diabetic populations.
Keywords: Phase Angle, Sarcopenia, Type 2 Diabetes Mellitus, Bioelectrical Impedance Analysis, Aging, Muscle Integrity

"SKELETAL AGE" FOR CUMULATIVE IMPACT OF CIGARETTE SMOKING ON POST-FRACTURE MORTALITY

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Background: Cigarette smoking is associated with an increased mortality risk, though its impact on post-fracture mortality is unclear. We determined the impact of cigarette smoking on post-fracture mortality risk and proposed the *"Skeletal Age"* metric to communicate the risk of smoking on mortality.
Methods: We analysed data of 1084 fracture patients (average age at fracture: 82.6±6.6 years) from the Osteoporotic Fractures in Men Study in USA. Smoking conditions, including smoking status (current, past or never), cumulative smoking exposure (tertiles of pack-years) and time since smoking cessation (< 10, 10-30 or > 30 years of quitting) were self-reported, and deaths were confirmed via death certificates. A Cox regression was conducted to quantify the association between smoking conditions and post-fracture mortality, accounting for known confounders. *"Skeletal Age"* is the sum of chronological age and the number of years of life lost associated with a fracture or a risk factor.
Results: Over a median follow-up of 5.1 years (IQR: 2.1-9.3), 639 fracture patients died (~ 10.2 deaths/100 person-years). Current and past smokers with the highest tertiles of smoking exposure or < 10 years of smoking cessation were independently associated with 90%, 42% and 60%-greater risk of post-fracture mortality than non-smokers, respectively. By contrast, past smokers who had smoked less or quit for > 10 years were not associated with post-fracture mortality risk, suggesting the reversibility of smoking's impact on post-fracture mortality. Additionally, a 60-year-old fracture patient who was currently smoking had *"Skeletal Age"* of 65.1 years, indicating 5 years of life lost related to current smoking. Similarly, those who had either smoked heavily or quit within 10 years had *"Skeletal Age"* of 62.9 or 63.8 years, respectively.
Conclusion: The association between cigarette smoking and post-fracture mortality is reversible, indicating the benefits of smoking cessation on mortality. *"Skeletal Age"* can be employed to improve doctor-patient risk communication.
Keywords: Smoking Cessation, Post-fracture Mortality Risk, Skeletal Age, Reversibility

DIFFERING MECHANISMS OF ANABOLIC EFFECTS BETWEEN TERIPARATIDE AND ROMOSOZUMAB: A BONE HISTOMORPHOMETRIC ASSESSMENT

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Background: Anabolic therapy for severe osteoporosis is commonly used in clinical practice. We examined the different effects of two anabolic agents, Teriparatide and Romosozumab, using bone histomorphometry on iliac bone biopsies.
Methods: The Teriparatide group consisted of 4 patients (aged 72.3 ± 2.3 years) who received 1 month of treatment, and 7 patients (aged 73.7 ± 8.2 years) who received 5 months of treatment prior to surgery. The Romosozumab group consisted of 4 patients (aged 83.8 ± 8.4 years) who received 1 month of treatment, and 5 patients (aged 72.8 ± 2.1 years) who received 5 months of treatment prior to surgery. Iliac bone biopsies were performed during spinal surgeries with informed consent. Bone histomorphometric assessments were conducted in the usual manner.
Results: 1-month effects of Teriparatide vs. Romosozumab: Osteoid surface (OS/BS): 22.3 ± 9.3% vs. 23.2 ± 13.1%, Mineralized surface (MS/BS): 4.5 ± 4.1% vs. 6.3 ± 10.6%, Eroded surface (ES/BS): 1.5 ± 1.3% vs. 2.1 ± 0.4%, Osteoclast surface (Oc.S/BS): 0.27 ± 0.19% vs. 0.08 ± 0.02%. 5-month effects of Teriparatide vs. Romosozumab: Osteoid surface (OS/BS): 34.5 ± 16.6% vs. 18.2 ± 17.3%, Mineralized surface (MS/BS): 9.5 ± 8.7% vs. 2.6 ± 2.4%, Eroded surface (ES/BS): 2.3 ± 0.9% vs. 0.8 ± 0.4%, Osteoclast surface (Oc.S/BS): 0.65 ± 0.46% vs. 0.05 ± 0.09%.
Conclusions: The 1-month treatments with Teriparatide and Romosozumab revealed similar anabolic effects, as both treatments increased the osteoid surface and mineralized surface. However, the 5-month treatment with Teriparatide showed sustained high levels of both osteoid and mineralized surfaces. In contrast, the 5-month treatment with Romosozumab showed lower levels in these parameters. These two anabolic agents for osteoporosis exhibit completely different bone dynamics in bone histomorphometry, suggesting that the properties of the bone tissue after treatment may differ significantly.
Keywords: Teriparatide, Romosozumab, Bone Histomorphometry

"POSTPONEMENT OF FRACTURE" AS A NOVEL METRIC FOR EXPRESSING ANTI-FRACTURE EFFICACY: AN IPD META-ANALYSIS

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Background: The interpretation of osteoporosis treatment effects remains challenging, contributing to its global undermanagement crisis. We propose the *"Postponement of Fracture"* as a novel and intuitive metric to express anti-fracture efficacy.
Methods: *"Postponement of Fracture"* is defined as the gain in fracture-free survival time attributable to osteoporosis treatment, calculated as the restricted mean fracture-free survival time (RMST) difference between the intervention and control groups. A two-stage individual patient data (IPD) meta-analysis was conducted, including randomized controlled trials (RCTs) that assessed anti-fracture efficacy, used a 1:1 allocation ratio, and reported at least one statistically significant result with Kaplan-Meier curves. First, we reconstructed individual patient-level data using the *IPDfromKM* application, and then calculated RMST differences at 12, 24, and 36 months post-intervention for each analysis result included in the meta-analysis. Secondly, a random-effects meta-analysis was performed to pool RMST differences by specific medications and fracture sites.
Results: The meta-analysis included 32 analysis results from 18 RCTs (median sample size: 1776 participants; IQR: 1085–4093), with 78% of trials having a maximum follow-up of 24 or 36 months. Osteoporosis treatment, treated for 12, 24, and 36 months, postponed fractures by 2.6 (95% CI: 2.2–2.9), 9.1 (8.1–10.0), and 16.7 months (14.1–18.6), respectively. Parathyroid hormone analogs and romosozumab yielded the longest postponement for osteoporotic fractures, while calcium supplementation (± vitamin D) was associated with the shortest postponement for wrist fractures. "Postponement of Fracture"-related advice, such as *"a 3-year treatment would give you 17 extra months of health, and only 8 out of 100 people like you will fracture, compared to 20 without treatment"* is more intuitive and informative than the conventional *"the treatment would reduce fracture risk by 60%"*.
Conclusions: "Postponement of Fracture" offers a complementary, patient-centered metric for interpreting treatment effects, thus improving doctor-patient risk communication and treatment uptake.
Keywords: IPD Meta-analysis, Postponement of Fracture, Anti-fracture Efficacy, Risk Communication