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Materials and methods: EOOP patients with suspected hereditary cause were analyzed by a SureSelect XT gene panel comprising bone affecting genes. Assessment of skeletal status included turnover parameters (n=33), BMD by dual-energy X-ray absorptiometry (DXA; n=33) and microstructure *via* high-resolution peripheral quantitative computed tomography (HR-pQCT; n=25) compared to age- and sex-matched reference values. Values are presented as mean ± standard deviation (SD).

Results: We detected 28 *LRP5*- and 5 *LRP6*-variants in 33 EOOP patients (49.5 ± 17.0 years), including 8 novel variants. Biochemical analysis revealed low formation in all patients. Vertebral and peripheral fractures occurred in 11/33 and 16/33 patients, respectively, whereas 12/33 patients had no history of fractures. Z-score ≤-2.0 was detected in 22/33 and values in the spine were significantly lower compared to the hip (-2.3 ± 1.3 vs. -1.8 ± 0.7; $p< 0.05$). HR-pQCT analysis revealed moderately impaired microstructure in both trabecular and cortical parameters. Moreover, a significant correlation between DPD levels and Z-score was detectable ($r=0.412$, $p< 0.05$). No significant difference between patients with *LRP5*- or *LRP6*-variants was detectable.

Conclusion: LRP5-/LRP6-variants represent a relevant proportion of genetic alterations in EOOP patients. These show low bone formation, reduced Z-scores and impaired bone microstructure, leading to an increased risk of fractures. This detailed skeletal characterization improves the interpretation of novel variants, while the effect of other variants remains to be elucidated.

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COP16

Bone peripheral microarchitecture in type 1 diabetes with and without neuropathy; a cross-section study

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Fracture risk is increased in diabetes, especially in type 1 diabetes. The mechanisms involved are not established. Some evidence suggests that abnormalities in microarchitecture might be involved, especially in patients with microvascular disease.

We assessed bone microarchitecture using high resolution peripheral quantitative computed tomography in patients with type 1 diabetes with (T1DN+, n=20) and without (T1DN-, n=20) distal symmetric polyneuropathy and in controls (n=20). Participants were scanned at the standard site and at 14% bone length at the radius and tibia. We used non-parametric tests to compare the groups.

At the 14% length site, favourable trabecular microarchitecture was found in diabetes at both sites (table). At the standard site, tibial cortical porosity was 56% higher (p=0.009) and tibial connectivity was 120% higher (p=0.001) in T1DN+ compared to T1DN-.

Diabetes is associated with low bone turnover; the low bone turnover likely preserved trabecular microarchitecture, resulting in favourable findings at the 14% site.

At distal sites, the major feature was the increase in cortical porosity which was found only at the tibia and in patients with neuropathy. This finding suggested that microvascular complications, especially neuropathy, could affect bone vascularization and innervation and impact on cortical porosity. Overall, impaired microarchitecture is unlikely to be the main mechanism of bone fragility in diabetes.

	Radius			
	T1DN- vs control (%)	p	T1DN+ vs control (%)	p
Trabecular density (mgHA/cm3)	↑50	0.006**	↑14	0.057
Inner trabecular density (mgHA/cm3)	↑113	0.002**	↑29	0.031*
Trabecular number	↑27	0.002**	↑11	0.072
Trabecular BV/TV (no units)	↑50	0.006**	↑14	0.064
Meta/Inn trabecular density (no units)	↓45	0.002**	↓32	0.035*
Trabecular separation	↓23	0.001**	↓9	0.076
Trabecular inhomogeneity	↓24	0.001**	↓17	0.118

	Tibia			
	T1DN- vs control (%)	p	T1DN+ vs control (%)	p
Trabecular density (mgHA/cm3)	↑43	0.003**	↑35	0.046*
Inner trabecular density (mgHA/cm3)	↑53	0.002**	↑64	0.034*
Trabecular number	↑15	0.005**	↑15	0.023*
Trabecular BV/TV (no units)	↑43	0.003**	↑36	0.047*
Meta/Inn trabecular density (no units)	↓19	0.002**	↓19	0.044*
Trabecular separation	↓15	0.005**	↓18	0.021*
Trabecular inhomogeneity	↓25	0.001**	↓22	0.008**

Percentage differences in trabecular features between T1DN- and T1DN+ and control
*p<0.05 **p<0.017

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COP17

Cortical porosity does not predict incident fractures in postmenopausal women

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Fracture risk is frequently assessed measuring areal bone mineral density (aBMD) or using Fracture Risk Assessment Tool (FRAX) including clinical risk factors. However, these tools have limitations and additional bone measurements may enhance the predictive ability of these tools. In cross-sectional studies, higher cortical porosity is found in women with fractures, and cortical porosity and cortical thickness are associated with fracture risk independent of aBMD and FRAX. Whether cortical porosity predicts incident fractures, is still elusive. In this prospective study, we examined whether cortical porosity of the proximal femur predicts incident fractures independent of aBMD in postmenopausal women. We pooled 211 postmenopausal women with fractures aged 54-94 years at baseline (cases) and 232 fracture-free age-matched controls in a nested case-control study. The cases had prevalent fractures (181 forearm, 26 proximal humerus and 4 hip). We assessed femoral neck (FN) aBMD, calculated FRAX 10-year probability of major osteoporotic fracture, and quantified femoral subtrochanteric cortical porosity, thickness, and cross-sectional area (CSA) from CT images using StrAx software. During a mean follow-up of 6.4 years, 114 of all 443 women suffered an incident fracture (33 forearm, 11 proximal humerus, 13 hip, 10 ankle, 15 vertebral, 32 others). Per SD higher total cortical porosity, thinner cortices, and smaller cortical CSA, hazard ratio (HR) (95% confidence interval) for fracture were 1.09 (0.91-1.30), 0.99 (0.82-1.20), and 1.08 (0.90-1.29), respectively, all $p > 0.100$. Cortical porosity of the inner transitional zone predicted incident fractures adjusted for prior fracture, HR 1.22 (1.00-1.48), $p = 0.045$, but not after additionally adjusted for FN aBMD, HR 1.15 (0.95-1.39), $p = 0.160$. Per SD higher FN aBMD and FRAX, HRs