SVGO
Schweizerische Vereinigung gegen die Osteoporose
ASCO
Association Suisse contre l'Ostéoporose

SBMS
The Swiss Bone and Mineral Society

Annual Meeting SVGO/ASCO and SBMS 2023

9. June 2023, Kursaal Allegro

08.40 *Registration*

09.00 Welcome from SVGO and SBMS Presidents in **«Aare» Meeting room**

09.10 ***"State of the Art"- Basic***
Cellular players of human bone remodeling under physiological and pathophysiological conditions
T.L. Andersen (Denmark)

09.50 **Short communications 1 (4 selected abstracts)**

09.50 – 10.00: Late diagnosis of childhood-onset hypophosphatasia in an adult with recurrent fractures: the impact of enzyme replacement therapy. *M. Messikommer et al.*

10.00 – 10.10 : A dietary plus exercise intervention improves bone turnover in patients with metabolic syndrome and type 2 diabetes. *M. Gerbaix et al.*

10.10 – 10.20 : Muscle parameters in fragility fracture risk prediction in older adults: a scoping review. *C. Vendrami et al.*

10.20 – 10.30: Effect of vitamin D3, omega-3s and a simple home exercise program on BMD in European older adults: preliminary findings from the DO-HEALTH randomized controlled trial. *M. Kistler-Fischbacher et al.*

10.40 *Coffee Pause* in **"Aare Foyer"**

11.00 **Short communications 2 (4 selected abstracts)**

11.00 – 11.10: Hip fracture and refracture rate in subjects with an incident hip fracture at the Geneva University Hospital: a retrospective analysis. *I. Padlina et al.*

11.10 – 11.20: Improving fracture prediction in patients with osteoporosis using machine learning techniques: a nationwide, registry-based cohort study. *J. Everts-Graber et al.*

11.20 – 11.30: Assessment of total and bioactive serum sclerostin levels and its association with bone metabolism in type 2 diabetes mellitus. *C. Traechslin et al.*

11.30 – 11.40: Ischemic stroke is associated with reduced sclerostin expression in human atherosclerotic plaques. *F. Burger et al.*

11.50 ***"State of the Art"- Translationnal***
Osteoporosis and CVD: Common mechanisms and impact of OP drugs on arterial calcifications
S. Papapoulos (Greece)

12.35 *Lunch in* **"Aare" Foyer**

(13.00 – 13.30: **SGBond members only**: Voting of the new committee in "Aare" Meeting room)

ASCO/SVGO Symposium 1: MANAGEMENT OF VERTEBRAL FRACTURES

13.30 Neurosurgical guidelines
D. Bellut (Zurich)

13.55 Osteoporosis treatments
S. Ferrari (Geneva)

ASCO/SVGO Symposium 2: MANAGEMENT OF FRACTURE RISK IN CANCER PATIENTS

14.20 MGUS: Does it increase fracture risk and how to prevent it?
R. Schmidmaier (Germany)

14.45 Fracture prevention in hormone-ablative therapy for breast and prostate cancer
Ch. Meier (Basel)

15.10 BPs or denosumab for the prevention of SRE in advanced cancer
E. Biver (Geneva)

15.35 *Coffee Pause* in **"Aare Foyer"**

ASCO/SVGO/SG BOND symposium: THERAPEUTIC MANAGEMENT OF RARE BONE DISEASES (in **"Aare" Meeting room**)

16.00 SGBond and Reference Centers for Rare Bone Diseases : our mission
B. Aubry-Rozier (Lausanne)

16.10 Is there a place for burosumab in fibrous dysplasia?
E. Gonzalez Rodriguez (Lausanne)

16.35 Bone manifestations of the different type of EDS
M. Rohrbach (Zurich)

16.50 **Awards ceremony**

17.00 End of Meeting

17.10 SVGO: General Assembly

18.00 Adjourn

13.30 – 16.30: PARRALEL PROGRAMM SBMS «Gaarten 2» Meeting room

LIST OF ALL SUBMITTED ABSTRACTS

1. **Preventing post-denosumab bone loss with zoledronate: a randomized trial in post-menopausal women without and with pre-exposure to bisphosphonates**. *S. Ferrari, M. Hars, E. Biver, B. Uebelhart, AC. Joly, F. Herrmann, Ch. Meier, K. Lippuner*

2. **Ischemic stroke is associated with reduced sclerostin expression in human atherosclerotic plaques**. *F. Burger, A. Roth, F. Mach, C. Thouverey, S. Ferrari, K. Miteva*

3. **ESCEO and IOF recommandations for the clinical use of trabecular bone score (TBS) in the management of osteoporosis. A systemic review**. *E. Shevroja, J-Y. Reginster, NC. Harvey, for the expert group*

4. **Body composition comparison between Hologic Horizon A and GE Lunar iDXA: The OsteoLaus cohort**. *C. Vendrami, E. Shevroja, G. Gatimeau, E. Gonzalez Rodriguez, D. Hans, O. Lamy*

5. **Late diagnosis of childhood-onset hypophosphatasia in an adult with recurrent fractures: the impact of enzyme replacement therapy**. *M. Messikommer, A. Popp, M. Hochuli*

6. **Muscle parameters in fragility fracture risk prediction in older adults: a scoping review**. *C. Vendrami, E. Shevroja, J. Elmers, E. Gonzalez Rodriguez, D. Hans, O. Lamy*

7. **PDGFRβ signaling in osteoprogenitors contributes to the pathogenesis of fibrous dysplasia**. *C. Thouverey, A. Corsi, M. Riminucci*

8. **A dietary plus exercise intervention improves bone turnover in patients with metabolic syndrome and type 2 diabetes**. *M. Gerbaix, D. Courteix, G. Lac, B. Lesourd, R. Chapier, A. Vinet, G. Walther, P. Obert, F. Dutheil, S. Ferrari*

9. **Evaluation of a deep learning spine segmentation (SpS) algorithm for accurate and reproducible monitoring of lumbar spine DXA scans**. *G. Gatineau, EH. Ahmed, K. Hind, O. Lamy, E. Gonzalez Rodriguez, L. Beaugé, D. Hans*

10. **Plasma sodium increase is associated with an increase in bone formation in outpatients with chronic SIAD – a predefined secondary analysis of the SANDx trial.** *S. Monnerat, J. Refardt, L. Potasso, C. Meier, M. Christ-Crain*

11. **Hip fracture risk and refracture rate in subjects with an incident hip fracture at the Geneva University Hospital: a retrospective analysis**. *I. Padlina, M. Portela, E. Biver, T. Chevalley, S. Ferrari.*

12. **Improving fracture prediction in patients with osteoporosis using machine learning techniques: a nationwide, registry-based cohort study**. *J. Everts-Graber, I. Lehmann, O. Mineeva, H. Häuselmann, L. Guyer, S. Reichenbach, T. Lehmann, O. Demler, and the Osteoporosis registry of the swiss society of rheumatology study group.*

13. **Effect of vitamin D3, omega-3s and a simple home exercise program on BMD in European older adults: preliminary findings from the DO-HEALTH randomized controlled trial**. *M. Kistler-Fischbacher, G. Armbrecht, S. Gängler, W. Lang, J. Kanis, B. Dawson-Hughes, R. Rizzoli, GA. Wanner, HA. Bischoff-Ferrari, for the DO-HEALTH investigators.*

14. **Assessment of total and bioactive serum sclerostin levels and its association with bone metabolism in type 2 diabetes mellitus**. *C. Traechslin, L. Sewing, S. Baumann, L. Grize, J. Vavanikunnel, M. Triantafyllidou, M. Kraenzlin, C. Henzen, C. Meier.*

ABSTRACT BOOK

Preventing post-denosumab bone loss with zoledronate: a randomized trial in post-menopausal women without and with pre-exposure to bisphosphonates

S. Ferrari[1], M. Hars[1], E. Biver[1], B. Uebelhart[1], AC. Joly[1], F. Herrmann[1], Ch. Meier[2], K. Lippuner[3]

[1]*Division of Bone Diseases, Department of Internal Medicine Specialties, Geneva University Hospital & Faculty of Medicine, Geneva, Switzerland*
[2]*Division of Endocrinology, Diabetes and Metabolism, University Hospital Basel*
[3]*Department of osteoporosis, Bern University Hospital, University of Bern, Switzerland*

Objective: To evaluate the effects of Zol administration and the need for multiple injections to prevent bone loss after stopping denosumab in long-term users, and the influence of previous bisphosphonates (BPs) exposure therein.

Methods: Fourty-four post-menopausal women treated with denosumab >2 yrs (median 4.7 yrs, range 3.6-5.7) for primary osteoporosis and reaching BMD T-scores > -2.5 at spine and hip were included. Those without pre-denosumab BPs were randomized to Zol at 6 months (gr.1, n=12) or 9 months (gr.2, n=11) after the last denosumab, or to an observational group receiving Zol if CTx >644 ng/ml, -i.e. 50% above the upper normal pre-menopausal value- (gr.3, n=11). Those exposed to BPs during ≥1yr pre-denosumab (gr.4, n=10) also received Zol if CTx >644 ng/ml. In addition, Zol was re-administered in all a group if subsequent CTX > 644 ng/ml at any time or BMD decreased > 5% at 6 months after Zol. In this interim analysis, median LS BMD changes from baseline to 12 months after the end of the last denosumab dose and to 12 months after the initial Zol infusion are reported.

Results: Mean age (±SD) was 69.5 ±6.6 yrs, baseline spine and hip BMD T-scores -1.41 ±0.77 and -1.33 ±0.61 respectively, without differences between groups. Mean pre-Zol CTx values were 160 ± 163, 718 ± 381, 888 ± 163, and 778 ± 281 ng/ml in gr. 1-4 respectively. Most patients randomized to gr- 1-3 received multiple Zol injections according to the CTx criteria (median = 2 Zol, range 1-5), whereas 8 out of 10 patients in gr. 4 (previous BPs) received Zol, only 3 requiring more than one injection. Median LS BMD changes 12 months post-Zol were similar between groups (-4.71, -4.77, -3.15, and -3.03%, respectively in gr. 1-4). However, LS BMD changes 12 months after the end of the last denosumab dose tended to be greater in gr. 2 (-8.25%) and 3 (-8.13%) than in gr. 1 (-4.71%) and 4 (-4.62%) (ns).

Conclusions: Most patients treated long-term with denosumab require more than one Zol injection to counteract the post-treatment bone turnover rebound, unless previously treated with BPs. In BPs-naïve patients, administering the first Zol 6 months post-denosumab may provide better protection against bone loss than delaying Zol injections.

Acknowledgements: Trial sponsored by AMGEN.

Ischemic Stroke is Associated with Reduced Sclerostin Expression in Human Atherosclerotic Plaques

Fabienne Burger[1], Aline Roth[1], François Mach[1], Cyril Thouverey[2], Serge L Ferrari[2], Kapka Miteva[1]

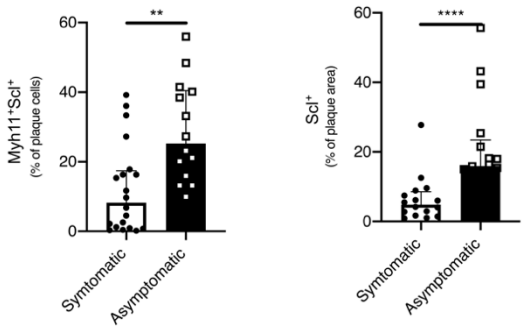
[1]Division of Cardiology, Foundation for Medical Research, Department of Medicine Specialized Medicine, Faculty of Medicine, University of Geneva, Av. de la Roseraie 64, CH-1211 Geneva 4, Switzerland
[2]Division of Bone Diseases, Department of Internal Medicine Specialties, Geneva University Hospital & Faculty of Medicine, Geneva, Switzerland

Objectives: Sclerostin (Scl) expression levels have been linked to vascular calcification (VC) of atherosclerotic plaques. In osteoporotic women, Scl inhibition with romosozumab has been associated with a higher incidence of major adverse cardiovascular events (MACE) compared to alendronate. This increases in MACE call into question the safety of romosozumab use, particularly in patients with cerebrovascular and cardiovascular history or at high cardiovascular risk. However, whether sclerostin expression levels in VC or atherosclerotic plaques are associated with clinical ischemic events remains unknown. Here we explored the association between Scl expression in human atherosclerosis plaques and the extend of VC, vascular smooth muscle cells (VSMCs) phenotypic switch to osteoblast-like cells (OBL), and its correlation to clinical cerebrovascular events.

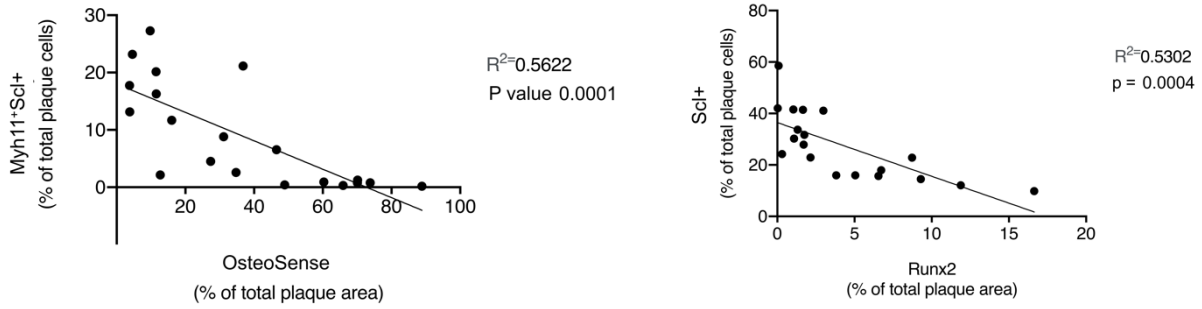
Methods: Carotid plaque specimens of symptomatic (ischemic stroke) and asymptomatic patients undergoing endarterectomy for severe carotid stenosis were co-stained with VSMCs specific marker (Myh11), OBL marker (RUNX2), microcalcification sensitive fluorescent imaging probes (OsteoSense) and Scl and used for quantification analyses.

Results: Carotid plaque specimens from asymptomatic patients exhibited a significantly higher percentage of VSMCs expressing Scl ($Myh11^{+}Scl^{+}$) in parallel with a greater Scl+ area versus symptomatic patients. A negative correlation was observed between the percentage of $Myh11^{+}Scl^{+}$ cells and the extent of microcalcification (OsteoSense) as well as between the percentage of total Scl^{+} cells and induction of VSMCs phenotype switch to osteoblast-like cells (quantified as RUNX positive area).

Conclusion: In atherosclerotic plaques of patients with ischemic stroke, total and VSMCs -specific Scl expression levels were reduced as compared to asymptomatic patients. Furthermore, reduction in Scl levels was positively associated with the extent of microcalcification, and VMSCs phenotypic switch to OBL. The presented findings suggest that sclerostin expression in human atherosclerotic plaques could contribute to plaque stabilization and be protective against ischemic stroke.



Bar graph represents median with interquartile range of the percentage of $Myh11^{+}Scl^{+}$, and Scl^{+} positive area in asymptomatic and symptomatic carotid artery disease patients, respectively, Mann-Whitney test, ** $p < 0.01$, **** $p < 0.0001$.



Negative correlation between the percentage of $Myh11^{+}$ Scl^{+} cells with the area of vascular micro calcification (OsteoSense positive areas) and Scl^{+} cells and VMSCs phenotypic switch to OBL in atherosclerotic plaques of carotid artery disease patients.

ESCEO and IOF Recommandations for the clinical use of trabecular bone score (TBS) in the management of osteoporosis. A systematic review

Shevroja E[1], Reginster J-Y[2], Lamy O[1], Harvey NC[3], for the expert group

[1]University of Lausanne, UNIL, CHUV, Lausanne, Switzerland, [2]World Health Organization Collaborating Centre for Epidemiology of Musculoskeletal Health and Aging, Liège, Belgium, [3]MRC Lifecourse Epidemiology Centre, University of Southampton, Southampton, UK

Background: TBS is a grey-level textural measurement acquired from DXA images; which predicts fractures independently of BMD.

Aim: To review the evidence base published between 2015-2022 and provide expert consensus statements and corresponding operational guidelines that can be used to guide the use of TBS.

Methods: An Expert Working Group was convened by the ESCEO and a systematic review of the evidence was undertaken, with defined search strategies for four key topics on the use of TBS: 1) fracture prediction in postmenopausal and male osteoporosis; 2) initiating and monitoring treatment in postmenopausal osteoporosis; 3) fracture prediction in secondary osteoporosis; 4) treatment monitoring in secondary osteoporosis. Twenty-five statements to guide the clinical use of TBS were derived from the review during a face-to-face meeting of the working group and anonymously graded by consensus using the Grades of Recommendation, Assessment, Development and Evaluation (GRADE) approach.

Results: 96 articles were included, from 20 countries. TBS enhances fracture risk prediction in primary and secondary osteoporosis; when taken with BMD and clinical risk factors, TBS informs treatment initiation and the choice of antiosteoporosis treatment. TBS provides useful adjunctive information in monitoring treatment with long-term denosumab and for as well as with anabolic agents. All expert consensus statements were voted as strongly recommended.

Conclusion: The addition of TBS to FRAX and/or BMD enhances fracture risk prediction in primary and secondary osteoporosis, and is useful in treatment decision-making and monitoring. The expert consensus statements provided from this work can be used to guide the integration of TBS in clinical practice for osteoporosis assessment and management.

Body composition comparison between Hologic Horizon A and GE Lunar iDXA: The OsteoLaus Cohort

C. Vendrami[1], E. Shevroja[1], G. Gatineau[1], E. Gonzalez Rodriguez[1], D. Hans[1], O. Lamy[1,2]

[1] *Interdisciplinary Center of Bone Diseases, Rheumatology Unit, Bone and Joint Department, Lausanne University Hospital and University of Lausanne, Switzerland*

[2] *Internal Medicine Unit, Internal Medicine Department, Lausanne University Hospital and University of Lausanne, Switzerland*

Background: Dual-energy X-Ray Absorptiometry (DXA) is the reference techniques for body composition assessment thanks to its reliability, low irradiation, and its ability to estimate fat, lean and bone masses. However, DXA measurements vary among devices.

Objectives: To compare body composition measures between two densitometers of latest generation: Hologic Horizon A System™ and GE Lunar iDXA™.

Methods: Post-menopausal women from the 5th visit of the OsteoLaus cohort underwent total body DXA assessment with both devices within one hour interval. We compared total fat mass (TFM) and percent fat (TPF), total lean mass (TLM), appendicular lean mass (ALM), total bone mineral content (BMC) and density (BMD) between the two DXAs with numerical analysis (mean an T-test) and with a Bland Altman analysis (regression, constant agreement, relative agreement).

Results: 926 participants were analyzed (age 72.9±6.9 years, BMI 25.7±4.8 kg/cm^2). Compared to Lunar iDXA, Horizon A measures higher ($p<0.001$) mean values for TFM +1392g.($r=0.99$) and TPF +0.85%($r=0.97$). Horizon A measures lower ($p<0.001$) mean values for TLM -661g.($r=0.96$), ALM -749g.($r=0.96$), BMC -209g.($r=0.84$) and BMD -0.049g./cm^2($r=0.82$). The Bland Altman visually demonstrate how each comparison relatively or constantly varies.

Conclusion: A trend of higher fat tissues values were seen for Horizon A System™, and of bone and lean tissues for Lunar iDXA™. These results suggest the presence of systematic differences and potential confounders between these devices. These differences might be particularly impactfull on the use of cut-offs in clinical setting (eg. sarcopenia, obesity). Further analysis on subgroups, cross-calibration equations and DXA phantom are planned.

Late diagnosis of childhood-onset hypophosphatasia in an adult with recurrent fractures: the impact of enzyme replacement therapy

Manuela Messikommer 1, Albrecht W Popp 1, Michel Hochuli 1
1 Department of Diabetes, Endocrinology, Nutritional Medicine and Metabolism, Inselspital, Bern University Hospital, University of Bern, 3010 Bern, Switzerland

Background/Introduction: Hypophosphatasia (HPP) is a rare inherited disorder of bone metabolism caused by loss of function mutations in the ALPL gene. This leads to a reduced activity of the tissue non-specific isoenzyme of alkaline phosphatase (TNSALP) resulting in extracellular accumulation of its endogenous substrates, mainly of inorganic pyrophosphate (PPi), Pyridoxal 5' phosphate (PLP) and phosphoethanolamine (PEA). The inability to generate phosphate from PPi inhibits bone mineralization, resulting in rickets or osteomalacia as well as dental problems. In some patients, relative deficiency of pyridoxal with a resulting defect in Gamma-amino butyric acid (GABA) metabolism in the CNS leads to neurological manifestations such as seizures. Overall, the clinical spectrum of the disorder is very heterogeneous and depends on the age at presentation. Enzyme replacement therapy (ERT) with recombinant alkaline phosphatase (asfotase-alfa) is available for treatment of individuals with a confirmed diagnosis of pediatric-onset HPP.

Methods: We describe the clinical and laboratory findings of a patient with childhood-onset hypophosphatasia diagnosed in adulthood, including results of treatment with asfotase-alfa.

Results: A 53-years old man was hospitalized with subtrochanteric and intertrochanteric femoral fractures left after a standing fall and, as an incidental finding, an insufficiency fracture of the right proximal femur. Consequently, the patient was dependent on crutches with a markedly limited quality of life (QoL) because of slowed recovery and persistent pain. The medical history revealed various bone fractures in the past after inadequate trauma and poor bone healing. Furthermore craniosynostosis, dental problems as well as a short stature and a waddling gait have existed since childhood. Additionally, ancient radiologic findings from childhood revealed curved tubular bones. Current laboratory evaluation showed a reduced alkaline phosphatase (AP) (16 U/l [ref 40 – 129 U/l]) immediately after surgical treatment of the femur fractures as well as a markedly elevated PLP (1400 nmol/l [ref 10 – 289 nmol/l]) and an elevated urinary PEA (40 mmol/molCr [ref < 6 mmol/molCr]). The subsequent genetic analysis revealed two compound heterozygous mutations of the ALPL gene confirming the suspected diagnosis of HPP. Enzyme replacement therapy with asfotase-alfa was started to enhance bone healing and to reduce the risk of bone fracturing in future, with the overall goal to improve QoL. After 4 months of treatment, advanced fracture healing with consolidation of the bilateral femur fractures was observed radiologically. Furthermore, PLP and urinary PEA levels normalized under ERT, a distinct proof of biochemical efficacy of ERT. The six-minutes walk test significantly improved (428 m before and 585 m under ERT) with associated improved patient-reported QoL. After 10 months of therapy with asfotase alfa, the fracture clefts of both femora showed complete consolidation on X-ray. Accordingly, a significant improvement in mobility was achieved with a fluent gait pattern with no more need for a walking aid and pain relief.

Conclusion: Rapid improvement of bone healing with consolidation of fractures as well as significant improvement of patient-reported QoL and biochemical normalization of PLP und PEA were observed in this patient soon after starting ERT, suggesting that ERT is effective even in late-diagnosed patients with clearly symptomatic childhood-onset HPP. Therefore, awareness of HPP in patients with suggestive clinical findings is important.

Muscle parameters in fragility fracture risk prediction in older adults: A Scoping Review

C. Vendrami[1], E. Shevroja[1], J. Elmers[2], E. Gonzalez Rodriguez[1], D. Hans[1], O. Lamy[1,3]

[1]*Interdisciplinary Center of Bone Diseases, Rheumatology Unit, Bone and Joint Department, Lausanne University Hospital and University of Lausanne, Switzerland*
[2]*University Library of Medicine, Faculty of Biology and Medicine, Lausanne University Hospital, Switzerland*
[3]*Internal Medicine Unit, Internal Medicine Department, Lausanne University Hospital and University of Lausanne, Switzerland*

Background: Half of fragility fractures occurs in patients with normal bone density or medium/low estimated risk. The effect of muscle parameters on incident fragility fractures (IFF) and their prediction is abundantly studied but remains unclear.

Objectives: To review the association between muscle health (mass, strength, or function) and IFF.

Methods: This scoping review follows the PRISMA-ScR guidelines. We retrieved 13'434 references from Medline Ovid SP, EMBASE, Web of Science and Google Scholar, using a search equation based on the concepts of "muscle measurements", "fragility fractures" and "risk". We included original and prospective studies analysing at least one muscle parameter with IFF. We systematically extracted 17 items including methodology, general characteristics and results.

Results: 67 articles met the inclusion criteria; 2,8 million person-years (M) were accounted in multiple analyses with 60 muscle parameters and 320 fracture risk ratios. Medians (IQR) of each characteristic were: 1642(921-5756) participants, age: 71.7(65-75) years, follow-up: 10(4.35-12) years, IFF number: 166(88-277). Lower muscle mass was negatively/not/positively associated with IFF in 10(2,3M), 64(2,5M) and 28(2,0M) analyses, lower muscle strength in 0, 57(1.7M), and 53(1.3M) analysis, and lower muscle function in 0, 45(1.0M), and 63(1.9M) analysis. Our in-depth analysis shows how each single muscle parameter was associated with each IFF subtypes (all, hip, major, vertebral, humeral, forearm) using multiple stacked forest plots.

Conclusion: Muscle strength and function are the best to predict IFF. More studies on muscle and fracture risk quantification models are needed. Since muscle mass fails to predict IFF, further research should focus on its indexes.

PDGFRβ signaling in osteoprogenitors contributes to the pathogenesis of fibrous dysplasia

Cyril Thouverey[1], Alessandro Corsi[2], Mara Riminucci[2]

[1]Service of Bone Diseases, University Hospital of Geneva, Geneva, Switzerland, [2]Department of Molecular Medicine, Sapienza University, Rome, Italy

Fibrous Dysplasia (FD) is a rare bone disorder caused by somatic gain-of-function mutations of the *GNAS* gene, which encodes Gsα protein. FD bone lesions are characterized by the replacement of normal bone and marrow by a fibro-osseous tissue containing proliferating fibroblast-like osteoprogenitors (OPs) and elevated number of osteoclasts. Platelet-derived growth factor B (*PDGFB*) and PDGF receptor type β (*PDGFRB*) are overexpressed in human FD bone lesions. To determine whether PDGF/PDGFRβ signaling contributes to FD pathogenesis, we generated a mouse model of FD that lacks PDGFRβ in leptin receptor-positive (LEPR+) OPs (*GnasR201C;Lepr-Cre;Pdgfrbf/f*) and compared its phenotype with that of *Lepr-Cre* and *GnasR201C;Lepr-Cre* mice at 5 months of age. Bone lesions of *GnasR201C* mice exhibited increases in *Pdgfb* and *Pdgfrb* expressions in comparison to healthy bone tissue of wildtype littermates. *GnasR201C* mice showed increased cortical bone volume (+39%, p=0.028) with elevated number of osteolytic cavities (x14.3 per total volume, p=0.0001), decreased cortical volumetric bone mineral density (vBMD; -2%, p=0.04), and altered bone mechanical properties (plastic energy: -55%, p=0.005) at femoral midshaft lesions. Deletion of PDGFRβ in LEPR+ cells in *GnasR201C* mice decreased number of osteolytic cavities (-62% vs *GnasR201C;Lepr-Cre*, p=0.002), augmented cortical vBMD (+1.2% vs *GnasR201C;Lepr-Cre*, p=0.04) and restored bone mechanical properties (plastic energy: +107% vs *GnasR201C;Lepr-Cre*, p=0.02). Those beneficial effects were associated with reduced osteoclast number (-44% vs *GnasR201C;Lepr-Cre*, p=0.0001), osteoid surfaces (-63% vs *GnasR201C;Lepr-Cre*, p=0.002) and fibrotic bone marrow volume (-66% vs *GnasR201C;Lepr-Cre*, p=0.02). In conclusion, our results indicate that PDGFRβ signaling in OPs contributes to the pathogenesis of FD.

A dietary plus exercise intervention improves bone turnover in patients with metabolic syndrome and type 2 diabetes

Gerbaix Maude[1], Daniel Courteix[2], Gérard Lac[2], Bruno Lesourd[3], Robert Chapier[3] Agnès Vinet[4], Guillaume Walther[4], Philippe Obert[4], Dutheil Frédérique[5], Ferrari Serge[1]

[1]Geneva University/Medicine/Geneva University Hospital, Geneve, Switzerland,[2]Clermont Auvergne University/Laboratory of Metabolic Adaptations to Exercise in Physiological and Pathological conditions /Research Centre in Human Nutrition, Clermont Ferrand, France, [3]Clermont Auvergne University/Laboratory of Metabolic Adaptations to Exercise in Physiological and Pathological conditions/ Research Centre in Human Nutrition, Clermont Ferrand, France, [4]Laboratory of Pharm-Ecology Cardiovascular/University of Avignon, Avignon, France, [5]Université Clermont Auvergne/ LaPSCo Physiological and Psychosocial Stress/CHU Clermont-Ferrand/University Hospital of Clermont-Ferrand /Preventive and Occupational Medicine, Clermont Ferrand, France

Objectives: Low bone turnover and higher fracture risk are commonly been reported in Type 2 Diabetes Mellitus (T2D) patients. Besides, T2D is often associated with cardiovascular risk factors including central obesity, dyslipidemia, and hypertension as clustered in the Metabolic Syndrome (MetS). We aim to investigate the effects of a dietary plus exercise intervention on bone turnover in obese patients with MetS ± T2D.

Methods: This study is a nested subpopulation analysis of The ReSOlve (Reverse metabolic SyndrOme by Lifestyle and Various Exercises) randomized control trial. Here, we studied the effects of a 6-month endurance and resistance training plus dietary restriction (-500 kcal/d) in 97 obese men and post-menopausal women with MetS (n= 68) and Mets-T2D (n= 29) aged 59±5 yrs. 50 healthy age-matched controls (Ctr) served for baseline comparisons. ELISA measured HbA1C, fasting serum glucose (FSG), serum osteocalcin (OCN), CTX, P1NP, Sclerostin (Scl) and Pigment epithelium derived factor (Pedf). Body composition, BMC and BMD were evaluated using DXA.

Results: At baseline, T2D had higher Hb1Ac, FSG and Pedf levels than MetS and Ctr (+16%, +27%; +31%, +56%; +13%, +38%, $p<0.01$), and lower OCN, CTX and P1NP levels than MetS and Ctr (-37%; -44%; -44%; -55%; -25%, -40%; $p<0.01$). P1NP was also lower in MetS than Ctr (-19%, $p<0.05$). BMD was not different between groups. The intervention decreased body weight and fat mass similarly in T2D and MetS (-5 and -7%; -14 and -17%, respectively vs baseline; $p<0.001$). BMD and BMC were preserved (pNS). HbA1C and FSG improved significantly in both groups but remained higher in T2D. Bone turnover markers increased significantly but remained lower in T2D, with similar results in men and women. Hb1Ac correlated positively with Scl and Pedf ($r =0.195, 0.438$; $p<0.001$), whereas HbA1c, Scl and Pedf correlated negatively with CTX, OCN and P1NP (range $r =-0.431$ to -0.192, all $p<0.001$). Interestingly, improvement of bone turnover markers by intervention was not anymore significant when Scl and Pedf were added as covariates.

Conclusion: A 6-month dietary and exercise intervention increases bone turnover in relation to better glycemic control in Mets and T2D. Sclerostin and Pedf may be involved in this mechanism.

Evaluation of a deep learning spine segmentation (SpS) algorithm for accurate and reproducible monitoring of lumbar spine DXA scans

G Gatineau*1*, E H Ahmed*2*, K Hind*2*, O Lamy*1*, E Gonzalez Rodriguez*1*, L Beaugé*2*, D Hans*1, 2*

1Center of Bone Diseases, Rheumatology Unit, Bone and Joint Department, Lausanne University Hospital, & University of Lausanne, Lausanne, Switzerland
2Medimaps group SA, Plan-les-Ouates, Switzerland

Background: The antero-posterior (AP) lumbar spine (LS) dual energy X-ray absorptiometry (DXA) scan is a critical diagnostic tool used to assess osteoporosis. However, the manual validation of the default spine segmentation (SpS) required to reduce technical error can be time-consuming in practice.

Hypothesis: This study aimed to evaluate if a new artificial intelligence (AI)-based model for automated SpS. could improve the accuracy and efficiency of the analysis of LS DXA scans.

Methods: A sub-sample of 130 women (age: 67.1; BMI: 25.2; no vertebral anomalies) were selected from the OsteoLaus cohort, having previously received two LS DXA (GE Lunar iDXA, encore v 18) 2.5 years apart. Scans were analyzed using the default, clinical expert and AI method to derive bone mineral density (BMD), trabecular bone score (TBS) and surface area. The coefficient of variation (CV%) for reproducibility of bone surface area was also computed.

Results: Significant differences in bone outcomes were found between the default method and expert, but not between the AI and expert (Table 1). The reproducibility for surface area was superior for the clinical expert and the AI model compared to the default (Table 2).

Conclusion: The new AI-based model showed enhanced accuracy and reproducibility in LS measurements compared to the default method and demonstrated close agreement with the clinical expert. These results suggest that the AI-based model for automated SpS may be a valuable and time-efficient tool for the analysis of lumbar spine DXA scans. Future work should validate the model in larger cohorts and different DXA systems.

Table 1: Comparison of bone mineral density (BMD) and trabecular bone score (TBS) between three spine segmentation methods: default, clinical expert and deep learning AI-model

Mean (SD)				Mean (SD)	**p-value**
L1L4 BMD	Expert	1.003 (0.156)	AI	1.006 (0.158)	0.67
L1L4 BMD	Expert	1.003 (0.156)	Default	1.034 (0.145)	0.01*
L1L4 TBS	Expert	1.326 (0.084)	AI	1.325 (0.084)	0.84
L1L4 TBS	Expert	1.326 (0.084)	Default	1.296 (0.091)	< 0.001*

Table 2: Bone surface area reproducibility (CV%) for the default, clinical expert and deep learning AI model

	A	B	Mean (SD)	Mean 2 (SD)	**p-value**
L1L4 surface CV%	Default	AI	1.61 (1.56)	0.932 (0.685)	< 0.001*
L1L4 surface CV%	Expert	Default	0.985 (0.898)	1.61 (1.56)	< 0.001*
L1L4 surface CV%	Expert	AI	0.985 (0.898)	0.932 (0.685)	0.496

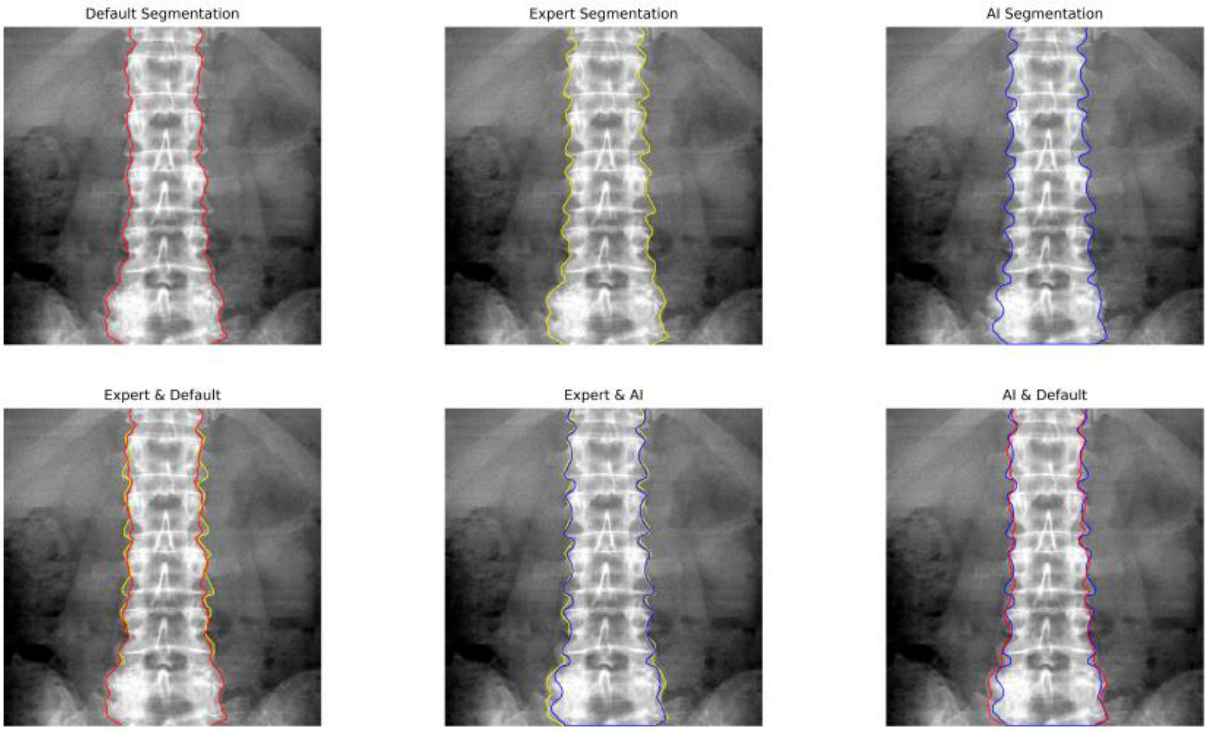


Figure 1: Comparison of the default, expert, and AI SpS

Plasma Sodium Increase Is Associated With an Increase in Bone Formation in Outpatients With Chronic SIAD - A Predefined Secondary Analysis of the SANDx Trial

Sophie Monnerat* 1,2, Julie Refardt*1, Laura Potasso1, Christian Meier1,2, Mirjam Christ-Crain1,2
*equally contributing first authors
1 Department of Endocrinology, Diabetology and Metabolism University Hospital Basel, Basel, Switzerland;
2 Department of Clinical Research, University of Basel, Basel, Switzerland

Background: Hyponatremia is associated with increased risk for osteoporosis.

Hypothesis: An increase in plasma sodium levels in patients with chronic hyponatremia increases osteoblast markers and decreases osteoclast markers.

Methods: This is a secondary analysis of a double-blind, crossover, placebo-controlled trial investigating the effect of 4-week treatment with empagliflozin 25mg/day in outpatients with a chronic syndrome of inappropriate antidiuresis (SIAD). The primary objective was to investigate the relationship between changes in bone formation index (BFI), defined as PINP/CTX, and changes in plasma sodium. Linear mixed models included bone markers as dependent variables, patients as random-effect and the following fixed-effects: week of treatment, serum cortisol, serum 25-OH-vitamin D, baseline serum bone marker, age, gender and smoking status.

Results: Six out of the 11 outpatients with chronic SIAD were female (median [IQR] age 73 years [66, 78]). A sodium increase of 1 mmol/L was associated with an increase of 5.21 in BFI (95%-CI: 1.41, 9.00, p=0.013) and with an increase of 1.48 ug/L in P1NP (95%-CI: 0.26, 2.62, p=0.03). Plasma sodium was not associated with a change in osteocalcin (β=0.32; 95%-CI: -0.09, 0.72, p=0.18), nor with a change in CTX (β=0.003; 95%-CI: -0.008, 0.014, p=0.324). The effect of sodium was independent from empagliflozin.

Conclusion: An increase in plasma sodium levels in outpatients with chronic SIAD was associated with an increase in P1NP/CTX, which was triggered by an increase in the osteoblast marker P1NP. This supports the importance of treating hyponatremia, particularly in older adults in whom chronic hyponatremia is also associated with falls.

Hip Fracture Risk and Refracture Rate in Subjects with an Incident Hip Fracture at the Geneva University Hospital: A Retrospective Analysis

Ivan Padlina[1], Marina Portela[1], Emmanuel Biver[1], Thierry Chevalley[1], Serge Ferrari[1].

[1]Division of Bone Diseases, Geneva University Hospitals and Faculty of Medicine, Geneva, Switzerland

Purpose: Fracture risk and contralateral hip fracture rates in subjects with a recent hip fracture may vary from country to country. To estimate the potential benefits of prophylactic surgical interventions to reduce the incidence of contralateral hip fractures, we analyzed the fracture risk profile with a recent hip fracture.

Methods: Patients ≥50 years admitted with a hip fracture to the Geneva University Hospital over 4 years (2013-2016) were retrospectively assessed for re-fracture rates between 2013 and 2018. Charlson comorbidity index (CCI) and FRAX±BMD scores were determined at the time of index fracture.

Results: 1253 patients (323 men and 930 women) were included. Mean age at index fracture was 83.2 yo±9.8 SD, Men 80.4±10.9, women 84.1±9.1. DXA values in 582 patients showed that 35.6% and 59.9% of them were osteopenic and osteoporotic, respectively. A contralateral hip fracture occurred in 144 (11.5%) patients, respectively 38 men and 106 women. Age at 2nd hip fracture was 77.6±11.9 and 87.6±7.9 years in men and women, respectively. Median time to 2nd hip fracture was 1.39 years. Mean age adjusted CCI was 5.5±2.0 with no sex difference. FRAX calculated for hip without BMD before and after index fracture were 16.7±11.5 and 21.0±12.3% respectively.

Conclusions: Among subjects with a recent hip fracture, more than one in ten had a contralateral hip fracture during follow-up, about half occurring within 18 months after the index fracture. CCI and FRAX hip scores at the time of the index were not worse in those sustaining a controlateral hip fracture.

Improving fracture prediction in patients with osteoporosis using machine learning techniques: a nationwide, registry-based cohort study

Judith Everts-Graber [1,2], Oliver Lehmann [3], Olga Mineeva [4], HansJörg Häuselmann [5], Laura Guyer [6], Stephan Reichenbach [2,7], Thomas Lehmann [1], Olga Demler [4,8] and the Osteoporosis Registry of the Swiss Society of Rheumatology Study Group

[1] OsteoRheuma Bern, Bahnhofplatz 1, Bern, Switzerland
[2] Department of Rheumatology and Immunology, Inselspital, Bern University Hospital, University of Bern, Switzerland
[3] ETH Zürich, Department of Information Technology and Electrical Engineering, Zürich, Switzerland
[4] ETH Zürich, Department of Computer Science, Zürich, Switzerland
[5] Zentrum für Rheuma- und Knochenerkrankungen, Klinik Im Park, Hirslanden Zürich, Switzerland
[6] Faculty of Medicine, University of Bern, Bern, Switzerland
[7]Institute for Social and Preventive Medicine, University of Bern, Switzerland
[8] Division of Preventive Medicine, Brigham and Women's Hospital, Harvard Medical School, Boston, MA, USA

Objectives: Fracture prediction is essential for the adequate management of patients with osteoporosis and might be improved by using machine learning techniques. The aim of this study was to analyse the performance of different machine learning models and to identify the most relevant clinical factors for fracture prediction.

Methods: This prospective, multicentre cohort study analysed a prognostic fracture risk- prediction model using clinical risk factors, T-scores, trabecular bone score (TBS) and treatment information from subjects in the nationwide Osteoporosis Registry of the Swiss Society of Rheumatology. Survival analysis was used to predict the 2-year risk of vertebral, hip, wrist and any fractures in a training subset. The C-index was estimated in the test set to evaluate the quality of the model using cumulative or dynamic areas under the curve, and was compared with the performance of state-of-the-art machine learning techniques such as Random Survival Forest and eXtreme Gradient Boosting with an accelerated failure time model. Both Cox proportional hazard model and machine learning models were externally validated using data from the UK biobank.

Results: A total of 15,383 postmenopausal women (mean age 68 ± 9 years) with 26,986 dual-energy X-ray absorptiometry scans and clinical visits were enrolled between January 2015 and October 2022. Of these women, 6,202 were followed-up for a median of 4.1 years [2.7 to 6.0]. During follow-up, 1,227 women suffered a fragility fracture, including 902 fractures within 2 years of follow-up. The C-index for fracture prediction for this 2-year follow-up period reached 0.68 for vertebral fracture, 0.76 for hip fracture and 0.67 for any fracture, and further increased with longer follow-up periods of up to 7 years. In comparison, the 10-year fracture prediction C-index calculated with FRAX® Switzerland was 0.61 for major osteoporotic fracture and 0.66 for hip fracture. The five most important variables in the Lasso-Cox model were age, bone density and prevalent fracture. In addition, TBS was relevant for vertebral and wrist fractures, while the number of falls was an important predictor of hip and wrist fractures. The T-score at the lumbar spine predicted vertebral fracture, while the T-score at the hip predicted vertebral, hip and wrist fractures. Performance of both Cox proportional hazard models as well as machine learning models showed similar prediction scores in the UK biobank dataset consisting of 5,474 postmenopausal women with 290 fractures during follow-up.

Conclusions: Fracture risk prediction by FRAX® can be improved by modifying fracture prediction models to include the T-score at the lumbar spine, TBS, number of falls and recent fractures. Age, low bone mineral density and prevalent fracture were the strongest predictors of both vertebral and non-vertebral fractures in these two cohorts of postmenopausal women.

Disclosures: JEG, OL, OM, LG, SR and TL have nothing to declare. HJH: Amgen, Sandoz, Eli Lilly and Labatec. OD: KOWA (all unrelated to this research).

Top 5 Features of the Lasso-Cox model

	Vertebral Fx	**Hip Fx**	**Wrist Fx**	**Any Fx**
1	Age	Previous Fx	Previous Fx	Previous Fx
2	Previous Fx	T-Score Total Hip	T-Score Total Hip	Age
3	TBS	Age	Number of Falls	T-Score Total Hip
4	T-Score LS	Recent Fx	GC dose	Number of Falls
5	T-Score Neck	Number of Falls	TBS	T-Score Neck

Table 1 Top five features of the Lasso-Cox model.
These features were obtained by performing incremental feature selection, where the lasso algorithm was limited to five features only. Thus, it represents which variables were considered most important in the model. «Recent fractures" is a subgroup of "previous fractures", defined as fractures that occurred within 2 years before study entry. All variables are continuous (e.g., number of previous fractures, dosage of steroids etc.).
Abbreviations: Fx: fractures, GC: Glucocorticoids, LS: lumbar spine, TBS: trabecular bone score.

Effect of vitamin D3, omega-3s and a simple home exercise program on BMD in European older adults: preliminary findings from the DO-HEALTH randomized controlled trial

Kistler-Fischbacher M[1,2], Armbrecht G[3], Gängler S[1,2], Lang W[1,2], Kanis J[4], Dawson-Hughes B[5], Rizzoli R[6], Wanner GA[7], Bischoff-Ferrari HA.[1,2,8], for the DO-HEALTH investigators

[1] Department of Aging Medicine, University Hospital Zurich, Zurich, Switzerland
[2] Centre on Aging and Mobility, University Hospital Zurich and University of Zurich, Zurich, Switzerland
[3] Klinik für Radiologie, Charité-Universitätsmedizin Berlin, Corporate Member of Freie Universität Berlin and Humboldt-Universität zu Berlin, Berlin, Germany
[4] Center for Metabolic Diseases, University of Sheffield Medical School, Sheffield, England.
[5] Jean Mayer USDA Human Nutrition Research Center on Aging, Tufts University, Boston, Massachusetts
[6] Division of Bone Diseases, Geneva University Hospitals and Faculty of Medicine, Geneva, Switzerland
[7] Spine Clinic and Traumatology, Private Hospital Bethanien, Zurich, Switzerland
[8] University Clinic for Acute Geriatric Care, City Hospital Waid & Triemli, Zurich, Switzerland

Background: Vitamin D, omega-3s and exercise are the most promising non-pharmacological interventions to improve bone health.

Objective: We examined whether vitamin D3, omega-3s, or a strength-training exercise program (SHEP), alone or in combination, improve lumbar spine (LS), femoral neck (FN) or total hip (TH) aBMD, or LS TBS, among European older adults.

Methods: This is a secondary analysis of DO-HEALTH, a 3-year multicenter, double-blind, randomized 2×2×2 factorial design trial in generally healthy older adults (≥70 years). The interventions were 2000 IU/d of vitamin D3, 1g/d of omega-3s, and a SHEP (3×30 min/wk), applied alone or in combination. Change in LS, FN, and TH aBMD and LS TBS was assessed by DXA at baseline and year 1, 2 and 3. Mixed effect models were used. Analyses were based on the intention-to-treat principle and adjusted for age, sex, BMI, prior fall, study site and baseline level of the outcome.

Results: DXA scans were available for 1486 participants (75 years, 63% women, FN T-score -1.4). Preliminary results show a significant difference in mean 3-year change in TH aBMD for vitamin D3 vs. no vitamin D3 (Δ least square means [LSMs]: 0.0035 [95% CI 0.0011, 0.0059] g/cm2) and vitamin D3+omega-3s vs. no vitamin D3+no omega-3s (ΔLSM: 0.0038 [95% CI 0.003, 0.0072] g/cm2). There were no significant effects on FN and LS aBMD. TBS analyses are in preparation.

Conclusions: Among generally healthy and active older adults, daily vitamin D3 supplementation, alone or in combination with omega-3s supplementation, showed a small benefit for total hip aBMD

Assessment of total and bioactive serum sclerostin levels and its association with bone metabolism in type 2 diabetes mellitus

Cyril Traechslin[1], Lilian Sewing[1], Sandra Baumann[1], Leticia Grize[2], Janina Vavanikunnel[3], Maria Triantafyllidou[4], Marius Kraenzlin[5], Christoph Henzen[4], Christian Meier[1,5]

[1]*Division of Endocrinology, Diabetes and Metabolism, University Hospital Basel,* [2]*Swiss Tropical and Public Health Institute, Basel,* [3]*Division of Endocrinology, Kantonsspital Olten;* [4]*Department of Internal Medicine, Kantonsspital Luzern;* [5]*Endocrine Clinic and Laboratory, Basel, Switzerland*

Background: Sclerostin has been linked to decreased bone turnover in patients with type 2 diabetes mellitus (T2DM). Several sclerostin assays with different binding sites of the sclerostin molecule have become commercially available. Their relationship with bone turnover and bone mineral density (BMD) remains unclear.

Hypothesis: We aimed to investigate the relationship between different sclerostin assays and markers of bone metabolism and BMD in patients with T2DM.

Methods: Baseline data from the cross-sectional multicenter DiabOS Study were analyzed. Total and bioactive serum sclerostin levels were measured with three different ELISA-based sclerostin assays (Sclerostin Biomedica [SCL-BM], Sclerostin bioactive Biomedica [SCLbio-BM] and Sclerostin hsTECO [SCL-hsTECO]). Sclerostin values between patients with T2DM and healthy controls were compared and correlation analysis with biochemical markers of bone metabolism and BMD was performed.

Results: Data from 115 postmenopausal women and men, aged from 50-75 years was analyzed. The mean diabetes duration was 13.4±7.0 years and mean HbA1c was 7.7±1.3% in patients with T2DM (n=78).
Unadjusted sclerostin levels were higher in men with T2DM measured with all sclerostin assays. After adjustment for renal function and BMI, only bioactive sclerostin levels remained significantly elevated in men with T2DM compared to controls (T2DM, 106.8±39.9 pmol/l; controls, 88.3±21.3 pmol/l, p=0.03).
Univariate analysis showed consistent significant associations with all sclerostin assays for age, eGFR, HbA1c and diabetes duration. In multivariate analysis in patients with T2DM, eGFR remained the only significant determinant of serum sclerostin levels. Elevated bioactive sclerostin values in patients with T2DM showed significant positive associations with BMD at all different skeletal sites as well as a trend to negative associations with bone turnover markers.

Conclusions: Measurement of bioactive sclerostin levels may support the assessment of bone metabolism in men with T2DM. Further studies are needed to assess its value for fracture prediction.