Bone Mineral Density and Trabecular Bone Score Values in Novel Subgroups of Adult-Onset Diabetes

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Introduction

Diabetes mellitus is a chronic metabolic disease with many adverse health outcomes (1).

Outcomes are not universal and require differing needs.

Bone mineral density (BMD) is lower in type 1 diabetes (2), but similar or higher in type 2 diabetes compared to healthy controls (3).

Both have lower trabecular bone score (TBS) (4).

These differences lead to difficulties understanding disease progression and treatment pathways.

Recently new subgroups for diabetes have been devised to improve precision medicine (5).

These are: mild age-related diabetes (MARD), mild obesity-related diabetes (MOD), severe insulin-resistant diabetes (SIRD), severe insulin-deficient diabetes (SIDD), and severe autoimmune diabetes (SAID).

It is not known whether bone health differs across the groups.

This study aims to investigate differences in BMD and TBS between the subgroups and normoglycaemia.

Methods

Data was from the Geelong Osteoporosis study (GOS).

Sampled from the electoral roll using and age stratified sampling method.

1170 men were assessed for glycaemia status at baseline (2001-06) and the 5-year follow-up (2007-10).

Diabetes was classified as a fasting plasma glucose (FPG) test ≥7.0mmol/L, self-report of diabetes, or the use of antihyperglycaemic medications.

Normoglycaemia was classified as FPG<5.6mmol/L.

Bone measures

Bone mineral density (BMD) was measured using dual-energy x-ray absorptiometry (DXA).

TBS iNsight software (version 2.2; Medimaps Group, Geneva, Switzerland) was used to retrospectively analyse DXA scans for TBS.

Statistical analysis

ANOVA and Kruskal-Wallis tests were used to examine differences between groups.

Linear regression models were set-up to examine the size of these differences, adjusting for age, and weight as confounders.

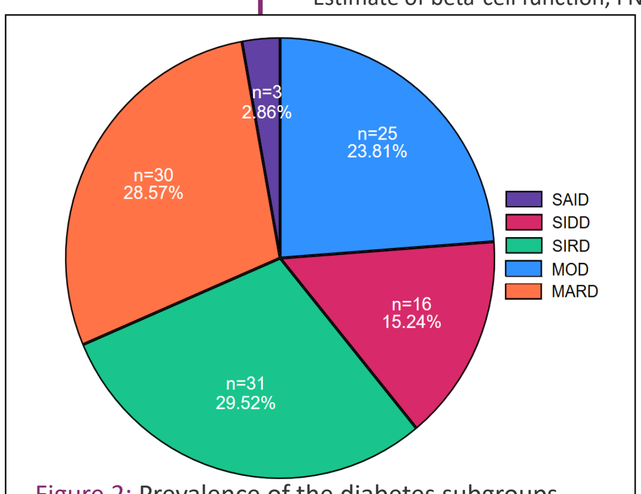

Figure 2: Prevalence of the diabetes subgroups within the Geelong Osteoporosis study.

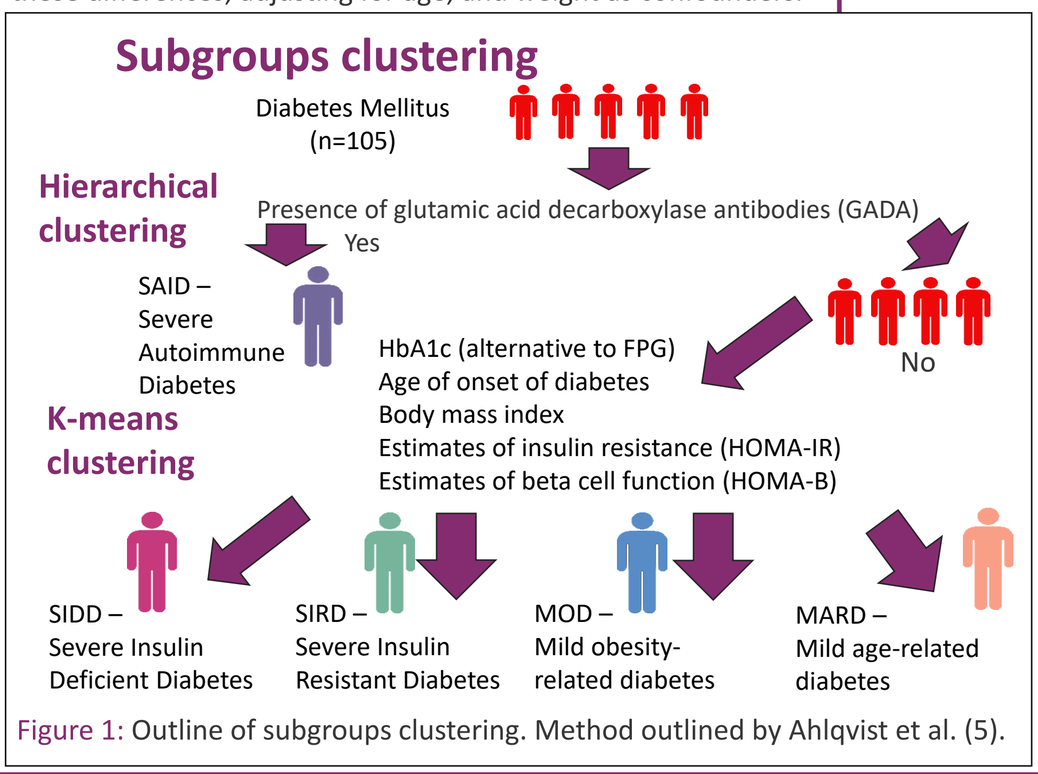

Figure 1: Outline of subgroups clustering. Method outlined by Ahlqvist et al. (5).

Results

Table 1: Characteristics of the subgroups compared to normoglycaemia. Data presented as mean±sd, or median (IQR).

	Normoglycaemia (n=790)	MOD (n=25)	MARD (n=30)	SIRD (n=31)	SIDD (n=16)	SAID (n=3)	p
Age (y)	57.0 ± 19.4	73.3 ± 5.6	82.6 ± 4.7	65.0 ± 7.3	58.6 ± 12.5	39.1 ± 10.6	<0.001
Age of onset (years)	N/A	68.4 ± 3.8	80.2 ± 4.5	58.2 ± 3.1	45.8 ± 6.0	27.0 ± 11.5	<0.001
Weight (kg)	81.2 ± 13.9	88.7 ± 15.3	79.0 ± 12.0	86.9 ± 14.5	86.8 ± 11.6	83.4 ± 8.1	0.011
Height (m)	174.7 ± 7.4	171.5 ± 7.6	170.8 ± 7.8	172.0 ± 6.1	174.3 ± 4.4	179.3 ± 2.6	0.004
BMI (kg/m^2)	26.6 ± 4.0	30.2 ± 5.2	27.1 ± 3.8	29.4 ± 4.7	28.6 ± 3.7	25.9 ± 1.9	<0.001
FPG (mmol/L)	5.0 (4.7-5.2)	7.5 (6.3-8.6)	7.3 (5.9-8.7)	7.6 (6.5-8.6)	8.1 (6.4-9.8)	5.4 (4.2-10.8)	<0.001
HbA1c (ug/ml)	56.7 (46.1-117.2)	51.9 (39.6-73.6)	63.9 (485-113.6)	116.6 (50.4-129.8)	120.9 (62.4-635.4)	40.0 (21.0-47.0)	<0.001
HOMA-IR	0.13 ± 0.06	0.27 ± 0.16	0.29 ± 0.24	0.29 ± 0.15	0.25 ± 0.15	0.05	<0.001
HOMA-B	9.6 ± 1.1	4.9 ± 3.5	5.9 ± 6.5	5.6 ± 7.4	3.9 ± 2.9	2.1	0.001
FN BMD (g/cm^2)	0.998 ± 0.159	0.937 ± 0.145	0.903 ± 0.128	0.990 ± 0.148	0.979 ± 0.120	1.007 ± 0.123	0.048
L2-L4 BMD (g/cm^2)	1.281 ± 0.198	1.360 ± 0.239	1.311 ± 0.209	1.283 ± 0.201	1.269 ± 0.209	1.188 ± 0.069	0.510
TBS	1.286 ± 0.118	1.230 ± 0.096	1.210 ± 0.134	1.233 ± 0.125	1.233 ± 0.149	-	0.008

SAID= Severe auto-immune diabetes, SIDD= Severe insulin-deficient diabetes, SIRD= Severe insulin-resistant diabetes, MOD= Mild obesity-related diabetes, MARD= Mild age-related diabetes, BMI= Body mass index, FPG= Fasting plasma glucose, HbA1c= Glycated haemoglobin, HOMA-IR= Estimate of insulin resistance, HOMA-B= Estimate of beta-cell function, FN BMD= Femoral neck bone mineral density, L1-L4= Lumbar vertebra 1-4, TBS= Trabecular bone score.

Clustering characteristics

Age, weight, and height of the subgroups and normoglycaemia were all significantly different (Table 1).

The SIRD and SIDD groups had the highest HbA1c.

SIRD had the highest estimate of insulin-resistance.

The SIDD group had the lowest estimate of beta-cell function.

Bone characteristics

Femoral neck BMD was different among the groups, lowest in the MARD group (Table 1).

The MARD group had lower femoral neck BMD in an unadjusted model (Table 2), this was no longer significant after adjustment.

TBS was lower in the subgroups (Table 1) and were significantly lower in the unadjusted regression model (Table 2).

Only the SIDD remained significantly lower than normoglycaemia after adjustment.

Table 2: Linear regression models comparing normoglycaemia to the diabetes subgroups adjusted for age and weight.

	Unadjusted Mean	95% Confidence Interval	p value	Adjusted Mean	95% Confidence interval	p value
FN BMD (g/cm^2) – normoglycaemia	0.998	0.986 – 1.011	Referent	0.940	0.869 – 1.011	Referent
MOD	0.937	0.860 – 1.014	0.123	0.929	0.827 – 1.030	0.730
MARD	**0.903**	**0.843 – 0.964**	**0.003**	0.951	0.858 – 1.043	0.684
SIRD	0.990	0.910 – 1.069	0.717	0.950	0.850 – 1.049	0.768
SIDD	0.979	0.876 – 1.082	0.842	0.912	0.800 – 1.025	0.517
L1-L4 BMD (g/cm^2) – normoglycaemia	1.250	1.235 – 1.265	Referent	0.925	0.824 – 1.025	Referent
MOD	1.319	1.235 – 1.402	0.113	0.949	0.809 – 1.089	0.571
MARD	1.275	1.204 – 1.345	0.506	0.929	0.800 – 1.057	0.910
SIRD	1.247	1.154 – 1.340	0.940	0.896	0.755 – 1.036	0.538
SIDD	1.235	1.118 – 1.353	0.806	0.888	0.732 – 1.044	0.537
TBS - normoglycaemia	1.276	1.263 – 1.288	Referent	1.672	1.586 – 1.758	Referent
MOD	**1.119**	**1.041 – 1.198**	**<0.001**	1.605	1.487 – 1.723	0.064
MARD	**1.118**	**1.027 – 1.209**	**0.001**	1.625	1.500 – 1.750	0.263
SIRD	**1.170**	**1.101 – 1.239**	**0.003**	1.616	1.506 – 1.726	0.079
SIDD	**1.146**	**1.062 – 1.230**	**0.003**	**1.557**	**1.440 – 1.675**	**0.003**

*Severe auto-immune diabetes subgroups was removed due to low numbers

MOD= Mild obesity-related diabetes, MARD= Mild age-related diabetes, SIRD= Severe insulin-resistant diabetes, SIDD= Severe insulin-deficient diabetes, FN BMD= Femoral neck bone mineral density, L1-L4= Lumbar vertebra 1-4, TBS= Trabecular bone score.

Discussion

The MOD and MARD groups were older which may explain the difference in BMD compared to normoglycaemia (6).

After adjusting for age and weight these were no longer different.

The subgroups were found to have significantly lower TBS than those with normoglycaemia and remained after adjustment.

Suggesting a potential link insulin deficiencies and poor TBS.

Diabetes mellitus as a group is highly heterogenous, these subgroups present as a way to classify these people into more distinct groups.

This allows for more precise classification and understanding of diabetes.

BMD and TBS both varied within the subgroups, and further research may improve our understanding within this space.

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