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Effect of Anthropometric Adjustments on BMD and BMC Z-Scores in a Population of Prader-Willi Syndrome Pediatric Patients

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Methods: (ASP8)-Liposome-Icaritin was synthesized by thin film evaporation method with extruding through polycarbonate filter membranes to obtain unilamellar vesicles with bone targeting molecules ASP8 attached. Eighty four-month-old C57/BL6 female mice were divided into 8 groups (n=10): Baseline (BL), Sham surgery (SH), Ovariectomized (OVX), Estradiol for oral administration(O-E2), Icaritin for oral administration (O-ICT), low dose (8mg/kg, once a week) targeting delivery system with Icaritin injected via caudal vein (IV-LIP+ICT+ASP8-L), high dose (8mg/kg, twice a week) targeting delivery system with Icaritin injected via caudal vein (IV-LIP+ICT+ASP8-H), delivery system with Icaritin injected via caudal vein (IV-LIP+ICT, 8mg/kg, twice a week). Administrations of gavage and IV injection were applied respectively for 6 weeks from the day right after the OVX surgery. Lumbar spine and lower limbs were harvest 6 weeks after surgery for bone quality analysis. The 5th vertebra body of lumbar region was scanned by micro-CT (Scanco micro-CT 40). Trabecular bone was identified and parameters were analyzed for evaluation of bone quality and microarchitecture. For confirming the specificity of the targeting delivery system, Xenogen IVIS spectrum was used to semi-qualify the distribution of bone targeting system ex vivo by injecting labelled targeting delivery system.

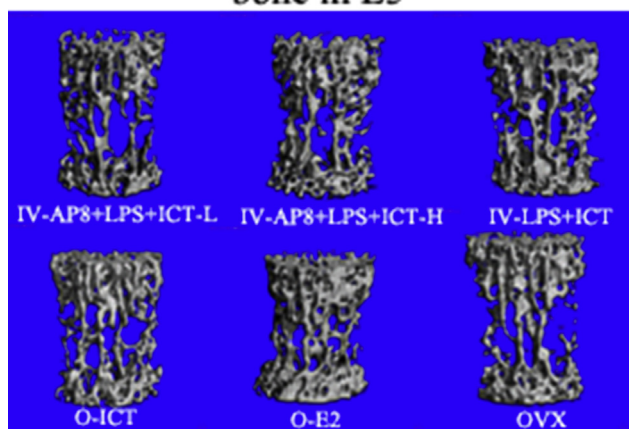
Results: By comparing to the OVX group, bone quality in groups with IV injection were enhanced reflected in the increased BMD ($p<0.05$), bone volume ($p<0.05$), trabecular bone number and connectivity density ($p<0.05$) and decreased in trabecular bone separation ($p<0.05$). Also the efficacy of the targeting icaritin delivery system tended to be dosage dependent (BV increased 14.16% in high dose group, Tb.N increased 10.34% and connectivity density of trabecular bone increased 19.70%). Moreover from Structure Model Index (SMI) value, we concluded that the morphology of trabecular bone in icaritin injection groups tends more to be plat-like: $SMI(OVX)=2.19\pm 0.30$, $SMI(IV-AP8+LPS+ICT-1)=2.07\pm 0.36$, $SMI(IV-AP8+LPS+ICT-H)=2.01\pm 0.23$. More signals retain in bone 72 hours after injection by comparing to the delivery system without bone targeting molecules ASP8 shown in IVIS image.

Conclusion: The novel bone-targeting delivery system carrying osteopromotive phytomolecule(s) Icaritin was confirmed that was capable of preventing the estrogen depletion induced osteoporosis in a dose dependent manner.

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Micro-CT 3D images of trabecular bone in L5.

Micro-CT 3D images of trabecular bone in L5



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FRACTURE RISK OF ELDERLY POPULATION: LIKELIHOOD OF OSTEOPOROTIC FRACTURE RISK IN ELDERLY POPULATION AND INDOOR AIR POLLUTION

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Background: Harmful particulate contaminants (such as PM_{2.5}) that indoor coal combustion produced can increase the incidence of cardiovascular disease and risk of death, while there is considerable evidence that cardiovascular disease, dyslipidemia, and osteoporosis among elderly population have common risk factors. Our hypothesis was that the osteoporotic fractures may be associated with indoor air pollution. The purpose of this study was to explore the risk of osteoporotic fracture of elderly population associated with likelihood of indoor air pollution.

Methods: Forty-eight cases with osteoporotic fractures and 91 controls were selected from the elderly population in Ordos region, Inner Mongolian. The risk factors were compared between the two groups in demographic characteristics, exercise, sleep, room environmental conditions, dietary, behavioral habits, history of medicine use, bone disease and chronic disease by using descriptive analysis. Multivariate logistic regression model was performed to analyze environmental risk factors associated with the risk of fractural etiology.

Results: The age range of case-control groups was 60-88 years old. There were no statistically significant differences between two groups in age, sex and occupation ($p>0.05$). The variables with statistically significant differences in the univariate analysis were included in Logistic Regression model. After adjustment for the education, ethnic factors, health status during childhood, behavioral habits, history of bone disease and medicine use, the findings showed that the exposure factors, such as indoor air conditions during the winter heating, weekly exercise, sleep quality, consumption of carbonated beverages, were associated with risk of elderly fracture. When compared to elderly population who had good air quality of habitable room in winter, elderly population with poor air quality had an elevated risk for fracture (OR 40.29, 95% CI 8.75-185.38); elderly population who had no weekly exercises had an increased risk for fracture (OR 4.28, 95% CI 1.20-15.24) when compared to those who had weekly exercises; elderly persons with poor quality of sleep was associated with a 6.85-fold increase in risk of fracture when compared to those with better quality of sleep (95% CI 1.61-29.14).

Conclusion: The findings suggest that poor indoor air quality during the winter heating may be the risk factors of osteoporotic fractures for the elderly population. It is necessary to further investigate those factors in a larger sample population.

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EFFECT OF ANTHROPOMETRIC ADJUSTMENTS ON BMD AND BMC Z-SCORES IN A POPULATION OF PRADER-WILLI SYNDROME PEDIATRIC PATIENTS

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Objective: Two adjustment models were applied to a dataset of bone-mineral density (BMD) and bone-mineral content (BMC) from dual-energy x-ray absorptiometry (DXA) measurements of pediatric patients with Prader-Willi Syndrome (PWS). One model used weight, height and % body fat (WHF) in the calculation of Z-scores in addition to race, sex and age already included in the standard model. As percent body fat is not always available, a second model with only weight and height was also examined (WH).

Methods: Fifty-six patients with PWS, a neurogenetic disorder caused by the absence of paternal expression of imprinted genes localized in the 15q11-q13, were recruited. PWS is characterized by an insatiable appetite leading to obesity, short stature, cognitive and behavioral problems, hypogonadism and osteoporosis. All patients had spine and hip DXA measurements; 31/56 also had whole-body measurements (needed for body-fat correction). Several patients show lower than normal height or higher than normal weight for age. The percent body fat for all patients is either at the upper limit of or above the normal range. Patients with extreme anthropometric values were most affected by the anthropometrically corrected Z-scores.

Results: In the analysis of Z-scores, patients below -2.0, the critical region, are of most interest. By analyzing which patients cross the -2.0 boundary

IBDW2014-00142-F0065 Table I Association between pQCT muscle outcomes and fractures with adjustment for covarlates and the CaMos Frailty Index (CFI). *In this model, CFI was examined as an interaction with each muscle measurement.

pQCT variables	Odds Ratio (OR) (95%CI)			
	A) Base model	B) age, BMI, aBMD	C) B + Falls	D) C + CFI*
Muscle density	1.34 (1.09, 1.65)	1.39 (1.09, 1.77)	1.40 (1.09, 1.78)	1.35 (1.05, 1.74)
Muscle area	1.04 (0.85, 1.26)	1.19 (0.94, 1.50)	1.19 (0.94, 1.50)	1.05 (0.82, 1.35)
Muscle mass	1.14 (0.93, 1.38)	1.31 (1.03, 1.65)	1.30 (1.03, 1.65)	1.16 (0.90, 1.48)

after applying the anthropometric corrections, we can gain insight into the relevance of such adjustments. Whereas 8/31 (26%) patients cross from the non-critical to the critical region with WH corrections applied to sub-head whole-body BMD, 6/31 (19%) cross the same boundary when WHF corrections are applied. The numbers are similar for BMC, with 9/31 (29%) crossing the critical boundary with WH or WHF corrections applied. The number of patients crossing from critical to non-critical is 23% for BMC with the WH correction and 29% for BMC with the WHF correction applied. However, when BMD is considered, that change in classification is smaller for the WH correction (13%) but not for the WHF correction (19%). The patterns are similar for the other body sites.

Conclusion: Anthropometric correction for the calculation of Z-scores appears to affect a considerable fraction of patients with PWS. This is due to the large abnormality in body size, and DXA measurements, being projection measurements, are affected by body size. However, fracture risk has not yet been studied in connection with DXA parameters in individuals with PWS, and the full implication of anthropometric corrections needs to be evaluated pending such investigations.

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MUSCLE DENSITY IS ASSOCIATED WITH FRAGILITY FRACTURES IN POSTMENOPAUSAL WOMEN WHO ARE LESS FRAIL: THE CaMOS MUSCLE QUALITY STUDY

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Muscle is the largest source for energy production and storage and is a determinant of frailty. Muscle has been linked to bone strength and fractures previously. It is unknown how muscle relates to fractures independently of frailty.

Objectives: To determine how muscle associates with fragility fractures in postmenopausal women in the context of frailty.

Methods: A subset of women 60-85 years old participating in the Canadian Multicentre Osteoporosis Study (CaMOS) completed peripheral quantitative computed tomography (pQCT) (20 mm/s, 38 kVp, 500 µm in-plane resolution) scans using XCT 2000 (Stratec Medizintechnik) at 66% of the tibial length (at year 16). Muscle density, mass, and area were derived using manufacturer's software. Comorbidities, cognition, energy level, function and mobility questions obtained at year 10 were used to compute the CaMOS frailty index (CFI). Incident fractures from baseline to year 15 were derived from the CaMOS database. A binary logistics regression analysis measured odds ratios (OR) for fragility fractures per standard deviation difference in each muscle measure, adjusting for age, body mass index (BMI), lowest areal bone mineral density (aBMD) T-score of total hip or lumbar spine and having fallen within the last 12 months. The interaction of muscle outcomes and CFI was examined in a second model, exploring the effect of muscle on fractures at different values of CFI.

Results: Women (N=525, mean age: 71.4 ± 6.4 years; BMI: 26.90 ± 4.85 kg/m²) with one or more fragility fractures since baseline had a lower muscle density than those without (p=0.004). Muscle density and mass but not muscle area, were associated with increased odds for fractures independent of age, BMI, aBMD and falls. Further adjustment for CFI abolished the relationship between fractures and muscle mass but not muscle density (Table I). A

plot of ORs and confidence intervals against CFI revealed that the significance of associations between muscle density and fractures were preserved only for CFI values less than 0.13. Above this value, confidence intervals overlapped 1.0 (Figure 1). For CFI ≤ 0.13, the association between CFI and each of muscle density (p=0.023) and mass were significant (p<0.001) but weak (R² < 0.03). For CFI values above 0.13, these relationships were not present.

Conclusions: Muscle density and muscle mass are associated with a history of fragility fractures independent of frailty for those who were less frail (CFI ≤ 0.13). For those who are frailer, muscle density and muscle mass did not associate with fractures.

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STRUCTURAL AND FUNCTIONAL INVESTIGATION OF GASTROCNEMIUS MUSCLE AND LUMBAR 5 OF SENESENCE-ACCELERATED MOUSE P8 (SAMP8) – A MUSCULOSKELETAL SENESENCE MODEL FOR SARCOPENIA RESEARCH

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Objective: Sarcopenia is an age-related systemic syndrome characterized by a progressive loss of skeletal muscle mass and muscle strength as well as a poor physical performance. Previous studies also suggested that sarcopenia might be associated with low bone mineral density (BMD). A good animal model is needed to explore the mechanism of sarcopenia and its relationship with low BMD.

Methods: Senescence-accelerated mouse P8 (SAMP8) was selected as the animal model and the target muscle was gastrocnemius. Parameters were investigated at 6, 7, 8, 9, 10-month old (6 mice per timepoint). Functional outcomes were measured with ex vivo muscle functional test system (800A, Aurora Scientific Inc). H&E staining was performed for fiber cross-sectional area evaluation and ATPase staining for muscle fiber typing. BMD of L5 was measured with viva CT. Data analysis was done with one-way ANOVA followed by Tukey post-hoc test with p<0.05 as significant difference.

Results: The peak of muscle mass (MM) appeared in 7-month group and significant decrease was observed in 10-month group (-12.41%, p<0.01). Compared with 10-month group, the 8-month group showed the largest specific twitch force (SF0, 11.54%, p<0.01) and muscle cross-sectional area (MCSA, 6.4%), while the peak of specific tetanic force (SFT, 13.23%, p<0.05) appeared in 7-month group with the largest fatigue rate (34.5%, p<0.05). Though there was no significant change in muscle stiffness and muscle contractility in 8-month, it was still better than 10-month with a higher contraction speed (35.1%, p<0.05). Animals in month 8 showed the largest fiber cross-sectional area of type IIA (12.1%, p<0.05). Meanwhile, type IIB and type I showed a decreasing trend from 6-month to 10-month. From 6-month, BMD of L5 showed a continuous decreasing trend (-10.39%).

Conclusion: Sarcopenia is defined by the decline of muscle mass and muscle strength and is divided into pre-sarcopenia, sarcopenia and severe sarcopenia stages by the onset of decreased muscle mass, muscle strength and quality of life. Based on this criteria, our result suggested that sarcopenia started between 7 and 8-month in SAMP8 animals and the 8-month animals were at pre-sarcopenia stage and 10-month animals were at sarcopenia stage. The result also indicated that the bone loss occurred earlier than the reduction of skeletal muscle mass and muscle strength.