.5 and 3.71 for Italian, and 212 and 2.72 for Chinese, $p<0.05$ for SDI mean), more likely to be multiple ($p<0.001$), more likely to have severe grade and collapsed grade ROVD ($p<0.001$, table-1).

	HK	% of total (HK)	IL	% of total (IL)	Ratio: HK/IL	p
total cases: all-inclusive ROVD*	77	38.5%	123	61.5%	0.626	<0.0001
Cases: apparent ROVD	53	26.5%	92	46%	0.576	<0.0001
Cases: multiple ROVDs	39	19.5%	74	37%	0.527	<0.001
Cases: multiple apparent ROVDs	21	10.5%	59	29.5%	0.356	<0.0001
Cases: ≥ severe grade ROVD	19	9.5%	52	26%	0.365	<0.0001
Cases: collapsed grade ROVD	16	8%	34	17%	0.471	<0.001

Table-1. A comparison of osteoporotic vertebral deformity characteristics between elderly Chinese and Italian women

HK: Hong Kong; IL: Italian. ROVD: radiological osteoporotic vertebral deformity

* ROVD of all severity grades.

For the older participants, both Chinese and Italian women had more subjects showing ROVD, and the ROVDs tended to be more severe with higher SDI (Fig-1). SDI ratio's difference between Chinese subjects and Italian subjects was greater for the younger group (65-68 yrs, sum score: 7.5 vs. 49) than for the older group (79-87 yrs, sum score: 94.5 vs. 190), suggesting a trend of earlier onset of ROVD in Italian subjects (Fig-1).

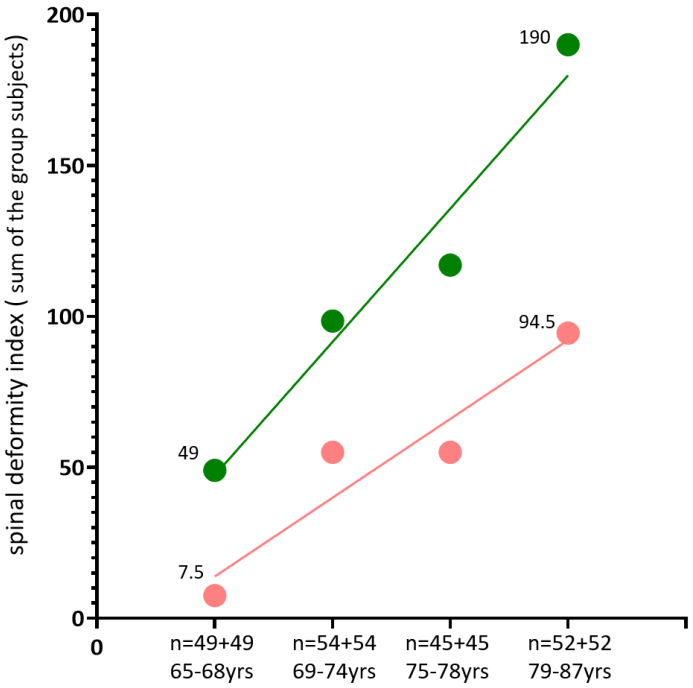

Fig-1, Total spinal deformity index score of four different age groups. Light red ball and line indicate Hong Kong subjects and dark green ball and line indicate Italian subjects. Lines denote linear fit of the four values of total spinal deformity index of the four age groups, with the slope steeper for Italian than for Chinese. N=49+49 means there are 49 Chinese subjects and 49 Italian subjects in this age group.

Discussion

The most important strength of this study is that population-based epidemiological study radiographs of age-marched elderly women of an East Ascian sample (i.e., Chinese) and a Caucasian sample (i.e., Italian) were read in parallel, by two experienced radiologist readers in Hong Kong and in Rome respectively, and consensus was achieved for each case. It is estimated that ¾ of the vertebral fractures are clinically silent, and diagnosis of true OVF on radiograph is challenging [1, 13, 20]. It may less be a problem for identifying moderate to severe OVF in daily clinics, while for epidemiological studies, asserting a minimal or mild OVF and precise grading of OVF are rather difficult [18, 20, 25-32]. Despite the limited number of participants, this study provides insights into the epidemiology difference of OVF among elderly Chinese women and Italian women. This study shows, compared with age-

matched Italian women, Chinese women in Hong Kong have much lower prevalence of OVF. OVF in Chinese women tend to be less severe, and onset of prevalent OVF in Chinese women tend to be later. It is interesting to note that the apparent ROVD (with ≥20% height loss) prevalence of Italian women was 74% higher than that of Chinese. For degenerative spondylolisthesis, Wang *et al* [34] estimated that Chinese and Japanese demonstrated similar prevalence, while its prevalence was 60%-70% higher in American Caucasians, both for men and women. The more novel finding of this study is that, for those with ROVD, the severity of ROVDs is much higher in Italian women. The findings in this study concur with the reports that, compared with Caucasian subjects, and based on BMD measurements, elderly Chinese loss bone much more slowly [5, 6, 35].

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References:

1. Kim DH, Vaccaro AR (2006) Osteoporotic compression fractures of the spine; current options and considerations for treatment. Spine J. 6:479-487

2. Lauderdale DS, Jacobsen SJ, Furner SE, Levy PS, Brody JA, Goldberg J (1997) Hip fracture incidence among elderly Asian American populations. Am J Epidemiol 146:502–509

3. Silverman SL, Madison RE (1988) Decreased incidence of hip fracture in Hispanics, Asians, and blacks: California Hospital Discharge Data. Am J Public Health 78:1482-3

4. Bow CH, Cheung E, Cheung CL, Xiao SM, Loong C, Soong C, Tan KC, Luckey MM, Cauley JA, Fujiwara S, Kung AW (2012) Ethnic difference of clinical vertebral fracture risk. Osteoporos Int. 23:879-85.

5. Morin SN, Berger C, Liu W, Prior JC, Cheung AM, Hanley DA, Boyd SK, Wong AKO, Papaioannou A, Rahme E, Goltzman D; CaMos Research Group (2020) Differences in fracture prevalence and in bone mineral density between Chinese and White Canadians: the Canadian Multicentre Osteoporosis Study (CaMos). Arch Osteoporos. 15:147.

6. Shin MH, Zmuda JM, Barrett-Connor E, Sheu Y, Patrick AL, Leung PC, Kwok A, Kweon SS, Nam HS, Cauley JA; Osteoporotic Fractures in Men (MrOS) Research Group (2014) Race/ethnic differences in associations between bone mineral density and fracture history in older men. Osteoporos Int. 25:837-45.

7. Ross PD, Norimatsu H, Davis JW, Yano K, Wasnich RD, Fujiwara S, Hosoda Y, Melton LJ 3rd. (1991) A comparison of hip fracture incidence among native Japanese, Japanese Americans, and American Caucasians. Am J Epidemiol. 133:801-9.

8. Lau EM, Chan HH, Woo J, Lin F, Black D, Nevitt M, Leung PC (1996) Normal ranges for vertebral height ratios and prevalence of vertebral fracture in Hong Kong Chinese: a comparison with American Caucasians. J Bone Miner Res. 11:1364-8.

9. Tsai KS (1997) Osteoporotic fracture rate, bone mineral density, and bone metabolism in Taiwan. J Formos Med Assoc. 96:802-5.

10. Ross PD, Fujiwara S, Huang C, Davis JW, Epstein RS, Wasnich RD, Kodama K, Melton LJ 3rd. (1995) Vertebral fracture prevalence in women in Hiroshima compared to Caucasians or Japanese in the US. Int J Epidemiol. 24:1171-7.

11. Tsang SW, Bow CH, Chu EY, Yeung SC, Soong CC, Kung AW (2011) Clinical risk factor assessment had better discriminative ability than bone mineral density in identifying subjects with vertebral fracture. Osteoporos Int. 22:667-74.

12. Kung AW (2004) Epidemiology and diagnostic approaches to vertebral fractures in Asia. J Bone Miner Metab 22:170–175

13. Lentle B, Koromani F, Brown J, Oei L, Ward L, Goltzman D, Rivadeneira F, Leslie WD, Probyn L, Prior J, Hammond I, Cheung AM, Oei EH; Vertebral Fracture Research Groups of the CaMos, STOPP, and Rotterdam Studies (2019) The Radiology of Osteoporotic Vertebral Fractures Revisited. J Bone Miner Res 34:409-418.

14. Kwok AW, Gong JS, Wang YX, Leung JC, Kwok T, Griffith JF, Leung PC (2013) Prevalence and risk factors of radiographic vertebral fractures in elderly Chinese men and women: results of Mr. OS (Hong Kong) and Ms. OS (Hong Kong) studies. Osteoporos Int. 24:877-85.

15. Wáng YX, Che-Nordin N, Deng M, Leung JCS, Kwok AWL, He LC, Griffith JF, Kwok TCY, Leung PC (2019) Osteoporotic vertebral deformity with endplate/cortex fracture is associated with higher further vertebral fracture risk: the Ms. OS (Hong Kong) study results. Osteoporos Int. 30:897-905.

16. Wáng YX, Che-Nordin N, Leung JCS, Kwok TCY (2020) Existing severe osteoporotic vertebral fractures in elderly Chinese males were only weakly associated with higher further vertebral fracture risk at year-4 follow-up. Osteoporos Int. 31:1593-1594.

17. Karlsson MK, Kherad M, Hasserius R, Nilsson JÅ, Redlund-Johnell I, Ohlsson C, Lorentzon M, Mellström D, Rosengren BE (2016) Characteristics of Prevalent Vertebral Fractures Predict New Fractures in Elderly Men. J Bone Joint Surg Am. 98:379-85.

18. Lentle BC, Berger C, Brown JP, Probyn L, Langsetmo L, Hammond I, Hu J, Leslie WD, Prior JC, Hanley DA, Adachi JD, Josse RG, Cheung AM, Kaiser SM, Towheed T, Kovacs CS, Wong AKO, Goltzman D (2020) Vertebral Fractures: Which Radiological Criteria Are Better Associated With the Clinical Course of Osteoporosis? Can Assoc Radiol J. 2020 Aug 5 doi: 10.1177/0846537120943529.

19. Wáng YX, Che-Nordin N, Deng M, Leung JCS, Kwok AWL, He LC, Griffith JF, Kwok TCY, Leung PC (2019) Osteoporotic vertebral deformity with endplate/cortex fracture is associated with higher further vertebral fracture risk: the Ms. OS (Hong Kong) study results. Osteoporos Int. 30:897-905.

20. Wáng YX, Lentle BC (2020) Radiographic osteoporotic vertebral fractures in elderly men: a brief review focusing on differences between the sexes. Quant Imaging Med Surg 10:1863-1876.

21. Wáng YXJ, Deng M, He LC, Che-Nordin N, Santiago FR (2018) Osteoporotic vertebral endplate and cortex fractures: A pictorial review. J Orthop Translat. 2018;15:35-49

22. Wáng YX (2020) Osteoporotic Vertebral Deformity: Radiological Appearances and Their Association With a History of Trauma and the Risk of Further Fragility Fracture. Can Assoc Radiol J. 2020 Sep 16 doi: 10.1177/0846537120958471.

23. Wang YX, Diacinti D, Yu W, Cheng XG, Nogueira-Barbosa MH, Che-Nordin N, Guglielmi G, Ruiz Santiago F (2020) Semi-quantitative grading and extended semi-quantitative grading for osteoporotic vertebral deformity: a radiographic image database for education and calibration. Ann Transl Med. 8:398.

24. Wang YX, Liu WH, Diacinti D, Yang DW, Iannacone A, Wang XR, Kripa E, Che-Nordin N, Diacinti D (2020) Diagnosis and grading of radiographic osteoporotic vertebral deformity by general radiologists after a brief self-learning period. J Thorac Dis 2020;12:4702-4710

25. Leidig-Bruckner G, Limberg B, Felsenberg D, Bruckner T, Holder S, Kather A, Miksch J, Wüster C, Ziegler R, Scheidt-Nave C (2000) Sex difference in the validity of vertebral deformities as an index of prevalent vertebral osteoporotic fractures: a population survey of older men and women. Osteoporos Int. 11:102-19.

26. Gao C, Xu Y, Li L, Gu WQ, Yi CT, Zhu Q, Gu HA, Chen BH, Wang QQ, Tang F, Xu JL, Hou JM, Song HJ, Wang H, Wang ZL, Zhang ZL (2019) Prevalence of osteoporotic vertebral fracture among community-dwelling elderly in Shanghai. Chin Med J (Engl). 2019;132:1749-1751.

27. Diacinti D, Vitali C, Gussoni G, Pisani D, Sinigaglia L, Bianchi G, et al; Research Department of FADOI (2017) Misdiagnosis of vertebral fractures on local radiographic readings of the multicentre POINT (prevalence of osteoporosis in INTernal medicine) study. Bone 101:230–235

28. Fechtenbaum J, Briot K, Paternotte S, Audran M, Breuil V, Cortet B, Debiais F, Grados F, Guggenbuhl P, Laroche M, Legrand E, Lespessailles E, Marcelli C, Orcel P, Szulc P, Thomas T, Kolta S, Roux C; bone section of the French Rheumatology Society (2014) Difficulties in the diagnosis of vertebral fracture in men: agreement between doctors. Joint Bone Spine. 2014;81:169-74.

29. Wu CY, Li J, Jergas M, Genant HK (1995) Comparison of semiquantitative and quantitative techniques for the assessment of prevalent and incident vertebral fractures. Osteoporos Int. 5:354–70.

30. Wáng YX, Wang XR, Che-Nordin N, Xu FR, Huang QL (2019) On the possibility of over-diagnosis of osteoporotic vertebral fracture at mid-thoracic level. J Thorac Dis. 11:5708-5711.

31. Buckens CF, de Jong PA, Mol C, Bakker E, Stallman HP, Mali WP, van der Graaf Y, Verkooijen HM (2013) Intra and interobserver reliability and agreement of semiquantitative vertebral fracture assessment on chest computed tomography. PLoS One.;8:e71204.

32. Wang XR, Xu FR, Huang QL, Wáng YXJ (2020) Radiological features of traumatic vertebral endplate fracture: an analysis of 194 cases with 263 vertebral fractures. Chin Med J (Engl). 2020;133:2696-2702.

33. Wáng YX, Che-Nordin N, Leung JCS, Man Yu BW, Griffith JF, Kwok TCY (2020) Elderly men have much lower vertebral fracture risk than elderly women even at advanced age: the MrOS and MsOS (Hong Kong) year 14 follow-up radiology results. Arch Osteoporos. 15:176.

34. Wang YX, Káplár Z, Deng M, Leung JCS (2016) Lumbar degenerative spondylolisthesis epidemiology: A systematic review with a focus on gender-specific and age-specific prevalence. J Orthop Translat. 11:39-52.

35. Sheu Y, Cauley JA, Wheeler VW, Patrick AL, Bunker CH, Ensrud KE, Orwoll ES, Zmuda JM, Osteoporotic Fracture in Men (MrOS) Research Group (2011) Age-related decline in bone density among ethnically diverse older men. Osteoporos Int 22:599–605