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ORIGINAL ARTICLE

Bone mineral density in diabetes and impaired fasting glucose

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Abstract

Summary We report that compared with normoglycaemia, post-menopausal women (non-obese and obese) with diabetes had higher lumbar spine bone mineral density (LSBMD). Femoral neck bone mineral density (FNBMD) was higher in obese post-menopausal women with diabetes. Only non-obese post-menopausal women with impaired fasting glucose (IFG) had a higher LSBMD than normoglycaemia. No other associations with IFG were observed.

Introduction Individuals with diabetes have a higher or normal bone mineral density (BMD) compared with those without diabetes. However, paradoxically, they also have a higher fracture risk. It is not clear whether those with IFG also have altered BMD. This study aimed to determine whether individuals with IFG have elevated or normal BMD.

Methods Women ($n = 858$) and men ($n = 970$) (aged 20–80 years) from the Geelong Osteoporosis Study were included. IFG was defined as fasting plasma glucose (FPG) 5.5–6.9 mmol/L and diabetes as FPG ≥ 7.0 mmol/L, use of antihyperglycaemic medication and/or self-report. Using multivariable linear regression, the relationships between glycaemia and BMD at the femoral neck and lumbar spine were examined, and adjusted for age, body mass index (BMI), and other variables. In women, two interaction terms were identified: menopause × glycaemia and BMI × glycaemia, and thus, the analyses were stratified by menopause and obesity status (BMI cut point ≥ 30 kg/m^2).

Results There were no associations between glycaemic status and BMD for pre-menopausal women. For non-obese post-menopausal women, there was no association between FNBMD and glycaemic status, but women with IFG or diabetes had higher LSBMD than those with normoglycaemia (7.1% and 9.7%, respectively, both $p < 0.01$). Obese post-menopausal women with diabetes had a higher FNBMD (8.8%, $p = 0.008$) and LSBMD (12.2%, $p < 0.001$), but those with IFG were not different from the normoglycaemia group. There were no associations detected between glycaemic status and BMD in men.

Conclusions In this study, we report that compared with normoglycaemia, post-menopausal women (non-obese and obese) with diabetes had higher LSBMD. FNBMD was higher in obese post-menopausal women with diabetes. Only non-obese post-menopausal women with IFG had a higher LSBMD than normoglycaemia. No other associations with IFG were observed.

Keywords Bone mineral density · Diabetes · Impaired fasting glucose

Introduction

Fracture risk is elevated for individuals with diabetes [1–5], but fractures are not often recognised as a complication the condition. Fractures sustained by individuals with diabetes are also associated with increased mortality, as well as longer time of and increased complications during fracture healing [6, 7]. Despite this, fracture risk prediction for individuals with diabetes is challenging. Those with diabetes have a normal or higher bone mineral density (BMD), as measured by dual-energy X-ray absorptiometry (DXA) [5] and in addition, fracture risk prediction using the FRAX tool underestimates fracture risk for individuals with diabetes [8].

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An intermediate stage between normoglycaemia and diabetes, known as impaired fasting glucose (IFG), is increasing in prevalence [9]. We have previously reported that one-third of Australian women aged 20 years and older are affected by IFG [10]. IFG is characterised by an elevated fasting plasma glucose (FPG) and it is defined by the American Diabetes Association (ADA) as a FPG level between 5.5 and 6.9 mmol/L (100–125 mg/dL) in the absence of treatment with antihyperglycaemic medication [11]. IFG has not been extensively studied in terms of BMD or fracture risk.

The aim of this study was to determine whether men and women with IFG have an elevated or normal BMD and to compare with diabetes and normoglycaemia.

Methods

Participants

This study utilised cross-sectional data from participants enrolled in the population-based, longitudinal, Geelong Osteoporosis Study (GOS). Details of the study are described elsewhere [12]. Participants were recruited using Australian electoral rolls of the Barwon Statistical Division. Since voting is compulsory in Australia, the electoral roll captures almost all adults in the region. This population of south-eastern Australia is ideal for epidemiological research as it is large (~ 290,277), stable, and broadly representative of the Australian population [12]. At baseline, the GOS included 1494 women and 1538 men, who ranged in age from 20 to 94 years. Women were recruited and underwent baseline assessment from 1993 to 1997 and men from 2001 to 2006, with 77% and 67% participation, respectively. A further 246 women aged 20–29 years on the 2005 electoral roll were recruited from 2006 to 2007.

Eligibility criteria for inclusion into this study were as follows: known glycaemic status and a DXA measurement at the femoral neck and/or lumbar spine. This study included 863 women from the 10-year follow-up visit (2004–2008), as well as 971 men from the 5-year follow-up visit (2006–2011). A small number of participants were known to have type 1 diabetes through an examination of medical records (one man, five women) and were excluded from the analyses, leaving 858 women and 970 men for this study.

All participants provided written, informed consent. Barwon Health Human Research Ethics Committee approved the study.

Measurements

Femoral neck bone mineral density (FNBMD) and lumbar spine bone mineral density (LSBMD, L2–L4, posterior-anterior projection) were measured using a Lunar DPX-L DXA machine (Lunar; Madison, WI, USA) for women and GE-Prodigy (Prodigy; GE Lunar, Madison, WI, USA) for men. The long-term reproducibility, coefficient of variation, assessed over 180 days using a phantom, was 0.23% [13]. Body weight (± 0.1 kg) was measured using electronic scales and height (± 0.1 cm) using a wall-mounted stadiometer. Body mass index (BMI) was calculated as weight/height^2 and obesity classified as BMI ≥ 30 kg/m^2 [14].

Fasting plasma glucose concentration was measured using an adaptation of the hexokinase-glucose-6-phosphate dehydrogenase method [15]. Participants were classified as having normoglycaemia (FPG ≤ 5.5 mmol/L), IFG (fasting plasma glucose (FPG) 5.5–6.9 mmol/L), or diabetes (FPG ≥ 7.0 mmol/L and/or use of antihyperglycaemic medication and/or self-report). Measurements of FPG were completed at the same time as other clinical measures and questionnaires.

Data were obtained from questionnaires completed by participants including mobility, smoking status, alcohol consumption, medication use, and menopause status. In detail, participants reported their level of mobility ranging from bedfast to very active and were separated into two groups classed as low mobility (bedfast, chair, inactive, limited, and sedentary) or medium/high mobility (active or very active). Current smoking was determined by self-report. Ex-smokers were considered as non-smokers. Alcohol consumption was determined from a food frequency questionnaire developed by the Victorian Cancer Council [16] and dichotomised into < 30 g or ≥ 30 g of alcohol per day. Data regarding current and past use of medications with positive (e.g. bisphosphonates, sex hormone supplementation, selective oestrogen receptor modulators) or negative (e.g. oral glucocorticoids, pioglitazone) effects on bone were also collected. Post-menopausal status was determined by questionnaire answers to menstruation frequency, date of last menstrual period, and history of oophorectomy (surgical or functional), and, if ambiguous, a review of medical records and/or pathology was conducted. Women were considered post-menopausal if they had amenorrhoea for one year or longer.

Statistics

The ANOVA or Kruskal–Wallis test was used to determine differences for continuous variables according to glycaemia status. A chi-square test was used for categorical variables. Multivariable linear regression models were developed to ascertain the relationship between glycaemic status and BMD, which included an adjustment for potential confounders, such as age, menopause status, BMI, mobility, smoking status, alcohol consumption, and use of medications with positive or negative effects on bone. Models were checked for effect modification.

As there was a glycaemia × age interaction in the model for FNBMD in women ($p = 0.010$), data were stratified by menopause status. Following stratification, there was a glycaemia × BMI interaction term for LSBMD in post-menopausal women ($p = 0.037$) and thus data for post-menopausal women were also stratified by BMI (< 30 or ≥ 30 kg/m^2), giving three groups: pre-menopausal, non-obese post-menopausal, and obese post-menopausal. No interaction terms were identified for men.

All analyses were completed using Minitab (Minitab, version 18, State College, PA, USA).

Results

Descriptive characteristics

In women, there were 657 participants with normoglycaemia (76.6%), 143 with IFG (16.7%) and 58 with diabetes (6.8%). In men, these proportions were 615 (63.4%), 275 (28.4%), and 80 (8.2%), respectively.

Descriptive characteristics of the sample, stratified by sex, and glycaemic status are shown in Table 1. For women, those with IFG and diabetes were older, heavier, shorter, and had lower mobility than those with normoglycaemia. For men, those with IFG and diabetes were also older, heavier, and shorter; however, those with diabetes consumed less alcohol than those with normoglycaemia or IFG. Men with diabetes were also more likely to be using a medication with a negative effect on bone (e.g. glucocorticoids, pioglitazone) than those with normoglycaemia or IFG. Pioglitazone was used by one man and two women in this study.

Pre-menopausal women

Pre-menopausal women with IFG had a 5.9% higher unadjusted mean FNBMD than women with normoglycaemia ($p = 0.009$, Table 2). There was no difference in FNBMD for women with diabetes compared with normoglycaemia ($p = 0.326$). After adjustment for age, weight, height, mobility, smoking, alcohol, and medication use, the associations for IFG ($p = 0.103$) and diabetes were attenuated ($p = 0.472$).

There were no differences detected between the glycaemia groups for mean LSBMD in the unadjusted (IFG, $p = 0.176$,

Table 1 Descriptive characteristics of women and men in the study, stratified by glycaemia status. Data presented as mean ± SD, median (IQR), or *n* (%)

Women	Total ($n = 858$)	Normoglycaemia ($n = 657$)	Impaired fasting glucose ($n = 143$)	Diabetes ($n = 58$)	*p*
Age (years)	51.7 (37.8–64.6)	47.8 (33.2–61.2)	59.9 (50.3–70.3)	67.2 (56.7–74.0)	*< 0.001*
Weight (kg)	69.8 (61.9–80.8)	67.8 (61.1–78.2)	76.6 (67.3–89.7)	76.6 (65.8–91.5)	*< 0.001*
Height (cm)	162.5 ± 6.6	163.0 ± 6.5	161.1 ± 6.5	159.6 ± 6.7	*< 0.001*
BMI (kg/m^2)	26.3 (23.5–31.0)	25.6 (22.9–29.3)	30.0 (26.2–33.4)	31.9 (25.6–36.2)	*< 0.001*
Mobility (low)	160 (18.7)	99 (15.1)	36 (25.2)	25 (43.1)	*< 0.001*
Smoking status (yes)	108 (12.6)	83 (12.6)	21 (14.7)	4 (6.9)	0.320
Alcohol consumption (≥ 30 g/day)	55 (6.4)	45 (6.9)	9 (6.3)	1 (1.7)	0.311
Medication with positive effect on bone (yes)	91 (10.6)	68 (10.4)	14 (9.8)	9 (15.5)	0.445
Medication with negative effect on bone (yes)	56 (6.5)	40 (6.1)	10 (7.0)	6 (10.3)	0.440
Past medication with positive effect on bone (yes)†*	2 (0.2)	1 (0.2)	1 (0.7)	0 (0.0)	–
Past medication with negative effect on bone (yes)†*	5 (0.6)	5 (0.8)	0 (0.0)	0 (0.0)	–
Men	Total ($n = 970$)	Normoglycaemia ($n = 615$)	Impaired fasting glucose ($n = 275$)	Diabetes ($n = 80$)	*p*
Age (years)	56.9 (42.6–70.0)	52.4 (38.4–66.7)	62.0 (50.5–72.5)	67.7 (60.1–73.8)	*< 0.001*
Weight (kg)	82.7 (74.5–92.0)	81.3 (73.0–89.1)	85.4 (77.4–95.5)	86.7 (78.8–94.1)	*< 0.001*
Height (cm)	175.2 ± 7.1	175.6 ± 7.2	174.8 ± 7.1	173.0 ± 6.4	*0.005*
BMI (kg/m^2)	26.9 (24.5–29.6)	26.3 (23.9–28.6)	28.1 (25.5–30.5)	28.7 (26.7–31.0)	*< 0.001*
Mobility (low)	291 (30.0)	180 (29.3)	85 (30.9)	26 (32.5)	0.778
Smoking status (yes)†	141 (14.6)	98 (16.0)	33 (12.0)	10 (12.5)	0.260
Alcohol consumption (≥ 30 g/day)†	232 (24.5)	138 (22.9)	82 (30.9)	12 (15.4)	*0.006*
Medication with positive effect on bone (yes)	9 (0.9)	4 (0.7)	3 (1.1)	2 (2.5)	–
Medication with negative effect on bone (yes)	74 (7.6)	46 (7.5)	16 (5.8)	12 (15.0)	*0.024*
Past medication with positive effect on bone (yes)†*	4 (0.4)	4 (0.7)	0 (0)	0 (0)	–
Past medication with negative effect on bone (yes)†*	12 (1.2)	8 (1.3)	1 (0.4)	3 (3.8)	–

*Too few for statistical analysis. † Missing data. For men: smoking; $n = 1$, alcohol consumption; $n = 23$, past medications; $n = 4$. For women: past medications; $n = 1$

Italics indicate where statistically significant differences were observed between the three glycaemia groups

Table 2 Mean values for femoral neck bone mineral density in women and men with impaired fasting glucose or diabetes, stratified by menopause status (women only)

	Unadjusted model	p	Adjusted model*	p
Pre-menopausal women				
Normoglycaemia	1.020 (1.006–1.034)	–	1.021 (1.009–1.034)	–
Impaired fasting glucose	1.080 (1.037–1.122)	*0.009*	1.056 (1.017–1.096)	0.103
Diabetes	0.972 (0.879–1.066)	0.326	0.990 (0.905–1.075)	0.472
Post-menopausal women (BMI < 30 kg/m^2)				
Normoglycaemia	0.842 (0.825–0.860)	–	0.837 (0.822–0.852)	–
Impaired fasting glucose	0.828 (0.794–0.862)	0.467	0.829 (0.799–0.859)	0.636
Diabetes	0.852 (0.798–0.907)	0.730	0.887 (0.839–0.935)	0.055
Post-menopausal women (BMI ≥ 30 kg/m^2)				
Normoglycaemia	0.918 (0.882–0.953)	–	0.920 (0.889–0.950)	–
Impaired fasting glucose	0.937 (0.893–0.981)	0.505	0.937 (0.899–0.975)	0.484
Diabetes	1.010 (0.952–1.068)	*0.008*	1.001 (0.951–1.051)	*0.008*
Men				
Normoglycaemia	1.018 (1.006–1.030)	–	1.009 (0.999–1.020)	–
Impaired fasting glucose	0.990 (0.972–1.008)	*0.012*	0.997 (0.982–1.013)	0.220
Diabetes	0.978 (0.944–1.012)	*0.033*	1.011 (0.982–1.041)	0.901

Analysis for post-menopausal women was further stratified by BMI (< 30 kg/m^2 and ≥ 30 kg/m^2) due to an interaction term with glycaemia status and BMI. Normoglycaemia was set as the referent group. Data presented as mean (95%CI)

*Adjusted for age, weight, height, mobility, smoking, alcohol, and medication use. Models in men also adjusted for past medication use

Italics indicate where statistically significant differences were observed between the three glycaemia groups

diabetes, $p = 0.673$, Table 3) or adjusted models (IFG, $p = 0.998$, diabetes, $p = 0.569$).

Post-menopausal women (BMI < 30 kg/m^2)

There was no association detected between mean FNBMD and IFG for non-obese post-menopausal women in either the unadjusted ($p = 0.467$, Table 2) or adjusted models ($p = 0.636$). For women with diabetes, there was no association detected in unadjusted models ($p = 0.730$). However in the adjusted model, mean FNBMD was higher in women with diabetes compared with normoglycaemia, but this did not quite reach statistical significance ($p = 0.055$).

However, for LSBMD, women with IFG had a 6.4% higher unadjusted value ($p = 0.008$, Table 3), whereas non-obese post-menopausal women with diabetes were not different to women with normoglycaemia ($p = 0.079$). After adjusting for other confounders, both the IFG and diabetes groups had higher LSBMD than the normoglycaemia group (IFG, 7.1%, $p = 0.003$, diabetes, 9.7%, $p = 0.006$).

Post-menopausal women (BMI ≥ 30 kg/m^2)

Obese post-menopausal women with diabetes had a 10.0% higher unadjusted mean FNBMD than those with normoglycaemia ($p = 0.008$, Table 2); however, there was no difference between IFG and normoglycaemia ($p = 0.505$). After adjusting for other confounders, the associations remained unchanged; the IFG group was not different to normoglycaemia ($p = 0.484$) and women with diabetes had an 8.8% higher mean FNBMD ($p = 0.008$).

For LSBMD, a similar pattern was observed. Women with diabetes had a 10.7% higher unadjusted mean LSBMD than the normoglycaemia group ($p = 0.004$, Table 3), and women with IFG were not different ($p = 0.909$). Following adjustment for other confounders, the associations were sustained (diabetes, 12.2% higher, $p < 0.001$, IFG, $p = 0.710$).

Men

In the unadjusted models for FNBMD, both men with IFG and diabetes had lower mean values than the normoglycaemia group (IFG, −2.8%, $p = 0.012$, diabetes, −3.9%, $p = 0.033$, Table 2). However, following adjustment for other factors, the associations were attenuated (IFG, $p = 0.220$, diabetes, $p = 0.901$).

There were no associations detected between glycaemia status and mean LSBMD in men, in either the unadjusted (IFG, $p = 0.075$, diabetes, $p = 0.228$, Table 3) or adjusted (IFG, $p = 0.587$, diabetes, $p = 0.846$) models.

Table 3 Mean values for lumbar spine bone mineral density in women and men with impaired fasting glucose or diabetes, stratified by menopause status (women only)

	Unadjusted model	p	Adjusted model*	p
Pre-menopausal women				
Normoglycaemia	1.281 (1.266–1.297)	–	1.285 (1.270–1.300)	–
Impaired fasting glucose	1.317 (1.268–1.365)	0.176	1.285 (1.237–1.333)	0.998
Diabetes	1.258 (1.151–1.366)	0.673	1.255 (1.152–1.357)	0.569
Post-menopausal women (BMI < 30 kg/m^2)				
Normoglycaemia	1.102 (1.078–1.126)	–	1.098 (1.075–1.121)	–
Impaired fasting glucose	1.173 (1.126–1.221)	*0.008*	1.176 (1.130–1.221)	*0.003*
Diabetes	1.173 (1.097–1.249)	0.079	1.205 (1.132–1.278)	*0.006*
Post-menopausal women (BMI ≥ 30 kg/m^2)				
Normoglycaemia	1.191 (1.148–1.235)	–	1.185 (1.145–1.225)	–
Impaired fasting glucose	1.195 (1.141–1.249)	0.909	1.197 (1.147–1.247)	0.710
Diabetes	1.318 (1.245–1.391)	*0.004*	1.329 (1.262–1.396)	*< 0.001*
Men				
Normoglycaemia	1.274 (1.259–1.289)	–	1.285 (1.270–1.299)	–
Impaired fasting glucose	1.299 (1.276–1.322)	0.075	1.277 (1.254–1.299)	0.587
Diabetes	1.302 (1.260–1.344)	0.228	1.289 (1.247–1.331)	0.846

Analysis for post-menopausal women was further stratified by BMI (< 30 kg/m^2 and ≥ 30 kg/m^2) due to an interaction term with glycaemia status and BMI. Normoglycaemia was set as the referent group. Data presented as mean (95%CI)

*Adjusted for age, weight, height, mobility, smoking, alcohol, and medication use. Models in men also adjusted for past medication use

Italics indicate where statistically significant differences were observed between the three glycaemia groups

Discussion

Adjusted LSBMD values were higher in post-menopausal women (both non-obese and obese) with diabetes. Adjusted FNBMD values were higher in obese post-menopausal women with diabetes. For those with IFG, adjusted FNBMD and LSBMD were not different from normoglycaemia, except for post-menopausal non-obese women, where adjusted LSBMD was higher than normoglycaemia.

It is not clear why we observed a higher LSBMD in non-obese post-menopausal women with IFG, but not in obese post-menopausal women. A pattern of increasing BMD was observed (Table 3), though we did not detect a difference between IFG and normoglycaemia. This could be due to insufficient numbers or could be related to obesity status. Obese post-menopausal women in the normoglycaemia group had a higher LSBMD than the corresponding non-obese group, which may result in a smaller difference between normoglycaemia and the other groups, and consequently, we were unable to detect a difference in LSBMD.

In this study, we observed differences in BMD for post-menopausal women with diabetes, but not for pre-menopausal women. Many previous studies have focussed on post-menopausal women, and those that have included pre-menopausal women are largely focussed on those with type 1 diabetes. However, there are several studies describing differences in BMD for pre-menopausal women with type 2 diabetes, such as Christensen et al. [17], which reported no differences between BMD at the spine (L2–L4), total hip, distal forearm, or total body, after adjustment for other potential confounding factors, similar to what we report in our study. Zakeri et al. [18] also reported the same results in a sample of pre-menopausal women from Iran; there were no differences in femoral neck or L2–L4 BMD between those with type 2 diabetes and controls. Another study of pre-menopausal women from Kuwait showed slightly different results. Gupta et al. [19] reported that, following adjustment for age and BMI, total hip BMD was not different from controls; however, (L1–L4) spine BMD was higher. This difference could be due to different sampling methods or differences in the population of the countries. Overall, it appears that differences in BMD associated with type 2 diabetes affect pre- and post-menopausal women differently. Further research is needed to determine the reasons for this difference.

To our knowledge, there are few other publications describing differences in FNBMD or LSBMD for individuals with IFG compared with diabetes and normoglycaemia. The pattern observed appears to be similar to that reported for diabetes; BMD in IFG is either higher or not different from normoglycaemia. A study by Mitchell et al. [20], which included 150 participants with IFG defined according to ADA criteria, the same as in our study, showed that total hip and femoral shaft BMD was higher in men and not different in women with IFG compared with normoglycaemia. As part of a study investigating fracture risk in elderly men, Napoli et al. [21] reported a higher unadjusted total hip BMD for men with

IFG (ADA criteria) compared with normoglycaemia. Another study by Jiajue et al. [22], which included post-menopausal women from China that showed similar finding to our study, showed that there were no differences in FNBMD or LSBMD between IFG (WHO criteria; FPG 6.1–6.9 mmol/L) and normoglycaemia, after adjusting for age, years since menopause, and BMI. Additionally, there are a few studies reporting on differences in BMD between individuals with impaired glucose tolerance (IGT) and normoglycaemia, such as Moseley et al. [23], which reported no differences in FNBMD, LSBMD, or total hip BMD between those with IGT and normoglycaemia, even after adjusting for potential confounders. De Liefde et al. [24] also reported a similar finding; there were no differences in FNBMD and LSBMD between men and women with IGT compared with normoglycaemia. All these studies indicate that BMD is not different from those with IFG or IGT, compared with normoglycaemia; however, other studies needed to determine whether these individuals are at a higher risk of fracture, similar to those with diabetes.

There are several studies reporting on the risk of fracture for individuals with IFG. Our research group has previously reported that individuals with IFG (using ADA criteria) had a similar rate of fracture to normoglycaemia [25]. Napoli et al. [21] used the same criteria as in our study to define IFG in elderly men and report the same finding; those with IFG do not have an elevated fracture risk. Using different criteria for defining IFG (WHO), both Gagnon et al. [26] and Strotmeyer et al. [27] have also reported similar findings; IFG is not associated with increased fracture risk. Thus, despite showing a similar pattern to diabetes in terms of BMD, those with IFG do not appear to be at increased risk for fracture.

In this study, we also observed that men and women with diabetes had BMD that was either higher, or not different to, those without diabetes. This is despite many studies reporting an increased fracture risk for individuals with diabetes. One reason that has been suggested for this observation is that individuals with diabetes have a greater BMI than those without diabetes, as BMD is reported to increase with increasing BMI [28]. Despite having a higher BMD, several studies have reported a higher fracture risk at specific skeletal sites in those with higher BMI [29–33]. The suggested reason for this paradox is that although BMD increases with increasing weight, it is not in proportion to the amount required for excessively increased weight [34, 35]. However, in this study, the statistical models were adjusted for weight and we still observed higher or normal BMD in men and women with diabetes compared with normoglycaemia. Consequently, it is likely that multiple factors influence BMD in the setting of diabetes.

Another potential explanation could be related to impaired bone microarchitecture. We have previously reported that although trabecular bone score (TBS) is not different in men and women with IFG compared with normoglycaemia, values for diabetes were lower [36]. Other studies have also reported lower TBS values for individuals with type 2 diabetes [37–41]. Additionally, other studies have reported impaired microarchitecture in individuals with diabetes using HR-pQCT. For example, de Waard et al. [42] reported that individuals with poorly controlled type 2 diabetes (HbA1c>7%) have poorer cortical bone values; lower cortical volumetric BMD, reduced cortical thickness, and higher cortical porosity of the radius. Interestingly, trabecular bone values at the radius (increased trabecular number) and tibia (higher trabecular number and lower trabecular thickness) were better for those with type 2 diabetes compared with controls. Another study by Samelson et al. [43] have also reported similar results, that cortical bone is negatively affected; specifically that individuals with type 2 diabetes have lower cortical volumetric BMD, higher cortical porosity, and smaller cross-sectional area at the tibia, although the radius was not affected. Trabecular variables showed a trend to be greater in diabetes compared with controls. Another study by Farr et al. [44] also supports these findings; cortical bone is negatively affected, while trabecular bone appears to be positively affected.

Additionally, lowered bone turnover can lead to accumulation of microdamage, which can increase fracture susceptibility [45]. We have previously reported changes in bone turnover markers for those with IFG compared with normoglycaemia [46], similar to the reduction in bone turnover markers observed for individuals with diabetes [5, 44, 45, 47]. Together, the results from these studies may indicate that although individuals with IFG do not have altered BMD, TBS, or elevated fracture risk, some early changes of bone fracture susceptibility may already occur with slightly elevated glycaemia, which may be detected using bone turnover markers. Advanced glycation end-products (AGEs) have also been implicated in the pathophysiology of diabetes-related bone fragility [4]. These compounds are produced by non-enzymatic glycation of proteins including type 1 collagen, which is found in bone [1]. Accumulation of these compounds can interfere with the functioning of osteoclasts and osteoblasts, thus impairing bone strength. AGEs can be measured easily using skin autofluorescence and may be useful in determining which individuals are at a higher risk of fracture [48].

This study has several strengths. The participants were randomly selected and are representative of the Australian population. The study also includes both men and women and it was possible to adjust for a variety of potential confounders. Some limitations exist, however; as the presence of impaired glucose tolerance (IGT) was not identified in participants, a proportion of those with prediabetes may not have been identified. Thus, some data may not have been analysed in appropriate groups. We also did not have information about insulin or HbA1c; however, we did exclude participants with known type 1 diabetes. We also utilised multiple sources of data to categorise participants into groups based on glycaemia status (self-report, fasting glucose, and medication use). Another limitation includes the cross-sectional nature of the study.

Conclusions

In this study, we did not detect a difference in FNBMD between IFG and normoglycaemia in either men or women. However, non-obese post-menopausal women with IFG had a higher adjusted LSBMD compared with normoglycaemia. There were no other differences detected between IFG and normoglycaemia for adjusted LSBMD. Diabetes showed higher adjusted FNBMD in obese post-menopausal women but was not different from normoglycaemia for all other participant groups. LSBMD was higher for diabetes than normoglycaemia for both non-obese and obese post-menopausal women.

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Compliance with ethical standards

All participants provided written, informed consent. Barwon Health Human Research Ethics Committee approved the study.

Conflicts of interest None.

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