Reasons for referral to bone densitometry in men and women aged 20-49 years:

Population-based data

Alice MJ Torpy¹, Sharon L Brennan^{1,2,3}, Mark A Kotowicz^{1,2,4}, Julie A Pasco^{1,2}

¹*School of Medicine, Deakin University, PO Box 281, Geelong, VIC 3220, Australia*

²*NorthWest Academic Centre, Department of Medicine, The University of Melbourne, Sunshine Hospital, 176 Furlong Road, St Albans, VIC 3021, Australia*

³*Australian Institute of Musculo-Skeletal Science, The University of Melbourne, 176 Furlong Road, St Albans, VIC 3021, Australia*

⁴*Department of Endocrinology and Diabetes, Barwon Health, Ryrie Street, Geelong, VIC 3220, Australia*

Corresponding author:

Dr Sharon L Brennan,

Barwon Epidemiology and Biostatistics Unit, School of Medicine, Deakin University

Kitchener House, Level 1

PO Box 281, Geelong, VIC 3220, Australia

Ph: +61 3 5226 7915

Fax: +61 3 5246 5165

sbrennan@unimelb.edu.au

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Abstract

Introduction: Osteoporosis poses a significant public health problem for ageing Australians. However, approximately 25% of Australian adults aged 20-49 years have osteopenia, a precursor condition to osteoporosis. Despite this, little is known about bone density testing in this age group.

Methods: Reasons for referral to dual energy x-ray absorptiometry (DXA) were examined in 2,264 patients aged 20-49 years, referred 2001-10 to the Geelong Bone Densitometry Service, Geelong Hospital, Victoria. Referral reasons were determined from clinical-indication codes derived from patient-records. Age, sex, and bone mineral density (BMD) T-scores were ascertained for each patient.

Results: The most common reason for referral for women reflected glucocorticoid use, and for men reflected fracture. Compared to women, men were more likely to have been referred because of minimal trauma fracture or low BMD (41.7% versus 27.1%, $p < 0.001$). No further differences were identified between the sexes, with similar numbers of referral observed for secondary osteoporosis, and monitoring of drug therapy. At the spine, and for all indications, men had a significantly greater BMD deficit compared to women (all $p \leq 0.002$). After age-adjustment, men who were tested due to fracture or glucocorticoid reasons had significantly greater BMD at the total hip ($p \leq 0.03$). No further associations were seen after age-adjustment between referral reason and BMD.

Conclusions: Our study presents the first data examining reasons for referral to DXA among Australians aged 20-49 years. Understanding health service utilisation regarding bone health in young adults is fundamental to understanding future risk, informing effective public health messages, and raising awareness of osteoporosis.

Introduction

Osteoporosis has a major influence on the health status and quality of life of Australians, with 3.4% of the total population having a clinical diagnosis of the disease in their lifetime, nationwide [1], [2]. However, the prevalence of osteoporosis is likely to be considerably higher, as it is a condition which often exists undetected until the occurrence of a fragility fracture [3]. Furthermore, management of this chronic disease has a significant impact on the Australian health expenditure budget, with the direct costs associated to osteoporosis in 2004-5 estimated at over \$300 million; double that of five years previous [4].

Osteoporosis is generally considered a condition of aging, with 82% of sufferers being aged ≥ 55 years [1]; however, data suggest that over one quarter of the Australian population aged 20-49 years suffer from osteopenia[2]; the precursor of osteoporosis [5]. Furthermore, little is known about reasons for referral to dual energy x-ray absorptiometry (DXA) for individuals less than 50 years of age. Published criteria for DXA referral primarily focus upon those aged ≥ 65 years [6], yet approximately 7% of major osteoporotic fractures occur in those aged between 35-49 years [7], contributing to the high lifetime fracture risk in women and men after age 50 years [8]. It is plausible that understanding the reasons for DXA referral prior to the age of 50 years may be useful in elucidating the risk of developing osteoporosis in later years.

To date, little is known about the reasons for referral to DXA testing in younger Australians; information which is integral to understanding future risk and informing effective public health messages. To a certain degree, this information can be determined through indentifying the reasons for referral to DXA to assess bone mineral density prior to the age of 50 years. Therefore, we aimed to examine the reasons for referral to DXA in all referred young adults (20-49 years) presenting to the Bone Densitometry Service, Geelong Hospital.

Methods

Subjects

Data were derived from the electronic records of the Geelong Bone Densitometry Service, Geelong Hospital, Victoria, for all patients who underwent a DXA test during the period 2001-10. The Geelong Bone Densitometry Service is the major service provider in the Barwon Statistical Division (BSD); a region with a population of n=106,607 (50.2% female) in the eligible age group of 20-49 yrs as at the 2005 Australian Census [9]. It is estimated that approximately 95% of the DXA examinations in the region are undertaken by this service. Of the total 21,128 patient records, we excluded those with missing data regarding reason for referral (n = 196), those aged ≥ 50 years (n = 17,744), and those aged < 20 years (n = 114), leaving 3,074 **potentially** eligible patient records. Barwon Health Human Research Ethics Committee approved this study (11/126).

Clinical indications for referral to DXA

Reasons for referral to DXA among patients were derived from Medicare item numbers recorded in the patient database. Medicare item numbers were: 12306 (minimal trauma fracture or monitoring of low BMD as detected by a previous scan); 12312 (prolonged glucocorticoid therapy, excess glucocorticoid secretion or hypogonadism in both sexes); 12315 (secondary osteoporotic conditions such as chronic liver or kidney disease, primary hyperparathyroidism, malabsorption disorders, rheumatoid arthritis or excess thyroxine excess); and 12321 (changes in class of drug therapy). Of the eligible 3,074 patient records, a further 798 patients were excluded because DXA was performed as part of an osteoporosis research project [10], and 12 were excluded because the referral reason was deemed ambiguous. All patients included in these analyses were attending DXA for an initial BMD measurement; no subsequent measures were included. The remaining 2,264 patients were categorized into 10 year age strata of 20-29 years (n=267), 30-39 years (n=526), and 40-49 years (n=1,471). The **site (total hip or spine), and lowest** BMD T-scores, were ascertained for each patient.

Statistical Analysis

Differences in subject characteristics for men and women were examined using the chi-square test or Kruskal-Wallis, where appropriate. Crude numbers of those referred to DXA during the period 2001-10 were stratified by age, sex and reasons for referral. Sex-specific BMD at the spine and total hip were examined using multivariable regression analyses, adjusting for age (as a continuous variable). Statistical analyses were performed using Minitab (Version 15; Minitab, State College, PA), and significance set at $p < 0.05$.

Results

Characteristics of the total study population are presented in Table 1 (81.6% female). The most common reason for referral for women reflected glucocorticoid use, and for men was related to fracture. Men were younger than women at the time of referral ($p < 0.001$).

Reasons for referral, stratified by sex and 10 year age groups are presented in Table 2. There was an age-related increase in the numbers of men and women referred to DXA; observed for each of the reasons for referral. For men, referrals were seen in 17% of those aged 20-29 years, 26% of those aged 30-39 years, and 57% of those aged 40-49 years. For women, referrals were observed in 11% of those aged 20-29 years, 22% of those aged 30-39 years, and 67% of those aged 40-49 years.

BMD T-scores for men and women for each of the different referral reasons are presented in Table 3, stratified by skeletal site. At the spine, sex differences were observed for BMD (T-score) for referral reasons; fracture ($p < 0.001$), glucocorticoid use ($p = 0.002$), and secondary osteoporosis ($p = 0.001$). The lowest BMD T-score was observed in men who were referred to DXA due to changes in drug therapy (men -2.8, and women -1.1). With the exception of fracture, where no sex-differences were observed ($p = 0.24$), similar sex-differences in BMD T-scores for referral reasons were observed at the total hip for glucocorticoid use ($p = 0.04$) and secondary osteoporosis ($p < 0.001$).

Table 4 presents the site- and sex-specific multivariable models examining the association between BMD T-score and the reason for referral, after adjustment for age. After adjusting for age, and compared to those scanned for monitoring of drug therapy (referent group, with the lowest BMD T-score), men who were scanned for evaluation of a fracture or glucocorticoid use had a significantly greater BMD T-score at the total hip (both $p \leq 0.03$), with a trend observed for secondary osteoporosis ($p=0.05$). No further associations were observed between reasons for referral and BMD at the spine for either sex, or for BMD at the total hip for females (Table 4).

Discussion

Our study presents the first data to examine reasons for referral to DXA in young adults aged 20-49 years. The most common reason for referral for men was for evaluation of a low trauma fracture or having low BMD, and for women, the most common reason reflected glucocorticoid use.

We observed the median age of women at the time of DXA referral to be older than that of men in this study population; an observation which has previously been reported in a British study of DXA referral in under-65 year olds [6]. Ageing is one of the major risk factors for the onset and progression of osteoporosis [11], and sex differences associated with the ageing processes offer a potential explanation for these disparities in DXA referral. For instance, oestrogen deficiency in women, occurring as a result of menopause, is documented as having dramatic effects on bone health; women may potentially lose up to 20% of their bone mass during the first 5 to 7 years following menopause [12]. Pasco et al have previously shown that oral contraceptive use is associated with greater BMD at the lumbar spine in this population [13]. Data have also shown that premenopausal bone loss begins in females soon after the attainment of peak bone mass in adolescence [14]. Hormone therapy use is associated with greater BMD at axial and appendicular sites [15], and a causative link has been reported between reduced oestrogen levels and decreased bone density [16]. Although ageing is a major risk factor for the onset of osteoporosis and fragility fracture [17] women are known to be more at risk of developing osteoporosis once they have reached menopause and oestrogen production and secretion begins to diminish. Given those data, a marked increase would be expected in the number of women being referred for DXA scans in the peri-menopausal years (in the 40-49 year age group), whereas no such increase would be expected for their male counterparts. Whilst we were unable to determine menopausal

status from the available data, we have previously reported that the mean age of menopause in this region is 48 years [18].

Glucocorticoid use is associated with various adverse effects, including development of secondary osteoporosis. In patients who have used glucocorticoids for six months or longer, the glucocorticoid-induced osteoporosis frequency is estimated by as high as 50% [19]. Indeed, our data show that the median T-score for men and women fell into the normal or osteopenic range, with almost equal proportions of males to females undergoing a DXA for this reason.

Other data have shown greater fracture incidence in younger men compared to women. For example, in a prospective Scottish study of ~15,000 young adults, males were observed to have almost three times the fracture rates of women [20]. With all ages combined, our data showed that men were 17.5% more likely to undergo a DXA after having sustained a low trauma fracture or to be tested for low BMD compared to women. When examining referral reasons stratified by age groups, this was also observed in the 20-29 and 30-39 year age groups. Sanders et al have previously reported that fracture rates are higher in young adult men compared to young adult women in this population [7]; an observation also reported elsewhere [21], supporting the hypothesis that young men may have greater exposure to trauma and sport-related injuries compared to women, and also more likely to engage in risk-taking behavior.

It would be expected that BMD would differ depending on the reason for referral to DXA. For example, the lowest BMD was observed for those who were referred to evaluate the effect of changes in their drug therapy (4 men, and 15 women; ~79% of whom were aged 40-49 years). This group is most likely to already have a diagnosis of low BMD and/or osteoporosis, and therefore being monitored.

Our study has some strengths. Our data provide an improved understanding of preventive health for young adults prior to the traditional osteoporotic age. Comprehensive data were collected from the only major public health care provider servicing the entire Geelong region and surrounding areas. However it did not include data from the smaller, private provider also located in the BSD. Given this, we speculate that our data comprises the majority of DXA referrals; however we acknowledge that we are unable to account for individuals who access

DXA from the smaller service provider. Another limitation of our study relates to the possibility of inaccurate information on the referrals for the Bone Densitometry Service. Based on our method of data acquisition, we were unable to differentiate between minimal trauma fracture and monitoring for low BMD that may have been detected by previous bone densitometry. However, given that we obtained data from the initial scan at the Bone Densitometry Service, which is the major service provider of DXA in the region, it would be reasonable to assume that the vast majority of these scans were for evaluation of low trauma fracture.

In conclusion, we present the first data to examine reasons for referral to DXA in young Australian adults 20-49 years. Furthermore, work is needed to consider whether young men are under-treated and tested for osteoporosis, similar to that observed in the older men [22].

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Table 1: Age and referral reasons for men and women aged 20-49 years referred to DXA (2001-10). Data presented as median (range), or n (%).

Variables	All (n=2,264)	Men (n = 417)	Women (n = 1,847)	<i>p</i> value
Age, years	43.4 (20.0 - 50.0)	42.1 (20.2 – 50.0)	44.1 (20.0 – 50.0)	<0.001
Fracture or low BMD ^a	675	174 (41.7%)	501 (27.1%)	<0.001
Glucocorticoid use ^b	1,118	173 (41.5%)	945 (51.2%)	0.55
Secondary osteoporosis ^c	452	66 (15.8%)	386 (20.9%)	0.82
Monitoring of drug therapy ^d	19	4 (1.0%)	15 (0.8%)	0.46

The full description of indication codes are: ^aminimal trauma fracture or monitoring low BMD; ^bprolonged glucocorticoid therapy, excess glucocorticoid secretion or hypogonadism; ^csecondary osteoporotic conditions including primary hyperparathyroidism, chronic renal and liver diseases, malabsorption disorders, rheumatoid arthritis and conditions associated with thyroxine excess; and ^dchanges in class of drug therapy.

Table 2: Reasons for referral to DXA, stratified by sex and 10 year age groups, presented as n (%).

	Fracture or low BMD^a	Glucocorticoid use^b	Secondary osteoporosis^c	Monitoring of drug therapy^d	Total
<i>Men</i>					
(age, years)					
20 – 29	27 (15.5)	32 (18.5)	11 (16.7)	-	70 (16.8)
30 – 39	43 (24.7)	47 (27.2)	17 (25.7)	1 (25.0)	108 (25.9)
40 – 49	104 (59.8)	94 (54.3)	38 (57.6)	3 (75.0)	239 (57.3)
<i>Women</i>					
(age, years)					
20 – 29	45 (8.9)	108 (11.4)	44 (11.4)	-	197 (10.7)
30 – 39	108 (21.6)	202 (21.4)	105 (27.2)	3 (20.0)	415 (22.5)
40 – 49	348 (69.5)	635 (67.2)	237 (61.4)	12 (80.0)	1,232 (66.8)

The full description of indication codes are: ^aminimal trauma fracture or monitoring low BMD; ^bprolonged glucocorticoid therapy, excess glucocorticoid secretion or hypogonadism; ^csecondary osteoporotic conditions including primary hyperparathyroidism, chronic renal and liver diseases, malabsorption disorders, rheumatoid arthritis and conditions associated with thyroxine excess; and ^dchanges in class of drug therapy.

Table 3: Lowest median BMD T-score (range) stratified by skeletal site, sex and clinical indications

Variables	Men (n = 417)	Women (n = 1,847)	p value
<i>Spine</i>			
Fracture or low BMD ^a	-1.7 (-4.6, 1.8)	-1.1 (-3.8, 2.1)	<0.001
Glucocorticoid use ^b	-1.4 (-6.3, 2.9)	-1.1 (-4.8, 2.3)	0.002
Secondary osteoporosis ^c	-1.4 (-3.3, 1.6)	-1.0 (-3.2, 1.7)	0.001
Monitoring of drug therapy ^d	-2.8 (-3.2, -2.2)	-1.1 (-3.6, 0.4)	*
<i>Total hip</i>			
Fracture or low BMD ^a	-1.2 (-5.0, 1.4)	-1.0 (-4.3, 2.0)	0.24
Glucocorticoid use ^b	-1.1 (-4.3, 0.7)	-0.9 (-4.4, 1.9)	0.04
Secondary osteoporosis ^c	-1.8 (-3.0, 1.5)	-0.6 (-2.9, 2.2)	<0.001
Monitoring of drug therapy ^d	-3.8 (-)	-1.4 (-2.3, -0.2)	*

The full description of indication codes are: ^aminimal trauma fracture or monitoring low BMD; ^bprolonged glucocorticoid therapy, excess glucocorticoid secretion or hypogonadism; ^csecondary osteoporotic conditions including primary hyperparathyroidism, chronic renal and liver diseases, malabsorption disorders, rheumatoid arthritis and conditions associated with thyroxine excess; and ^dchanges in class of drug therapy.

* Due to small numbers, p values for between sex differences could not be determined

Table 4: Multivariable model examining sex-specific, age-adjusted BMD (T-score) at the spine and total hip, and presented as coefficient and ($\pm$ SE)

Variables	Men coefficient ($\pm$ SE)	<i>p</i> value	Women coefficient ($\pm$ SE)	<i>p</i> value
<i>Spine</i>				
Age (years)	-0.01 (0.10)	0.12	-0.002 (0.004)	0.59
Fracture or low BMD ^a	0.91 (0.74)	0.22	0.19 (0.32)	0.56
Glucocorticoid use ^b	1.14 (0.74)	0.12	0.13 (0.32)	0.68
Secondary osteoporosis ^c	1.28 (0.75)	0.09	0.50 (0.33)	0.13
Monitoring of drug therapy ^d	(referent)	-	(referent)	-
<i>Total hip</i>				
Age (years)	-0.12 (0.01)	0.33	0.001 (0.005)	0.83
Fracture or low BMD ^a	2.36 (1.10)	0.03	0.32 (0.45)	0.48
Glucocorticoid use ^b	2.48 (1.10)	0.02	0.49 (0.45)	0.28
Secondary osteoporosis ^c	2.17 (1.11)	0.05	0.75 (0.45)	0.10
Monitoring of drug therapy ^d	(referent)	-	(referent)	-

The full description of indication codes are: ^aminimal trauma fracture or monitoring low BMD; ^bprolonged glucocorticoid therapy, excess glucocorticoid secretion or hypogonadism; and ^csecondary osteoporotic conditions including primary hyperparathyroidism, chronic renal and liver diseases, malabsorption disorders, rheumatoid arthritis and conditions associated with thyroxine excess. Due to small numbers of patients undergoing DXA for changes in drug therapies (n=19), this group is not presented.