higher BMD and FIs than non-diabetic participants (p-values<0.001). During follow-up, 611 (19.4%) fragility fractures were observed: 35 (25.4%) in T2DM and 576 (19.1%) in controls. Compared with non-fractured, significantly higher FIs were found in those with incident fragility fractures in analyses conducted in all participants, in controls, and in participants with T2DM (all p-values<0.001). A higher FI was significantly related to risk for incident fragility fractures in the adjusted models: HR=1.02 (95%CI: 1.01 – 1.03), p<0.001 for per-0.01 increment of the FI; HR=1.21 (95%CI: 1.12- 1.32), p<0.001 for per-0.10 FI increment.

Conclusion: Frailty is significantly related to increased risk for incident fragility fractures in T2DM despite their higher BMD values. Assessing frailty status may aid in the fracture risk evaluation and management of those with T2DM.

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NEW USEFUL MARKER FOR DIAGNOSIS OF OSTEOPOROSIS IN RHEUMATOID ARTHRITIS

L. Sivordova[1], J. Polyakova[1], Y. Akhverdyan[1], N. Fofanova[1], V. Kravtcov[1], B. Zavodovsky[1]

[1]Federal State Budgetary Institution "Research Institute of Clinical and Experimental Rheumatology named after A.B. Zborovsky", Volgograd, Russia

Objective: In recent years, we have been studying the role of cytokines in the pathogenesis of osteoporosis (OP) in patients with rheumatic diseases (1,2). We studied the clinical and diagnostic value of serum Adiponectin determination in rheumatoid arthritis (RA) patients complicated by osteoporosis.

Methods: We examined 88 women with documented diagnosis of RA and mean disease duration of 6.56±0.88 years and control group of 45 healthy females. Serum adiponectin levels (μg/ml) using human adiponectin ELISA commercial test systems (BioVendor). OP diagnosed using DXA with LUNAR DPX PRO (GE, USA).

Results and discussion: Serum adiponectin levels in the control group were 12.5±0.9 μg/ml (M±m). Adiponectin levels in healthy subjects measured as M±2d, ranged between 0.44 and 24.56 μg/ml. Patients with OP and RA had significantly higher levels of serum Adiponectin (p<0.001). Mean serum Adiponectin levels in RA patients who had normal bone density and had no OP were 35.21±0.6 μg/ml. Mean serum Adiponectin levels in RA/OP patients with low BMD were 52.42±0.69 μg/ml. Adiponectin levels of 44 μg/ml and higher were associated with osteoporosis. Adiponectin levels of 43.9 μg/ml and lower were associated with normal bone density. Thus, we revealed that adiponectin levels depend on osteoporosis presence in RA patients. We suppose that Adiponectin determination may be useful laboratory marker for osteoporosis diagnosis.

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HEPCIDIN REGULATE BIOMINERALIZATION OF BONE BY BMP SIGNALING IN ZEBRAFISH

J. Yu[1]

[1]The Second Affiliated Hospital of Schoow University, Suzhou, China

Iron overload, as a risk factor for osteoporosis, can result in the upregulation of *Hepcidin*, and *Hepcidin* knockout mice display defects in their bone microarchitecture. However, the molecular and genetic mechanisms underlying *Hepcidin* deficiency-derived bone loss remain unclear. Here, we used CRISPR-Cas9, a versatile genome-editing tool, to generate a zebrafish *hepcidin* mutant. Iron overload and a mineralization delay were observed in osteoblast cells in *hepcidin-/-* zebrafish larvae, and these defects could be partially restored with a microinjection of *hepcidin* mRNA. Quantitative real-time PCR analyses revealed the downregulation of the osteoblast-specific genes *alp*, *runx2a, runx2b,* and *sp7* in homozygous *hepcidin* mutant zebrafish. Luciferase reporter assays further showed that bone morphogenetic protein 2a(Bmp2a) enhanced the expression of *runx2a*, while iron overload repressed its expression through *bmp2a* (independent of*hjv*). High-throughput transcriptome analysis of *hepcidin-/-* zebrafish revealed multiple pathways involved in osteoblast metabolism. Together, these findings show that iron overload derived from *hepcidin* deficiency represses bone formation, possibly through the BMP pathway, and affects *runx2* in zebrafish.

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COST-EFFECTIVENESS OF SEQUENTIAL TREATMENT WITH ABALOPARATIDE VS. TERIPARATIDE FOR THE PREVENTION OF OSTEOPOROTIC FRACTURES IN POSTMENOPAUSAL US WOMEN AT INCREASED RISK OF FRACTURE

M. Hiligsmann[1], S. A. Williams[2], L. A. Fitzpatrick[2], S. Silverman[3], R. Weiss[2], J.-Y. Reginster[4]

[1]Maastricht University, Maastricht, The Netherlands, [2]Radius Health, Inc., Waltham, USA, [3]Cedar-Sinai Medical Center and UCLA School of Medicine, Los Angeles, USA, [4]University of Liege, Liege, Belgium

Objective: To assess the cost-effectiveness of sequential treatment with abaloparatide (ABL) followed by alendronate (ABL/ALN) vs. teriparatide (TPTD) followed by ALN (TPTD/ALN) for the treatment of postmenopausal osteoporosis from the US payer perspective using a lifetime horizon.

Methods: A Markov microsimulation model was developed to estimate the cost-effectiveness of sequential ABL/ALN compared with sequential TPTD/ALN with a lifetime horizon from the US payer perspective. Patients were assumed to receive ABL or TPTD for 18 months followed by 5 years of ALN as per treatment guidelines. The effects of ABL on fracture risk was derived from the ACTIVExtend trial. The effects of TPTD was assumed to be maintained during subsequent ALN treatment, consistent with ACTIVExtend findings for ABL. Evaluation was completed for high-risk patients 50-80 years of age with a BMD T-score ≤-3.5 or with a BMD T-score between -2.5 and -3.5 and a history of at least one osteoporotic fracture. Sensitivity analyses were performed to test the robustness and uncertainty of the model results.

Results: In all simulated populations, sequential ABL/ALN therapy was dominant (lower healthcare costs and higher QALYs) compared with sequential TPTD/ALN therapy. In patients aged 70 years with BMD T-score ≤-3.5, sequential ABL/ALN therapy reduced the expected number of fractures per patient by 0.125, increased lifetime QALY gained by 0.036 and saved $33,381 over a patient's lifetime. Probabilistic sensitivity analyses suggested that ABL/ALN was dominant in about 90% of the simulations.

Conclusions: Sequential ABL/ALN therapy is a cost-effective (dominant) strategy compared with sequential TPTD/ALN therapy for the treatment of women at increased risk of fractures in the US.

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