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IOF Regionals – 6th Asia-Pacific Osteoporosis Meeting

Poster Presentations

P100

MICRORNA-1187 INHIBITS OSTEOBLAST FUNCTIONS BY SUPPRESSING BMP-INDUCED ACTIN CYTOSKELETAL ORGANIZATION

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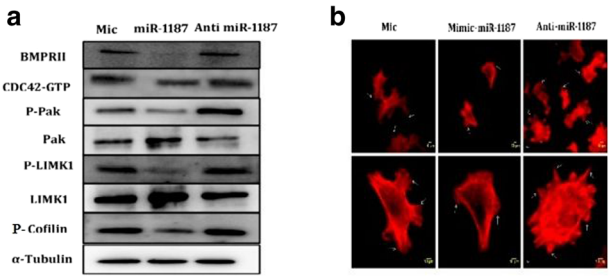
Aims: MicroRNAs (miRNAs) are small noncoding RNAs (approximately 22 nucleotides long) that have emerged as critical post-transcriptional regulators of gene expression. There is increasing evidence that miRNAs play an important role in osteoblast commitment and differentiation. The main aim of this study was to identify and characterize novel microRNAs regulating osteoblast functions. We report the role of mmu-miR-1187 in osteoblast differentiation and the mode by which it regulates osteogenesis.

Methods: MiRNA expression pattern in control and Medicarpin (Med) treated cells was analyzed by miRNA microarray and further validated by quantitative RT-PCR (qRT-PCR). Effect of mmu-miR-1187 on osteoblast differentiation and mineralization was validated by transfection of mmu-miR-1187 and its anti-miR in mice calvarial osteoblast cells using biochemical assays and qRT-PCR. Luciferase reporter gene assay was performed to confirm mmu-miR-1187 target. Protein expression levels were determined by western blotting and chemiluminescence. Further F-actin polymerization and cortical protrusion formation was analyzed using confocal microscopy.

Results: MicroRNA profiling of calvarial osteoblasts revealed that mmu-miR-1187 was ~8.5-fold downregulated in response to Med treatment. This data was further validated by qRT-PCR in calvarial osteoblasts. Overexpression of mmu-miR-1187 inhibited osteoblast differentiation, whereas inhibition of mmu-miR-1187 function promoted osteoblast differentiation and mineralization. Target prediction analysis tools and experimental validation by luciferase 3′ UTR reporter assay identified BMPRII as a direct target of mmu-miR-1187. Overexpression of mmu-miR-1187 in osteoblasts led to downregulation of BMP-2 induced and cdc42 mediated actin cytoskeletal organization. All these results were reversed on transfection with anti-miR-1187. Additionally, after visualizing actin with TRITC-conjugated phalloidin, it was revealed that over expression of anti-miR-1187 resulted in increased actin polymerization and cortical protrusions formation.



Conclusion: Our data suggest that binding of mmu-miR-1187 represses BMPRII thus inhibiting BMP2 signalling pathway which is required to activate cdc42 and phosphorylate LIMK1. LIMK1 is not able to inactivate cofilin which is an actin depolymerizing factor. Mmu-miR-1187 may thus be inhibiting osteoblast functions by suppressing actin polymerization. Our findings suggest that therapeutic approaches targeting mmu-miR-1187 for enhancing osteoblast functions may be useful.

P101

THE HISTOLOGICAL STRUCTURE OF THE LOWER INCISOR IN RATS OF VARIOUS AGES AFTER APPLYING PERFORATED TIBIAL DEFECTS

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Aims: To analyze histological structure of the lower incisor in rats of various ages after applying perforated tibial defects and finding possibility of medication with quercetin.

Methods: The experiment involved 252 male rats (young, adult, and senile): the 1st control group; the 2nd group - animals with 2.2 mm defect in the both tibiae; the 3rd group animals with defect in the tibia that received *per os* quercetin in dosage of 0.32 g/kg daily. The animals were withdrawn from the experiment by the 7th, the 15th, the 30th, and the 90th day after applying tibial defects by means of anaesthetized decapitation. Cross-sections of the lower incisor sampled as a segment next to the second molar tooth were HE stained. Morphometry included measurements of odontoblast layer (OL), predentin (PD), and mature dentin and mesiodistal size (MDS) (V. Luzin, 2011).
Results: A plain defect in the tibia had inhibiting effects on activities of odontoblasts. In young rats peak of alterations was registered by the 7th day for OL, by the 15th day for PD and by the 30th day for MDS where were narrower than of controls by 6.16 %, 7.62 % and 5.06 %. In adult rats peak of alterations was registered by the 30th day when OL, PD and MDS were narrower than of controls by 6.83 %, 6.54 % and 3.68 %. And in senile animals peak of alterations was registered by the 90th day when OL, PD and MDS were narrower than of controls by 7.67 %, 7.94 % and 4.87 %. Restoration of registered alterations also depended on age of experimental animals: in young rats by the 90th day after applying perforated tibial defects significant differences from the control values some differences were still observed, in adult rats in the same period most differences were still observed, and in senile rats histological structure of the lower incisor did not restore. Application of quercetin in dosage of 0.32 g/kg of body weight daily significantly reduced negative effects of experimental conditions on structure of lower incisor. Maximum value gap between the 3rd and the 2nd groups in young and adult rats were observed by the 30th day: OL, PD and MDL were wider than those of the 2nd group by 4.52 %, 3.88 % and 3.15 %, and 4.52 %, 3.88 % and 3.15 %, respectively. In senile rats maximum value gap was observed on 90th day: OL, PD and MDL were wider than those of the 2nd group by 5.78 %, 5.75 % and 4.43 %.
Conclusion: A plain defect in the tibia had inhibiting effects on morphofunctional activities of lower incisor odontoblasts. Deviations degree and recovery rate depend on age of animals. Faster recovery rate was observed in young animals while old animals exhibited few signs of recovery. Application of quercetin in dosage of 0.32 g/kg of body weight reduced negative effects of experimental conditions on structure of lower incisor.

P102
COMBINATION OF METFORMIN AND SEVERE HYPERTHERMIA ACTIVATES BAX/BID-DEPENDENT APOPTOSIS IN OSTEOSARCOMA CELLS IN VITRO

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Aims: Metformin used in type 2 diabetes treatment exerts its anticancer effects by inhibiting glucose metabolism. Meanwhile, hyperthermia sensitizes cancer cells. It is known that both metformin and hyperthermia deregulate mitochondrial metabolism in cancer. However, if there is a possible additive effect is not known. Targeting the Warburg effect, we investigated the combined effect of metformin and hyperthermia on osteosarcoma cell viability, DNA damage, glucose metabolism, regulation of apoptotic genes and proteins.
Methods: Osteosarcoma (MG-63) cells were treated with metformin IC_{50} 30 M (clinically relevant) for 48 h followed by exposure to moderate (39 °C) and severe (45 °C) hyperthermia for 2 h meanwhile 37 °C served as control. DNA damage was accessed by comet assay. The type of cell death was determined via annexin V-FITC and PI staining. Gene and protein expression of AKT1 & GSK3β (glucose metabolism), DR5, Bax, Bid, Bcl-2, AIF, cytochrome c, Apaf1, Caspase 8, 9 & 3 (apoptosis) were measured using real-time PCR and ELISA.
Results: The combination of metformin and hyperthermia significantly downregulated the expression of AKT1 and GSK3β, which in turn led to a reduction in cell viability and an increase in DNA damage. Metformin induced apoptosis (57.9 ± 1.2 %) and necrosis (18.8 ± 1.2 %) while the combination with 45 °C significantly reduced necrosis (0.23 ± 0.08 %) and increased apoptosis (92.1 ± 5.6 %). The combined effect caused an upregulation of DR5, Bax, Bid found upstream of mitochondrial signalling molecules and a downregulation of antiapoptotic Bcl-2. The intrinsic pathway was not activated as the expression of AIF and cytochrome c was downregulated. Although Apaf-1 upregulated caspase 9, caspase 3 remained downregulated.
Conclusion: This study suggests that the combination of metformin with hyperthermia particularly at 45 °C, enhances apoptosis via Bax/Bid-dependent pathway. This pathway is either directly p53-mediated or through direct activation of caspase 7.
Acknowledgement: This study was fully funded by the Fundamental Research Grant Scheme (FRGS) under the Malaysian Ministry of Higher Education (MOHE) (600-RMI/FRGS 5/3(109/2013).

P103
ASSOCIATION BETWEEN OSTEOCALCIN AND CORONARY CALCIUM SCORE IN KOREAN ADULTS

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Aims: The relationship between bone metabolism and atherosclerosis has not been well known. However, recent studies suggested that both entities share common physiological mechanisms. There was a study that serum osteocalcin was associated with risk of coronary heart disease in Chinese adults. The purpose of this study was to assess whether serum osteocalcin levels were associated with coronary calcium score in Korean adults.
Methods: A total of 315 subjects (44 with significant coronary artery stenosis and 271 without significant stenosis) who underwent coronary CT and serum osteocalcin at the same time were included in this study. Coronary calcium score was determined by coronary CT and using software program. Severity of atherosclerotic stenosis was estimated by number of significant stenotic vessels.
Results: Calcium score was significantly higher in the stenosis group (230.0 ± 355.9) than in the non stenosis group (18.5 ± 52.5) and was inversely associated with serum osteocalcin by regression analysis ($\beta = -3.63$, $p = 0.003$).
Conclusion: Our data suggested that serum osteocalcin levels were significantly associated with coronary calcium score in Korean adults.

P104
ESSENTIAL ROLES OF C-C CHEMOKINE-MEDIATED SIGNALING IN MATURE OSTEOCLAST FUNCTION

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Aims: A G-protein-coupled receptor, CCR5 is a coreceptor of HIV cell entry. Epidemiological and pathological findings have reported that functional changes in CCR5 correlate with bone destruction diseases as well as HIV transmission. However, pathophysiological roles of CCR5 in bone metabolism have not been well documented. We experimentally assessed bone morphology and metabolism in CCR5-deficient (*Ccr5*−/−) mice.
Methods: We first analyzed bone phenotypes in *Ccr5*−/− mice, and then applied a RANKL-induced bone loss model to *Ccr5*−/− mice and their wildtype littermates. Femoral bones obtained from male mice of these two genetic backgrounds at 8 weeks of age were analyzed by μCT and histomorphometrical analyses. To further elucidate the roles of CCR5 in osteoclastogenesis in vitro, we generated *Ccr5*−/− and wildtype osteoclasts from bone marrow macrophages in the presence of M-CSF and RANK, and compared their functions. We also took integrative approaches of proteomics (MS-based phosphoproteomics, LC-MS/MS) and transcriptomics (RNA sequencing) to identify CCR5-mediated molecular mechanisms in osteoclast function.
Results: *Ccr5*-deficient bone had significantly increased osteoclasts number, although they did not show difference in BMD compared to their wildtype littermates, indicating dysfunction of *Ccr5*-deficient osteoclasts in vivo. Interestingly, in histological bone sections, *Ccr5*-deficient osteoclasts were observed to be flattened in shape with covering wider bone surface compared to those in wildtype. Furthermore, *Ccr5*-deficient mice were less susceptible to RANKL-induced bone loss model. *Ccr5*-deficient osteoclasts in vitro showed decreased bone resorption activity accompanied with disorganized cellular architecture and impaired motility, supporting in vivo findings. Multimodal and multidimensional super-resolution microscopy facilitated to observe irregular microtubule network and disorganized podosome arrangement in *Ccr5*−/− osteoclasts, suggesting malfunctions in cell polarity, adhesion and locomotion. Molecular analyses suggested that CCR5-mediated signaling, with cooperating with RANKL-mediated signaling, regulated small GTPases, thus controlling cellular architecture and motility of differentiated osteoclasts. Lastly, blockades of human CCR5-mediated signaling by anti-hCCR5 neutralizing antibody obviously inhibited human osteoclastogenesis with disorganized podosomes as was observed in mouse *Ccr5*−/− cells, whereas this antibody treatment did not affect human osteoblast differentiation.
Conclusion: Our findings uncovered critical roles of CCR5-mediated signaling in osteoclast function and a pathological bone destruction model, which could be at work in human cases.

P105
VITAMIN D STATUS AND ITS ASSOCIATION WITH PARATHYROID HORMONE CONCENTRATIONS IN A REPRESENTATIVE POPULATION IN RIYADH, SAUDI ARABIA

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Aims: There is a lack of large-scale studies on vitamin D status and its relationship to PTH in adults living in Riyadh Saudi Arabia. The objectives were to determine vitamin D statues in adults living in Riyadh and to investigate the relationship of 25(OH)D with parathyroid function in order to determine the threshold for plasma 25(OH)D above which there is no further suppression of PTH.

Methods: This cross-sectional study involved 373 men and 720 women aged 50.7 ± 13.9 y who randomly sampled from Riyadh. Serum concentrations of 25(OH)D, PTH, calcium and albumin were measured.
Results: Prevalence of vitamin D insufficiency (25–50 nmol/) was 57 % in males and 42 % in females. The prevalence of vitamin D deficiency (<25 nmol/L) was 72 % in males and 27.5 % in females. With increasing serum 25(OH)D concentrations mean PTH gradually decreased in both sexes ($p < 0.001$).
Conclusion: There was an inverse relationship between the serum 25(OH)D and PTH concentrations in both genders, but no threshold of 25(OH)D at which PTH levels plateaued was observed.

P106
LACTOBACILLUS ACIDOPHILUS INHIBITS BONE LOSS IN OSTEOPOROTIC MICE BY MODULATING TH17-TREG CELL BALANCE

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Aims: The intestinal gut microbiota (GM) plays an important role in the host immune system. Perturbed microbial composition of the gut has been postulated to be involved in a range of inflammatory conditions including inflammatory bowel diseases, rheumatoid arthritis, multiple sclerosis, diabetes, etc. The GM affects the host's immune status and it is now well established that there is a connection between the immune system and bone metabolism, suggesting that the GM might affect bone metabolism via altered immune status of the host. One of the most important but often neglected bone disease associated with aging and postmenopausal condition is osteoporosis. Earlier reports have suggested that probiotics can increase bone mass and help reduce osteoporosis by different ways but the exact mechanism of the same is still unclear. Thus to delineate the mechanism of action of probiotics on bone metabolism via the host immune system, we selected *Lactobacillus acidophilus* strain (no study done so far) for studying its effect on bone health in ovariectomy (ovx) induced osteoporotic mice model.
Methods: In the present study postmenopausal osteoporotic mice model was used. Mice were divided into three groups viz. 1. Sham, 2. Ovx and 3. Ovx + *L. acidophilus* with each group containing not less than 10 mice. After 6 weeks of *L. acidophilus* administration (oral) mice were sacrificed and analysed for various parameters to access the role of *L. acidophilus* on bone health by using various cutting edge technologies such as μCT, AFM, SEM, FACS, ELISA, qPCR, etc.
Results: In the present study we found that administration of *L. acidophilus* protected mice from ovx-induced bone loss which was confirmed by μCT, atomic force microscopy and SEM analysis of bone samples. Both the cortical and trabecular bone content of *L. acidophilus* administered group was significantly higher than control groups. Interestingly the percentage of osteoclastogenic Th17 cells in lymphoid organs (bone marrow, spleen, lymph nodes, etc.) were significantly enhanced, whereas the number of anti-osteoclastogenic regulatory T cells (Treg) were significantly reduced in ovx groups, thereby resulting in enhanced bone loss. Interestingly the *L. acidophilus* administered groups had decreased percentage of Th17 cells but enhanced number of Treg cells. The serum cytokine analysis further supported our data with a significant decrease in proinflammatory cytokines (IL-6, TNF-α) and increase in anti-inflammatory cytokines (IL-10, IFN-γ) in *L. acidophilus* administered groups.
Conclusion: Thus we propose for the first time that the inhibitory effect of *L. acidophilus* on bone mass is mainly mediated via its effects on the Treg-Th17 axis, which in turn regulates osteoclastogenesis, thereby validating the use of probiotics as possible novel therapeutics for the treatment of various inflammatory conditions such as RA, osteoporosis to name a few.
Acknowledgement: UGC-FRPS, Govt. of India for financial support and Dept. of Zoology, DHGSU for infrastructural facilities.

P107
SEVERE VITAMIN D DEPLETION CAUSING BILATERAL QUADRICEPS TENDON RUPTURE DUE TO SECONDARY HYPERPARATHYROIDISM

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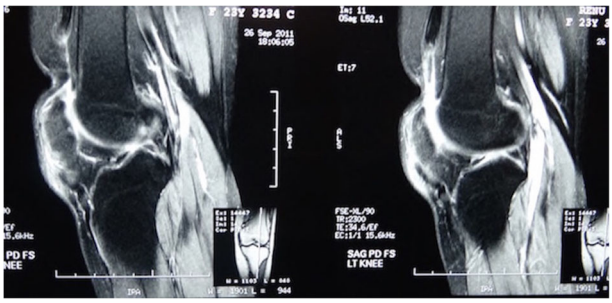
Aims: To highlight a very rare complication of a very common disorder. Severe vitamin D deficiency and consequent secondary hyperparathyroidism leading to bilateral quadriceps tendon rupture is extremely rare and is likely to be missed, hence we thought of presenting this case.
Methods: A 24 years old young lady presented with pain, swelling and difficulty in walking following a minor fall in bathroom 6 weeks ago.
Results: Examination: Height 155 cm, weight 51 kg, atrophy of the quadriceps muscles and gaps in bonding places of the tendons to the patella (palpable soft tissue depression proximal to the superior pole of the patella) were observed. Anteroposterior and lateral X-rays of both knees showed inferior displacement of the patella; which were not fractured and there was no calcium deposit in the quadriceps tendon. CBC, renal and liver functions were normal except a slightly raised serum alkaline phosphatase. Urine examination was

normal. MRI: complete thickness tear in quadriceps tendon with step defect in overlying soft tissue at this level. Repair of bilateral quadriceps tendon with reconstruction of extensor apparatus was done. Three years later she presented with severe pain in both the knees and shins. She had generalized muscle weakness. There was no H/O trauma, urolithiasis, deformities, fractures, dental problems. CBC, renal functions were normal. Serum alkaline phosphatase: 574(24–78), T4: 4.2, TSH: 25, B12: 172, 25OHD3: 3.1 ng/ml, PTH: 1166 pg/ml, calcium: 8.2, Phos: 2.4, albumin: 4.0. Radiology: x-ray knees, bony flake related to quadriceps tendon bilaterally. Bilateral pseudofractures, serial x-rays revealed healing of these fractures. USG neck: B/L parathyroids enlarged, heterogeneous echotexture. MIBI scan: no sestamibi avid lesion.



Conclusion: Unlike the other cases published in the literature, a young female patient had spontaneous and simultaneous quadriceps tendon rupture related with hyperparathyroidism secondary to vitamin D deficiency. S. PTH >500 pg/dL is significantly seen in all these cases. Bilateral simultaneous quadriceps tendon rupture is a rare pathology and the rate of misdiagnosis is high. Good results would be achieved with early diagnosis and an appropriate physical therapy program. Vitamin D depletion leading to quadriceps tendon rupture has not been reported from India. It usually occurs in males in middle age and is usually unilateral. It is mostly seen in people with chronic metabolic disease or those who are involved with strenuous physical activity. None of these were present in our case.

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P108
VITAMIN D LEVELS IN PATIENTS WITH ACUTE CORONARY SYNDROME

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Aims: To evaluate vitamin D levels in patients with acute coronary syndrome (ACS) and correlate it with vitamin D levels in patients without ACS. Other aim was to compare the relationship between persons with and without ACS and cardiometabolic risk factors among which in our opinion the vitamin D belongs as well.
Methods: 52 patients with ACS and 46 controls were examined. Levels of 25(OH) D2 + D3 were tested by electrochemiluminescence immunoassay (ECLIA). Results were evaluated by nonparametric tests such as Mann–Whitney test, interquartile range and Fischer exact test.
Results: Normal vitamin D levels were found in 11.54 % patients in a group with ACS and 19.54 % in healthy controls. 34.62 % of patients in the ACS group and 23.91 % in the control group had severe deficiency of vitamin D. Average level of vitamin D was 45.06 nmol/l in the group with ACS and 53.28 nmol/l in the control group. Statistically significant difference in vitamin D levels between both groups was found only at significance level $p=0.1$. Significant difference in vitamin D levels $p= 0.001$ was confirmed between women with ACS and women in control group and between men and women in the group with ACS. No other statistically significant difference was found in monitored groups.
Conclusion: We confirmed statistically significant difference of vitamin D levels depending on gender and in women with and without ACS. We confirmed also higher incidence of ACS in women with severe deficiency of vitamin D.

P109
HISTOLOGICAL STRUCTURE OF LOWER INCISOR IN RATS OF DIFFERENT AGES AFTER 60-DAY INHALATION OF TOLUENE VAPORS

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Aims: To study histological structure of lower incisor in rats of different ages after 60-day inhalation of toluene vapours and administration of thiotriazoline and *Echinaceae tinctura* as medication.
Methods: The study involved 420 male rats of three ages (young, adult and old). The animals were split into the groups: 1st group comprised control animals, the 2nd group comprised the animals that received inhalations of toluene vapours in dosage of 10 MPC as a single 5-h exposure per day, 3rd group - inhalations of toluene vapours and intraperitoneal thiotriazoline in dosage of 117.4 mg/kg, 4th group - inhalations of toluene vapours and intragastric *E. tinctura* in dosage of 0.1 mg of active substance per 100 g of body weight. After toluene vapours discontinued, cross-sections of the lower incisor sampled as a segment next to the second molar tooth

were HE stained. Morphometry included measurements of odontoblast layer, predentin, and mature dentin and mesio-distal size (V. Luzin, 2011).

Results: By the 1st day upon toluene vapours discontinued, width of odontoblasts layer, predentin layer, dentin layer and mesio-distal size in young rats were lower than that of the controls (1st group) by 11.93 %, 8.54 %, 8.18 % and 10.70 %. In mature rats all the values listed were lower by 10.14 %, 9.33 %, 7.62 %, and in old rats 9.75 %, 7.05 % and 4.65 %. In readaptation period after toluene vapours discontinue, alterations gradually restored by the 30th day, in adult animals alteration persisted up to the 60th day, and in old animals restoration of the cartilage was not observed. After administration of thiotriazoline, restoration of dentin structures in young rats was registered from the 1st to the 60th day, in adult rats from the 1st to the 60th day, and in old rats from the 7th to the 60th day. After administration of *E. tinctura,* positive effects in young and adult rats were observed from the 7th to the 60th day and in old rats from the 15th to the 60th day.

Conclusion: 60-day inhalation of toluene vapours results in inhibition of functional activities of dentin secreting structures of the lower incisor. Restoration of dentin structure well depended on age of animals. Young animals exhibited faster restoration while in old animals such manifestations were scarce. Administration of thiotriazoline or *E. tinctura* resulted in restoration of structure of the lower incisor. Thiotriazoline appeared to be more effective than *E. tinctura.*

P110

LUPEOL ACETATE AMELIORATES COLLAGEN-INDUCED ARTHRITIS AND OSTEOCLASTOGENESIS OF MICE THROUGH IMPROVEMENT OF MICROENVIRONMENT

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Aims: Lupeol has been shown with anti-inflammation and antitumor capability. However, the poor bioavailability limiting its applications in living subjects. Lupeol acetate (LA), a derivative of lupeol, shows similar biological activities as lupeol but with better bioavailability. Here RAW 264.7 cells and bone marrow derived macrophages (BMDMs) stimulated by lipopolysaccharide (LPS) were treated with 0–80 mM of LA, and assayed for TNFα, IL-1β, COX-2, MCP-1 using western blotting. Moreover, osteoclastogenesis was examined with reverse transcription PCR (RT-PCR) and tartrate-resistant acid phosphatase (TRAP) staining.

Methods: For in vivo study, collagen-induced arthritis-bearing DBA/1 J mice were randomly separated into three groups: vehicle, LA-treated (50 mg/kg) and curcumin-treated (100 mg/kg). Therapeutic efficacies were assayed by the clinical score, expression levels of serum cytokines including TNFα and IL-1β, 18 F-fluorodeoxyglucose (18 F-FDG) μPET/CT and histopathology.

Results: The results showed that LA could inhibit the activation, migration, and formation of osteoclastogenesis of macrophages in a dose-dependent manner. In RA-bearing mice, the expressions of inflammation-related cytokines were suppressed, and clinical symptoms and bone erosion were ameliorated by LA. The accumulation of 18 F-FDG in the joints of RA-bearing mice was also significantly decreased by LA. The results indicate that LA significantly improves the symptoms of RA by downregulating expressions of inflammatory cytokines and osteoclastogenesis.

Conclusion: LA suppresses the progression of RA by inhibiting the activation of macrophages and osteoclastogenesis through downregulations of TNFα, IL-1β, MCP-1, COX-2, VEGF and granzyme B. LA may have the potential as an alternative medicine for anti-rheumatoid arthritis in clinic. Furthermore, the 18 F-FDG PET/CT imaging modality not only benefits the assessment of inflammatory activity, but also substantially impacts on the development and the outcome prediction of new treatments in RA.

P111

NAMPT SERVES AS AN APPLICABLE MARKER FOR OSTEOBLAST DIFFERENTIATION OF BONE MARROW-DERIVED MESENCHYMAL STEM CELLS

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Aims: To study whether the nicotinamide phosphoribosyltransferase (Nampt) will be able to regulate the osteogenic differentiation of primary murine bone marrow-derived mesenchymal stem cells (MSCs).

Methods: MSCs were obtained by the whole bone marrow adherent culture, and then the surface markers were analyzed by using flow cytometry. The expression of Nampt during MSCs osteogenic differentiation was detected by western blot and qRT-PCR. The suppression of Nampt was achieved by pharmaceutic inhibition and gene silencing. Nampt inhibitor FK866 was used and Nampt deficient MSCs were generated by transfecting with Nampt shRNA lentiviral transduction particles. ALP activity was quantified by phosphatase substrate kit and matrix mineralization was indicated by alizarin red S staining. Specific markers for osteoblasts were further examined by qRT-PCR. Sirt1 deacetylase activity was measured by fluorometric SIRT1 assay kit and the intracellular

NAD concentration was examined with NAD +/NADH quantification kit.

Results: MSCs displayed fibroblast-like morphology, which were positive for CD29, CD44 and CD90, but negative for CD34 and CD45. During MSCs osteogenic differentiation, Nampt expression at both protein and mRNA levels was progressively elevated. Nampt inhibitor FK866 or knockdown of Nampt in MSCs led to the declined osteoblastogenesis, including attenuated ALP activity, diminished bone matrix mineralization and downregulated osteoblast specific marker genes. In addition, declined osteoblastogenesis by Nampt deficiency or addition of FK866 was related to the lower intracellular NAD concentration and decreased Sirt1 activity.

Conclusion: Taken together, the present findings demonstrate that osteogenic differentiation in MSCs can be modulated by intracellular NAD metabolism, in which Nampt may serve as an applicable marker for the osteoblast determination.

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P112

ASSOCIATIONS BETWEEN APPENDICULAR SKELETAL MUSCLE MASS AND ANTHROPOMETRIC MEASURES AMONG MIDDLE-AGED WOMEN: A STUDY IN SOUTHERN SRI LANKA

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Aims: This study investigated the association between anthropometric measures and appendicular skeletal muscle mass (ASMM) among middle-aged women in order to find a suitable formula to predict the ASMM.

Methods: A cross-sectional study was conducted in Galle, southern Sri Lanka with 197 healthy women aged 30–60 y. ASMM (skeletal muscle mass of all four limbs) was measured with DXA scanner (Hologic Inc, Bedford, MA, USA). Body weight (BW), height, skin-fold thicknesses over biceps (BSF), triceps (TSF), thigh (ThSF), calf (CSF), anterior superior iliac spine (ASISSF), subscapular area (SSSF), circumferences at mid-upper arm (MUAC), thigh (TC), calf (CC), waist (WC) and hip (HC) were measured adhering to the standard protocols. Correlations between ASMM and anthropometric measures were determined by Pearson correlation. Linear regression model was fitted with ASMM as the dependent variable and all anthropometric measures as independent variables. Weak associations were excluded by stepwise manner (backward) to find the strongest anthropometric predictor of ASMM.

Results: Mean(SD) age of the sample was 45.5(8.14) y. Mean(SD) ASMM was 15.64(2.64) kg. ASMM showed significant correlations (r) with all the anthropometric measurements; with BW = 0.88 (<0.001), WC = 0.69 (<0.001), HC = 0.74 (<0.001), height = 0.52 (<0.001), TSF = 0.22 (<0.001), SSSF = 0.43 (<0.001), BSF = 0.45 (<0.001), UAC = 0.48 (<0.001), ASISSF = 0.19 (0.003), TC = 0.41 (<0.001), CSF = 0.27 (<0.001), ThSF = 0.24 (<0.001), CC = 0.33 (<0.001). In the regression analysis, BW emerged as the strongest predictor of ASMM. The predictive equation developed for ASMM using anthropometric measurement: $ASMM = 2.636 + 0.227(BW)$ ($R^2 = 0.775$, SEE = 1.255, p = <0.001).

Conclusion: This study shows that ASMM is related to all selected anthropometric measures although body weight is the strongest predictor of ASMM of these middle-aged women. The regression equation shown can be used to predict the ASMM using the BW.

Acknowledgement: Faculty Research Grant, Faculty of Medicine, University of Ruhuna, Sri Lanka and National Research Council, Sri Lanka for funding this study.

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AGE-RELATED DIFFERENCES IN LEAN MASS AND PHYSICAL FUNCTIONS AMONG MIDDLE-AGED WOMEN IN SOUTHERN SRI LANKA

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Aims: To investigate the age-related differences in lean mass and physical functions among middle-aged healthy women in Sri Lanka.

Methods: A cross-sectional study was conducted in Galle, Sri Lanka with 204 healthy women aged 30–60 y. Total lean mass (TSMM), appendicular lean mass (ASMM), upper limb lean mass (ULSMM) and lower limb lean mass (LLSMM) were measured with DXA Scanner (Hologic Inc, Bedford, MA, USA). hand grip strength (HGS), gait-speed (GS), time taken for time get up go test (TGUG) and time taken for five repeated chair stands (RCS) were also measured. Appendicular lean mass index (ASMI) was calculated by dividing the ASMM by height square (kg/m^2).

Results: Mean age (SD) of the total sample was 45.3 (8.1) y. Women were categorized to 6 age groups (5-year gaps); Gp1: 30-35(n = 27), Gp2: 36-40(n = 40), Gp3: 41-45(n = 41), Gp4: 46-50(n = 40), Gp5: 51-55(n = 30), Gp6: 56-60(n = 26).

Mean(SD) of skeletal muscle mass and physical function measures from Gp 1 to 6 were as follows:
TSMM = 34.77(4.29), 35.99(4.40), 36.06(4.57), 34.59(5.17), 43.00(5.79), 33.82(5.31)
ASMM = 15.72(2.23), 16.38(2.46), 16.29(2.46), 15.35(2.80), 14.84(2.90), 15.07(2.83)
ULSMM = 4.69(0.92), 4.80(0.91), 4.73(0.82), 4.52(1.06), 4.42(1.08), 4.38(1.16)
LLSMM = 11.02(1.42), 11.58(1.63), 11.56(1.72), 10.89(1.81), 10.42(1.91), 10.68(1.77)
ASMI = 6.78(0.90), 6.95(0.87), 7.00(0.95), 6.69(1.10), 6.59(1.01), 6.65(1.04)
GS = 1.18(0.14), 1.26(0.12), 1.25(0.20), 1.19(0.19), 1.13(0.12), 1.16(0.21)
HGS = 19.86(6.48), 19.37(6.40), 19.63(5.52), 18.20(5.76), 14.56(5.19), 17.03(4.08)
RCS = 15.11(2.27), 14.07(2.21)), 14.66(2.81), 16.71(3.29), 15.49(2.79), 15.19(4.42)
TGUG = 8.45(1.62), 8.36(1.24), 8.76(1.73), 9.61(1.94), 9.60(1.65), 9.88 (2.67)
LLSMM was significantly different between age groups ($p = 0.029$) and other lean mass measures were not significantly different ($p > 0.05$). All the tested physical function measures were significantly different between the age groups ($p = 0.012$ for GS), ($p = 0.001$ for HGS), ($p = 0.007$ for RCS) and ($p = 0.004$ for TGUG).
Conclusion: No significant change of lean mass occurs in healthy community-dwelling women aged between 30–60 y. Physical functions, however, decline with advancing age and the reason for this is unclear.
Acknowledgement: Faculty Research Grant, Faculty of Medicine, University of Ruhuna, Sri Lanka and National Research Council, Sri Lanka for funding this study.

P114
AGE-RELATED TRENDS IN TOTAL AND REGIONAL BONE MINERAL DENSITIES OF MIDDLE-AGED WOMEN IN SOUTHERN SRI LANKA

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Aims: This study investigated the total and regional BMDs among a group of community-dwelling healthy women in southern Sri Lanka as this information is not readily available.
Methods: For this cross-sectional study randomly selected 204 healthy women aged 30–60 y were recruited from Galle, southern Sri Lanka. Total body (TB), total spine (TS), total hip (TH) and femoral neck (FN) BMDs were measured with DXA scanner (Hologic Inc, Bedford, MA, USA). Prevalence of osteoporosis/osteopenia among postmenopausal women was determined according to the WHO criteria based on T-scores of lumbar spine, FN or TH, calculated using Asian reference data.
Results: Mean (SD) age of the total sample was 45.3 (8.1) y. There were 147 (72.1 %) pre- and 57 (27.9 %) postmenopausal women in the study sample. Women were categorized to 6 age groups (5 year gaps); Gp1: 30-35(n = 27), Gp2: 36-40(n = 40), Gp3: 41-45(n = 41), Gp4: 46-50(n = 40), Gp5: 51-55(n = 30) and Gp6: 56-60(n = 26). Mean(SD) TB BMD, TS BMD, TH BMD and FN BMD of Gp1 to 6 were as follows:
TB BMD = 1.017(0.064), 1.041(0.606), 1.051(0.093), 1.043(0.093), 0.978(0.112), 0.948(0.091)
TS BMD =0.848(0.072), 0.890(0.091), 0.875(0.117), 0.892(0.138), 0.809(0.145), 0.809(0.125)
TH BMD =0.879(0.072), 0.908(0.108), 0.908(0.110), 0.923(0.150), 0.872(0.143), 0.854(0.124)
FNBMD = 0.780(0.082), 0.803(0.103), 0.799(0.105), 0.800, (0.125), 0.755(0.121), 0.745(0.113)
Only TB ($p = <0.001$) and TS BMDs ($p = 0.006$) showed significant differences among the age groups. The prevalence of osteoporosis and osteopenia among the postmenopausal women were 31.6 % (18) and 45.6 % (26), respectively.
Conclusion: This study provides the total and regional BMDs of healthy middle-aged women in southern Sri Lanka. BMDs remain unchanged between 30–50 y and they all start declining after 50 y at all the skeletal sites measured.
Acknowledgement: Faculty Research Grant, Faculty of Medicine, University of Ruhuna, Sri Lanka and National Research Council, Sri Lanka for funding this study.

P115
SEXUAL AND RACIAL DIMORPHISM IN BONE MICROARCHITECTURE REQUIRES ADJUSTMENT OF THE REGION OF INTEREST FOR SKELETON DIMENSIONS

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Aims: Bone size, shape, and microarchitecture vary point by point around and along the length of a bone, especially at metaphyses, irregularly designed ends of long bones. Image acquisition using HR-pQCT is achieved by scanning fixed region of interest (ROI) without considering bone length. Given the heterogeneity in structure, sex and racial differences may be a consequence of measuring different regions rather than true differences in bone. To quantify sexual and racial differences in bone microarchitecture we examined effects of placement of the ROI to ensure anatomical identity was maintained by sex and race.

Methods: In 77 women (40 Asian and 37 Caucasian) and 85 men (37Asian and 48 Caucasian), age range 22–52 y, the distal part of nondominant radius was scanned using HR-pQCT. Images were analysed slice by slice using StrAx 1.0. Total vBMD and porosity of total and compact cortex were assessed using the standard-fixed method (110 slices) vs. a region of 4.3-6.2 % of the radius length before and after adjustment for total cross-sectional area (TCSA) of the ROIs.
Results: The standard-fixed method produced either no differences in porosity or higher porosity in males than females. After adjusting for bone length to ensure the same anatomical location, differences in porosity either disappeared or reversed. However, when the standard-fixed or adjusted ROI was adjusted by total CSA, the same result was found; females had higher porosity than males in both races and there are no racial differences in men and women.
Conclusion: Differences in the relative to position of the ROI has biologically significant effects on cortical porosity which may result in erroneous reporting of age, sex and racial differences in this trait. Adjustment for total CSA is sufficient to correct for anatomical variation in the ROI in persons with differences in radius length.
Disclosure of Interest: A. Ghasem-Zadeh Patent licensing: One of the inventors of the StrAx1.0 algorithm, R. Zebaze Grant/research support from: Amgen, Merck Sharp & Dohme, Servier, Warner-Chilcott, AKP, Genzyme, Sanofi, Other Conflict with: Director and shareholder in StraxCorp, is remunerated by StraxCorp as president of R&D, and is one of the inventors of the StrAx1.0 algorithm. No financial compensation was derived from this work, E. Seeman Grant/research support from: Amgen, Allergen, Asahi, Genzyme and Warner Chilcott, Consultant/speaker's bureau/advisory activities: Lectured at national and international meetings funded by Allergan, Asahi, Amgen and Merck Sharp and Dohme, Other Conflict with: Director of the board and shareholder in StraxCorp, is remunerated by StraxCorp as Chief Medical Officer, and is one of the inventors of the StrAx1.0 algorithm. No financial compensation was derived from this work.

P116
LUMBAR MUSCLE LOSS IN POSTMENOPAUSAL WOMEN WITH OSTEOPOROTIC COMPRESSION FRACTURES: QUANTITATIVE MRI STUDY

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Aims: To investigate the relation of paraspinal muscle loss and osteoporotic/osteopenic lumbar compression fracture in postmenopausal women.
Methods: Subjects were divided into two groups. In group 1, 18 postmenopausal women who received lumbar MRI done the same day for acute compression fractures after falls were reviewed. In group 2, 14 postmenopausal healthy women who received lumbar MRI were reviewed. The cross-sectional areas (CSA) of paraspinal and psoas muscles were obtained using MRI at the lumbar intervertebral disc level. The CSA of multifidus and erector spinae muscles in the paraspinal muscles as well as psoas muscles were separately measured on the bilateral sides. The proportions of the multifidus, erector spinae and psoas muscles to the lumbar muscles (paraspinal and psoas muscles) were calculated by dividing each CSA of the muscles by the sum of the CSA of the paraspinal muscles and the psoas muscles. All values were normalized with BMIs.
Results: There were no significant differences in age and BMI between the two groups. CSA of erector spinae muscle and the proportion of the area to lumbar muscles (paraspinal and psoas muscles) at L3/4, L4/5, L5/S1 level in group 1 were significantly smaller than that of the group 2 (all $p < 0.05$). The mean value of CSA of multifidus muscle at L4/5, L5/S1 level in group 1 was significantly smaller than that of the group 2 (all $p < 0.05$). CSA of psoas muscles at L3/4 level and all values measured at all level were significantly different between the groups (all $p < 0.05$).
Conclusion: Postmenopausal women with osteoporotic/osteopenic lumbar compression fracture are associated with paraspinal and psoas muscle loss at the low lumbar level.

P117
PREVALENCE OF OSTEOPOROSIS AND LOW BONE MASS IN POSTMENOPAUSAL WOMEN WITH VERTEBRAL COMPRESSION FRACTURES

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Aims: Vertebral compression fractures in postmenopausal women are usually caused by osteoporosis. We aimed to determine the prevalence of osteoporosis and low bone mass in postmenopausal women who had compression fractures by using Asian and USA/Northern Europe reference population.
Methods: We conducted a retrospective study from 2010.02 to 2015.03 on 228 postmenopausal women who had undergone multiple-site BMD measurement by Lunar DXA within 24 months before compression fracture that the fractures were confirmed by lumbar MRI study. Subsequently, gender-specific lowest T-scores measured from multiple sites (lumbar, right and left hips) were calculated using the Asian and USA/Northern Europe reference population.
Results: The standardized prevalence of osteoporosis, low bone mass, and normal BMD in multiple sites from lowest T-score were 58.3 (81.6 %), 36.4 % (17.5 %) and 5.3 % (0.9 %) in T-score Asian (USA/Northern Europe) references, respectively. In subjects who had spine compression fractures,

osteoporosis was diagnosed at a higher rate if the USA/Northern Europe reference rather than the Asian reference was used to calculate the T-score from multiple skeletal sites. **Conclusion:** Our findings indicated that more than 40 % subjects with spine compression fractures were not classified in the osteoporosis category if the Asian reference was used. Thus, a more sensitive risk assessment USA/Northern Europe reference was recommended to screen and diagnose osteoporosis in Asia.

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CHANGES OF TYPE H VESSEL IN BONE FROM PATIENTS WITH OSTEOPOROTIC AND NONOSTEOPOROTIC HIP FRACTURE

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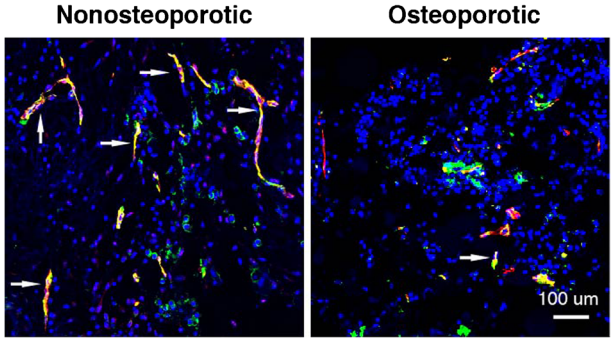
Aims: A recent study discovered a new capillary subtype in murine skeletal system, termed as type H vessel and strongly positive for both CD31 and Endomucin ($CD31^+Emcn^+$), coupled osteogenesis to angiogenesis[1–3]. The aim of this study is to confirm a special vessel subtype in human bone and explore the changes of the capillary in bone samples form patients with osteoporotic and nonosteoporotic hip fractures.
Methods: Postmenopausal patients with hip fracture were admitted to our clinic for surgery intervention and bone samples were collected during artificial joint replacement or proximal femoral nails by a special instrument. The patients aged from 60–70 y old (an average age of 64.30 ± 4.67 y) were divided into osteoporotic (N = 10) and nonosteoporotic groups (N = 10) based on BMD measured by DXA. Fresh bone specimens were washed by 0.9 % normal saline, fixed immediately by 4 % paraformaldehyde, decalcified by 0.5 M EDTA, dehydrated by 20 % sugar, embedded and made for slices for histological observation. For immunostaining, bone sections were incubated with primary antibodies and then fluorescein conjugated secondary antibodies. Difference of type H vessel in two groups was observed by confocal microscope.
Results: The patients in both groups have similar BMI (P = 0.9361). Blood routine examination and liver and kidney functions are normal (P > 0.05). There are significant differences in BMD and biochemical markers of bone metabolism (P < 0.0001). Our study established for the first time that type H vessel was found in human bone samples. What's more, the area of type H vessel in patients with osteoporotic fractures was less than nonosteoporotic fractures (9.28 ± 2.71 % vs. 23.12 ± 3.14 %). The area of type H vessel showed significantly different between two groups (t = 26.66, P < 0.0001).



Conclusion: Type H vessel is confirmed in human bone from hip fracture and remarkably decreases in osteoporotic patients, which suggests that there is correlation between type H vessel and BMD. That will provide a new target for prevention and treatment of osteoporotic fracture by promoting type H vessel formation.

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ASSOCIATION BETWEEN QUANTITATIVE ULTRASOUND AND FRAX® IN THE MIDDLE-AGED AND OLD COMMUNITY PEOPLE IN TAIWAN

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Aims: Quantitative ultrasound and FRAX® are both the convenient tools to evaluate the fracture risk. However, nearly none of the study had focused on the association between quantitative ultrasound and FRAX.
Methods: From March 2009 to February 2010, 1200 community-dwelling people (male/female = 524/676) 40 y old and over were collected by epidemiologically systemic sampling method in Yunlin County, mid-Taiwan. Structural questionnaires including socioeconomic status, living status, smoking and drinking habits, exercise and medical history were completed. Speed of sound (SOS) by quantitative ultrasound (QUS) at the nondominant distal radial area (QUS-R) and broadband under attenuation (BUA) by the left calcaneal area (QUS-C) were measured. FRAX score without BMD was calculated according to the Taiwan calculator. Continuous FRAX without BMD including major or hip score were analyzed as dependent variables.

Results: The correlation coefficients between major or hip FRAX without BMD and SOS by QUS-R were −0.38 and −0.37 ($p<0.01$), respectively. The correlation coefficients between major or hip FRAX without BMD and BUA by QUS-C were 0.41 and −0.39, respectively. In FRAX major scores without BMD, the SOS by QUS-R (OR: −0.30, 95%CI: −0.01 ~ −0.01, $p<0.01$) and BUA by QUS-C (OR: −0.35, 95%CI: −0.11 ~ −0.08, $p<0.01$) were negatively associated factors. In FRAX hip scores without BMD, the SOS by QUS-R (OR: −0.26, 95%CI: −0.01 ~ −0.00, $p<0.01$) and BUA by QUS-C (OR: −0.30, 95%CI: −0.06 ~ −0.04, $p<0.01$) were also negatively associated factors.

Conclusion: BUA or SOS derived from quantitative ultrasound were negatively associated with FRAX without BMD score in middle-aged and old people in Taiwan.

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Acknowledgement: We sincerely thank the Bureau of Health Promotion-Department of Health R.O.C (Taiwan) for the data authorization. We also sincerely thank Mr. Ting-Hsing Chao and the staff working at the health promotion center of the Dou-Liou branch of National Cheng-Kung University Hospital for administrative assistance.

P120
VITAMIN D STATUS IN POLYCYSTIC OVARIAN WOMEN: CASE–CONTROL STUDY

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Aims: Polycystic ovary syndrome (PCOS) is the commonest endocrine metabolic disorder in women of reproductive age, affecting between 5–18 % worldwide. PCOS is characterized by polycystic ovaries, hyperandrogenism, and chronic anovulation. The aim of this study was to evaluate 25-hydroxyvitamin D [25(OH)D], intact-PTH and BMD in Saudi women diagnosed with PCOS.

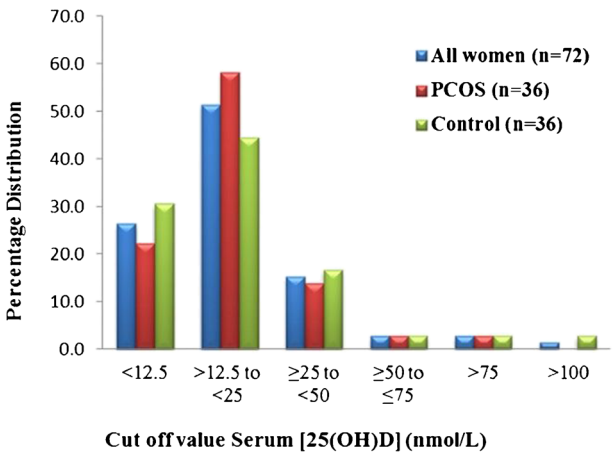
Methods: In a total of 72 Saudi women; 36 women with PCOS were matched with 36 healthy women (referred as control group) for their age and BMI. Each study group was stratified according to BMI into lean (BMI <30 kg/m^2) and obese (BMI ≥30 kg/m^2) subgroups. All participated women visited a special clinic in the Center of Excellence for Osteoporosis Research (CEOR), Jeddah, Saudi Arabia during the period March-July 2010. Blood samples were obtained for assessment of [25(OH)D]and PTH. BMD was measured by DXA at the lumbar spine (L1-L4) and mean femoral neck.

Results: The distribution frequencies for various [25(OH)D] cut-off levels are presented in Table 1 and Figure 1. Almost 90 % of studied women showed serum [25(OH)D]levels <50.0 nmol/L with only 7 % of all women (2.8 % PCOS and 4.2 % control women) were considered with adequate vitamin D status (i.e., serum [25(OH)D] ≥75.0 nmol/L). Serum [25(OH)D] and serum intact-PTH did not show significant differences between PCOS and control group or between lean and obese subgroups. There was an inverse relationship between [25(OH)D] and intact-PTH, in all studied women ($r^2=-0.381$, $P<0.001$), in PCOS women ($r^2=-0.351$, $P<0.005$) and in control group ($r^2=-0.404$, $P<0.005$). In the present study, women with or without PCOS did not show any significant differences in BMD values and T-score, at both lumbar spine (L1-L4) and femoral neck.

Table 1. Distribution of serum [25(OH)D] values according to different cutoffs among studied women.

Cutoff values of serum [25(OH)D] (nmol/L)	All women (n = 72)	PCOS (n = 36)	Control (n = 36)
<12.5	19 (26.4 %)	8 (22.2 %)	11 (30.6 %)
>12.5 to <25	37 (51.4 %)	21 (58.3 %)	16 (44.4 %)
≥25 to <50	11 (15.3 %)	5 (13.9 %)	6 (16.7 %)
≥50 to ≤75	2 (2.8 %)	1 (2.8 %)	1 (2.8 %)
>75	2 (2.8 %)	1 (2.8 %)	1 (2.8 %)
>100	1 (1.4 %)	–	1 (2.8 %)

Figure 1.



Conclusion: Vitamin D deficiency is rather highly prevalent among Saudi women, with or without PCOS. Future studies with larger sample size are needed to verify these outcomes.

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OSTEOPOROSIS SCREENING RECOMMENDATIONS VERSUS CLINICAL PRACTICE: DO WE NEED TO REVISIT AND REDEFINE OF FRAX-BASE THRESHOLDS AND FOREARM BONE MINERAL DENSITY UTILIZATION

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Aims: In clinical practice physicians are in need of simple but optimal screening guideline for osteoporosis. Well known US Preventive Services Task Force (USPSTF) missed three-quarters of women suffering from osteoporosis of 50–64 y. On the other hand, widely used assessment tools underestimate fracture risk as well. In such context, this study was aimed to observe the outcome of assessment tools in osteoporosis and forearm BMD status in patients <65 years of age.
Methods: A semistructured questionnaire was maintained for the clinically suspected patients of osteoporosis from January 15 to May 2016 in the private office of a tertiary care center at Dhaka, Bangladesh. A total 256 patients demographics, anthropometric, risk factors for osteoporosis and FRAX score were obtained. DXA at lumbar spine, hip and left forearm was performed in all cases. Age, menopause, BMI and FRAX were considered as screening modalities. Observation was made on age groups, i.e., subjects <65 y and >65 y. Determinants considered as risk factors were determined by univariate and multivariate analysis.
Results: Total study subjects were 256, male 26 female 230, mean age 69.5 ± 10.4 and 65.2 ± 8.7 y, respectively. 114 subjects were <65 y among them 10 male (age 59.3 ± 3.2 y) and 104 female (age 57.7 ± 4.7 y), BMI of all patients 24.3 ± 4.6 kg/m^2 and age at menopause 45.9 ± 4.7 y. Considering the FRAX treatment thresholds >20 % for major osteoporotic fracture (MOF) and >3 % for hip fracture in <65 age group, out of 114 subjects without and with BMD, FRAX able to identify 4 and 1 subjects for MOF respectively but in >65 years age group 41 and 32 subjects (p = <0.001) respectively, in hip without and with BMD, in <65 years group, 9 and 10 subjects respectively but in >65 years group 93 and 71 patients (p = <0.001) respectively. WHO definition of osteoporosis, osteopenia and normal BMD were observed in dual femoral neck mean (13.75 %, 55.5 % and 30.9 %) respectively, lumbar spine (L1-L4) total (44.3 %, 35.3 % & 20.4 %) respectively, and left radius total (78.5 %, 17.2 % and 4.3 %) respectively. The risk factor based screening modalities associated with forearm BMD were; BMI, OR = 0.85, CI (0.77-0.91) p = 0.00 and age at menopause, OR = 0.91, CI (0.83-0.99), p = 0.03.
Conclusion: In <65 years of age, FRAX treatment thresholds underestimate osteoporosis and additionally two sites (lumbar and hip neck) BMD also under diagnose the condition. Maximum cases of osteoporosis were identified by distal forearm BMD in clinically suspected situation in this series. The BMI and age at menopause may be better screening tools need to be evaluated in large sample. We recommend it is time to rethinking and redefine FRAX thresholds both for screening and treatment as well as forearm BMD for diagnosis of osteoporosis.

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OSTEOPOROSIS IN MONGOLIAN MEN

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Aims: To determine association between BMD and risk factors in Mongolian men.
Methods: Our study group is 627 men who are over 18 years and participated from Uvs, Arkhangai, Dundgovi, Sukhbaatar province and Ulaanbaatar. We have evaluated serum calcium, phosphorus, estradiol, PTH, calcitonin, 25-hydroxyvitamin D level and BMD via bone sonometer. Lifestyle risk factors were evaluated through a specific questionnaire.
Results: SOS was inversely correlated with age ($r = -0.247$, $p < 0.01$), estradiol ($r = -0.253$, $p < 0.01$), PTH ($r = -0.216$, $p < 0.05$). In contrast, SOS was correlated with weight ($r = 0.094$, $p < 0.05$). Serum concentration of 25-hydroxyvitamin D ranged from 7.85-154.89 ng/ml and 26.5 % were below 20 ng/ml (deficient), 35.3 % ranged from 20–29.9 ng/ml (insufficient) and 38.2 % were above 30 ng/ml (sufficient). Mongolian men's peak bone mass achieved between 36–45 years of age.
Conclusion: Compared to women osteoporosis, male BMD decreases gradually and aging is the main factor. In Mongolian men, age related changes in serum calcium level and calcium induced PTH elevation are determinant factor in decline of BMD.
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QUANTITATIVE COMPUTED TOMOGRAPHY BASED BONE MINERAL DENSITY AT L4 VERTEBRAL BODY IN 523 KOREAN FARMERS

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Aims: The standard diagnostic tool for osteoporosis is made based on DXA)(T-score ≤ −2.5). In computed tomography (CT), the trabecular regions of vertebral bodies expressed by Hounsfield units (HU) providing a source of information reflecting BMD. The purpose of this study was to determine association of L4 trabecular bone attenuation measurements at abdominal CT with BMD at DXA.
Methods: This was the cross-sectional study of the second wave of the Farmers' Cohort for FARM study (from October 2014 to March 2015). 523 Korean farmers were recruited: male 259 and female 264. Cross-sectional abdominal CT scan was acquired at the mid-L4 vertebral level. Lumbar trabecular bone attenuation was measured using an ovoid region-of-interest on the transverse series of abdominal CT (CT-TBMD, HU). BMD was also estimated by lumbar DXA (DXA-BMD, g/cm^3). Linear regression was performed to compare DXA-BMD and CT-TBMD results. The diagnostic performance for CT-TBMD was measured by the area under the receiver operator characteristics curve (AUC).
Results: Mean age of participants were 60.1 ± 7.4 y, of which 151 (28.9 %) had osteoporosis according to DXA. Mean value of CT-TBMD at L4 was 131.9 ± 49.7 HU (135.1 ± 48.4 HU for men and 128.8 ± 50.8 HU for women). DXA-BMD at L4 was 1.15 ± 0.20 g/cm^3 (1.19 ± 0.20 g/cm^3 for men and 1.10 ± 0.18 g/cm^3 for women). There was a significant association of DXA-BMD with CT-TBMD as dependent variable in linear regression analysis ($\beta = 0.513$, $P < 0.001$). We found an AUC was 0.785 (0.740-0.829).
Conclusion: We confirmed a significant association between trabecular vertebral density measurements at abdominal CT measured at L4 vertebral body and BMD at DXA, and found the good diagnostic performance of CT-TBMD.
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Acknowledgement: This study was supported by Research Grant for Kangwon Center for Farmers' Safety and Health from Korean Ministry of Agriculture, Food and Rural Affairs.

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HIGH PREVALENCE OF OSTEOPOROSIS AND MORPHOMETRIC VERTEBRAL FRACTURES IN INDIAN MALES AGED 60 YEARS AND ABOVE: SHOULD AGE FOR SCREENING BE LOWERED?

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Aims: Current guidelines recommend BMD measurement in asymptomatic men above age 70 years and vertebral fracture assessment above 80 years with T-score < −1.0 with risk factors. We studied the prevalence of osteoporosis and morphometric vertebral fractures (VF) in asymptomatic males aged 60 years and above in north India.
Methods: Free living community dwelling men (n = 241, mean age 68.0 ± 6.2 y) underwent a detailed history, physical examination, biochemical evaluation, and BMD measurements at 3 sites (lumbar spine (LS) and hip [total (TH) and femoral neck (FN)]. Morphometric VF was assessed by Instant Vertebral Assessment™ (IVA™) using Genant's semi-quantitative method.
Results: We observed osteoporosis, osteopenia and normal BMD in 19.1 %, 56 %, and 24.5 % subjects, respectively. The decade wise prevalence of osteoporosis in age group 60–70 y, 71–80 y and >80 y was 16.9 %, 17 % and 50 %, respectively. Mean serum 25OHD levels were 17.2 ± 10.3 ng/ml with vitamin D deficiency (<20 ng/ml) and secondary hyperparathyroidism (SHPT, plasma iPTH >65 ng/ml) in 68.8 % and 45.4 %, respectively. VF were present in 29.6 % subjects (Grade I: 58 %, Grade II: 32.4 % and Grade III: 8.8 %). Age and iPTH had significant negative correlation with BMD at FN and TH. Serum 25OHD had no correlation with BMD at any site. The prevalence of VF was positively associated with age ($p = 0.018$) and negatively associated with BMD at FN ($p = 0.002$) and TH ($p = 0.013$).
Conclusion: Osteoporosis and VF are common in asymptomatic Indian males aged 60 years and above. Screening for osteoporosis and IVA can be recommended earlier than currently existing guidelines.

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BONE MINERAL DENSITY AND METABOLISM IN THE VERY ELDERLY PATIENTS WITH CONGESTIVE HEART FAILURE

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Aims: To study BMD and features of bone metabolism in very elderly patients with heart failure.
Methods: 95 hospital patients (females - 78.9 %, males - 21.1 %) aged 86.5 ± 4.8 y with coronary artery disease (CAD) were included in the study. Study group included 41 patients (mean age 86.9 ± 4.8 y) with moderate to severe congestive heart failure (CHF); the control group 54 patients (mean age 86.3 ± 4.8 y) without CHF. The study and control

groups were similar regarding main baseline characteristics and medical history except for myocardial infarction and atrial fibrillation more often registered in study group ($p = 0.006$ and $p = 0.02$, respectively). Main exclusion criteria were disorders or medications causing secondary osteoporosis. All patients underwent measurements of BMD in lumbar spine and proximal femur using DXA. Also, physical performance evaluation was conducted. Biochemical assessments included measurement of β-crosslaps and osteocalcin levels and routine biochemical tests.

Results: BMD was significantly lower in CHF-patients compared to control group (both the absolute units and T-score). Largest differences were observed in proximal femur and femur neck: mean femur BMD in CHF-patients was 709.97 ± 167.45 mg/cm^3, in control group 807.22 ± 171.61 mg/cm^3 ($p = 0.007$). Similar changes of BMD were registered in lumbar spine but differences between groups did not reach statistical significance ($p = 0.07$). Greater differences in BMD were detected in female patients, mainly concerning T-score ($p = 0.03$ for lumbar spine; $p = 0.0001$ for proximal femur). Normal BMD in proximal femur was revealed only in 2 patients with CHF but in control group normal BMD was observed in 17 patients ($p = 0.003$ Fisher's exact test). According to FRAX model, probability of proximal femur fractures achieved 6.2 %, the main osteoporotic fractures 13.5 % on average. Mean osteocalcin level was 0.9 ± 1.47 (from 0 to 6.1) ng/ml. Osteocalcin concentrations below lower limit of normal were detected in 68.4 % of patients. β-crosslaps level varied from 0.22 to 1.62 ng/ml (mean value 0.58 ± 0.33); only in 2 patients this parameter was slightly higher than upper limit of normal. There were no significant differences between groups in osteocalcin and β-crosslaps concentrations. CHF-patients were more likely to have poor physical performance. 93 % patients with CHF had very low physical activity, 21 % prolonged immobilization. The mean value of Get up and Go test was 16.45 (±7.1) s, 6-min walk test 73 m.

Conclusion: Study results demonstrated lower BMD (especially in proximal femur) in very elderly patients with CHF as compared to similar patients without CHF. The data suggest that in very elderly patients there is reduced osteoblast function without significant bone resorption. Further studies are required to better understand relationships between heart failure and osteoporosis.

P126
AN AUTOMATED TABLET-BASED, WEB-ENABLED TOOL (I-GYNE) FOR OSTEOPOROSIS RESEARCH AND CLINICAL CARE IN A GYNAECOLOGICAL UNIT

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Aims: Many women consider their gynaecologist their primary physician. This may increase as family medicine grapples with rapid aging. Adopting a life course approach, gynaecology can deliver holistic care to mid-life women. Since the 1970s, a 5-fold increase in hip fractures in this group has occurred in Singapore. As part of a comprehensive evaluation, patients were assessed for osteoporosis (OP) and clinical risk factors which may be associated with low BMD. A data collection tool was developed in order to consolidate the assessment and data management. We report on methodology and findings from 512 participants.

Methods: The cohort comprised 45–69 y olds attending gynaecology clinics for wellness checks, excluding cancer. The study used i-Gyne, an automated, web-based tool collecting data relating to OP through validated questionnaires. In addition, all participants underwent biophysical assessment (height, weight, waist/hip circumference, blood pressure and pulse) and completed a Short Physical Performance Battery, including grip strength. Whole body BMD was measured by DXA using an Asian reference. Subjects entered their responses into tablets. Stored on password-protected hospital servers, the set up allowed automatic analysis of the data using decision tree matrices and generation of a patient summary.

Results: Femoral neck and spinal OP was reported in 8.2 % and 6.8 % women, respectively. The i-Gyne's summary included the woman's 10-y fracture risk using FRAX®. In the clinical setting, the report enabled a rapid and comprehensive assessment of the woman's holistic well-being including information on concomitant health issues, medication use and lifestyle factors related to bone health. In the research setting, the incorporated prompts prevented missing/invalid data entry and data entry errors.

Conclusion: The i-Gyne's comprehensive assessment has enabled the integration of osteoporosis research and health care delivery in gynecology, facilitating the identification of our women's bone health needs. We anticipate the summary, with fracture risk prediction and clinical recommendations, will enhance health care delivery. Concurrently, the quality of data, captured across multisystems, will advance knowledge on factors associated with poor bone outcomes in Asian women, guiding the development of innovative interventions in this important health area.

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SEX AND AGE DIFFERENCES IN FAT AND LEAN MASS DISTRIBUTION IN CHINESE WITH NORMAL BMI POPULATION

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Aims: Sex and age in fat and lean mass distribution in normal BMI Chinese population have not been described before. The aim of this study was to evaluate sex and age differences in body fat distribution in Chinese with normal BMI population.
Methods: Analysis of covariance was used to explore fat and lean mass distribution in 2531 subjects with normal BMI (18.5 ≤ normal <24) and age over 20 y old, using Lunar DXA scanner in a cross-sectional study. Extremity and trunk lean mass as well as gynoid and android fat was evaluated for covariates including sex and age and interactions. All the participants were grouped by sex and age at intervals of 10 years (20-29….and 70+).
Results: Both sexes reach their peak lean mass in young adults (women by 30–39, 34198 g; men by age 20–29, mean 50261 g), whereas mean fat mass in women was 16404 g and 17554 g in their age of 20–29 and over 70, respectively, and in men was 13849 g and 14022 g in their age of 20–29 and over 70, respectively. Both men and women declined lean mass and gained fat by age with advancing age, with men losing almost twice as much lean mass as women (−2 % vs. -1 % per 10 y) whereas women gaining almost twice as much fat as men (−2 % vs. -1 % per 10 y).
Conclusion: This study of adults Chinese with normal BMI population showed that extremity and truck lean mass as well as body fat distribution are reversely vary by sex and age. Additional studies are needed to explore the metabolic and health risk implications of these findings.

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TRABECULAR BONE SCORE (TBS) PREDICTS INCIDENT LUMBAR VERTEBRAL FRACTURES IN POSTMENOPAUSAL CHINESE WOMEN INVERSELY OF LOWEST BMD T-SCORE TRENDS

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Aims: Osteoporotic compression fractures predominately affect women. However, vertebral compression fractures may occur in BMD with a T-score ≥ −2.5 measured with DXA. This study aimed to examine whether trabecular bone score (TBS) predicts the risk of vertebral fractures in postmenopausal Chinese women.
Methods: Of 114 consecutive postmenopausal women with compression fractures confirmed at lumbar MRI study, we reviewed data from 33 women (mean age 72.85 ± 10.57 y) who had at least one DXA for lumbar areal BMD (aBMD) measurement within 2 years before the fracture incidents. TBS was obtained from spine DXA scans archived in the baseline study. Both TBS and T-score BMD were obtained from isolated value of L1, L2, L3 and L4 segment, respectively.
Results: Among compression fractures in L1 (n = 6), L2 (7), L3 (8) and L4 (9), the lowest TBS at L1, L2, L3, and L4 was associated with incident fractures at the same site or adjacent site in 64.0 %, 40.0 %, 0 % and 33.3 %, respectively; whereas the lowest T-score BMD in 27.3 %, 52.4 %, 66.7 % and 0 %, respectively.
Conclusion: TBS predicts vertebral fracture independently and reversely associated with aBMD. TBS could effectively improve vertebral fracture risk assessment in the L1, whereas aBMD in L3 segment, thereby providing potential clinical impact in fracture prevention.

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BONE MINERAL DENSITY AND SPATIOTEMPORAL GAIT PARAMETERS AMONG FALLS IN THE COMMUNITY-DWELLING ELDERLY IN TAIWAN

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Aims: Falls in the elderly are multiclausal phenomenon with a complex interaction between intrinsic (patient-related), extrinsic (environment-related), and behavior (activity-related) factors. Walking gait has found to be associated with risk of falls. Only a few studies reported relationship between BMD and walking gait parameters. The aim of the study was to evaluate the relationship BMD and spatiotemporal gait parameters of falls among the elderly in community-dwelling in Taiwan.
Methods: Design: Cross-sectional study. Setting: A community in Taiwan. Participants: Subjects were divided into two groups – Group 1: Elderly subjects with history of falls on standing height; Group 2: Elderly age- and gender-matched subjects without history of falls. Main Outcome Measure: Gait parameters were assessed using GAITRite® electronic walkway system. Participants walked forward on a GAITRite walkway. These parameters were calculated separately for the right and left legs. The measurement session for each participant consisted of five consecutive trials in forward walking (FW) directions. BMD measurement was performed by Lunar DXA. BMD of the spine and both hips were measured and the lowest BMD was used for diagnosis according to WHO criteria.
Results: A total of 29 subjects (age 72.86 ± 5.98) were enrolled in this study. There was no statistical significance between BMD and spatiotemporal gait parameters in both groups (falls group and without falls history group).

However, the results demonstrated statistically significant with negative relationship between BMD and walking speed, cadence, swing phase and stride length. The results also revealed statistically significant with positive relationship between BMD and CV% stand phase.

Conclusion: Our results indicated that osteoporosis is associated with spatiotemporal gait parameters in FW directions. Finding may add to the knowledge and practice of prevent fall among the elderly in community-dwelling.

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RACIAL DIFFERENCES IN BONE LENGTH OVERSTATE DIFFERENCES IN CORTICAL POROSITY IN CHINESE AND CAUCASIANS

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Aims: Chinese have lower hip and forearm fracture rates, appendicular bones with a smaller total cross-sectional area (CSA) but thicker and less porous cortices. As morphology differs along the length of a bone, and the region of interest (ROI) is more proximal in a shorter bone, positioning errors may influence racial difference in bone microarchitecture.

Methods: Distal radius images acquired using HR-pQCT (XTreme CT, Scanco) in 76 healthy Chinese (40 women) and 80 Caucasians (32 women) aged 20–55 y. The manufacturer method started at 9.5 mm from the endplate. The corrected ROI started at 4 % of the forearm length. StrAx 1.0 algorithm was used to segment the matrix and void volumes of the compact-appearing cortex (CC), the transitional and trabecular regions.

Results: Chinese were shorter and leaner. The forearm length was 1.2 cm and 1.5 cm shorter in Chinese women and men respectively compared to Caucasians ($p < 0.001$). Using the manufacturer method in women, total CSA was smaller (−0.67SD, $p = 0.001$), CSA of CC was greater (0.59 SD, $p = 0.026$) in Chinese with lower porosity of CC (−0.97 SD, $p < 0.001$) and higher matrix mineral density (MMD, 0.59SD, $p = 0.006$) in Chinese than Caucasians. Using the corrected ROI, differences were smaller but significant (total CSA: −0.64SD, $p = 0.002$; CSA of the CC: 0.47 SD, $p = 0.078$; porosity of the CC: −0.76 SD, $p = 0.002$; MMD: 0.52SD, $p = 0.017$). Chinese men had smaller total CSA but similar CSA of CC compared to Caucasians using both the manufacturer and corrected method. The lower porosity of CC and higher MMD in Chinese men were not presented in the corrected ROI.

Conclusion: The lower cortical porosity in Chinese is exaggerated compared to Caucasians, especially in men. Bone length differences need to be addressed when comparing racial differences in morphology.

Disclosure of Interest: A. Ghasem-Zadeh Patent licensing: one of the inventors of StrAx, R. Zebaze Patent licensing: one of the inventors of StrAx, E. Seeman Patent licensing: one of the inventors of StrAx

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EXAMINING DISCORDANCE OF LOW BMD DIAGNOSIS IN ADULT THALASSEMIC PATIENTS: DOES COMPARISON WITH NORMAL REGIONAL POPULATION MAKE A DIFFERENCE?

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Aims: Diagnostic discordance for osteoporosis is determined when the T-score varies from one site to another site (for example from femoral region to spinal region) that makes different diagnosis identified in any region. Discordance is a known phenomenon in secondary osteoporosis, but is less studied in thalassemia major patients. Thalassemia major is a hemoglobinopathy, an endemic disease in Iran and Mediterranean countries. We checked discordance in thalassemic patients, and for examining the rule of ethnicity, we examined discordance also, when they compared with reference of Iranian normal population.

Methods: BMD of 177 adult β-thalassemia major patients (20–39 y/o) and 490 age and sex matched normal Iranians compared. Normals selected from participants of Iranian Multicenter Osteoporosis Study (IMOS). As in BMD reporting of premenopausal and in young males, Z-scores are preferred and a Z-score of −2.0 or lower is defined as "below the expected range for age", we checked discordance in our patients according to Z-score. Also after mean and standard deviation of normal Iranians determined, Z-score of patients recalculated based of Iranian reference. As BMD of normal participants and thalassemic patients performed by devices of different brands, analyses were done based of calculated standard BMD of all participants.

Results: BMD of patients was significantly lower than normal participants in femoral and spinal regions (both P-value <0.001). Mean of femoral and spinal Z-scores according to original device reference range (American) was -1.89 ± 1.12 and -2.09 ± 0.901, respectively. Frequency of Z-score ≤ -2 found in 52 % and 56 % of thalassemic patients in femoral and spinal region, respectively. When they compared with normal Iranians, mean and standard deviation of these femoral and spinal Z-scores was -1.12 ± 1.107 and -2.80 ± 1.23, respectively; and Z-score ≤ -2 found in 16 % and 72 % of thalassemic patients in femoral and spinal region, respectively.

Conclusion: Thalassemia major patients have diagnosis discordance when their mean Z-scores of femoral and spinal regions are compared and this fact does not change when they compare with reference range of same geographical region. As difference in mean of Z-scores is more prominent when they compare by regional references, we conclude that in secondary osteoporosis patients, maybe other cutoff points is needed, especially based on comparison with normal population of same geographical region.

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EFFECT OF SWITCH FROM TENOFOVIR TO RALTEGRAVIR ON TRABECULAR BONE SCORE

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Aims: To examine the effect of tenofovir cessation on trabecular bone score (TBS) compared to the change in BMD.

Methods: Patients with a spine T-score ≤ -1.0 and plasma HIV RNA <50 copies/mL for at least 3 months were switched from tenofovir to either raltegravir. Lumbar spine DXA images were obtained at baseline, 12 and 24 months. Student's paired t-test was used to compare the change in TBS and BMD at 12 and 24 months.

Results: Seventeen patients were enrolled for the study: mean age 49.9 y (SD: 8.99), mean lumbar BMD was 1.11 g/cm^2 (SD: 0.13), mean T-score of −0.9 (SD: 1.1) and Z-score −0.9 (IQR: −1.7-0.3). The mean TBS was 1.28 (SD: 0.16). Lumbar BMD increases were significant at 12 and 24 months. At 24 months, lumbar BMD increased by 4 % (0.03 g/cm^2) from baseline (95%CI: 0.02-0.05, P = 0.0003). However, there was no significant change in TBS at two years (−0.01, 95%CI: −0.06-0.04 P = 0.64).

Conclusion: In HIV-infected men with low bone mass, tenofovir switch to another antiretroviral therapy increased BMD without any significant increase in TBS.

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MALE OSTEOPOROSIS AWARENESS IN THE ELDERLY: AN ANALYSIS OF DXA USE IN AUSTRALIA 1995–2015

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Aims: To investigate gender differences of DXA utilization in the elderly in the Australian context.

Methods: Data from the Australian Federal Government's Medicare were obtained to quantify all funded male and female DXA claims between 1995–2015.

Results: In females and males aged 64–74, 75–84 or ≥ 85 years of age there was a progressive increase in DXA claims per capita between 1994–2002, with little change thereafter in females but slow increase in males until 2007. After 2007, following introduction of Medicare eligibility criterion for age over 70, claims increased sharply in all three age groups, with ongoing increase in Medicare claims per capita subsequently. The male/female claim ratio in all age groups demonstrate low relative DXA use in males compared to females with the male/female ratio significantly below 1.0. Following the 2007 Medicare criterion for age over 70, the male/female ratio DXA scans improved slightly in the 64–74 and 75–84 age groups with little subsequent change thereafter. Conversely in males over 85 the relative use of DXA, compared to females, has improved steadily over the last 20 years predating, and continuing since, the 2007 Medicare change.

Conclusion: In Australian elderly males aged over 85, there is an ongoing improvement in DXA utilization possibly reflecting increasing awareness of high fracture risk in this group by healthcare professionals. Importantly however in the age groups 64–74 and 75–84, while DXA use per capita has increased in Australia, the male/female ratio of DXA utilization remains low with little improvement after the introduction of the Medicare rebate for age over 70. There is a need for improved education of health professionals about the risk of osteoporosis in males aged 64–85.

P134

FEMORAL GEOMETRY AS INDEPENDENT RISK FACTORS FOR HIP FRACTURES IN UKRAINIAN PATIENTS

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Aims: According to the literature data, some parameters of the femur are independent predictors of hip fractures (HF), but such studies among Ukrainian patients are absent. The purpose of this research was to study the some geometric parameters of the upper third of the hip and in patients with intra- and extra-articular HF.

Methods: 94 patients aged 50–89 y (median age 70.98 ± 0.99 y) were examined, 74 of whom (37 women and 37 men) were hospitalized with intra- and extra-articular HFs. Assessment of geometry parameters of the femur was performed on the contralateral limb in relation to fracture.

Results: It was established the significant effect of age on femoral geometry parameters in men and women with intra- and extra-articular fractures, but this effect was not present in patients without fractures. In men with intra-articular hip fractures the indices of the length of hip axis, length of femoral neck, intertrochanteric distance, basis of the head and head diameter were significant lower in comparison with indices of patients without fractures. In men with extra-articular hip fractures the indices of length of hip axis, intertrochanteric distance, basis of the head and head diameter were also significant lower in comparison with indices of patients without fractures. We did not find the significant differences of hip geometry parameters in women depending on the hip fractures.

Conclusion: Femoral geometry indices are independent risk factors for hip fractures in Ukrainian patients. Identified differences should be considered for both planning surgery after hip fracture and for predicting the risk of hip fracture in older age patients.

P135
EPIDEMIOLOGY OF LOWER LIMB FRACTURES IN UKRAINE

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Aims: Lower limb fractures (LLF) account for approximately third of all fractures and may result in substantial mortality/morbidity. Fractures are a considerable public health burden, but information on their epidemiology in Ukraine is limited.

Methods: We identified 665 subjects from 76765 citizens, living in Vinnitsa region, who had a first time (incident) diagnosis of LLF, recorded in the regional Hospital database (1.01.2011-31.12.2011).

Results: Frequency the LLF of was 42.4 % from the total fractures in all patients and 44.4 % from the total fractures in patient aged 50 y and older. The most common anatomic site of LLF was the tibia and/or fibula (48.9 % of all incident LLF), followed by the hip (29.5 %), and the tarsal/metatarsal bones (21.6 %). Incidence of fracture in patient 50 y and older was 519.8 per 10000 patient for all LLF, 212.3 per 10000 patient for tibia and/or fibula fractures and 226.9 per 10000 patient for hip fracture. LLF were more common among males than among females in the younger age groups (up to 39 y old). Among subjects 50 y and older the incidence of tibia and/or fibula fractures was 340.7 per 10000 patient in the age group 60–69 y old, 44.9 per 10000 patient in age group 70–79 y old, and 102.4 per 10000 patient in age group 80–89 y old.

Conclusion: Our study provided the new information about the epidemiology of lower limb fractures in Ukrainian population according the age. This information is important for planning of the prevention and treatment strategy in patients of different ages.

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COMMUNITY-DWELLING MEN WITH DEMENTIA ARE AT HIGH RISK OF FRACTURE: THE CONCORD HEALTH AND AGEING IN MEN PROJECT

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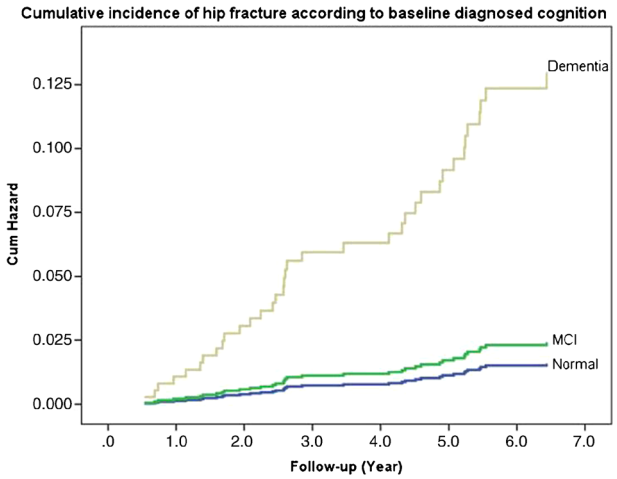
Aims: To examine the association between cognitive status and fractures in older community-dwelling men after accounting for other risk factors for fracture.

Methods: In the Concord Health and Ageing in Men Project (CHAMP), 1541 community-dwelling men aged 70–97 were screened for dementia using the Mini-Mental State Examination (MMSE) and the Informant Questionnaire on Cognitive Decline at baseline. Screen positives were then assessed for dementia, mild cognitive impairment (MCI) or no cognitive impairment by a panel of geriatricians and neuropsychologist. During a mean follow-up of 6 y, data were collected on radiologically verified fractures (all, nonvertebral or hip). Data collected at baseline included potential confounders such as age, BMI, smoking, alcohol, comorbidity, depression, falls, physical activity, gait speed, BMD and vitamin D metabolites (25D and 1,25D) measures. The relationship between cognitive status and fractures was analyzed using Cox's Proportional Hazard regression.

Results: 93 (6 %) men had dementia and 120 (7.0 %) had mild cognitive impairment (MCI). There were 162 (11 %) first incident fractures, including 131 (9 %) nonvertebral and 43 (3 %) hip fractures. Dementia, but not MCI, was a very strong predictor of all, nonvertebral and hip fractures. Almost 20 % of men with dementia suffered any fracture compared to 10 % without dementia. Whereas 12 % of men with dementia suffered a hip fracture compared to 2 % in men without dementia. In univariate models, men with dementia at baseline predicted increased incidence of all (HR: 2.67, 95%CI: 1.65-4.33), nonvertebral (HR: 2.59, 95%CI: 1.51-4.45), and hip (HR: 6.95, 95%CI: 3.47-13.96) fracture. Similar findings were observed in the multivariable-adjusted models.



Conclusion: Dementia was a high risk for fracture, especially for hip fracture, in older men. This was not related to BMD, falls or any other potential risk factors for fractures.

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THE INCIDENCE AND RISK OF OSTEOPOROSIS IN PATIENTS WITH ANXIETY DISORDERS: A POPULATION-BASED RETROSPECTIVE COHORT STUDY

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Aims: To investigate the relationship between anxiety disorder (AD) and the subsequent development of osteoporosis.
Methods: We conducted a cohort analysis according to the data in the Longitudinal Health Insurance Database 2000 of Taiwan. We included 7098 patients in both the AD and no-anxiety cohort. The incidence rate and the risk ratios (RRs) of subsequent new-onset osteoporosis were calculated for both cohorts.
Results: The risk of osteoporosis was higher in the AD cohort than in the comparison cohort. In addition, the incidence of newly diagnosed osteoporosis remained significantly increased in all of the stratified follow-up durations (0–1, 1–5, 5–10, ≥10 y).
Conclusion: The incidence of osteoporosis in Taiwan is associated with an a priori AD history. The risk ratios are the highest for osteoporosis within 1 year of AD diagnosis, but the risk remains statistically significant for more than one year. Clinicians should pay particular attention to osteoporotic comorbidities in AD patients.
Acknowledgement: The study is based on data from the National Health Insurance Research Database provided by the Bureau of National Health Insurance (BNHI) in Taiwan and managed by National Health Research Institutes (NHRI). We express our particular gratitude to the government organization BNHI and the nonprofit foundation NHRI.

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RISK OF HIP FRACTURE IN PATIENTS WITH DEPRESSION: A NATIONWIDE POPULATION-BASED RETROSPECTIVE COHORT STUDY

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Aims: Some studies have revealed that depression may play a vital role in the occurrence of osteoporotic fractures. However, a clear correlation between depression and osteoporotic fractures has not been established.
Methods: We investigated patients who were diagnosed with depressive disorders by a psychiatrist according to the data in the Taiwan National Health Insurance Research Database. A comparison cohort comprised age- and sex-matched patients without depressive disorders. The incidence rate and the hazard ratios of subsequent hip fractures were evaluated in both cohorts.
Results: The depression and control cohorts each consisted of 11,207 patients. The incidence risk ratio (IRR) between these 2 cohorts was indicated that patients with depression may have higher risk of developing subsequent hip fractures (IRR = 1.60, 95%CI = 1.29–1.99, $P < 0.001$). After adjusting potential confounding factors using multivariate analysis in the Cox regression model, the depression cohort still showed higher risk of hip fractures development than the comparison cohort (adjusted hazard ratio = 1.34, 95%CI = 1.08-1.65, $P = 0.008$).
Conclusion: Depression might increase the risk of subsequent new onset hip fractures. A prospective study is necessary to confirm these findings.

P139

THE ASSOCIATED FACTORS OF SEVERE OSTEOPOROSIS AT FRACTURE LIAISON SERVICE IN TAIWAN

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Aims: First fragility fracture increased risk for further fracture for 2–4 folds. However, most fracture sufferers did not receive secondary prevention for osteoporosis to decrease future fracture risks. The International Osteoporosis Foundation (IOF) launched the Capture the Fracture campaign with 13 specific criteria to help healthcare organizations setting up their own fracture liaison service (FLS).This aim was to determine the associated factors of the osteoporosis in FLS at China Medical University Hospital (CMUH).

Methods: Data from the FLS (2015–2016) at CMUH containing 100 elderly were analyzed. A total of 100 fracture patients (37 females and 63 males) aged 53–93 y old were recruited. BMD was measured by DXA. Those fracture patients were defined as severe osteoporosis were those whose average T-score ≤ −3. Chi-square test, student's t-test and multivariate logistic regression were applied to analyze the predictive ability of these factors on osteoporosis.

Results: The severe osteoporosis prevalence rates were 21 %. The average age of study subjects was 71.2 ± 9.12 with average T-score > −3 and 77.48 ± 6.59 with average T-score ≤ −3.Among those severe osteoporosis patients, 28.6 % no regular take the calcium and vitamin D. After multivariate adjustment, age, gender, used teriparatide and used denosumab were found to be significantly associated with severe osteoporosis. The odds ratios (95%CI) were as follows: 1.08 (0.996, 1.16) for age, 0.16 (0.03, 0.81) for males, 5.65 (1.01, 31.74) for using teriparatide, and 5.73 (1.38, 23.83) for using denosumab.

Conclusion: Osteoporosis is an important issue in rapid aged Taiwan. From the FLS model, the osteoporosis-related assessments, treatments, consultations on diet, medications, exercise, fall preventions are given mainly by care managers and will improve the care quality of fragility fracture patient In Taiwan.

P140

ORTHOGERIATRIC ADMISSION RATES AND OUTCOMES IN AUSTRALIA: CURRENT TRENDS AND FUTURE PROJECTIONS (UP TO 2050)

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Aims: To (i) evaluate trends in the age- and gender-specific admission incidence rates and short-term outcomes among public orthogeriatric patients (60 y and over) in the Australian Capital Territory (ACT) over a 15-y period (2000–2014), and (ii) predict the absolute number and rates of orthogeriatric admissions through 2050.

Methods: The data obtained from electronic medical records for all orthogeriatric patients in ACT admitted to public hospitals between 2000–2014 were analysed in 5-y periods: 2000–2004, 2005–2009, and 2010–2014. Age- and gender-specific admission rates were calculated using ACT population data from the Australian Bureau of Statistics (series B). Projections of rates and numbers of admissions were conducted using two models: negative binomial regression and Poisson regression.

Results: The mean absolute annual number of elderly orthopaedic patients increased from 1055 ± 144 in 2000–2004 to 1301 ± 95 (+23.3 %) in 2005–2009 and 1464 ± 59 (+38.8 %) in 2010–2014. The proportion of patients aged 85 y and over increased from 12.5 % to 13.7 % and 15.7 %, respectively. Age-specific admission rates (cases/100,000 population/year) changed in the opposite direction: from 2636 in 2000–2004 to 2663 (+1.1 %) in 2005–2009 and to 2450 (−7.0 %) in 2010–2014, while the female: male ratio rose (1.59, 1.64 and 1.66, respectively). The mean length of hospital stay in the three periods fluctuated (10.5 ± 16.1, 8.4 ± 13.4 and 8.9 ± 12.8 days, respectively) and the in-hospital mortality rates slightly increased (2.24 %, 2.39 % and 2.66 %, respectively). In ACT, the annual number of orthogeriatric admissions is estimated to increase in 2030 by 113.4 % (negative binomial regression) - 132.8 % (Poisson regression) and in 2050 by 196.0 % - 217.0 %, respectively, according to the two predictive models used. The proportion of patients aged 85 y is expected to increase in 2030 by 18.4 % - 17.8 %, and in 2050 by 24.8 % - 25.2 %, respectively. Age-specific admission rates are projected to decrease in 2030 by 15.0 % - 7.2 %, and in 2050 by 20.0 % -13.9 %, respectively. If similar trends in public orthogeriatric admissions occur in other Australian states and territories, the nationwide admission numbers may reach by 2030 and 2050 to 160,403 and 211,407, respectively (negative binomial model), or 174,974 and 227,128, respectively (Poisson regression).

Conclusion: As the population ages, despite the declining incidence of orthogeriatric admission rates, the absolute number of elderly persons requiring in-hospital orthopaedic treatment continue to increase, and may double by 2030 and triple by 2050. The strategies, goals of care and resources will have to be tailored to the coming socioeconomic burdens.

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DO MEASURES OF MUSCLE STRENGTH, MUSCLE MASS AND PHYSICAL PERFORMANCE CORRELATE? A PILOT STUDY IN OLDER SINGAPOREAN ADULTS

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Aims: Singapore has one of the most rapidly aging populations in Asia. Low Handgrip Strength and Gait Speed are markers of frailty status in the elderly and even are associated with increased mortality risk (1). No published data regarding these parameters exists in Singapore; a multi-ethnic nation. We aimed to evaluate these parameters and to assess their

correlation with muscle mass and components of the SARC-F questionnaire; a predictive score of poor functional outcomes in sarcopenia.

Methods: Cross-sectional evaluation of Hand Grip Strength and Gait Speed in community dwelling adults >50 years attending an Osteoporosis Public forum at Singapore's largest public hospital. Muscle mass and Hand Grip Strength were measured by Bio Impedance Analysis and by using a Jamar dynamometer respectively. Gait Speed was assessed through a timed 5-metre walk test. SARC-F score which assesses capacity to conduct activities of daily living was calculated by administering a questionnaire regarding ability to carry a heavy load, walking, rising from a chair, climbing stairs, and falls frequency.

Results: 108 subjects were analysed. Mean age was 63.9 (7.5). 77 % of the subjects were female and 23 % were male. Mean Hand Grip Strength of the dominant hand in males was 33.5 kg (5.7) and that in females was 19.4 kg (5.2) ($p < 0.001$). Mean Gait Speed in males was 1.5 m/s (0.5) and in females it was 1.4 m/s (0.5) ($p = 0.395$). Mean Muscle Mass amongst males was 19.4 kg/m^2 (2.5) and that amongst females was 15.6 kg/m^2 (2.3) ($p < 0.001$). Hand Grip Strength correlated with Gait Speed ($p = 0.039$) and with Muscle Mass ($p = <0.01$). There was no significant correlation between Gait Speed and Muscle Mass. Neither Hand Grip Strength nor Gait Speed correlated with total SARC-F score or with any of its individual components. Gait Speed correlated with history of active osteoarthritis of the knees ($p < 0.001$).

Conclusion: Measures of muscle strength (Hand Grip Strength) correlate well with measures of physical performance (Gait Speed) and Muscle Mass in older Singaporean adults. The lack of correlation between Gait Speed and Muscle Mass can potentially be explained by the fact that Gait Speed may be influenced by other factors such as osteoarthritis and knee pain. The lack of correlation seen between Hand Grip Strength (an early manifestation of sarcopenia/frailty) and the SARC-F is likely because the components of the latter are likely to be compromised only in severe sarcopenia and when activities of daily living are compromised. Our pilot study will serve as an impetus to not only ascertain normative data for these important health indicators in Singapore's elderly but will also potentially facilitate the constructive incorporation of these markers of frailty in routine clinical assessment of older subjects.

References: 1. Chainani V et al. Int J Cardiol 2016;215:487.

P142

ARE THERE CUT-OFFS FOR ASSOCIATIONS BETWEEN MUSCLE STRENGTH AND BALANCE IN CHINESE OLDER WOMEN?

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Aims: Poor balance is a major risk factor for falls. Muscle strength is associated with balance in older people, but cut-offs for the associations have not been well estimated. We aimed to describe the association between muscle strength and balance in Chinese older women and investigate whether cut-offs exist for the associations, which can be used to identify women at higher risk of reduced balance.

Methods: This was a cross-sectional study of 441 community-dwelling Chinese women aged 60–88 y. Associations of handgrip and lower limb muscle strength (LMS) with static (one-leg standing time with eyes closed) and dynamic (timed up and go (TUG) test) balance tests were assessed using linear regression, and thresholds for the associations were estimated using locally weighted smoothing (LOWESS) plots and piecewise regressions.

Results: After adjusting for confounders, weaker LMS was associated with poorer performance on the TUG [β -0.018 (95%CI: −0.025, −0.011) s/kg] and log-transformed one-leg standing time [β 0.004 (0.001, 0.007)], while handgrip strength was only associated with TUG [β -0.065 (95%CI: −0.096, −0.033) s/kg]. LOWESS analyses showed potential nonlinear associations for handgrip strength (cut-off = 18 kg) and LMS (cut-off = 83 kg) with TUG but not one-leg standing time; there was significant difference in the associations of handgrip strength [β -0.241 (−0.366, −0.116) kg/s] and LMS [β -0.056 (−0.081, −0.031) kg/s] with TUG for women below and above their identified cut-offs.

Table. Cut-points for associations between muscle strength and timed up and go test, and associations in participants with muscle strength below or above the identified cut-offs and the difference in the associations.

	Cut-offs		Below cut-off		Above cut-off	Difference in associations
	n	β (95 % CI)	n	β (95 % CI)	Δβ (95 % CI)	
Lower limb muscle strength (kg-force)	83	112	**−0.067 (−0.091, −0.044)[b]**	329	**−0.011 (−0.019, −0.004)[a]**	**−0.056 (−0.081, −0.031)[b]**
Handgrip strength (kg)	18	66	**−0.265 (−0.374, −0.157)[b]**	374	−0.024 (−0.062, 0.013)	**−0.241 (−0.366, −0.116)[b]**

Higher values of timed up and go test represent poorer performance whereas higher values of all the other tests represent better performance.
Adjusted for age, weight, height, physical activity, calcium intake and serum vitamin D status.
[a]$p < 0.01$; [b]$p < 0.001$.
Conclusion: In Chinese older women, poorer muscle strength was associated with reduced balance, and cut-offs were identified for associations between muscle strength and TUG; associations in women below the cut-offs were much stronger than those above. Older women with muscle strength below those cut-offs may be an effective target group for future randomized controlled trials aiming to improve muscle strength and balance and reduce falls risk in later life.

P143
NARRATIVE REVIEW ON THE RELATIONSHIP BETWEEN HYPERTENSION AND OSTEOPOROSIS

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Aims: Numerous studies have discussed hypertension as a potential risk factor for osteoporosis. To date, there is no systematic review synthesising the data on the relationship between hypertension and osteoporosis. We thus aimed to perform a systematic review to close this gap.
Methods: Articles between 2000 and April 2016 were searched from Embase, Medline and Scopus databases based on the search term "'hypertension' AND ('fracture' OR 'fractures')". After duplicates were removed, articles which were not in English, involved cadavers or animals were excluded. Case reports, basic science studies and articles with poor methodology or data analysis techniques were excluded as well. Randomised controlled trials, retrospective studies, case series and reviews were included in this study.
Results: Out of a total of 8307 articles, 26 articles were included within our review. The presence of hypertension was generally associated with a lower BMD. Regardless, there were studies which also showed no relation between hypertension and osteoporosis. There was even a study which revealed that hypertension was associated in higher BMD scores in males. Comorbidities such as diabetes mellitus, obesity and underlying metabolic syndrome were confounders to the relationship between hypertension and osteoporosis. The use of antihypertensives such as thiazides and β-blockers also influenced the BMD of patients.
Conclusion: Epidemiologically, current literature suggests that hypertension is a risk factor for lower BMD. However, this finding is not consistent in all studies. Regardless, there is still insufficient information on this topic. The current literature still remains to be strengthened for more rigorous quantitative reviews to be performed.

P144
MULTIPLE FRACTURES AND RISK FACTORS AMONG THE PATIENTS WITH OSTEOPOROSIS IN TAIWAN

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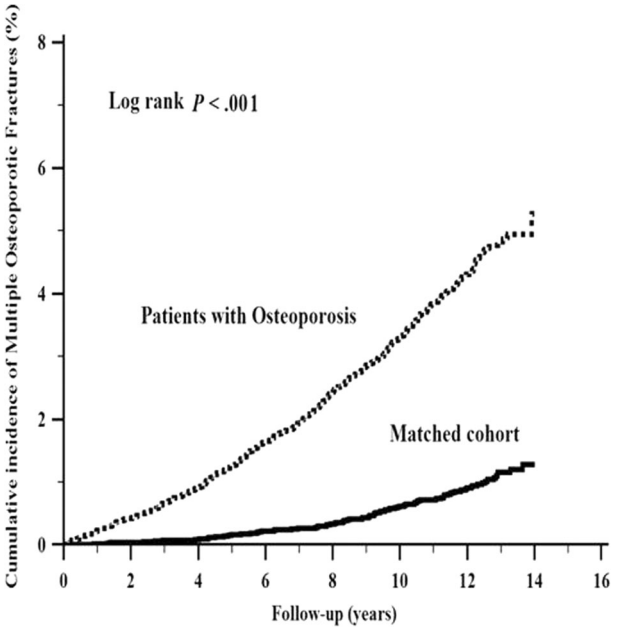
Aims: To evaluate the risk of multiple fractures in patients with osteoporosis by using the Taiwan National Health Insurance Research Database.
Methods: We conducted a retrospective study on 28,574 participants (14,287 patients with osteoporosis and 14,287 control patients). Patients were observed for a maximum of 13 years to determine the rates of multiple fractures which are highly associated with the osteoporotic changes including vertebral fracture, hip fracture, upper end humerus (closed) fracture and wrist fracture following an osteoporosis diagnosis. Multiple fractures are defined with at least 2 types of above mentioned fractures during the observational period. The Cox proportional hazards model was used to evaluate the risk of multiple fractures among the patients with osteoporosis and comparison cohort. In addition, the Cox model was also tried to investigate the possible risk factors of multiple fractures among the patients with osteoporosis.
Results: During the 13-year observational period, 544 (3.56 per 1000 person-years) patients with osteoporosis and 111 (0.73 per 1000 person-years) comparison patients were diagnosed with multiple fractures. The incidence risk ratio of multiple fractures between patients with osteoporosis and matched patients was 4.87 (95%CI, 3.96-6.03, $p < 0.001$). After adjustments for age, sex, comorbidities, urbanizations, and socioeconomic status, patients with osteoporosis were 4.57 times more likely to develop multiple osteoporotic fractures (95%CI, 3.72-5.62, $p < 0.001$) as compared to matched patients. Moreover, older age (more than 50 years old), female sex, and comorbidities of hypertension, dyslipidemia, congestive heart failure and cerebrovascular diseases may be seen as independent risk factors for development of subsequent multiple fractures among the patients with osteoporosis.



Conclusion: There is an increased risk for multiple fractures in patients with osteoporosis, and clinicians should take the risk of the multiple fractures into consideration when the osteoporosis patients present with the predictive risk factors.

P145
RISK OF VERTEBRAL FRACTURE IN PATIENTS DIAGNOSED WITH DEPRESSIVE DISORDERS: A NATIONWIDE POPULATION-BASED COHORT STUDY

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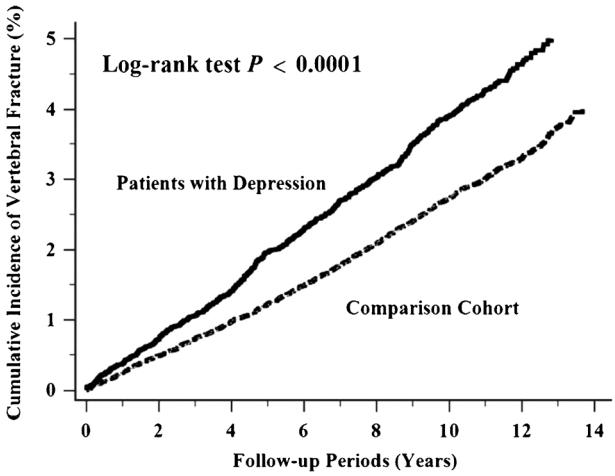
Aims: We explored the association between depression and subsequent new onset vertebral fractures. In addition, we tried to find potential risk factors of vertebral fractures in the patients with depression.
Methods: We investigated patients who were diagnosed with depressive disorders by a psychiatrist according to the data in the Taiwan National Health Insurance Research Database. A comparison cohort comprised age- and sex-matched patients without depressive disorders. The incidence rate and the hazard ratios of subsequent vertebral fractures were evaluated in both cohorts.
Results: The depression and control cohorts each consisted of 11,203 patients. The incidence risk ratio (IRR) between these 2 cohorts was indicated that patients with depression may have a higher risk of developing subsequent hip fractures (IRR = 1.41, 95%CI = 1.26-1.57, P < 0.001). After adjusting potential confounding factors using multivariate analysis in the Cox regression model, the depression cohort still showed higher risk of hip fractures development than the comparison cohort (adjusted hazard ratio = 1.24, 95%CI = 1.11-1.38, P < 0.001). In the risk factors analysis, aged more than 50, hypertension, diabetes mellitus, cerebrovascular disease, chronic obstructive pulmonary disease, autoimmune disease, osteoporosis and lower monthly income may be seen as predictive factors of vertebral fractures in the patients suffering from the depressive disorder.



Conclusion: Depression might increase the risk of subsequent new-onset vertebral fractures. A prospective study is necessary to confirm these findings.

P146
FRACTURE LIAISON SERVICE (FLS) PROGRAM: A NEW APPROACH FOR PATIENTS WITH LOW TRAUMA FRACTURES IN MALAYSIA

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Aims: Fracture liaison service (FLS) program: a new approach for patients with low trauma fractures in Malaysia.
Methods: The idea on FLS was first introduced to Assunta Hospital Petaling Jaya, Malaysia end of December 2013. It was approved early year 2014 and the program was first commenced on 1 April 2014 with a trial period of six months. Problems encountered were then analyzed and protocol revised. After running the program for second phase, the FLS was introduced into Assunta Hospital as part of the Standard Service for patients with low trauma fractures. Individuals

above age of 50 y old, both male and female, presenting with low trauma fractures (defined as fractures sustained following fall from standing height), both male and female, seen in outpatient and inpatient clinics are recruited into the program. Orthopaedic surgeons are the front line personnel and the main source of referral who decide on the eligibility of the individual patients with fracture for the FLS program. There are two FLS nurses identified from Assunta Hospital, one for outpatient and inpatient each. Patients with low trauma fractures are treated for their fractures accordingly. They are then captured into the FLS program and will be seen by individuals from FLS team such as physiotherapists, occupational therapists, dietitians and general physicians or geriatrician. Patients received appropriate treatment and support from different members of the FLS team. Individuals discharged from outpatient of inpatient services will then be followed up by FLS nurse for one year. Similar approach has been introduced into another private hospital in which the author is affiliated to. This is the first official FLS service introduced in hospital in Malaysia and with the hope that it will become the model for other hospitals in Malaysia.

Results: As the result of the trial and revised protocol of the FLS program in Assunta Hospital, FLS has been accepted, recognized and endorsed as the Standard Service for patients presenting with low trauma fractures in Assunta Hospital. They will receive a more complete care from members of the FLS team. This is the first FLS Service in Malaysia to date. Hope this will be the model for other hospitals in Malaysia too.

Conclusion: This is the first official FLS service introduced in Malaysia. It is recognized and endorsed by Assunta hospital with a team dedicated for this service. After periods of trial and protocol revision, FLS Service has been introduced as the Standard Service for patients with low trauma fracture.

Acknowledgement: Thanks to the Hospital Management, the Marketing team, the FLS team members consist of Nursing Managers and Nursing staff, Physiotherapist and Occupational Therapist, Dietitians, General Physicians, Geriatrician and all the participating Orthopaedic Surgeons of Assunta Hospital for their supports, input, advice and their patience in setting up this FLS Service in Assunta.

P147
SARCOPENIC OBESITY IN OLDER WOMEN: THE GEELONG OSTEOPOROSIS STUDY

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Aims: Sarcopenic obesity refers to age-related loss of muscle mass and function, in the face of obesity. We aimed to investigate the relationship between sarcopenic obesity, and its components, with physical inactivity and falls among older women.

Methods: Participants (n = 436) were women aged 60–97 y assessed in the Geelong Osteoporosis Study.[1] Total lean mass (LM, kg) was measured by DXA (Lunar) and low LM defined as T-score < -1.[2] We identified sarcopenia in terms of both low muscle mass and function. Obesity was defined as BMI ≥ 30.0 kg/m^2. Low muscle function was based on performance using the timed up-&-go (TUG) test (distance 3 m, cut-off 10 s). Physical activity scores were determined using a questionnaire for the elderly and low physical activity levels identified as scores below the median. Falls were self-reported over the previous 12 months. Associations between sarcopenic obesity (and its components), physical inactivity and falls were determined using logistic regression after adjusting for age.

Results: In this sample, 191 (43.8 %) had low LM, 179 (41.1 %) had TUG >10 s, 119 (27.3 %) were obese and 8 (1.8 %) had all three, thereby meeting criteria for sarcopenic obesity. Age-specific prevalence for sarcopenic obesity was 0.6 % 60–69 y, 2.4 % 70–79 y, 2.8 % 80+ y. Low physical activity was associated with low LM/height^2 (OR 1.55, 95%CI 0.88-2.73, p = 0.1), high TUG (OR 2.19, 95%CI 1.39-3.47, p < 0.001) and obesity (OR 1.97, 95%CI 1.25-3.12, p = 0.004). The likelihood of a fall was associated with TUG >10 s (OR 1.74, 95%CI 1.10-2.75, p = 0.02), had borderline significance with low LM/height^2 (OR 1.40, 95%CI 0.82-2.40, p = 0.2) and was not associated with obesity (OR 1.01, 95%CI 0.65-1.56, p = 0.9). Women with sarcopenic obesity all had low physical activity scores and 5 (62.5 %) reported a fall (p = 0.3); there were too few for multivariable analyses.

Conclusion: The prevalence of sarcopenic obesity was low in this group of older women. However, participation bias cannot be excluded and results were dependent on criteria for case. Our cross-sectional analyses suggest that women with sarcopenic obesity were habitually less active, but falls data were less clear.

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P148
THE AGEING, CHRONIC DISEASE AND INJURY STUDY: EPIDEMIOLOGY OF HIP FRACTURES ACROSS WESTERN VICTORIA, AUSTRALIA

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Aims: To map the burden of hip fractures across the western region of Victoria, in Australia (Figure 1).
Methods: Data from hip fractures resulting in hospital admission were extracted from the Victorian Admitted Episodes Dataset (VAED) for men and women aged 40+ during 2010–2013 inclusive. An age-adjusted incidence rate (per 10,000 population/y) was calculated for the entire region. Crude incidence rates and length of acute care hospital stay were calculated for smaller geographical regions under responsibility of Local Government Councils; called Local Government Areas (LGAs). The association between LGA level age (proportion of individuals aged 70 y or older), accessibility/remoteness Index of Australia (ARIA) and socioeconomic status (SES) on hip fracture rates was determined using Poisson regression.
Results: For both sexes combined, the age-adjusted rate of hospitalisations for hip fracture across the whole region was 30.0 (95%CI; 29.0-31.0) per 10,000 population/year. For men, the age-adjusted rate was 19.2 (95%CI; 18.0-20.4) and for women, 40.0 (95%CI; 38.3-41.7). The highest incidence rates for both sexes occurred in the rural LGAs of Yarriambiack and Hindmarsh, as well as the LGA with the lowest SES, Central Goldfields (Figure 1). In both sexes, approximately two thirds of individuals were discharged from acute hospital care after ≤14 d (men: 67.1 % and women: 67.3 %). Age and ARIA were significant predictors of hip fracture rates (incidence rate ratios: $2.4x10^{-4}$; 95%CI 0.2 $x10^{-4}$ to 28.0 $x10^{-4}$ and 3.3; 95%CI 3.2 to 3.4, respectively). Rates also varied by SES; there was a 7-fold difference between the LGAs with the highest and lowest SES.

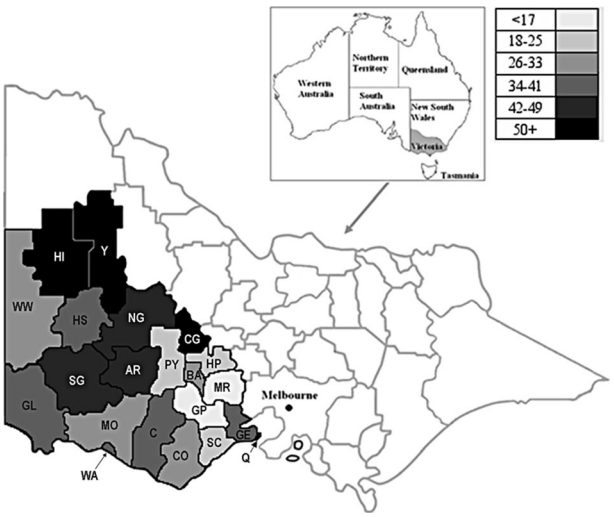

Figure 1. Legend: Heat map showing crude incidence rate for men and women combined aged 40+ y admitted to hospital for a hip fracture across the study region during 2011–2013 inclusive. The legend shows the shading as incidence rate per 10,000 population/y. AR = Ararat, BA = Ballarat, CG = Central Goldfields, CO = Colac-Otway, C = Corangamite, GL = Glenelg, GP = Golden Plains, GE = Greater Geelong, HP = Hepburn, HI = Hindmarsh, HS = Horsham, MR = Moorabool, MO = Moyne, NG = Northern Grampians, PY = Pyrenees, Q = Queenscliffe, SG = Southern Grampians, SC = Surf Coast, WA = Warrnambool, WW = West Wimmera and Y = Yarriambiack.
Conclusion: Crude incidence rates varied across the LGAs. Approximately two thirds of patients had acute hospital care of ≤14 d. Age, ARIA and SES were associated with hip fracture rates. Further research is required to understand the differences observed across LGAs.

P149
EVALUATING SUCCESSFUL DISEASE MANAGEMENT PROGRAMS

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Aims: To identify and determine the extent to which effective steps to change were/and were not present in the implementation of the Kaiser Permanente Southern California Healthy Bones Model of Care as perceived by physician champions and Healthy Bones Care Managers.
Methods: The subjects in the study included 20 Physician Champions and 35 Healthy Bones Care Managers employed in the Kaiser Permanente Southern California Healthy Bones Model of Care. 25 have been employed in their current role since the implementation of the program. Of those, 16 agreed to participate. The instrument for interviewing was an e-mail interview.
Results: Each participant was asked to respond to a set of nine standard questions. The results of their written responses were used to develop a set of themes characterizing steps and procedures thought to be particularly effective in support of a change initiative, and those thought to be particularly ineffective or counterproductive. Examination of qualitative data resulted in eight major findings. Among the findings were the following: nine effective and six ineffective themes were identified and as a result ten best practices for creating change efforts when implementing Disease Management Programs emerged.
1. Relentlessly informing, advocating, and networking.
2. Balancing the merits of consistency gained by centralized control, with the merits of creativity and innovation, guided by autonomous flexibility.
3. Creating strong multi-disciplinary champions.

4. Providing hands-on monitoring and management of change.
5. Creating inclusive feedback systems.
6. Leveraging external forces and available data to support change.
7. Rewarding meritorious or noteworthy behaviors, innovations, and ideas.
8. Personalizing interactions with potential change agents.
9. Providing adequate resources and administrative support.
10. Providing adequate short-term plans and goals.

Conclusion: This study utilized e-mail-based interviews to assess perceptions of the participants who were involved in the implementation of the Healthy Bones Program at their medical center within the Kaiser Permanente system in support of improved osteoporosis care for patients. An osteoporosis program was used as an example but any Disease Management Program could benefit from the results of this study. These steps will greatly increase the likelihood of success and long-lasting sustainability. The results of the study also support effective guides for healthcare reform initiatives at the national, corporate, and medical center levels. At this time there are many opportunities for the incorporation of Disease Management Programs in many avenues. Proponents of improvements to any healthcare system can use recommendations from this study to remove obstacles and barriers to change and foster supportive participation from involved health care professionals.

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VARIATION OF BONE TURNOVER MARKER (BTM) REFERENCE VALUES AMONG ASIANS

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Aims: Although BTMs have some clinical applications, they are not widely used in clinical decision making partly due to the wide variation of the reference values. This paper describes the geographical variation in BTMs reported from Asian countries.

Methods: A systematic search was conducted using the PubMed and Embase. We searched for BTMs or individual BTMs in Asia or different countries. Original research which published BTMs values were included, while reviews, comments and meta-analyses were excluded.

Results: Of 458 articles, 21 fulfilled the inclusion and exclusion criteria and considered for this study. A wide within-country and between-country variation of BTMs was seen in all age groups. Among premenopausal women, mean (SD) Intact OC ranged from 3.35(1.28) in Japan to 7.38(1.54) ng/mL in Thailand. Mean (SD) Total OC ranged from 9.26(3.17) in India to 15.4(6.0) ng/mL in Korea. Two studies in Japan involving subjects of same age group showed intact OC of 3.35(1.28) and 5.8(1.5) ng/mL. Similarly in India mean (SD) BAP were 15.9(4.18) and 53.7(32.7) U/L in two different studies involving subjects of same age. Observations were same among postmenopausal women. Mean (SD) intact OC ranged from 2.69(1.30) in China to 8.4(1.4) ng/mL in Japan. Total OC ranged from 10.02(1.68) in India to 29.8(10.8) ng/mL in Japan. Two studies in Japan involving subjects of same age showed Total OC of 14.5(5.4) and 29.8(10.8) ng/mL. BAP also showed similar variation and it ranged from 21.2(5.51) in India to 60.28(15.33) U/L in China. Urinary DPD, CTX and NTX, however, showed variations of lesser degree in both pre and postmenopausal women.

Conclusion: A wide between-country and within-country variation of serum BTMs was observed among pre- and postmenopausal women in Asia. Urinary BTMs showed a lesser variation. Differences in selection criteria of subjects and those inherited to analytical methods may have contributed to these differences.

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RELATIONSHIP BETWEEN BODY MASS INDEX AND PERCENT BODY FAT IN VIETNAMESE: IMPLICATIONS FOR THE DIAGNOSIS OF OBESITY

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Aims: The burden of obesity in Vietnam has not been well defined because there is a lack of reference data for percent body fat (PBF) in Asians. This study sought to define the relationship between PBF and BMI in the Vietnamese population.

Methods: The study was designed as a comparative cross-sectional investigation that involved 1217 individuals of Vietnamese background (862 women) aged 20 y and older (average age 47 y) who were randomly selected from the general population in Ho Chi Minh City. Lean mass (LM) and fat mass (FM) were measured by DXA (Hologic QDR 4500). PBF was derived as FM over body weight.

Results: Based on BMI ≥30, the prevalence of obesity was 1.1 % and 1.3 % for men and women, respectively. The prevalence of overweight and obesity combined (BMI ≥25) was

~24 % and ~19 % in men and women, respectively. Based on the quadratic relationship between BMI and PBF, the approximate PBF corresponding to the BMI threshold of 30 (obese) was 30.5 in men and 41 in women. Using the criteria of PBF >30 in men and PBF >40 in women, approximately 15 % of men and women were considered obese.

Conclusion: These data suggest that BMI underestimates the prevalence of obesity. We suggest that a PBF >30 in men or PBF >40 in women is used as criteria for the diagnosis of obesity in Vietnamese adults. Using these criteria, 15 % of Vietnamese adults in Ho Chi Minh City were considered obese.

Acknowledgement: This study is a part of Vietnam Osteoporosis Study (VOS) Project. We thank the following friends and colleagues for their support and help in the recruitment and providing logistic support for the study: Fr. Pham Ba Lam, Fr. Vu Minh Danh, Mr. Pham Doan Phong, Mr. Luong Thanh Phat, Mr. Nguyen Cong Phu, and Mr. Tien Ngoc Tuan. We also thank the doctors and medical students of the Pham Ngoc Thach University of Medicine, Ho Chi Minh City, Vietnam, for the data collection and clinical measurements.

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VITAMIN D STATUS IS LOW IN UNHEALTHY PEOPLE AGED ≥75, WHEREAS HEALTHY CONTROLS SHOW NEARLY OPTIMAL VITAMIN D LEVELS

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Aims: There is neither a consensus for how to define and assess vitamin D deficiency nor for optimal levels in elderly people. Objective: To compare vitamin D status in people ≥75 y selected from four groups with a frailty phenotype, combined with a control group free from serious illness, without prescribed vitamin D, and who considered themselves completely healthy.

Methods: S-25(OH)D) was measured using a LC-MS/MS method.

Results: Using the controls as a reference population for healthy adults ≥75 y, the observed reference interval for 25(OH)D for men and women was 31–123 nmol/L. Using the cut-off limit often suggested for vitamin D deficiency <50 nmol/L, only 13 % of the 169 controls were vitamin D deficient, in contrast to 49 % of orthopedic patients with hip fractures (n = 133), 31 % of stroke patients (n = 122), 39 % of frequent users of emergency departments (n = 81), and 75 % of homebound adult residents in long-term care nursing homes (n = 51). There was no significant correlation between skin type and vitamin D status. When all patients were included there was a small but significant seasonal variation, $p = 0.03$. In the controls, fracture patients and institutionalized group of patients, there were no seasonal variations.

Conclusion: The mean vitamin D concentrations in the healthy control group (74 nmol/L) was similar to suggested optimal levels based on physiological data and mortality studies, and much higher than that of the Swedish authority's recommended cut-off level for vitamin D deficiency (>50 nmol/L). The present study provides a basis for planning and implementing public guidelines for the screening of vitamin D deficiency, and vitamin D treatment for elderly frail patients

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THE CHANGING PROFILE OF HYPERCALCEMIA IN A TERTIARY CARE SETTING: AN 18-MONTH RETROSPECTIVE STUDY

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Aims: To determine the profile of hypercalcemia in a tertiary care hospital in north India.

Methods: All calcium measurements done on patient's sera over the period between 1 January 2014 and 30 June 2015 were retrieved from the Hospital Information System (eHIS) by the Information Technology department. The actual number of patients investigated for calcium status was determined. The initial serum calcium done on each patient was used to categorize hypercalcemia (serum total calcium of >10.4 mg/dL). A study was made to determine 1) the incidence of hypercalcemia and 2) frequency distribution of types of hypercalcemia.

Results: A total of 255,830 patients were registered in our hospital in a period of 18 months (January 1, 2014 till June 30, 2015). Serum calcium estimation was done in 26,297 (10.2 %) patients. Among them, 16,684 (63.5 %) presented in outpatient clinics, 8862 (33.7 %) as inpatients and 751 (2.8 %) as emergency patients. A total of 552 patients were found to have hypercalcemia, among them 347 (62.8 %) were inpatients and 205 (37.2 %) were outpatients. A total of 15 (2.7 %) patients had transient hypercalcemia (one calcium reading above 10.4 mg/d followed by at least 2 readings in normal range) and 537 (97.3 %) had sustained hypercalcemia (serum calcium above 10.4 mg/dL on more than two occasions). The incidence of hypercalcaemia was 2.09 %, being transient in 0.05 % and sustained in 2.04 %. The most common cause in the sustained group was malignancy (23.0 %). The second most common cause was primary hyperparathyroidism (18.2 %). Interestingly, we found emergence of two unusual groups of hypercalcemia, namely

hypercalcemia of chronic liver disease (CLD, n = 34) and hypervitaminosis D (n = 21) in the nonparathyroid group of hypercalcemia.

Conclusion: The profile of hypercalcemia in a tertiary care setting in India is changing. Hypercalcemia due to primary hyperparathyroidism is mostly asymptomatic. Hypervitaminosis D and hypercalcemia of advanced chronic liver disease are emerging as relatively newer causes of nonparathyroid hypercalcemia.

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P154
DOES THE IMPACT OF OBESITY ON BONE DENSITY DIFFER IN MEN AND WOMEN?

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Aims: Studies have reported the existence of obesity paradox in osteoporosis. However, the occurrence of obesity paradox by gender and menopausal status has not yet been thoroughly investigated, even though both genders differ in patterns and occurrence of obesity. Therefore, we investigate whether obesity effect on BMD by gender and menopausal status in Iranian patients referred for DXA scan.

Methods: 5892 consecutive patients (592 men, 1832 premenopausal, 3468 postmenopausal women) 20–91 y old referred for DXA scan were examined. All subjects underwent a standard BMD scans of hip (total hip, femoral neck, trochanter, Wards triangle, and femoral shaft) and lumbar spine (L1-L4) using a DXA scan and examination of body size. BMI was used to categorize these subjects as normal weight, overweight, and obese.

Results: BMD was higher in obese and overweight vs. normal weight men, pre- and postmenopausal women. Compared to men, pre- and postmenopausal women with normal weight, the age-adjusted odds ratio (95%CI) of osteopenia was 0.42 (0.22, 0.80), 0.31 (0.23, 0.41), and 0.38 (0.29, 0.51) for obese men, pre- and postmenopausal women. Corresponding figure for osteoporosis was 0.22 (0.11, 0.45), 0.16 (0.10, 0.26), and 0.16 (0.10, 0.26), respectively.

Conclusion: Obesity is associated with BMD of hip and lumbar spine and overweight and obesity seems to have similar influence on osteoporosis in both genders and menopausal status, and this might be worthy of further investigations

P155
BONE DISEASE IN PATIENTS WITH PRIMARY HYPERPARATHYROIDISM IN INDIA: PROSPECTIVE DATA FROM A SINGLE INSTITUTION

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Aims: Bone disease has been traditionally regarded as the predominant manifestation (77 %) of primary hyperparathyroidism (PHPT) in India[1]. Aim of this study was to evaluate the clinical and biochemical profile of patients with PHPT.

Methods: This was a prospective study conducted at a single institution in India. Consecutive patients diagnosed with PHPT from year 2014–2016 were included. Clinical, biochemical and radiological parameters were evaluated. Bone status was assessed by symptoms, radiographic evidence of bone disease and DXA scan. Dietary calcium intake was recorded. Patients lacking specific symptoms or signs traditionally associated with hypercalcemia or PTH excess were diagnosed as having asymptomatic PHPT.

Results: A total of 100 consecutive patients were studied prospectively. Among them 51 % were symptomatic and 49 % were asymptomatic. The mean age (SD) was 53.5 (14.5) y and the female to male ratio was 2.1:1. Predominant manifestations included renal calculi (23 %) followed by bone pains (21 %), polyuria (16 %) and pancreatitis (15 %). One patient reported history of fragility fracture. None of the patients had brown tumors or bone deformities. 36 patients had radiographic evidence of bone disease and 45 (21 asymptomatic and 24 asymptomatic) patients had osteoporosis by DXA scan. Abnormal parathyroid gland was localized by ultrasound in 94 patients, Tc-99-sestamibi scintigraphy (MIBI) scan in 91 patients and C-11 methionine PET scan in 2 patients. Eighty seven out of 100 patients met criteria for surgery and underwent parathyroidectomy. The asymptomatic group had significantly lower mean serum calcium (11.7 vs. 12.7 mg/dL), lower median intact PTH (iPTH) level (200.2 vs. 266 pg/mL), lower mean 24-h urinary calcium (237.5 vs. 294.5 mg/d), lower mean serum alkaline phosphatase (ALP) levels (118.1 vs. 187.7 U/L) and lower mean adenoma weight (1.87 vs. 3.59 g) compared to symptomatic group. Dietary calcium intake and serum 25-dihydroxyvitamin D levels were not significantly different between the two groups.

Conclusion: Symptomatic bone disease was seen in a small number of PHPT patients in this study. None of the patients had classical bone disease. This is in contrast to existing Indian studies on PHPT. Low prevalence of bone disease in PHPT patients in this study suggests a changing clinical profile of PHPT in India. Asymptomatic patients had lower serum calcium, iPTH, 24-h urinary calcium, serum ALP levels and adenoma weight compared to symptomatic group.

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REDUCED BONE MINERAL DENSITY IN HUMAN IMMUNODEFICIENCY VIRUS-INFECTED INDIVIDUALS: A META-ANALYSIS OF ITS PREVALENCE AND RISK FACTORS

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Aims: We systematically reviewed published literature on the prevalence of reduced BMD and its associated factors in HIV-infected individuals.

Methods: A literature search was conducted from 1989-May 2015, using 6 databases: Medline, CINAHL, Embase, Science Direct, Cochrane and Web of Science. Included were studies which recruited HIV-infected individuals ≥18 y of age, used DXA to measure BMD, were full text articles and published in English. Studies were excluded if the following were not reported: prevalence of osteopenia/osteoporosis without a comparison group, and the outcomes of interest (e.g., BMD or T-score). Articles that reported HIV-infected individuals co-infected with hepatitis B or hepatitis C were also excluded, as a systematic review has just been recently published on this topic. Data were extracted independently by two teams of researchers, and recorded in a standardised extraction form. Any differences were resolved by discussion between the two teams.

Results: A total of 21 cross-sectional and 11 longitudinal studies were included. However, this abstract will only focus on the outcomes obtained from the cross-sectional studies. The prevalence of reduced BMD was higher in both HIV-infected and antiretroviral therapy(ART)-treated individuals when compared to their respective controls, whereby the odds ratio of reduced BMD was 2.2(95%Cl 2.3,2.58) and 2.1(95%Cl 1.46, 2.88), respectively. Reduced BMD in protease inhibitor(PI)-treated individuals was 1.3 times higher that non PI-treated individuals (95%Cl 0.92,1.74), but this did not reach statistical significance. Only one study reported the effect of tenofovir on reduced BMD. A higher proportion of tenofovir-treated individuals (52.6 %) had lower BMD compared to non-treated individuals (42.7 %, $p = 0.248$). Older age, history of bone fracture, low BMI, low body weight, ethnicity, low fat mass and lean mass were found to be associated with low BMD.

Conclusion: The prevalence of reduced BMD in HIV-infected and ART-treated individuals was approximately two times more as compared to their respective controls. PI and tenofovir-treated individuals had a higher prevalence of reduced BMD as compared to their respective controls, but our results were not statistically significant. The risk factors that were associated with low BMD were older age, history of bone fracture, low BMI, low body weight, ethnicity, low fat mass and lean mass.

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THRESHOLD OF JOINT SPACE WIDTH FOR KNEE PAIN IN JAPAN: THE ROAD STUDY

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Aims: Knee pain is the principal clinical symptom of knee OA. Although much effort has been devoted toward a definition of knee pain, the correlation with radiographic severity of the knee OA by categorical methods such as Kellgren Lawrence grade was not as strong as one would expect. In this categorical system, joint space narrowing and osteophytosis are not assessed separately, while these accumulating lines of evidence have indicated that joint space narrowing and osteophytosis may have distinct etiologic mechanisms, and their progression may be neither constant nor proportional. Although osteophytosis also has some effect on ADL and QOL, joint space narrowing is the primary outcome in studies of OA. Thus, to examine the association between knee OA and pain, joint space narrowing should be assessed separately. Thus, an automatic system that can quantify the joint space width of knee OA on standard radiographs and allows for objective, accurate, and simple assessment of the structural severity of knee OA was developed. The objective of the present study was to clarify the association of joint space narrowing with knee pain in Japanese men and women using a large-scale population-based cohort of the Research on Osteoarthritis/osteoporosis Against Disability (ROAD) study.

Methods: From the 3040 participants in the ROAD study, the present study analyzed 2733 participants who completed the radiographic examinations and questionnaires regarding knee pain (975 men and 1758 women; mean age, 69.9 ± 11.2 y). This study examined the association between minimum joint space width (mJSW) in the medial compartment and pain at the knee. mJSW was measured in the medial and lateral compartments of the knee using a knee OA computer-aided diagnosis system.

Results: mJSW in subjects with and without knee pain were 2.4 ± 1.2 mm and 3.3 ± 0.9 mm, respectively, in men ($p < 0.05$) and 2.0 ± 1.1 mm and 2.8 ± 0.8 mm, respectively, in women ($p < 0.05$). Medial mJSW/lateral mJSW in subjects with and without knee pain were 57.2 ± 27.6 mm and 72.8 ± 20.8 mm,

respectively, in men ($p < 0.05$) and 52.2 ± 31.5 mm and 71.4 ± 33.0 mm, respectively, in women ($p < 0.05$). After adjustment for age and BMI, medial mJSW as well as medial mJSW/lateral mJSW were significantly associated with knee pain ($p < 0.05$). The threshold of medial mJSW by ROC curve analysis was 2.87 mm (sensitivity 0.67, specificity 0.65, AUC 0.70, 95%CI 0.64-0.75) in men and 2.01 mm (sensitivity 0.43, specificity 0.689, AUC 0.69, 95 % CI 0.66-0.73) in women, while that of medial mJSW/lateral mJSW was 55.2 % (sensitivity 0.45, specificity 0.68, AUC 0.66, 95 % CI 0.60-0.72) in men and 57.9 % (sensitivity 0.57, specificity 0.75, AUC 0.69, 95 % CI 0.66-0.73) in women.

Conclusion: The present cross-sectional study using a large-scale population from the ROAD study showed that joint space narrowing had a significant association with knee pain. The thresholds of joint space width for knee pain were approximately 3 mm in men and 2 mm in women.

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MALNUTRITION AND ANAEMIA ARE ASSOCIATED WITH HIP FRACTURE TYPE BUT NOT WITH AGE OR RESIDENTIAL STATUS

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Aims: Hip fractures (HF) in Australia remain a significant burden in the health system, Fisher et al. (J Trauma Manag Outcomes 2012;6:22012) found trochanteric HF is likely to be older, anaemic and hypoalbuminaemic. It is uncertain, however, if age and institutionalization has a direct influence on malnutrition, and thus indirectly, HF type. Furthermore, patients who readmit for 2nd HF may skew the nutritional profile of HF type.

Methods: Demographic and clinical data prospectively collected from 738 patients admitted to The Canberra Hospital between 1999–2011 with low energy HF (malignancy and 2nd HF admission excluded) were analysed regarding fracture type and pre-operative blood tests reflecting nutritional status specifically serum vitamin D, haemoglobin, albumin and blood lymphocyte count.

Results: Trochanteric (T) HF occur in older patients compared to cervical (C) HF (46.9 % vs. 40.9 % >85 y, $p = 0.0069$). No difference is found in institutionalisation between both HF types (C:T 60.6 % vs. 67 %, $p = 0.874$). There is a high incidence of nutritional deficiency in HF patients overall; 79 % hypovitaminosis D, 26 % anaemia, 57.8 % lymphocytopaenia, 32 % hypoalbuminaemia. Trochanteric HF patients are more undernourished in terms of anaemia and hypoalbunminaemia (C:T 20.0 %:34.2 % $p < 0.0001$ and 27.0 %:37.5 % $p = 0.0031$, respectively); this nutritional profile is not found to be associated with older age or institutionalisation.

Conclusion: This study reaffirms the close association between malnutrition and HF type; anaemia and hypoalbuminaemia are found to be independent of age and institutionalisation profile. Further studies may reveal the pathophysiology of anaemia and hypoalbuminaema underlying development of specific HF type.

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TRENDS IN HIP FRACTURE RATES IN TAIWAN: A NATIONWIDE STUDY FROM 1996–2010

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Aims: Fractures of the proximal femur remain a major cause of mortality and morbidity. Recent studies worldwide reported a trend of decrease in hip fracture rates. We aimed to examine recent trends in hip fracture rates, in-hospital mortality rates and length of hospital stay (LOS) due to hip fractures in people aged 55 and over in Taiwan.

Methods: This is a time trends study. We used national data from the National Health Insurance Research Database between 1996–2010 in Taiwan. Insurants aged 55 and over were included. The outcome measures were hip fracture rates, in-hospital mortality rates and LOS due to hip fractures. We classified hip fractures into femoral neck, trochanteric and subtrochanteric fractures.

Results: We identified 250,919 hospitalizations for hip fractures. The total number of hip fractures increased steadily from 12,479 to 19,841 cases. There was a trend towards initial increase and then later decrease in both hip fracture crude and age-adjusted rates (from 305.6 and 457.9 to 390.0 fractures per 100,000 person-years, respectively). LOS decreased by 46.5 % (17.53 to 9.38 days). By contrast, mortality rates for hip fractures decreased initially but re-emerged later with a total decrement of 16.5 % (2.10 to 1.88 deaths per 100 hip fracture admissions). Women outnumbered men in all types of hip fractures, but men had higher in hospital mortality rates. LOS was similar between genders and among age groups. The turning point for change in trends was year 2003.

Conclusion: While LOS shortened gradually since 1996, the absolute number of hip fractures in Taiwan continues to rise. There is still room for improvement in reducing mortality due to hip fractures.

Acknowledgement: This study is based in part on data from the National Health Insurance Research Database provided by the National Health Insurance Administration, Ministry of Health and Welfare and managed by National Health Research Institutes (Registered number NHIRD-101-534).

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HIP FRACTURE RATES IN ASIA; A SYSTEMATIC REVIEW

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Aims: To study the hip fracture rates (HFR) in Asia to find out between-country differences and secular trends in HFR.
Methods: A systematic search was done in PubMed and Embase using the terms "hip fracture incidence" or "hip fracture rate" or "new hip fracture" and specific Asian countries; Malaysia, Singapore, China, Japan, Taiwan, Thailand, Hong Kong, Korea, India, Pakistan, Sri Lanka and Bangladesh. Original studies publishing HFR/incidence were included in the review after agreement of two authors. Review articles, meta-analyses, comments and case reports were excluded. HFR given are for 100,000 population unless stated otherwise.
Results: In Singapore, the age-adjusted HFR for 1991–1998 were 152 in men and 402 in women. In another study in 1997, the corresponding values were 164 and 442. In Malaysia, the age-adjusted HFR in men and women were 88 and 218 in 1997. In 1995 the HFR in Hong Kong were 11/1000 in women and 5/1000 in men. In 1997, the age-adjusted HFR in men and women were 180 and 459 in Hong Kong. During 2001–2009, the age-adjusted HFR among the population aged 65 and over in Hong Kong decreased from 381.6 in men and 853.3 in women to 341.7 and 703.1. In Thailand, the age-adjusted HFR in men and women were 114 and 289 in 1997. A study in 2006–2007 in Thailand reported HFR of 203 in males and 487 in females. In Taiwan, during 1996 and 2000, the age-adjusted HFR reported were 225 and 505 in men and women. During 2004–2011 the reported HFR were 317 and 211 among women and men, in Taiwan. In 1990 the age-standardized HFR in China were 87 and 97 among women and men. In 1994 the corresponding values were 67 and 81. In Japan, the age-adjusted HFR were 75.7 and 296.1 in 1987/1988 and 123.6 and 420 in 2004 in men and women. In Korea from 2001 to 2004, the HFR in women increased from 250.9 in 2001 to 262.8 in 2004, in men decreased from 162.8 in 2001 to 137.5 in 2004. Another study in Korea showed hip fracture incidence to increase from 100.6 in men and 194.4 in women in 2002 to 114.2 in men and 278.4 in women in 2011. In 2007, a study in Southern Sri Lanka reported 73 hip fractures per 100 000 people aged over 50.
Conclusion: There is a wide variation of hip fracture incidence in Asian countries. Apart from Hong Kong, other countries reported an increase trend in the hip fracture occurrence during the past.

P161
FATTY ACID INTAKE IN RELATION TO RISK OF HIP FRACTURE IN THE SINGAPORE CHINESE HEALTH STUDY

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Aims: The relationship between fatty acid intake and risk of osteoporotic hip fractures is unclear. In this study, we examined the associations between dietary fatty acids and risk of hip fracture in the Singapore Chinese Health Study.
Methods: This is a prospective cohort of 63,257 Chinese men and women of ages 45–74 y during recruitment from 1993–1998 in Singapore. At baseline, fatty acid intake from habitual diet was assessed by using a validated food frequency questionnaire and the Singapore Food Composition database developed specifically for this Cohort. Incident hip fracture cases within the cohort were identified via linkage with nationwide hospital registry. We excluded those with prevalent hip fracture, baseline history of cancer and who reported extreme energy intakes (n = 3055). Multivariate Cox proportional regression model was used to estimate hazard ratio (HR) and its 95%CI, with adjustment for established and potential risk factors of hip fracture, including lifestyle and other diet factors.
Results: During a mean follow-up of 16.7 years, we identified 2374 incident cases of hip fracture. There were 658 cases among 26,795 men and 1716 cases among 33,407 women. Among the dietary fatty acids examined, saturated fatty acid and marine omega-3 polyunsaturated fatty acid intake displayed a dose-dependent inverse association with risk; the HRs (95 % CI) comparing extreme quartiles were 0.86 (0.75-0.98) (P for trend = 0.026) for saturated fatty acid, and 0.88 (0.78-1.00) (P for trend = 0.043) for marine omega-3 polyunsaturated fatty acid intake. These associations were not different by gender. Intake of monounsaturated, plant-based omega-3 and omega-6 polyunsaturated fatty acid had no significant association with hip fracture risk.
Conclusion: Our study concurred with other studies (1,2) in supporting a potential role of marine omega-3 polyunsaturated fatty acid in preventing hip fractures. Contrary to previous USA-based studies (3,4), we showed beneficial effects for bone health with increased saturated fatty acid intake in this Asian population, and this needs to be validated or refuted in further prospective studies.
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CHARACTERISTICS OF ELDERLY OSTEOPOROTIC FEMALES IN TAIWAN: AN ANALYSIS OF DATA FROM NAHSIT 2005–2008

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Aims: To explore the anthropometric and lifestyle characteristics of female osteoporotic adults.
Methods: Data collected from the participants in the Nutrition and Health Survey in Taiwan (NAHSIT) 2005–2008 was used. Female adults aged 50 y and older were grouped as osteoporotic if they had at least one BMD T-score below −2.5 at any of the bilateral femoral neck, ultradistal radius, or vertebrae 1–4 of lumbar spine.
Results: 48.1 % (52/108) of the females met the above mentioned criterion for osteoporosis. Comparing with their nonosteoporotic counterpart, osteoporotic women were significantly older (69.4 ± 8.7 vs. 61.2 ± 7.4 y, $p < 0.0001$), lighter in weight (56.1 ± 11.4 vs. 60.9 ± 7.5 kg, $p = 0.014$), shorter in height (151.2 ± 5.9 vs. 153.6 ± 5.7 cm, $p = 0.036$), less in percent body fat (34.0 ± 10.6 vs. 37.8 ± 5.9 %, $p = 0.027$), and higher in serum level of homocysteine (10.9 ± 5.2 vs. 9.2 ± 2.1 μmol/L, $p = 0.029$); they also had significantly lower intake of vitamin B6 (1.6 ± 0.9 vs. 2.0 ± 1.3 mg/d, $p = 0.045$) and a trend toward significantly lower intake of calories from protein (15.9 ± 5.0 vs. 17.5 ± 3.9 %, $p = 0.074$).
Conclusion: In female adults aged 50 y and older, higher percent body fat may be protective against osteoporosis, and the nutrition status such as vitamin B and protein intake may also play some roles in maintaining bone health.
Acknowledgement: The research project "Nutrition and Health Survey in Taiwan 2005-2008" is sponsored by the Food and Drug Administration, Department of Health, Executive Yuan (DOH101-FDA-31411). The assistance provided by the institutes and efforts made by all contributed to the survey are greatly appreciated. The views expressed herein are solely those of the authors.

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THE PERCEPTION AND BEHAVIOR OF CALCIUM AND VITAMIN D CONSUMPTION AMONG MIDDLE-AGED WOMEN IN TAIWAN

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Aims: To evaluate the awareness and behaviors of calcium and vitamin D consumption among middle-aged women in Taiwan.
Methods: A total of 1107 women aged 30 y and older living in Taiwan were invited by e-mail to complete an online-survey with valid questionnaires during Apr 6 and 11, 2016. OSTA index, as [body weight- age] x 0.2, was used to evaluate the risk of osteoporosis. OSTA index ≤ −1.0 was defined to be the moderate-high risk group of osteoporosis. The standard deviation of sampling error with 95%CI was less than 2.95 %.
Results: Of the 1107 subjects, 77(7.0 %) was defined as moderate-high risk group based on OSTA index. 937(84.6 %) reported they were in face of bone loss and 69.3 % considered they would suffer from osteoporosis in the future. Even so, approximately one-third of them did not know about bone loss and 89.8 % had misperceptions about the daily recommendations of vitamin D. 95.6 % subjects thought themselves the consumption of calcium was inadequate. However, only one-third of them were using the calcium supplement, and 22.0 % of them were using vitamin D supplement.
Conclusion: The discrepant perception and behavior among middle-aged women in calcium and vitamin D consumption is common in Taiwan. It is necessary for more education and communication to provide healthy strategies against bone loss and ameliorate the possible epidemic problem of osteoporosis in the future.
Acknowledgement: This work was supported by Grant from Taiwanese Osteoporosis Association.

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CLINICAL INCIDENCE AND MANAGEMENT OF ATYPICAL FEMORAL FRACTURES

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Aims: Osteoporosis is one of the growing problems to treat at a proper time. Despite the medication, atypical femoral fracture is another type of complication in osteoporosis. Our study aimed at incidence and characteristics assumed of increasing the risks of atypical femoral fracture. Also we examined the results of operation for atypical femoral fractures.
Methods: A retrospective search was conducted for patients hospitalized for femoral fracture between January 1, 2010 and December 31, 2014. The medical records regarding the characteristics supposed to increasing the risks of atypical femoral fracture were collected with radiographs. The data were compared to two controls with a femoral fragility fracture or a traumatic fracture, paired for sex and age.

Results: Fifty-four cases of atypical femoral fractures were collected during the period. The incidence of atypical femoral fracture represented 8.2 cases per 100,000 person-years. The association between the occurrence of atypical femoral fracture and bisphosphonates use showed statistically significant change. And compared to matched group, atypical femoral fracture patients had greater cortical thickening, more varus femoral neck angle, and higher femoral offset. All cases treated operation healed with a mean period of 18.4 weeks.
Conclusion: Our study confirms the low incidence and association between the increasing risks and the occurrence of atypical femoral fracture. Proper operative management appears to be reliable way of preventing the progress of atypical fracture.

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CHARACTERISTICS AND OUTCOMES OF PATIENTS WITH OSTEOPOROTIC HIP FRACTURE: A SINGLE CENTER EXPERIENCE

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Aims: Hip fracture is the most severe and economically most important complication of osteoporosis in aged people. This study aimed to determine characteristics of patients with osteoporotic hip fracture at KAMC-Riyadh and assess if care delivered is in accordance with international standards.
Methods: This is a retrospective cohort study done at KAMC-Riyadh involving patients above 40 years and admitted for hip fracture secondary to low-grade trauma last 2008–2012. Charts of eligible patients were collected and analyzed.
Results: A total of 264 patients (133 males and 131 females) were included. The most common fracture types involved the trochanter (49.3 %), followed by femur neck (46.2 %). History of fall accounted for 115 (43.6 %) of patients. BMD was assessed in only 15.5 % (N = 41) of patients. Almost all patients underwent surgery (N = 243, 92 %). Surgical complications were noted in 15 (5.7 %) patients and medical complications in 21 (7.9 %) patients. Vitamin D and calcium were the most common medications given. Post-op follow up revealed that 62 patients (23.5 %) patients died one year after surgery while 29 patients (11.1 %) died within one year after surgery.
Conclusion: The present study reveals that BMD testing is rarely documented or requested among adult patients diagnosed with hip fracture secondary to low-grade trauma in KAMC-Riyadh. Furthermore, mortality rate among these patients less than or one year post-operation is very high. Findings warrant urgent attention and reassessment of clinical care provided for these patients.

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MORPHOGENESIS OF RENAL PROXIMAL CONVOLUTED TUBULES AND CHEMICAL STRUCTURE OF BONES UNDER THE IMPACT OF TOLUENE VAPORS IN WHITE RATS

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Aims: To analyze chemical composition of bones (tibia, hipbone and third lumbar vertebra) and structure of renal proximal convoluted tubules in rats after 60-day exposure to toluene (Tol) and application of thiotriazoline (Th) and *Echinaceae tinctura (ET)* as medication.
Methods: The experiment involved 420 male rats (young, adult and old): the first group was control group; the second group animals that received inhalations of Tol; the third group received Tol and Th; the fourth group animals that received Tol and *ET*.
Results: Upon cessation of Tol exposure, shares of mineral content, calcium and calcium/phosphorus ratio were lower than those of the control group by 6.13-7.78 % 11.77-12.86 % and 16.96-18.40 %, in mature animals by 5.43-6.65 % 9.75-10.97 % and 13.46-16.20 % and in senile rats by 5.62-6.65 % 8.45-8.94 % and 11.86-12,55 % ($p < 0.05$ in all cases). Thus in immature, mature and senile rats diameters of proximal tubules and tubular lumen were higher than control data by 9.53 % and 17.66 %, 8.28 % and 15.47 %, 7.26 % and 18.84 %, respectively. The height of the epithelium in immature rats was higher than control data by 3.39 %, and in senile animals by 5.97 %. This demonstrates the significant failure of reabsorption (including calcium) in proximal convoluted tubules. In readaptation period macroelemental contents of bones in young animals restored after the 15th day of observation, in adult animals alterations persisted up to the 30th day of observation and gradually reduced. In old animals alteration persisted throughout the whole observation period. The structure of proximal convoluted tubules restored in a similar manner judging by the amplitude. After application of Th (117.4 mg/kg) on the background of Tol in comparison with non-medicated animals macroelemental contents of tibia, hipbone and third lumbar vertebra in young animals restored after the 15th day of observation, in mature animals restoration signs were registered in the period from the 15th to the 60th days of observation and in old animals from the 7th to the 60th days of observation. After application of *ET* (0.1 mg of dry substance per 100 g) changes of macroelemental contents of bones in young animals in comparison with control data restored after the 15th day of observation, in mature by the 30th day, in senile animals changes were registered by the 60th days of observation. Th thus appeared to be more effective than *ET*.

Conclusion: 60-day inhalation of Tol results in instability of chemical composition of bones and failure of reabsorption in proximal convoluted tubules. Deviations degree and recovery rate depend on age of animals. Faster recovery rate was observed in young animals while old animals exhibited few signs of recovery. Application of Th or *ET* reduces negative effects of Tol.

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EXPRESSION PROFILING OF MITOGEN ACTIVATED PROTEIN KINASE (MAPK) SIGNALLING PATHWAY IN SPORADIC PARATHYROID TUMORS

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Aims: Molecular mechanism associated with parathyroid tumorigenesis is partially understood. The present study was designed to study expression profiling of MAPK signalling pathway with cell cycle regulator molecules activated by Erk1/2 Pathway in sporadic parathyroid adenoma.
Methods: Gene expression of MAPK signalling pathway molecules were studied in 20 parathyroid adenoma and 4 normal parathyroid tissue samples. Total of 84 genes associated with MAPK signalling pathway including 15 activated transcription factors and 20 cell cycle regulatory molecules were analysed by real-time PCR based array. Fold change up/down-regulation of molecules were analysed in between parathyroid normal and adenoma tissue samples. Statistical analysis was performed to correlate the expression pattern of the genes with biochemical indices of the parathyroid adenoma.
Results: PHPT patients recruited have symptoms like weakness and fatigue (13.65 %), bone pain (12.60 %), renal stone disease (8.40 %), fracture (5.25 %) and gall stone disease (2.10 %). PCR array analysis revealed that overall 8 molecules were significantly upregulated and 14 were downregulated in parathyroid adenoma compared to normal parathyroid tissue samples. Upregulated genes (adenoma to control ratio >2.0, $p \leq 0.05$) in parathyroid adenoma were ARAF, MAP2K12, MAX, HSPB1, HRAS, CREBBP, CCND1 (cyclin D1) and CDK4 (cyclin dependent kinase 4). Downregulated genes (adenoma to control ratio <0.5, $p \leq 0.05$) were cell cycle regulatory molecules (CDKN2A (cyclin dependent kinase inhibitor 2A), CDKN2B (cyclin dependent kinase inhibitor 2B) and retinoblastoma1) and MAPK8, MAPK10, LAMTOR3, DLK1, FOS, ATF2, MAP3K4, MAP4K1, MEF2C, MYC and MOS. Expression of CDK4 was positively associated with plasma iPTH level ($r = 0.61$, $p = 0.04$) and the tumor weight ($r = 0.80$, $p = 0.02$) of the PHPT patients. Expression of HSPB1 was also positively associated with tumor weight ($r = 0.91$, $p = 0.002$). CDKN2A was negatively correlated with iPTH level ($r = 0.65$, $p = 0.04$) and expression of MYC was negatively correlated with alkaline phosphatase level ($r = -0.70$, $p = 0.01$) of the PHPT patients.
Conclusion: Cell cycle regulatory genes are highly dysregulated in sporadic parathyroid adenoma and also associated with the biochemical parameters of the disease. Molecules with dysregulated expression need to be studied for understanding their role in parathyroid tumorigenesis.
Acknowledgement: This work was supported by research grant from Endocrine Society of India (ESI) (Id- 201512003).

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THE ROLE OF CORTICAL BONE IN HIP FRACTURES: FEMORAL CORTICAL INDEX AS A DIAGNOSTIC TOOL FOR BONE FRAGILITY

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Aims: The femoral cortical index (FCI) assesses bone stock using the ratio between the diameter of the femoral shaft and the thickness of the cortical bone calculated 10 cm distal to the center of the small trochanter in an AP view X-Ray of the femur. Aim of our study is to evaluate a possible association among low values of FCI, risk factors, comorbidities and serum 25-hydroxyvitamin D levels and to establish the importance of FCI as a potential predictor of a new fracture
Methods: We conducted a retrospective study on 366 consecutive patients (90 men and 296 women) (range 60–103 y) surgically treated for hip fractures from March 2013 to June 2015, after informed consent in our Orthopaedic Department and that never received any medical treatment for osteoporosis. FCI has been calculated by routine clinical radiographs of the pelvis both on fractured femur and on the opposite side. For each patient, we analyzed the presence of comorbidities (such as diabetes, hypertension, IRC, rheumatoid arthritis), osteoporosis risk factors and blood levels of vitamin D, usually evaluated in our patients with fragility fractures.
Results: Average values of FCI were 0.42 (range 0.18-0.58) at the fractured femur and 0.48 at the opposite side (range 0.25-0.66) with a statistically significant difference ($p = 0.002$). At the fractured side an average value of 0.45 was found in men, and of 0.40 in women. Patients with severe hypovitaminosis D (serum concentration <12 ng/ml) had minor FCI compared to those with a moderate deficiency (0.41 vs. 0.46, $p < 0.01$). The presence of comorbidities or osteoporosis risk factors had a different influence on the values of FCI.

Conclusion: We found a correlation among low values of FCI, clinical factors related to bone fragility and severe hypovitaminosis D in elderly patients with hip fractures. Comorbidities and risk factors have a different weight in FCI variations, while the severe hypovitaminosis has a major impact on it. As described in the literature regard the DXA limitations in elderly, FCI could be a useful tool in terms of bone fragility evaluation and fracture risk prediction.

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NUCLEAR EXPRESSION OF VITAMIN D RECEPTOR AS A MOLECULAR LINK OF OSTEOPOROSIS-SARCOPENIA CONNECTION

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Aims: Bone and muscle are tissue in close relationship and emerging evidence suggests that vitamin D (Vit.D) may play a direct role in both muscle and bone homeostasis. Nevertheless, precise molecular mechanisms by which Vit.D affects the homeostasis of muscle and bone tissues are still unclear. The main aim of this study was investigated the role of Vit.D and their receptor (VdR) in regulation of muscle homeostasis of osteoporotic and osteoarthritis patients.

Methods: For this study, we analyzed 60 muscle biopsies of *vastus lateralis* in total*:* 30 biopsies of osteoporotic *patients* and 30 biopsies of osteoarthritic women, as control (OA/CTRL). Clinical report included anamnestic data, serum concentration of Vit.D and PTH and DXA. Muscle atrophy, VDR, BMP-2 and myostatin expression were evaluated by immunohistochemical reaction.

Results: The morphometric analysis of muscle fibers in OP patients showed more than 48.00 % of atrophic fibers with prevalence of type II fibers. As concern VdR, we note a significantly different expression of activated VdR (nuclear) in OA/CTRL muscle tissues respect to OP group. Conversely, no different was observed for cytoplasmic expressions of VdR (OP: 213.94 ± 127.51; OA: 193.90 ± 107.08). Surprisingly, we note that in muscle tissue of OP patients the absence of nuclear VdR was associated with atrophy of type II fibers and absence of BMP-2 expression. Unlike, the number of myostatin-positive fibers in OP patients (42.85 ± 59.52) was significantly higher compared to OA group (17.21 ± 17.66).

Conclusion: Our results demonstrated that activation of VdR, and their translocation into nucleus, is related to onset of sarcopenia. Indeed, we note low level of nuclear VdR in muscle samples characterized by high percent of atrophic fibers. Moreover, the evidence of relationship between type II fibers atrophy and impairment of VdR activation in OP patients, suggest a molecular correlation between Vit.D signaling and muscle regeneration. In conclusion, the identification of early and late mechanisms by which Vit.D affects muscle homeostasis could provide a rationale for the establishment of a clinical correlation between Vit.D levels and muscle health. In future, we will expect to identify patient's molecular profiles able to predict the clinical response to Vit.D supplementation.

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ULTRASTRUCTURE OF BIOMINERAL OF THE MANDIBULAR RAMUS IN RATS OF VARIOUS AGES AFTER EXCESSIVE PALM OIL INTAKE

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Aims: To analyze ultrastructure of biomineral of the mandibular ramus in rats of different ages after excessive palm oil (PO) intake and administration of thiotriazoline (T) and *Garciniae extract (GE)* as medication.

Methods: The experiment involved 216 rats of three ages: immature (1 month old), mature (6 months old) and elderly animals (22 months old). The animals were split into the groups as follows: the 1st group comprised intact animals (the controls), the 2nd group comprised the animals that received intragastric PO in dosage of 30 mg/kg of body weight (modeled alimentary obesity), and the 3rd group PO and intragastric *GE* in dosage of 0.25 mg/kg of body weight. The animals were withdrawn from the experiment by the 1st, 10th, 30th and 60th day after 6 weeks of PO intake. Burned and powdered mandibular rami were taken to X-ray scatter analysis (V.I. Luzin, 2005). The X-ray device employed Kα copper radiation with wavelength of 0.1542 ηM; anode voltage and amperage were 30 kV and 20 A, respectively. From the data obtained we calculated crystallographic parameters of the bone mineral. The data were analyzed by means of variation statistics using standard software.

Results: Excessive intake of PO resulted in derangement of the crystal lattice of biomineral of the mandibular ramus; deviations degree depends on age of animals. The alterations started manifesting from the 1st day of observation and continued growing throughout the whole experiment. In immature animals, crystallites dimensions increased as compared to

the control values from the 1st to 60th day of observation by 5.10 %, 5.53 %, 4.51 % and 5.01 % and microtexture coefficient decreased by 4.59 %, 4.65 %, 4.89 % and 5.39 %, respectively. In mature animals the same values changed in the same way by 4.95 %, 4.89 %, 6.02 % and 6.52 % and by 4.90 %, 4.91 %, 5.49 % and 6,78 % and in old animals by 4.21 %, 5.01 %, 7.14 % and 6.96 % and by 4.27 %, 5.10 %, 6.82 % and 7.59 %. Administration of *GE* reduced negative effects of PO as compared to the 2nd group (diminishing of elementary cells and crystallites and increase of microtexturing coefficient). After *GE* administration on the 60th day of observation in immature rats, crystallites dimensions decreased as compared to the 2nd group by 5.44 % and microtexture coefficient increased by 5.63 %, in mature rats by 5.87 % and 6.31 %, and in elderly rats by 3.31 % and 6.85 % respectively.

Conclusion: Long-term excessive intake of palm oil results in derangement of the crystal lattice of biomineral of the mandibular ramus. Terms and intensity of alterations depend on age of experimental animals. Administration of *GE* reduced negative effects of palm oil on the crystal lattice of biomineral of the mandibular ramus. Faster recovery rate was observed in young animals, slower in senile animals.

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VERTEBRAL FRAGILITY FRACTURES: FREQUENCY OF LOCALIZATION

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Aims: Vertebral deformities represent the most frequent and feared complication of osteoporosis together with the femur fracture they are associated to an increase of the morbidity, disability and of mortality. The evaluation of such deformities is assign from many years to the Genant semiquantitative method which establishes three degrees of reduction of vertebral height. Nowadays such deformities unfortunately are not always accurately described in the radiological report and so the patients delay the therapeutic approach. The aim of our study is to evaluate the prevalence of vertebral fractures from fragility in relation to the age, the sex and the eventual correlation of the mentioned fractures with the densitometric and BMI value.

Methods: We have conducted an observational study, of a duration of 4 y, over a sample of patients affected by osteoporosis assisted with the use of the CBM service offered by the operating unit of Geriatrics – University of Catania, hosted by the Cannizzaro Hospital. They have been enrolled 1062 subjects (average age 67.72 y old ±10.62 SD), 987 of them females and 75 males, who have arrived for the first time to our observation and have not been put under therapy for osteoporosis. All the patients have been put under radiological morphometry of the chest and lumbar tract from T4 to L4 using the Genant semiquantitative method in order to classify the vertebral fractures. The patients have been put also under densitometric exam at femoral level. The sample has been divided for range of age: subjects of age <65 (1st range), subjects of age between 65–74 y old (2nd range), subjects of age >75 (3rd range). It was also divided for BMI classes. The subsequent statistic significance studies of the confrontation of morphometric, densitometric and BMI data has been performed using chi-square - Yate's correction test or Fisher's exact test.

Results: From the data obtained by our sample, it is clear that are meanly interested vertebra T7, T8, T11 and T12. In the males the vertebra more frequently interested of fracture results to be the T5 while in the females the T7. With the coming of age the most interested vertebra are the T11 and T12. The presents of osteoporosis at femur neck level is correlated with a major probability of vertebral fracture at T10, T11, T12, L1, L2 and L3, while the presents of osteoporosis at ward level is correlated in a significantly way with a major prevalence of vertebra fractures at T4, T6, T10, T11, T12, L1, L2, L3 and L4. Obesity at general has a negative influence over the health of the spine and in particular the obesity of 1st degree in a significantly way in the deformation of the T11 and T12.

Conclusion: At the moment we can affirm that the osteoporosis is underdiagnosed and undertreated and so it remains the real obstacle to pass in order to reduce the sanitary cost and, most important, to protect the health of the skeleton.

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RELATIONSHIPS BETWEEN BONE FRAGILITY CAUSED BY VITAMIN D DEFICIENCY AND BONE TURNOVER MARKERS AS WELL AS SCLEROSTIN IN POSTMENOPAUSAL WOMEN

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Aims: The level of 25-hydroxyvitamin D [25(OH)D] is widely accepted as the best indicator of vitamin D status, and its deficiency is a clear risk factor for fractures. Since it has been reported that the majority of Japanese individuals meet the criteria for vitamin D deficiency, implementation of medical interventions for all individuals with vitamin D deficiency is not necessarily realistic. Therefore, the aim was to elucidate the factors that are useful for identifying individuals with vitamin D deficiency who are at high risk of fractures.

Methods: The subjects were 201 healthy postmenopausal women who underwent an osteoporosis examination. Blood tests were performed to measure serum levels of 25(OH)D, intact PTH, CTX, P1NP, osteocalcin (OC), and sclerostin, an inhibitor of bone formation. DXA was used to measure BMD at the lumbar (L2-4) and the femoral neck (FN), and the presence or absence of vertebral fractures was determined. Individuals with a vertebral or nonvertebral fragility fracture were regarded as having an osteoporotic fracture.
Results: Osteoporotic fractures were observed in 71 subjects. Subjects had a mean age of 63 ± 8 y, and the following values: 25(OH)D, 16.0 ± 4.2 ng/mL; CTX, 0.40 ± 0.15 ng/mL; P1NP, 53.9 ± 16.6 ng/mL; OC, 22.4 ± 8.4 ng/mL; sclerostin, 1.26 ± 0.39 ng/mL. Serum levels of 25(OH)D had significant negative correlations with age, PTH, CTX, P1NP, and OC and significant positive correlations with L2-4 and FN BMD, but no correlation with sclerostin was observed. Investigation of the presence or absence of fractures showed that the fracture group had significantly lower levels of 25(OH)D, as well as L2-4 and FN BMD, and significantly higher levels of sclerostin ($p < 0.01$), but no differences in bone turnover markers were observed. When subjects were classified into four groups based on 25(OH)D and CTX levels, no differences were seen in the proportion of fractures. In contrast, when subjects were classified into four groups based on 25(OH)D and P1NP levels, the low 25(OH)D/low P1NP group had a significantly higher proportion of fractures than the high 25(OH)D/high P1NP group. In addition, investigation of 25(OH)D and OC levels showed that the low 25(OH)D/low OC group had a significantly higher proportion of fractures than the high 25(OH)D/high OC and high 25(OH)D/low OC groups. Furthermore, investigation of 25(OH)D and sclerostin levels showed that the low 25(OH)D/high sclerostin group had a significantly higher proportion of fractures than the high 25(OH)D/high sclerostin and high 25(OH)D/low sclerostin groups. These results indicate that Inhibition of bone turnover, specifically reduced bone formation, may have some involvement in the increased bone fragility resulting from 25(OH)D deficiency.
Conclusion: Candidate indicators for identifying cases at high risk of fractures among individuals with vitamin D deficiency include measurements of bone formation markers such as OC and P1NP, as well as sclerostin, in addition to 25(OH)D.

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EFFICACY OF MICELLIZED VERSUS FAT-SOLUBLE VITAMIN D3 SUPPLEMENTATION IN HEALTHY SCHOOL CHILDREN FROM NORTHERN INDIA

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Aims: Vitamin D deficiency is a widely recognised public health problem. Efficacy of a recently developed micellized form of vitamin D3 has not been studied. We undertook this study to compare the efficacy of micellized vitamin D3 to fat-soluble vitamin D3 and assess if 60,000 IU of vitamin D3 per month is an adequate supplementation dose.
Methods: In this open-labelled non-randomised pilot study, we recruited 180 healthy children, aged 13–14 y in two groups and supplemented Group A (60 children) with 60,000 IU of fat-soluble vitamin D3/month with milk and Group B (120 children) with 60,000 IU/month of water miscible vitamin D3 under supervision for 6 months. Serum 25(OD)D, PTH, calcium, phosphates and alkaline phosphatase levels were evaluated before and after supplementation in 156 children (54 in Group A and 102 in Group B) who completed the study.
Results: We observed a significantly greater increase in the serum 25(OH)D levels in group B as compared to group A (31.8 ± 9.1 ng/mL *vs* 23.7 ± 10.4 ng/mL; $p < 0.001$). All children in group B achieved adequate levels of serum 25(OH)D (>20 ng/mL) as against 83.3 % children in group A. Serum PTH and ALP levels declined considerably in both the groups following supplementation.
Conclusion: Vitamin D supplementation significantly increased the serum 25(OH)D levels in both groups. This is the first study documenting effectiveness of micellized forms of vitamin D3 over the conventionally used fat soluble vitamin D3. Further studies with different dose regimens are required to establish its efficacy over fat soluble vitamin D3.

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OESTRADIOL DEPLETION IN PREMENOPAUSAL WOMEN WITH NONMETASTATIC BREAST CANCER IS ASSOCIATED WITH SEVERELY DETERIORATED CORTICAL AND TRABECULAR MICROSTRUCTURE

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Aims: Treatment of premenopausal women with breast cancer using ovarian suppression (OS) and aromatase inhibition (AI) causes more rapid and complete oestradiol depletion than natural menopause. Oestrogen deficiency increases remodelling rate, prolongs osteoclast lifespan, and shortens osteoblast life span.[1] Consequently, each of the many more remodelling events remove more bone, more rapidly. We therefore hypothesised that the remodelling imbalance produces severe

microstructural deterioration while the rapid remodelling reduces matrix mineral density (MMD) of the reduced matrix volume.

Methods: At this early stage of this case–control study, we have recruited 7 premenopausal women with breast cancer (mean age 45 y, range 38–51) treated with OS and AI for 38 months (range 11–118 months), 38 healthy age-matched premenopausal women and 38 healthy women at least ten years post natural menopause (mean age 62 y, range 60–65). Six cases had chemotherapy as part of their treatment. Women treated with tamoxifen for >6 months or antiresorptives were excluded. Images of the distal radius and distal tibia were acquired using HR-pQCT. Radial and tibial microstructure and MMD were quantified using StrAx1.0.[2] Independent t-tests were used to compare morphology. Interim analysis was performed using SPSS v22. Results are presented as mean difference (95%CI).

Results: Cases had 10.34 % (5.45 to 15.24) higher cortical porosity than premenopausal age matched controls ($p < 0.001$). Despite being nearly two decades younger than women 10 y post natural menopause, cases had comparable cortical porosity [4.38 % (−1.61 to 10.37), $p = 0.15$]. Cases also had −2.53 % (−4.24 to −0.81, $p = 0.002$) and −0.79 % (−1.58 to −0.01, $p = 0.048$) lower trabecular bone volume relative to pre- and postmenopausal controls, respectively, due to fewer, not thinner trabeculae, and −1.12 % (−1.81 to −0.42, $p = 0.002$) and −0.79 % (−1.58 to −0.01, $p = 0.048$) lower MMD than these controls, respectively. Results at the tibia were similar (not shown).

Conclusion: Severe and perhaps irreversible microstructural deterioration and the longevity of these women suggest that there is a need to investigate the role of early intervention to preserve bone strength.

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P175
CALCITRIOL SUPPLEMENTATION INCREASES FIBROBLAST GROWTH FACTOR 23 (FGF23) IN VITAMIN D DEFICIENT SUBJECTS

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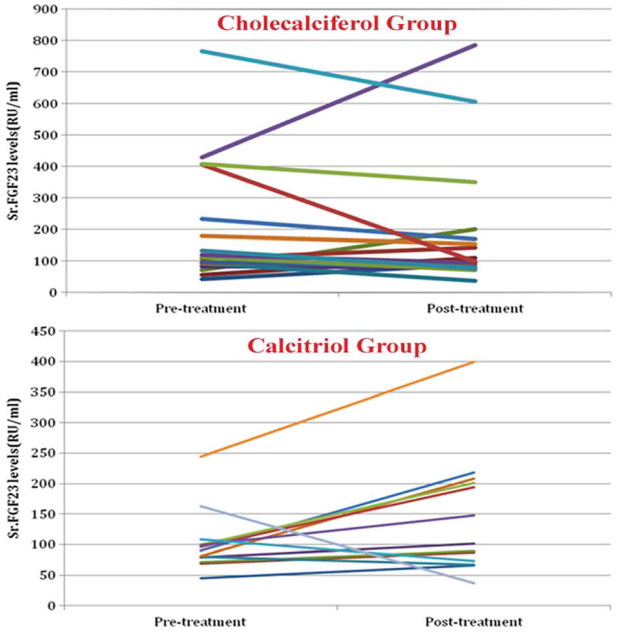
Aims: To determine the effect of cholecalciferol and calcitriol supplementation on FGF23 concentration in vitamin D deficient subjects

Methods: An 8-week prospective intervention study was conducted on healthy subjects with vitamin D-deficiency ($n = 30$). 17 subjects were allotted to cholecalciferol group (mean age 34.6 ± 9.6 y), whereas 13 subjects to calcitriol group (mean age 32.6 ± 8.8 y). Both the groups were administered 500 mg of elemental calcium twice a day. The cholecalciferol group was treated with cholecalciferol 60,000 IU once a week for 8 weeks, whereas the calcitriol group received calcitriol 0.25 μg twice a day for 8 weeks. FGF23 was assayed by Immunotopics which measures both intact and C-terminal fragment (normal value 50–150 RU/ml).

Results: The mean 25(OH)D($p = 0.000$) and $1,25(OH)_2D$($p = 0.002$) increased significantly in cholecalciferol group. In calcitriol group, the change in 25(OH)D($p = 0.944$) and $1,25(OH)_2D$($p = 0.279$) was non-significant. Serum ALP and iPTH declined significantly in both the groups [cholecalciferol group ALP ($p = 0.029$), iPTH ($p = 0.002$)], [calcitriol group ALP ($p = 0.007$), iPTH ($p = 0.009$)]. Sr.FGF23 declined in cholecalciferol group from 201.77 ± 193.08 RU/ml to 190.06 ± 205.78 RU/ml; however the decline was not statistically significant ($p = 0.287$). In calcitriol group, the FGF23 levels increased significantly from 102.24 + −50.78 to 145.47 ± 98.94 RU/ml ($p = 0.046$). The change in serum calcium and phosphorus was not significant in both the groups.



Conclusion: Cholecalciferol administration decreased FGF23 levels. The decline in PTH may be partly responsible for this. It may be possible that 25(OH)D has direct effects on FGF23 metabolism[1,2]. FGF23 levels increased in calcitriol group. This is because 1,25$(OH)_2$D increases the production from osteoblast by increasing the transcription of FGF23 gene[1]. Elevated FGF23 levels are associated with increased mortality in chronic kidney disease patients as well as healthy subjects. This is possibly due to direct effects of FGF-23 on the myocardium which leads to left ventricular hypertrophy. Thus, calcium supplements with calcitriol should be used with caution in healthy patients with vitamin D deficiency as elevated FGF23 levels may be predictor of increased mortality.

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P176
MICRORNA-467G INHIBITS NEW BONE REGENERATION BY TARGETING RUNX-2 SIGNALING

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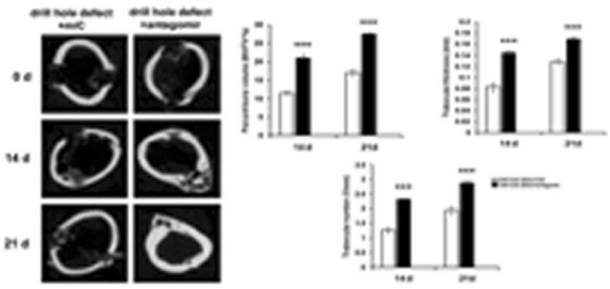
Aims: MicroRNAs (miRNAs) are short noncoding RNAs that interfere with translation of specific target mRNAs and thereby regulate diverse biological processes. Recent studies have suggested that miRNAs might play a role in osteoblast differentiation and bone formation. The main aim of this study was to identify and characterize novel miRNA candidates with differential expression in Medicarpin (positive regulator of bone formation) induced calvarial osteoblast cells, and determine the role of mmu-miR-467 g in osteogenesis.

Methods: MiRNA expression pattern in control and Medicarpin treated cells was analyzed by miRNA microarray and quantitative RT-PCR. Effect of mmu-miR-467 g on osteoblast differentiation and mineralization was validated by transfection of mmu-miR-467 g and its anti-miR in mice calvarial osteoblast cells using biochemical assays and real- time qPCR. Luciferase reporter gene assay was performed to confirm mmu-miR-467 g target. Protein expression levels were determined by western blotting and chemiluminescence. Silencing of mmu-miR-467 g was done to see the effect on new bone regeneration in a BALB/c mice drill hole injury model. Bones were collected for assessing various skeletal parameters.

Results: Over-expression of miR-467 g inhibited osteoblast differentiation, whereas inhibition of miR-467 g function promoted osteoblast differentiation and matrix mineralization. Target prediction analysis tools and experimental validation by luciferase 3′ UTR reporter assay identified Runx-2, the master osteogenic transcription factor, as a direct target of miR-467 g. Over expression of miR-467 g in osteoblasts led to down regulation of Runx-2 and associated signaling components while treatment with anti-miR-467 g reversed these effects. Runx-2 transfected human adipose stem cells have been shown to heal tibial and calvarial bone defects. Thus, silencing of miR-467 g was done to see its role in Runx-2 mediated bone healing and regeneration. Silencing of miR-467 g led to significant increase in new bone regeneration at injury site in a day dependent manner. Additionally, immunohistochemical localization and gene expression studies in the callus tissues at the drill site depicted increased expression of Runx-2 in antagomir treated mice.



Conclusion: MiR-467 g negatively regulates osteogenesis by targeting Runx-2 signaling. We thus propose that therapeutic approaches targeting miR-467 g could be useful in enhancing the new bone formation.

P177

METFORMIN, GENISTEIN AND THE COMBINATION ATTENUATE METHYGLYOXAL INDUCED INHIBITION OF OSTEOBLAST DIFFERENTIATION AND REDUCTION IN CELL VIABILITY

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Aims: Type 2 diabetes mellitus (T2DM) is associated with increased fracture risk and impaired bone healing due to excessive glucose and formation of advanced glycation endproducts (AGEs). Metformin, an oral glycemic drug and genistein, an isoflavone, have been suggested to trap reactive carbonyl compounds before they can form AGE by reacting with proteins, lipids and nucleic acids. AGE is a major causative agent of oxidative stress and cell death in T2DM patients. Osteopontin (OPN) and alkaline phosphatase (ALP) are markers of osteoblast differentiation and initiators of mineralisation. A lack of both is associated with impaired mineralisation and bone healing. What role OPN and ALP play in T2DM induced impaired bone healing is not clear. Therefore the aims of this study were to investigate the effect of methylglyoxal, metformin, genistein and the combination of metformin with genistein on the 1) expression of OPN and ALP, 2) osteoblast cell viability and 3) expression of caspase 3 in human foetal osteoblast (hFOB1.19) cells. hFOB1.19 cells were incubated 24 hours with 150 μM methylglyoxal (MG) with and without metformin, genistein and the combination of both.
Methods: hFOB1.19 cells were incubated 24 h with 150 μM methylglyoxal (MG) with and without metformin, genistein and the combination of both. The expression of OPN, ALP and caspase 3 were determined by ELISA, while the cell viability was measured by trypan blue and via DNA damage.
Results: Incubation with MG significantly reduced the expression of OPN and ALP indicating an inhibition of cell differentiation. This was accompanied by a significant reduction in cell viability and upregulation of caspase 3, indicating increased apoptosis due to DNA damage. Metformin, genistein and the combination of both significantly improved the measured parameters. Comparing the three treatments, metformin was more potent than genistein in reversing the MG-induced downregulation of OPN and ALP as well as the reduction of cell viability and an increase in DNA damage. No synergistic effect between metformin and genistein was observed
Conclusion: In conclusion, MG inhibits osteoblast cell differentiation and induces DNA damage followed by apoptosis which then leads to impaired bone healing. Metformin and genistein reverse the effects of MG by upregulating OPN and ALP expression and increasing cell viability. Therefore genistein can potentially be used for improving bone healing.
Acknowledgement: We would like to acknowledge the Malaysian Ministry of Higher Education for providing the grant (600-RMI/FRGS 5/3 (107/2013) for this project.

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BONE DENSITY PATTERN IN ADOLESCENT WOMEN WITH POLYCYSTIC OVARY SYNDROME (PCOS) FROM INDIA

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Aims: 1. To study BMD in subjects with polycystic ovarian syndrome (PCOS) aged 14–24 y and to compare them with age-matched controls. 2. To correlate BMD with BMI, serum total testosterone and serum insulin.
Methods: A total of 118 subjects (n = 60 PCOS by Rotterdam 2003 criteria and n = 58 age-matched healthy girls) were recruited. All subjects underwent a detailed medical history, anthropometry, Ferriman Gallwey scoring and a brief clinical examination. Biochemical and hormonal analysis included OGTT with 75 g glucose and measurement of plasma glucose and insulin at 0 h,1 h and 2 h, serum LH, FSH,T4, TSH, PRL,17 OHP, total testosterone and DHEAS. Transabdominal USG was done to record PCO morphology and to rule out any adrenal pathology. BMD was assessed by DXA (Hologic).The difference in BMD at various site between the two groups were compared by independent t-test.
Results: The mean age was comparable (20 ± 2.52 vs. 21 ± 1.9 y, p = 0.05). PCOS group had significantly higher BMI (25.6 ± 0.96 kg/m^2 vs. 22.0 ± 0.48 kg/m^2, p = 0.01), waist circumference (81.23 ± 1.32 cm vs. 70.5 ± 1.14 cm, p = 0.01). The number of cycles per year (8.7 ± 0.49 vs. 12 ± 0, p = 0.01) were lower in PCOS while as Ferriman-Gallawey score (10.58 ± 4.70 vs. 3.94 ± 1.14, p = 0.01) was higher. The two groups did not differ with respect to fasting blood glucose (86.0 ± 20.46 mg/dl vs. 84.27 ± 8.5 9 mg/dl, p = 0.53) but 1 h and 2 h values were significantly higher among PCOS subjects as were plasma insulin at all three intervals after OGTT. The PCOS subjects had higher serum total testosterone (0.81 ± 0.25 ng/ml vs. 0.26 ± 0.09 ng/ml, p = 0.01) and DHEAS (285.7 ± 118.9 μg/dl vs. 203.2 ± 96.9 μg/dl, p = 0.03). There was no significant difference in BMD between the two groups at any of the sites (total body BMD = 1.10 ± 0.07 g/cm^2 vs. 1.12 ± 0.08 g/cm^2, p = 0.12). There was no significant correlation of serum total testosterone levels or HOMA-IR with BMD at any of the sites.
Conclusion: There is no significant difference in BMD among Indian PCOS and healthy adolescents when compared to controls.

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P179

CORRELATION BETWEEN VITAMIN D LEVELS AND STATIC POSTURAL BALANCE OF BOTH FEET IN TYPE 2 DIABETES MELLITUS PATIENTS

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Aims: To analyze the differences in indicators of static postural balance in type 2 diabetes mellitus (T2DM) patients with different vitamin D levels and to investigate the association between vitamin D levels and fall risks in T2DM patients.
Methods: A total of 125 T2DM patients were selected between Dec. 2014 and Oct. 2015. The patients were divided into the following groups according to their $25(OH)D_3$ levels: severe deficiency group (group A), deficiency group (group B), insufficiency group (group C), and normal group (group D). Platform plantar pressure was measured to compare the differences in the total travelled way (TTW) of the center of pressure (COP) and the ellipse area (EA) enclosing the TTW of the COP among the 4 groups. Variables that affected the TTW of the COP and the EA enclosing the TTW of the COP were used for the Pearson correlation analysis. All factors with $P < 0.05$ were included in the stepwise multiple linear regression analysis.
Results: The TTW of the COP and the EA enclosing the 95 % TTW of the COP in the vitamin D severe deficiency and deficiency groups were significantly higher than those in the insufficiency and normal groups. The stepwise multiple linear regression analysis showed that the $25(OH)D_3$ level had an independent negative correlation with the TTW of the COP and the EA enclosing the 95 % TTW of the COP.
Conclusion: The vitamin D level had an independent negative correlation with the static postural balance. Thus, when the vitamin D level in T2DM patients was lower, the fall risk was higher.

P180

FUNCTION ANALYSIS OF OSTEOPOROSIS SUSCEPTIBILITY GENE BDNF INDICATE ITS POTENTIAL ROLE IN OSTEOBLAST DIFFERENTIATION MODULATION

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Aims: To investigate whether brain-derived neurotrophic factor (*BDNF*) is associated with osteoporosis in Han Chinese population and to explore its functional role in osteoblast differentiation.
Methods: 14 SNPs on *BDNF* gene was genotyped in a cohort of 1300 Han Chinese subjects. Candidate gene association study was performed to examine the relationships of hip and spine BMD with *BDNF* polymorphisms. To explore its functional role in bone formation, we then performed short interfering RNA (siRNA)-mediated knockdown of *BDNF* gene in differentiated mouse preosteoblast MC3T3 cells induced by BMP-2. qRT-PCR and western blot were used to detect expression levels of *BDNF* and osteoblast differentiation related genes, including alkaline phosphatase(*ALP*), type I collagen (*COL1*), runt related transcription factor 2 (*RUNX2*), and osteocalcin(*OCN*).
Results: The association analysis identified that 4 SNPs in *BDNF* gene were significantly associated with hip BMD (rs6265: $P = 0.0159$, rs11030104: $P = 0.0127$, rs7103411: $P = 0.0089$, rs16917237: $P = 0.0021$), SNP rs16917237 was still associated with hip BMD after Bonferroni correction. Real-time PCR revealed that differentiated osteoblasts had higher *BDNF* expression level than pre-osteoblasts. Knockdown of *BDNF* significantly suppressed the expression of marker genes *COL1*, *RUNX2*, and *OCN*, compared with the control siRNA treated group. The reduction was subsequently confirmed by the result of western blot. The protein levels of *COL1, RUNX2,* and *OCN* were significantly decreased.
Conclusion: *BDNF* gene is a candidate osteoporosis susceptibility gene which plays an essential role in osteoblast differentiation.
Acknowledgement: This work was supported by the National Natural Science Foundation of China (31371278, 31471188, 81573241, 31511140285); China Postdoctoral Science Foundation (2015 M570819); and the Natural Science Basic Research Program Shaanxi Province (2015JQ3089, 2016JQ3026).

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THE UPTAKE OF FLUORIDE AND STRONTIUM IN OSTEOPOROSIS TREATMENT AFFECTS THE COMPOSITION, STRUCTURE AND MECHANICAL PROPERTIES OF HUMAN CORTICAL BONE

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Aims: Strontium and fluoride are both used as therapeutic treatments to reduce fracture risk in osteoporosis. Incorporation of these elements in bone is accompanied by changes in remodeling, matrix composition and structure.

However, a direct comparison of the effectiveness of strontium and fluoride treatment in human cortical bone with a focus on the resulting mechanical properties remains to be established.
Methods: The study groups are composed of iliac crest biopsies from healthy controls, treatment-naïve osteoporosis cases and strontium ranelate or fluoride-treated osteoporosis cases. Concentrations of these elements were determined using instrumental neutron activation analysis. Quantitative backscattered electron imaging was carried out to investigate the degree of mineralization and the cortical microstructure. Mechanical properties were assessed via reference point indentation.
Results: The concentration of strontium in the bone matrix positively correlates to the treatment period. Fluoride and strontium-treated patients have a lower cortical porosity in comparison to osteoporotic patients indicating an improvement in bone's microstructure. Additionally, the control and fluoride-treated cases have a significantly higher bone mineralization in comparison to treatment-naïve osteoporotic bone. Strontium-treated bone has significantly lower total indentation distance values than the osteoporotic bone, measuring bone's resistance to deformation; however, the controls have the highest resistance to indentation.
Conclusion: Osteoporosis treatment with strontium and fluoride has positive effects on mineralization and mechanical characteristics beyond gains in bone volume but does not completely recover the properties of healthy cortical bone.

P182
OSTEOPOROSIS IN PATIENTS WITH POLYMYALGIA RHEUMATICA TREATED WITH LOW-DOSE GLUCOCORTICOIDS

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Aims: Polymyalgia rheumatica (PMR) is a chronic inflammatory condition affecting elderly persons. Clinical symptoms respond to low-dose glucocorticoids (GC), but many patients require long-term GC therapy. Osteoporosis is the one of the significant adverse events of GC. In Japan, guidelines on the management of GC induced osteoporosis (GIO) were updated in 2014[1]. Here we review the adverse events, especially osteoporosis, of patients with PMR.
Methods: This was a retrospective study in a single hospital. We studied 37 patients with a diagnosis of PMR according to the 2012 Provisional Classification Criteria for PMR (ACR/EULAR). They presented to our hospital from April 2011 to December 2015. Patients associated with giant cell arthritis were excluded. We collected the demographic and clinical data from the medical records.
Results: Among the 37 patients, 20 were women. The mean age was 76 y old (SD 6.9). The mean duration of GC therapy was 19 months (SD 11.3). All patients were treated with oral PSL. The median initial dose of PSL was 15 mg daily (0.28 mg/kg/d). The median cumulative dose of PSL was 2.2 g. Remission was achieved in 18/37 (49 %) as of June 2016. At the beginning of treatment, 7 patients had prior vertebral body fractures, and 5 patients showed less than 70 % of YAM. We prescribed bisphosphonate or selective estrogen receptor modulator (SERM) to 15 of 20 female patients to prevent GIO or treat osteoporosis. On the other hand, only 2 of 17 male patients were treated with bisphosphonate. The reasons for not starting the therapy were normal BMD (33 %), severe dementia (27 %). During GC therapy, 4 female patients suffered vertebral compression fractures despite drug therapy. The details are given in the table.

	At diagnosis of PMR	Initial dose of PSL	BMD at the beginning	Prior fragility fracture	GFR <60 mL/min	Drug	PSL treatment until new vertebral fracture			
	Age	Weight (kg)	BMI	mg/d	mg/kg/d					
1	71	45	19.2	20	0.44	64 %	-	-	M	34 months
2	75	40	17.8	10	0.25	63 %	-	-	R	12 months
3	78	40	19.0	15	0.38	ND	+	-	M	4 months
4	85	44.5	20.9	10	0.22	53 %	-	+	M	4 months

GFR, glomerular filtration rate; M, minodronate; R, raloxifene
Conclusion: In most female patients, we started the drug therapy for osteoporosis according to the Japanese guidelines. However, 4 female patients suffered vertebral fractures despite treatment. More aggressive treatment; teriparatide or denosumab, might be the first choice for high-risk patients.
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P183
DESTRESSING THE MIND, BUT STRESSING THE FEMUR? LOW-ENERGY FEMORAL SHAFT FRACTURE FROM A YOGA POSE

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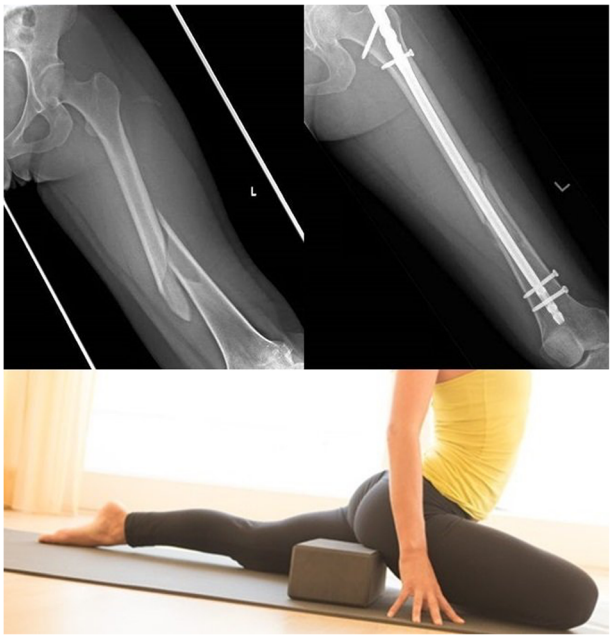
Aims: Yoga, touted as a panacea for problems of both body and soul is becoming increasingly popular. Though vertebral fractures have rarely been described in osteopenic patients doing certain yoga stances, only once before has a femoral shaft fracture sustained during yoga been reported. We describe the case of a young healthy woman who sustained a low-energy femoral shaft fracture while performing a yoga stance.
Methods: Case report.
Results: A previously healthy 38 y old woman, a practitioner of yoga for 2 y, assumed a "Pigeon Pose" during one of the sessions, extending her right hip, flexing her left hip and knee and pressing her left heel into her right groin. A yoga block was positioned beneath her left thigh. On passive rotation of her trunk to the left, she heard a crack and experienced pain in her left thigh. X-rays revealed an oblique mid-shaft fracture of the left femur. She underwent closed reduction and intramedullary nailing. Histological analysis of intramedullary reamings did not show any malignancy or other pathology. She had no clinical risk factors for low bone density or fragility fracture. She weighed 51.9 kg and had a BMI of 19.5 kg/m^2. Her dietary intake of calcium was adequate. She did not smoke. There was no history of medication, supplement or excessive alcohol intake or of anorexia or weight loss. She had regular monthly menstrual cycles since age 11 without any history of amenorrhoea. There was no history of prolonged lactation. There was no family history of fragility fractures. She had no features of Cushing's syndrome, hyperthyroidism or rheumatological disease on physical examination. BMD assessed by DXA was normal: 0.653 g/cm^2 (Z-score: −1.2) and 0.730 g/cm^2 (Z-score:-1.3) at the right femoral neck and total hip, respectively, and 0.921 g/cm^2 (Z-score: 0.6) at the lumbar spine (L1-L4). Thyroid and renal function, prolactin, 24-h urinary free cortisol, and myeloma screening were all normal. Serum calcium, phosphate, intact PTH and alkaline phosphatase were within normal limits and there was no evidence of biochemical vitamin D deficiency. Anti-gliadin and anti-endomyseal antibodies were negative. There was no evidence of hypercalciuria on a 24-h urine assay for calcium. 10 weeks after fracture fixation, bridging callus was seen at the fracture site indicative of appropriate healing.



Conclusion: Femoral shaft fractures occur almost exclusively due to high energy trauma. Low-trauma femoral shaft fractures have been described in patients with osteoporosis and with chronic antiresorptive use. However, it appears that tensile forces applied onto the femur by the "pigeon" stance described as a hip opener was sufficient to cause a fracture in this young woman with no apparent metabolic bone disease. This case serves as "*prima facie* evidence" that, though uncommon, low-energy fractures in healthy individuals may occur while attempting certain yoga poses.

P184
OSTEOPOROSIS AS A COMPLICATION OF TOTAL HIP ARTHROPLASTY

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Aims: Osteoporosis is currently one of the most common diseases with tremendous socioeconomic and medical significance. Fourth place among all causes of disability and death occupy fractures of the femur in osteoporosis. According to Aubrey Blumsohn (2013) osteoporosis is 2.7 times more common in women older age group, which is associated with the onset of menopause. The aim was to determine the optimal amount perioperative management of patients women of the senior age group with bilateral coxarthrosis 3.
Methods: In our study involved 32 patients of the senior age group orthopedics and trauma Department of the Clinic of Rostov State Medical University. Inclusion criteria: bilateral coxarthrosis 3: before surgery, after performing unilateral hip replacement, and, after bilateral hip replacement with cement

variant of the prosthesis. All patient was performed a study of bone resorption markers and bone formation, osteodensitometry of the lumbar spine and the hips before surgery, and at 3, 6 and 12 months after total arthroplasty of the first hip joint.

Results: In 28 patients 3 months after surgery on the first hip joint showed a reduction in mineral density of bone mass of the lumbar spine, a decrease in T criterion of 0.8. In 4 patients remained unchanged (within 0.2). In 27 patients, the decrease of bone mineral density in the zone of localization of the operated hip joint, the T criterion decreased on average by 2.1. The tendency to loss of bone mineral density in the following year was observed in 100 % of patients. In 17 women with the worst indicators of osteodensitometry, the increase in bone resorption (β-crosslaps test) history of diagnosed early menopause. Further x-ray observation during the year of instability of the components of the implant was not observed in 100 % of women.

Conclusion: It remains an undeniable fact that effects of menopause on the rate of development of osteoporosis in women with bilateral coxarthrosis. Treatment selection should be based on data osteodensitometry studies, biochemical markers of bone metabolism. Need extended preoperative preparation and dynamic observation of the patient after the implantation with the aim of preventing the development of instability of endoprosthesis components.

P185

OSTEOPOROSIS AS A CAUSE OF UNSTABLE COMPONENT OF THE KNEE ENDOPROSTHESIS

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Aims: The arthroplasty of a knee joint with an osteoporosis background is accompanied by a risk development of endoprosthesis loosening. Aim: comparison of the data from osteodensitometry and bone strength in patients undergoing knee replacement.

Methods: 50 patients underwent densitometry in the preoperative period. After surgery, the strength of the resected fragments of the femur and tibia were examined.

Results: A classification was developed for bone strength. Patients with the worst bone strength were classified in class 1. Pathological bone breakdown occurred for excess weights of not more than 3 times. The bone strength in this group was less than 240 kg of force (KgF). Patients with a bone strength of 241–400 KgF were set in class 2, 401–480 KgF to class 3, more than 480 KgF to class 4. There were more than 3 times more women in the classes 1 and 2, in classes 3 and 4 more men. The average ages by class were as follows: 1 – 63.93 y, 2 – 61.45 y, 3 – 64.11 y, 4 – 62.56 y. According to the data from the densitometry and bone strength of the femur in classes 1 and 2, osteoporosis and osteopenia were present. Classes 3 and 4 had normal indicators. The average weights of the patients for each class was as follows: classes 1 and 2 – 83.76 kg, classes 3 and 4 – about 10 kg more. The average BMI for each class was as follows: class 1 – 30.05, class 2 – 31.11, class 3 – 31.48, class 4 – 30.63.

Conclusion: A decrease in the bone strength depends on an increase in age, a decrease in weight and BMI. A gender dependence was found.

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ROLE OF FRACTURE PREVENTION PRACTITIONER IN LIAISON SERVICES IN JAPAN

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Aims: Fracture liaison services (FLS) are coordinator-based, secondary fracture prevention services for the treatment of osteoporotic patients. Japan Osteoporosis Society has started domestic program to improve the quality of care for both primary and secondary fracture prevention, named as Osteoporosis Liaison Service (OLS) in 2012. OLS has its educational program for medical staffs as fracture prevention practitioner (FPP). The society performed FPP qualifying test, and more than 1000 staffs has been qualified in 2014 and 2015. This paper showed the present distribution of FPP in Japanese hospitals and clinics, and their performances in OLS activity.

Methods: The data were obtained from the application form for FPP qualifying test in 2014 and 2015. We also sent questionnaire to FPP qualified in 2014 and asked about their activities in OLS services.

Results: A total 1108 persons (M/F = 324/784) were qualified in 2014 and 2015. They consist of nurses (50 %), physical therapists (19 %) pharmacists (18 %), radiological technologists (5 %), registered dietitians (4 %), medical technologists (2 %) and others. Majority of the population belong to

hospitals (71 %) and clinics (20 %). Interprofessional working for OLS was performed in 65 % of first year FPP, but interinstitutional liaison service exists in only 30 % of their institution. Generally, FPPs were well supported by their institution, but would like to have more information and established systems for interinstitutional services.

Conclusion: OLS including FLS started in Japan, and the number of FPPs is increasing. For improvement of efficacy of liaison services, interinstitutional working model should be provided by the society.

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THE EFFECTS OF DRUGS METABOLIZED BY CYTOCHROME P450 ON MALE BONE MINERAL DENSITY

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Aims: Drugs that induce cytochrome P450 (CYP450) may accelerate the metabolism of vitamin D, leading to vitamin D deficiency which decreases the amount of calcium and phosphorus ions in the blood, thus causing the loosening or weakening of the bone matrix. Therefore, this study investigated the correlation between the amount of drugs that inhibit or induce CYP450 and the increase or decrease in BMD.

Methods: This study focused on male patients who underwent two or more DXA scans to measure lumbar vertebrae BMD between 2006–2015 and received refillable prescriptions for chronic illnesses. After patients who took osteoporosis medication, steroids, or thyroid medication between the DXA scans or were bedridden were excluded, medical records were compared to review patients' drug use and changes in BMD. The refillable prescriptions given between the two DXA scans were the focus of investigation. SPSS 22.0 software was used to conduct logistic regression analysis on basic information, the number of drugs that inhibit or induce CYP450, and the changes in BMD.

Results: 83 men met the inclusion criteria for this study. The average age at the time of the two DXA scans was 60.6 ± 13.5 (42.7-89.1) y. The average time between the two DXA scans was 3.6 ± 1.9 (1.1-7.2) y. The average lumbar vertebrae BMD at the first DXA scan was 1.27 ± 0.26 (0.80-2.46) g/cm^2 and the average BMD at the second scan was 1.21 ± 0.26 (0.61-2.02) g/cm^2. 45 (54 %) of the patients experienced losses in BMD while 38 (46 %) experienced increases in BMD. Three groups were created according to the types of drugs prescribed in the chronic prescription: the inhibitory group (N = 28) included patients who took more drugs that inhibit CYP450 than those that induce CYP450, the inductive group (N = 19) included patients who took more drugs that induce CYP450 than those that inhibit CYP450, and the reference group (N = 36) included patients who took the same number of drugs that inhibit and induce CYP450 or used neither. The results indicated no significant difference between the BMD increases in the inhibitory group and the reference group (OR = 1.79, 95 % CI = 0.84-6.60) (p = 0.102); however, there was a significance increase in the risk of BMD loss in the inductive group compared to the reference group (OR = 7.61, 95%CI = 1.53-37.84) (p = 0.013).

Conclusion: The long-term use of drugs that induce CYP450 may decrease the BMD in males. The reason may be that these drugs increase the metabolism rate of vitamin D in the liver. Furthermore, insufficient vitamin D combined with a decrease in calcium ions may stimulate parathyroid gland secretions, which further utilize calcium from the bones. We suggest that male patients with long-term prescriptions for drugs that induce CYP450 undergo regular BMD scans to assess the influence of the drugs on BMD.

Acknowledgement: We would thank the Taiwanese Osteoporosis Association for subsidy of seminar allowance and transportation fee.

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THE IMPACT OF SMOKING ON BONE MINERAL DENSITY AT DIFFERENT AGE: A SUBSTUDY OF TAIWAN OSTEOPOROSIS SURVEY (TOPS)

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Aims: To investigate the association between current smoking and BMD change of lumbar spine and total hip at different life stages.

Methods: Database of this cross-sectional study was supported by Taiwan Osteoporosis Association, who conducted a nationwide osteoporosis survey by collecting clinical risk factors (CRFs) and BMD of participants in Taiwan during 2008 ~ 2011. All participants completed a FRAX® CRFs questionnaire in Chinese version, and measured BMD of lumbar spine and total hip. Current smoking is defined as tobacco smoking at present time. Participants were divided as current smoking and noncurrent smoking, and we compared BMD of lumbar spine and total hip by Student t test in each 10-y age group.

Results: Current study consisted of 9667 women and 2529 men, and characteristics are presented in Table 1. Lumbar spine BMD of current smoking women was slightly lower than noncurrent smoking women, but no statistical significance was identified (in age group of 40 ~ 50, 51 ~ 60, 61 ~ 70, 71 ~ 80, 81 ~ 90, p = 0.78, 0.18, 0.23, 0.15, 0.22, respectively; Figure 1A). Lumbar spine BMD of men did not show downward trend as age increased, and there was no statistical difference between smoking and nonsmoking men (P = 0.65, 0.75, 0.51, 0.47, 0.06, respectively; Figure 1A).

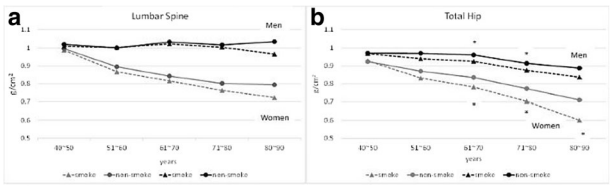
Current smoking women demonstrated profound reduction of total hip BMD since age of 61 y, compared to noncurrent smoking women (P = 0.89, 0.06, 0.01, <0.01, 0.02, respectively; Figure 1B). Current smoking men also revealed significant decrease of total hip BMD since age of 61 y, compared to noncurrent smoking men(P = 0.89, 0.06, 0.02, 0.02, 0.13, respectively; Figure 1B).

Table 1. Demographic data of participants in 10-y age group.

Women	40 ~ 50	51 ~ 60	61 ~ 70	71 ~ 80	81 ~ 90					
Smoking	+	–	+	–	+	–	+	–	+	–
Number	22	867	43	2704	36	2977	25	2291	8	694
Age (y)	45.4 ± 3.5	46.7 ± 2.9	55.3 ± 2.9	56.0 ± 2.8	65.5 ± 3.2	65.6 ± 2.9	74.5 ± 2.7	75.0 ± 2.8	86.1 ± 3.0	83.7 ± 2.5
BMI(kg/m^2)	22.5 ± 4.1	23.0 ± 3.4	23.3 ± 3.4	23.7 ± 3.5	23.9 ± 3.5	24.4 ± 3.7	25.0 ± 4.9	24.4 ± 3.7	21.7 ± 4.1	23.5 ± 3.8
Men	40 ~ 50	51 ~ 60	61 ~ 70	71 ~ 80	81 ~ 90					
Smoking	+	–	+	–	+	–	+	–	+	–
Number	43	89	111	363	144	656	110	666	26	321
Age (y)	45.7 ± 2.8	46.0 ± 3.0	55.9 ± 2.8	56.5 ± 2.7	65.5 ± 2.7	66.0 ± 2.8	75.5 ± 3.1	75.5 ± 2.9	82.8 ± 2.1	83.7 ± 2.5
BMI(kg/m^2)	24.3 ± 3.0	24.4 ± 3.5	24.3 ± 3.2	24.5 ± 3.1	23.7 ± 3.1	24.8 ± 3.1	23.3 ± 3.6	23.8 ± 3.3	22.6 ± 3.2	23.5 ± 3.4

Data are mean ± SD; +: current smoker; −: noncurrent smoker

Figure 1. Bone mineral density change of lumber spine and total hip at different age in current and non-current smokers.



Conclusion: Current smoking is associated with significant decrease of total hip BMD in men and women since age of 61 y, but no significant reduction on lumbar spine BMD at all age group compared to noncurrent smokers.

Acknowledgement: We are indebted to Taiwan Osteoporosis Association for authorizing to manage the database and grateful to the offering mobile DXA machine by Merck Sharp & Dohme pharmaceutical company (Taiwan) during the study period.

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EFFECT OF TNF-ALPHA BLOCKADE ON THE MINERAL METABOLISM IN CHRONIC INFLAMMATORY DISEASES

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Aims: To evaluate the effect of antiTNF-α treatments on BMD, bone turnover markers (BTMs), osteoprotegerin (OPG), serum RANKL (sRANKL) and the functional capacity of patients with chronic articular inflammatory diseases.

Methods: It is a longitudinal prospective study in every day practice conditions, involving 31 patients diagnosed with rheumatoid arthritis (RA), psoriatic arthropathy (PsA) and ankylosing spondylitis (AS) who were on treatment with antiTNF-α medications for one year. At the beginning and at the end of the study we evaluated BMD, OPG and, sRANKL. We also evaluated the Simple Disease Activity Index (SDAI), Bath Ankylosing Spondylitis Disease Activity Index (BASDAI), reactive C protein, Health Assessment Questionnaire (HAQ), Bath Ankylosing Spondylitis Functional Index (BASFI), BTMs and vitamin D at the beginning and on months 3, 6, 9 and 12 (end of study) visits.

Results: BMD did not experience a significant change after one year of treatment. Patients who were on corticosteroid treatment endured a decrease in the BMD of all the sites, but only the decrease in the lumbar BMD was statistically significant (3 % SD1.6; p = 0.02). P1NP increased and CTX decreased but neither one was statistically significant. Disease activity experienced a statistically significant decline according to the SDAI (p = 0.001) and BASDAI (P = 0.005), keeping an association with the improvement in the mineral metabolism parameters. Equally, HAQ declined significantly (p = 0.025) as BASFI, nonetheless its reduction was not statistically significant. OPG levels stayed stable during the whole year of treatment. On the other hand, the levels of sRANKL (0.28 ± 0.21 vs. 0.22 ± 0.15; p = 0.013) as well as the sRANKL/OPG ratio (0.05 ± 0.04 vs. 0.04 ± 0.03; p = 0.031)

showed significant reductions. No changes were observed in vitamin D levels. No statistically significant relation could be found between vitamin D levels and BMD and/or BTMs, independently from the basal levels of calcidiol. Correlations between parameters and diseases can be found in Table 1. No significant correlations was found among the responders, nor in the AS patients or the one with arthritis (AR and PsA).

Table 1. Correlations. (Whole=responders + non responders)

Disease	Correlation	r	p
Whole AS	BASDAI & BASFI	0,840	0.001
Whole AS	% increment BMD total HIP & BASDAI	-0,583	0.029
Whole AS	% increment BMD total HIP & RCP	-0,728	0.003
AS responders	BASDAI & BASFI	0,799	0.005
RA & whole PsA	HAQ & SDAI	0.633	0.011
PsA	HAQ & SDAI	0.678	0.04
RA & whole PsA	% increment lumbar BMD & SDAI	-0.582	0.037
PsA responders & RA	% increment lumbar BMD & SDAI	-1,000	0.000

Conclusion: TNF-α blockade depresses bone loss in patients with articular inflammatory diseases and improves the disease at the same time. The decrease in sRANKL and in the sRANKL/OPG ratio, endorses the protector effect these treatments have on bone through the improvement of the inflammatory activity. Still, we have shown that this protector effect is bigger in responders.

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TUMOR INDUCED OSTEOMALACIA IN TAIWAN

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Aims: We present our 16 cases of tumors induced osteomalacia (TIO) to show the location, multiplicity, diagnosis, imaging studies, molecular pathology and outcomes of the 10 tumors we found.
Methods: We routinely screen our patients with low impact vertebral fractures with serum calcium, phosphorus, alkaline phosphatase levels. The patients with low serum phosphorus level (<2.8 mg/dl) were further examined for inappropriate phosphatura (>800 mg/d), and elevated FGF-23. If FGF-23 is abnormally high and there was no evidence of congenital hypophosphatemia, we then search the location of the possible tumors causing TIO with bone X-ray, MRI and octreotide scan, after a thorough physical examination.
Results: Within the period of 2000–2014, a total of 16 patients were identified. In 8 patients, 10 tumors were identified, including two single subcutaneous tumors in two patients and 8 intraskeletal tumors in 6 patients. They resided mostly at femur, humorous, and jaws. Another patient was found to have ovarian adenocarcinoma and wide metastases. The 10 tumors were all phosphaturic mesenchymal tumors (PMT). We failed to find tumors in 8 patients. Most of the tumors showed either fibronectin – FGFR (fibroblast growth factor receptor) or fibronectin-FGF 1 fusion mutations. After resection of the two subcutaneous tumors, the two patients recovered completely. However, only one of the 6 patients had remission after surgical removed of the bone tumors.
Conclusion: TIO is not rare. Most of the tumors were phosphaturic mesenchymal tumors is nature. They were located at certain common site, and may be multiple. But about half of tumors could not be found. All patients with osteoporosis should be screened for hypophosphatemia. If PMT is found in bones, wide resection of tumors is preferred.

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BULLEYACONITINE A INHIBITS OSTEOCLAST FORMATION AND TITANIUM-PARTICLE-INDUCED OSTEOLYSIS

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Aims: Excessive osteoclast formation and bone resorption are key causes of osteoporosis. Natural plant-derived compounds have received great attention because they are considered to be attractive sources of therapeutic regimens, and some natural compounds may have advantages over traditional drugs. The aim of this study was to assess the effect of Bulleyaconitine A (BLA) on osteoclasts and titanium particle-induced osteolysis in vivo.
Methods: 1. BMMs were isolated from C57BL/6 mice. After plating cells at a density of 8000 BMMs/well into a 96-well plate and incubating for 24 h, BMMs were incubated in the presence of 30 ng/mL M-CSF, 50 ng/mL RANKL, and different concentrations of BLA. The cell culture medium was replaced every 2 d until mature osteoclasts had formed. Fixed with 4 % paraformaldehyde for 30 min, and stained using the TRAP kit. TRAP-positive cells were counted. The cytotoxic effect of BLA on BMMs were assessed using CCK-8 assays according to manufacturer's protocol.
2. BMMs were seeded at a density of 2.4×10^4 cells/cm^2 onto bovine bone slices, and treated with 30 ng/mL M-CSF, 50 ng/mL RANKL, and 0, 2.5, 5, or 10 μM BLA until mature osteoclasts were formed. Adherent cells were then completely removed from the slices. Resorption pits were imaged using a scanning electron microscope.
3. Total RNA was extracted using the Qiagen RNeasy® Mini kit, and then subjected to cDNA synthesis. Real-time PCR was performed using the SYBR Premix Ex Tag kit and an ABI 7500 Sequencing Detection System according to the manufacturer's protocols.
4. RAW264.7 cells were cultured to reach confluent and pretreated with or without 10 μM BLA for 4 h, followed by stimulation with 50 ng/mL RANKL for 0, 10, or 30 min. Cells

were lysed with RIPA buffer to extract proteins. Antibody reactivity was detected by exposure in an Odyssey V3.0 image scanning.
5. 24 healthy 8-week-old C57 mice were assigned randomly into four groups: sham PBS control (sham), Ti particles with PBS (vehicle), and Ti particles with low and high concentrations of BLA, respectively. After abdominal anesthesia, 30 mg of Ti particles were embedded under the periosteum at the middle suture of the calvaria. Mice in the low and high BLA groups were injected intraperitoneally with BLA at 80 or 160 μg/kg/d, respectively, for 10 d. Mice in the sham and vehicle groups received PBS daily. At the end of the experiment, the mice were sacrificed, and the calvaria of all mice were excised and fixed in 4 % paraformaldehyde for μCT analysis.
Results: In this study, we verified for the first time that BLA suppressed osteoclast differentiation, osteoclastogenesis gene expression and bone resorption in vitro, leading to the preventive effect of BLA on titanium induced osteolysis in vivo.
Conclusion: These results demonstrate BLA effectively inhibited osteoclastogenesis and prevented titanium particle-induced osteolysis in vivo.

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SERUM 25-HYDROXYVITAMIN D STATUS AMONG SAUDI CHILDREN WITH AND WITHOUT A HISTORY OF FRACTURE

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Aims: The significance of vitamin D deficiency in the incidence of fractures in children has been under investigated. Here we aimed to associate serum 25-hydroxyvitamin D levels and fractures in Saudi children.
Methods: This cross-sectional study was conducted in 1022 Saudi children without fracture history [476 boys (age: 14.56 ± 1.81, BMI: 22.38 ± 5.81) and 546 girls (age: 13.57 ± 1.67, BMI: 22.24 ± 4.94)] and 234 Saudi children with history of fracture [148 boys (age: 14.25 ± 1.39, BMI: 22.66 ± 6.08) and 86 girls (age: 13.76 ± 1.35, BMI: 21.33 ± 1.35)]. Anthropometric and fasting serum biochemical data were collected. Serum 25-hydroxyvitamin D level was assessed using electrochemiluminescence.
Results: Mean circulating 25-hydroxyvitamin (25OH) D level in subjects with a history of fracture were significantly lower in both boys ($p < 0.01$) and girls ($p < 0.01$) than those without, although both groups had low mean 25(OH)D levels. Furthermore, age was positively associated with 25-hydroxyvitamin D in boys ($p < 0.05$) and negatively in girls ($P < 0.05$) with a history of fracture. Vitamin D levels were significantly lower in children with a history of fractures in both boys and girls than those without such a history.
Conclusion: Even in the absence of fracture history, vitamin D status correction should be warranted in the general Saudi pediatric population.

P193
OSTEOPOROSIS IN PATIENTS WITH CHRONIC NONINFECTIOUS DISEASES

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Aims: To analyze the risk factors (RFs) of osteoporosis (OP), the risk of OP-related fractures, the specific features of osteopenic syndrome in patients with chronic noninfectious diseases (CNID) (coronary heart disease (CHD), hypertension, chronic obstructive pulmonary disease (COPD), and asthma).
Methods: The investigation enrolled 377 patients (mean age 55.3 ± 1.6 y) with CNID and 221 persons (mean age, 53.2 ± 1.3 y) who formed a control group. According to the nosological entity, the patients were divided as follows: Group 1 included 84 patients with CHD and hypertension; Group 2 comprised 99 hypertensive patients; Group 3 consisted of 70 patients with COPD; and Group 4 included 124 asthmatic patients. Prior to the examination, the patients had received no specific therapy for the prevention and treatment of OP. 10-y risk for OP-related fractures was calculated applying the FRAX computer program. To investigate BMD, bioenergy X-ray densitometry of the lumbar spine and proximal femur was carried out by means of a Lunar DPX apparatus (USA). The results were assessed using the t-test in standard deviations from the peak bone mass according to the WHO guidelines.
Results: The RFs of OP were more frequently recorded in the patients with CNID than in the healthy individuals. RFs, such as smoking, low physical activity, and low-energy fractures, were most common in the patients with cardiovascular disease or COPD. The frequent use of glucocorticoid therapy was also an important RF in the patients with COPD. CHID considerably increased the risk of fractures in the succeeding 10 y after disease onset. The high risk of fractures, those of the proximal femur in particular, provides a rationale for the need for timely antiosteoporotic therapy in the majority of patients with CNID. The performed investigation demonstrated that the BMD values in the patients with CNID corresponded, on the average, to the osteopenia criteria; the lowest BMD values were recorded in the patients with COPD and associated cardiovascular disease. The severe course of osteopenic syndrome (a BMD decrease that was diagnostically significant

for OP concurrent with fractures was observed in one-third of patients with CNID. The patients with cardiovascular disease or COPD showed a high incidence and degree of OP, which allows these diseases to be considered as a RF for decreased BMD. The long-term uncontrolled course of disease, the degree of organ and functional disorders in the patients with CNID, and concomitant use of glucocorticoid therapy contribute to a reduction in BMD.

Conclusion: RFs for OP were identified in the majority of patients with CNID. The high risk of fractures due to an obvious BMD decrease in patients with CNID requires timely diagnosis, treatment, and prevention of osteopenia.

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FINDING NEW IDEAS ON AN OLD PROBLEM: PREDICTING HIP FRACTURE TYPE BASED ON ANALYSIS OF VITAMIN D-PARATHYROID HORMONE-CALCIUM AXIS USING DATABASE STUDY OF THE PATIENTS WITH BOTH HIP FRACTURES.

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Aims: Hip fractures (HF) are clinical presentations of osteoporosis associated with significant mortality/morbidity. While older HF patients demonstrate heterogeneity in calciotropic hormone concentrations, independent serum PTH and Vit D measurements may lead to different pathophysiological mechanism of specific HF type formation. Since the second HF reflects ongoing pathogenesis of bone fragility, the possible high congruence level between index and second HF suggest similar processes causing similar pattern of proximal femur fault lines. In view of recent changes and doubts regarding the role of bisphosphonates in secondary prevention of HFs such confusion in literature may be related to a lack of differentiation in HF types and their pathogenesis, assumptions that anabolic or antiresorptive therapies affect both HF type equally as well as assumed linear time-size of effect relationship in anti-osteoporosis treatment. This study aims to identify if these causative factors includes the Vit D-PTH-Ca axis, using 10 years of database, by comparing the endocrinological profile in the same patient at admission for both HF.

Methods: Data on 1170 low-energy HFs (1438 patients) were prospectively collected at The Canberra Hospital between 1999–2011 excluding pathological fractures. 217 patients have sequential bilateral hip fractures, but only 158 with both HF occurred during the study period are considered. Demography and Vit D-PTH-Ca axis bloods test results are analysed.

Results: Congruence rate between index and second HF are 83 % for cervical type, 68 % trochanteric. Factors associated with congruent bilateral HF include age group and abnormal Vit D-PTH-Ca axis pattern, though isolated hypovitaminosis D does not appear to predict HF type by itself. We examine the abnormal responses of this endocrinal axis and correlate this with HF type. We also noted the temporal relationship in crossover of abnormal Vit D-PTH profile with change of HF type predominance

Conclusion: Changes in HF type predominance is related to PTH profile. Those with normal PTH profile [regardless of age or 25(OH)D] are more likely to have bilateral cervical HFs While it is not possible to control age in causation of HF, the role of Vit D-PTH-Ca profile abnormalities may represent a platform for further research in determining possibly different pathogenesis in cervical versus trochanteric HF types, thus individualising treatment and preventive regimen.

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PREGNANCY- AND LACTATION- ASSOCIATED OSTEOPOROSIS: CASE SERIES

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Aims: Pregnancy- and lactation- associated osteoporosis (PLO) is a rare disease with an incidence of 4 in 1000,000 women. We present four cases of PLO to show clinical courses and share treatment experiences. We hope to arouse awareness of this uncommon cause of secondary osteoporosis.

Methods: We retrospectively review charts of four patients of PLO diagnosed in National Taiwan University Hospital.

Results: These four patients were breastfeeding mothers aged from 29–38 y. Large amount of lactation was noticed in two patients, one of whom gave birth to twins. Symptoms included soreness and severe pain over the back since two to four months after delivery. All patients suffered from multiple fractures of the thoracolumbar spine with a decrease of 3 to 10 cm in body height. BMI ranged from 16.7-24.6 kg/m^2. BMD measured −3.3 to −4.1 SD and increased after treatment. Serum calcium and phosphate levels were normal, intact PTH levels were in the lower normal range (14.6-18.9 pg/mL), and 25-hydroxyvitamin D was insufficient (15.3-27.5 ng/mL). Exclusion of malignancy and other endocrine diseases was necessary for the diagnosis of PLO. Cessation of breastfeeding was crucial for treatment. Oral calcium and vitamin D supplement with or without denosumab injection were the most common medication prescribed. Back pain improved gradually within several months of treatment.

Conclusion: PLO may cause multiple fractures. Breastfeeding should be discontinued once PLO was diagnosed. Adequate calcium and vitamin D supplement must be proposed in all pregnant

and breastfeeding women. PLO with fracture should be kept in mind as one of the differential diagnosis of severe back pain in lactating mothers.

P196
EFFECT OF GLUCOCORTICOID ON HIGH FAT DIET INDUCED BONE LOSS IN BALB/C MICE

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Aims: Chronic glucocorticoid (GC) therapy leads to bone loss. This study aims to highlight the deleterious effect of glucocorticoid on bone in male and female BALB/c mice fed on high fat diet.
Methods: BALB/c mice of both sexes were assigned to eight groups of eight animals each. Female animals were segregated into four groups as control (fed with normal chow diet), high fat diet group (fed with HFD) and GC group (treated with glucocorticoid along with normal diet) and HFD + GC (animals fed on high fat diet and treated with glucocorticoid). Likewise male animals were divided in four groups as control, HFD, GC and HFD + GC. The treatment continued for 10 weeks. At the end of the study, animals were euthanized, autopsied and bone, muscle, serum samples were collected for μCT, gene expression and histological study. Comparisons of each parameter among the groups were analyzed by one-way ANOVA to determine the effects of treatment and diet in all groups.
Results: HFD induced deterioration in bone micro architecture was observed to be predominant in male mice. μCT analysis, histological study of femur and tibia exhibited sharp deterioration in bone in animals on HFD diet treated with GC. Osteoblast differentiation from bone marrow stromal cells was sharply reduced in animals on GC treatment. Expression of osteoblast genes *Runx2, Ocn, Col1* was decreased and osteoclast marker gene was increased in long bones. Muscle atrophy genes *Atrogin1* and *MuRF1* were elevated as result of treatment with GC. Muscle atrophy was evident from histological sections and increased creatine kinase activity in serum.
Conclusion: GC showed pronounced deleterious effect in female as compared to male. HFD further aggravated the effect of GC on both male and female mice. Our results showed that chronic glucocorticoid therapy is detrimental for bone in obese individuals. Increased body mass in obese individuals does not protect the bone from deteriorating on exposure to GC.

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BONE MINERAL DENSITY AND VITAMIN D STATUS IN WOMEN WITH PARKINSON'S DISEASE

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Aims: To determine the BMD and vitamin D status in patients with Parkinson's disease.
Methods: We examined 32 women with Parkinson's disease and 32 healthy women of appropriate age (average age: 64.5 ± 7.6 vs. 63.8 ± 8.1 y, $p = 0.5$). The duration of Parkinson's disease was at least 5 y. All patients received levodopa. BMD measurements using DXA. Serum 25-hydroxycholecalciferol (25-OHD) was determined by electrochemiluminescence immunoassay methods.
Results: BMD of women with Parkinson's disease was significantly lower compared with BMD of women of control group on the level of lumbar spine (BMD = 0.921 ± 0.028 vs. 0.984 ± 0.024, $p < 0.05$) and at the hip (BMD = 0.923 ± 0.022 vs. 0.984 ± 0.016, $p < 0.05$). The difference of the lumbar spine BMD was 14.7 % and at the hip 6.8 %.The incidence of vitamin D deficiency was significantly higher in patients with Parkinson's disease (76 % vs. 21 %). The level of the vitamin D was significantly lower in patients with Parkinson's disease in comparison with healthy persons (15.87 ± 3.43 vs. 23.82 ± 2.63 ng/ml, $p < 0.05$).
Conclusion: BMD and level of vitamin D in women with Parkinson's disease were significantly lower than in healthy women of the same age.

P198
NONVERTEBRAL FRACTURES IN UKRAINIAN WOMEN WITH OBESITY AND METABOLIC SYNDROME IN POSTMENOPAUSAL PERIOD

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Aims: The number of obesity in the world has been significantly increasing in population. Abdominal obesity leads to the metabolic syndrome (MS) development. It was researched that components of MS have influence on BMD, but data are contradictory. The aim of this study was to determine peculiarities of nonvertebral fractures in women with obesity and MS.
Methods: 590 women aged 50–79 y (mean age – 64.0 ± 8.0 y; mean weight −75.8 ± 13.6 kg, BMI – 29.4 ± 5.3 kg/m^2, mean duration of menopause – 14.6 ± 8.4 y) were examined. The women were compared into the three groups: **A** included 298 women without obesity BMI ≤ 29.9 kg/m^2), **B** involved 177 patients with obesity (BMI ≥ 30.0 kg/m^2). MS was diagnosed in women of the **C** group (115 people). Women were considered to have the MS according to IDF criteria (2005 y). BMD was measured by the DXA method (Prodigy, GEHC Lunar, Madison, WI, USA). Results are present as mean

(±SD) and categorical variables were expressed as frequencies. Significance was set at $p < 0.05$. We performed a one-way ANOVA test, multiple regression and correlation analysis. Data were analyzed using Statistika 6.0© StatSoft, Inc.

Results: Nonvertebral fractures were found in 37.92 % of the A group patients, 29.94 % of B group women and 35.56 % of the C group. We estimated that patients without obesity have significantly lower BMD of lumbar spine (A – 0.931 ± 0.168 g/cm^2, B −1.091 ± 0.191 g/cm^2, C −1.082 ± 0.190 g/cm^2), femoral neck (A – 0.772 ± 0.113 g/cm^2, B – 0.858 ± 0.132 g/cm^2, C −0.861 ± 0.135 g/cm^2) and ultradistal forearm (A – 0.347 ± 0.073 g/cm^2, B – 0.428 ± 0.083 g/cm^2, C −0.418 ± 0.088 g/cm^2) in comparison with women of the groups B and C. We did not find significant differences among BMD of the B and C group patients ($p > 0.05$). The results of the study showed significant better BMD of the C group patients without fractures compared to those with fractures. Differences of BMD in patients with and without nonvertebral fractures in other groups of the women were not found.

Conclusion: BMD is better in women with obesity and MS. Nonvertebral fractures are more common in patients without obesity.

P199

CELIAC DISEASE: AN UNRECOGNIZED PREDISPOSING FACTOR FOR HYPOCALCEMIA IN TAIWAN

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Aims: In the Western world, celiac disease globally affects 0.6-1.0 % of the population. The frequency of celiac disease is increasing in many developing countries because of westernization of the diet, changes in wheat production and preparation, increased awareness of the disease, or a combination of these factors. Only few case reports and short reports were recently available from Eastern world.

Methods: According to the guideline of the American College of Gastroenterology, small bowel biopsy together with positive disease-specific serology is recommended as the gold standard for diagnosing celiac disease.

Results: We present 2 cases manifesting with hypocalcemia. Both of them were diagnosed as having secondary hyperparathyroidism with unknown cause. The levels of minerals in urine demonstrated low level of daily calcium excretion. The serum 25-OHD levels both were lower than 20 ng/mL, indicating vitamin D insufficiency. The diagnosis of celiac disease was established following an agreement between the serologic results and the biopsy findings.

Conclusion: Although celiac disease was previously considered to be either nonexistent or very rare in Asia, this report of 2 cases supports the existence of celiac disease in Taiwan.

P200

A YOUNG ADULT WOMAN WITH SEVERE OSTEOPOROSIS DUE TO CUSHING'S DISEASE: A CASE REPORT

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Aims: Severe osteoporosis due to Cushing's disease was relatively uncommon in the clinical setting, especially for a young adult woman. Therefore, we present a case of a 35-year-old premenopausal woman with Cushing's disease who presented with multiple low trauma fracture. We hope that our experience of this case will remind doctors to be aware of this unusual complication of Cushing's disease.

Methods: We report the clinical presentation, laboratory results, and imaging studies of a case of a 35-year-old premenopausal woman who presented with multiple low trauma fractures due to Cushing's disease.

Results: A 35-year-old was admitted to our orthopedic department because of left pubic bone fracture after falling from a standing height on a rainy day. She had regular menstrual cycles and denied smoking, alcohol consumption, taking any medication and drug containing ingredients of steroid or Chinese herb. Physical exam showed no obvious finding except for overweight based on criteria in Taiwan. Initial lab data revealed Ca: 9.3 mg/dL, inorganic P: 3.5 mg/dL, albumin: 4.71 g/dL, alkaline phosphatase: 76 U/L, intact PTH: 24.8 pg/mL, serum creatinine: 0.62 mg/dL, hemoglobin: 13.9 g/dL, thyroid stimulating hormone: 0.485 μIU/mL, free T4: 1.00 ng/dL, normal serum and urine pattern of protein electrophoresis/immunofixation electrophoresis, cancer antigen 15–3: 12.0 U/mL, carbohydrate antigen 19–9: 21.02 U/mL, carcinoembryonic antigen: 0.90 ng/mL, serum 25-hydroxyvitamin D: 8.61 ng/mL. Initial image study with chest, thoracolumbar spine and pelvis X-ray showed old fractures at bilateral ribs, old compression fracture at T11 and new fracture of left superior/inferior pubic ramus (Figure 1). Computed tomography from neck to pubic symphysis confirmed the fractures corresponding to X-ray findings and no evidence of visceral malignancy. Bone scan demonstrated old fractures as mention-above and no possible uptake of malignancy (Figure 1). DXA revealed the lowest Z-score: −3.4 for her left hip. The screen test with 24-h urine free cortisol was 1298.7 μg/d (normal range: 20.9-292.3 μg/d) and serum ACTH was 68.4 pg/mL (normal reference in our hospital was ≤46 pg/mL). 2 mg 48-h high dose dexamethasone suppression test was performed and the result was positive. Pituitary MRI revealed pituitary microadenoma (7x5x5 mm) in the left-sided pituitary gland (Figure 2). Transsphenoidal surgery for tumor resection due to highly suggestive of pituitary adenoma was performed and the pathological result showed pituitary tissue with positive of immunohistochemical study for ACTH.

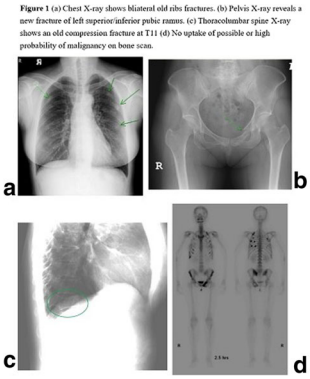

Figure 1 (a) Chest X-ray shows bilateral old ribs fractures. (b) Pelvis X-ray reveals a new fracture of left superior/inferior pubic ramus. (c) Thoracolumbar spine X-ray shows an old compression fracture at T11 (d) No uptake of possible or high probability of malignancy on bone scan.

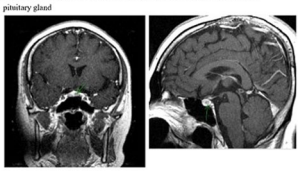

Figure 2 Pituitary MRI revealed microadenoma (7x5x5 mm) in the left-sided pituitary gland

Conclusion: A young adult woman with severe osteoporosis due to Cushing's disease was a relatively uncommon in our clinical practice. We hope that our experience of this case will remind physicians to be aware of this unusual complication of Cushing's disease.

P201
THE ROLE OF OSTERIX EXPRESSION IN FGF-23 SECRETION FROM CAUSATIVE TUMORS OF ONCOGENIC OSTEOMALACIA

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Aims: Oncogenic osteomalacia (OOM), or tumor induced osteomalacia (TIO), is a rare disease characterized by renal phosphate wasting and hypophosphatemic osteomalacia due to the secretion of FGF-23 from causative mesenchymal OOM tumors, which is physiologically secreted from osteocytes. To determine the role of osterix (OSX) in FGF-23 secretion from OOM tumors, the expressions of OSX and other osteoblast/osteocyte specific genes in OOM tumors were investigated. The role of OSX expression was also investigated in UMR106 osteoblastic cell line.
Methods: Sixteen causative OOM tumors and 7 histopathologic classification-matched non-OOM tumors were analyzed by quantitative real-time RT-PCR and immunohistochemistry. Fluorescent immunohistochemistry was also applied to investigate colocalization of the gene expressions in OOM tumors. The study was approved by the institutional ethics committees and was conducted in accordance with the principles of the Declaration of Helsinki. UMR106 cells were analyzed to identify the role of osteocyte/osteoblast specific genes in FGF-23 expression in vitro.
Results: Osteocyte/osteoblast specific genes such as OSX, osteocalcin (BGP), and DMP-1 were significantly elevated as well as FGF-23 in OOM tumors compared to non-OOM tumors. The elevated expressions of these genes were also confirmed by immunohistochemistry. Fluorescent immunohistochemistry revealed that localizations of these gene expressions were merged in some OOM tumors; however, the other OOM tumors exhibited different colocalizations of OSX and FGF-23, from those of osteocalcin and DMP-1. In gene knockdown analyses using UMR106 cells, OSX siRNA suppressed FGF-23 and DMP-1 expression, but not BGP expression. DMP-1 siRNA increased FGF-23 expression and FGF-23 siRNA decreased DMP-1 expression.
Conclusion: OOM tumors have osteogenic characteristics. Colocalization of OSX and FGF-23, and siRNA assays revealed that OSX is one of regulator in FGF-23 expression in OOM. The negative feedback loop between FGF-23 and DMP-1 is still remained in some tumors as well as normal bone tissue.

P202
PREDICTORS AND OUTCOME OF FRAGILITY HIP FRACTURE: A PROSPECTIVE MULTICENTRE STUDY FROM NORTH INDIA

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Aims: Fragility fracture of hip is a useful surrogate marker to determine the burden of osteoporosis. With improving life expectancy and progressive ageing of population, the global burden of osteoporotic fracture is increasing. Despite this, there is paucity of data regarding epidemiology, predictors and outcome of fragility hip fracture in Indian population
Methods: In this multicentre, cross-sectional, prospective observational study, total 264 patients of fragility hip fracture were followed up for 12 months.
Results: Men (46.2 %) and women (53.8 %) had a near equal distribution of fragility hip fracture. Mean (±SD) age of study population was 65.9 (12.6) y and men had earlier age (64.7 ± 12.6 y) of fracture as compared to women (66.9 ± 12.6 y). Out of these 89.7 % patients had osteoporosis, 7.6 % had osteopenia and 2.7 % patients had normal BMD. Fractures predominantly occurred inside home (229, 86.7 %) as compared to outside (35, 13.3 %). Female gender, hypertension, diabetes, anaemia, smoking and alcohol were associated with lower BMD, but not a predictor of morbidity. Aging (p 0.000), osteoporosis (p 0.012) and diabetes (p 0.008) were predictor of increased mortality. Total 243 (92 %) patients underwent surgery with hospital stay of 13.5 (±2.9) d and 34 (12.9 %) patients died. Maximum death (73.5) occurred in first 3 months and the commonest cause of death was cardiovascular (44.1 %) related.
Conclusion: Majority of fragility hip fractures occur inside home. Distribution of fracture in either gender is comparable.

Aging, osteoporosis and diabetes are predictors of poor outcome. Newer strategies to be developed to target male patients and prevent in-house fragility fracture.

P203
ANABOLIC BONE WINDOW WITH WEEKLY TERIPARATIDE THERAPY IN POSTMENOPAUSAL OSTEOPOROSIS

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Aims: Osteoporosis is a major public health problem which reduces bone strength and increases risk of fracture. Teriparatide has been approved for the treatment of postmenopausal osteoporosis (PMO) with recommended daily dose of 20 μg subcutaneously. However data regarding the long term effect of once-weekly teriparatide therapy on BMD, bone turnover markers (BTMs) and anabolic bone window is limited.
Methods: In this prospective observational study 26 patients with PMO were treated with weekly teriparatide therapy for 2 y. BMD was measured at baseline, 12 months and 24 months. The bone formation marker, type I collagen C-terminal propeptide (P1NP) and the bone resorption marker, C-terminal telopeptide of type I collagen (CTx) were measured at baseline, 6 weeks, 6 months, 12, 18 and 24 months.
Results: BMD at lumbar spine increased by 3.1 % and 10.8 %, respectively, after 1 y and 2 y of weekly teriparatide therapy. T-score significantly increased at lumbar spine as compared to baseline after 2 y (p 0.015). Serum P1NP levels increased significantly at 6th month (p 0.024), peaked at one year and remained above the baseline even after 2 y. Serum CTx levels decreased significantly at 6th month (p 0.025) and remained below the baseline at the end of 2 y of teriparatide therapy.
Conclusion: Weekly teriparatide therapy is effective for the treatment and prevention of PMO by achieving a sustained anabolic bone window.
Acknowledgement: Our sincere thanks to Ranbaxy India for providing teriparatide (recombinant human PTH).

P204
THE EFFECT OF VITAMIN D SUPPLEMENTATION ON LEVELS OF 25-HYDROXYVITAMIN D3 [25(OH)D], INTACT PARATHYROID HORMONE (IPTH) AND BONE MINERAL DENSITY (BMD)

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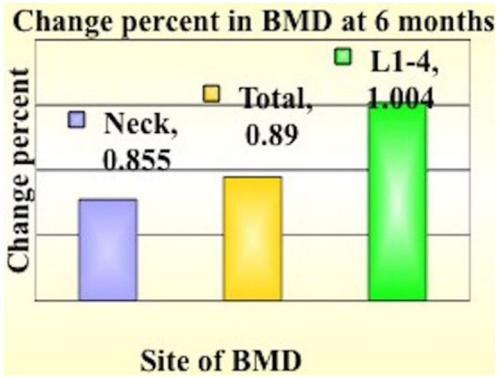
Aims: 1. To define the normal range of serum 25(OH)D and iPTH based on their relationship. 2. To analyze the effect of vitamin D supplementation on 25(OH)D and iPTH at end of 3 and 6 months in vitamin D deficient (VDD) group. 3. To study the BMD changes from baseline at end of 6 months of vitamin D supplementation
Methods: This study was conducted in tertiary care hospital, on apparently healthy subjects (detailed clinical history and examination, hemoglobin >11 g%.). 1800 subjects interviewed, (both sexes, 19–44 y). 200 sample size, collected randomly. 50 received cholecalciferol supplementation and BMD. Nutritionist assessed 3-d diet recall. Daily sun exposure was assessed. Visit 1: serum 25(OH)D, iPTH, calcium, albumin, phosphorus, alkaline phosphatase, bone profile, magnesium and creatinine measured in all. After randomization n = 50 had BMD by DXA and given cholecalciferol sachet (each containing 1500 μg (60 000 IU) vitamin D3; Cadila Pharmaceutical, India) per month (i.e., 2000 IU/d) and elemental calcium 1000 mg/d (each tablet containing 500 mg elemental calcium carbonate + 250 IU vitamin D3 (Elder Pharmaceutical, India)); i.e., total vitamin D_3 2500 IU/d. Repeated at end of 3 and 6 months (visits 2 and 3): serum 25-(OH)D, iPTH, and bone profile. BMD by DXA was repeated at the end of 6 months. Compliance assured by giving monthly prescriptions only and counting any unused tablets. Data analyzed by SPSS software version 15.
Results: Out of 200 asymptomatic healthy Asian Indian subjects, 82 % had VDD (<20 ng/ml), 12.5 % had insufficiency (<30 ng/ml), and only 5.5 % (>30 ng/ml) were in sufficient range. 50 VDD subjects were randomized and supplemented with cholecalciferol and calcium. 62.22 % had net increase in 25 (OH) D at end of 6 months. Group 1: iPTH > 72 pg/ml, change in 25(OH) D was significant at 3 and 6 months from baseline P < 0.001, but change in PTH was significant only between 3 and 6 months, as the PTH values rose again at end of 6 months, P < 0.05. Group 2: iPTH 12–72 pg/ml, the change in 25(OH) D was significant at 3 and 6 months from baseline P < 0.001, but change in PTH was significant neither at 3 nor at 6 months. The change in BMD by DXA was significant at L1-4, at neck femur and total femur at 6 months, P = 0.01, P = 0.001and 0.002, respectively. Significant correlation between 25(OH) D and BMD at baseline at all sites: L1-4, neck femur and total femur, P = 0.0220, 0.0105 and 0.0064, respectively.



Conclusion: Vitamin D deficiency is widely prevalent amongst apparently healthy individuals. Sustained supplementation of 2500 IU/d of cholecalciferol may not increase 25(OH)D levels above 30 ng/ml in all individuals. The serum 25(OH)D in some subjects decreased and then increased suggesting altered vitamin D metabolism related to vitamin D gene polymorphisms.

P205
REGULATION OF ACTIVE COMPOUNDS FROM EUCHEUMA COTTONII ON RECEPTOR FOR ADVANCED GLYCATION END PRODUCTS: IN SILICO STUDY

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Aims: The mechanisms underlying diabetes-mediated bone loss are not well defined. It has been reported that the advanced glycation endproducts (AGEs) and receptor for AGEs (RAGEs) are involved in diabetic complications. This study aimed to evaluate the active compounds of *Eucheuma cottonii* to the RAGE pathway as one pathway in diabetoporosis.
Methods: Three dimensional structure of the (−)- catechin and phloroglucinol was obtained from NCBI's PubChem. (−) – catechin ID was CID73160 and phloroglucinol ID was CID359. Analysis was performed in silico using the primary method of docking by the use of Hex 8.0 software and Haddock web server. Analysis of interactions was then performed to determine the interactions between the ligand and its receptors by using the software Discovery Studio Client 3.5.
Results: Ligand docking energy show that catechin have lowest binding energy with Nrf2 (−165.0 kJ/mol), while phloroglucinol have highest binding energy (−129.6 kJ/mol). A lower binding energy means that the catechin is easier to interact with the RAGE.
Conclusion: Catechin was more likely to bind with the RAGE pathway in diabetic osteoporosis.

P206
WHO AND HOW TREATS OSTEOPOROSIS IN A CASE AT THE BORDER BETWEEN SPECIALTIES?

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Aims: We present the case of a 72 y old female patient, who is hospitalized in the Rheumatology Clinic in May 2015 with suspicion of rheumatoid arthritis. She complains also of low back pain and polyarticular swelling and tenderness.
Methods: The patient was recently hospitalized in a Hematology Clinic where she was diagnosed with multiple myeloma IgG kappa (May 2015) but without starting a specific treatment. She is guided to our clinic due to painful joint symptoms.
Based on physical examination, laboratory tests (rheumatoid factor, anti-CCP antibodies, inflammation tests positive) and X-rays we confirm the diagnosis of rheumatoid arthritis. The X-ray for spinal column shows multiple vertebral compressions and spine bone densitometry (T-score) is −3. We begin treatment with bisphosphonate and corticosteroids in small doses, with favorable evolution.
Results: After 6 months of treatment the joint symptoms were remitted, the tests for inflammation are negative, but T-score now is −3.5. The Haematologist considers myeloma controlled and recommends continuation of treatment with bisphosphonates and corticosteroids.
Conclusion: At a patient with multiple myeloma controlled by bisphosphonate therapy with glucocorticoids, in which osteoporosis is widening, against the risk of fragility fracture, which is the appropriate treatment? Haematologist should interfere therapeutically, allowing elimination of corticosteroid treatment?

P207
THE EFFECTIVENESS OF SYNTHETIC BONE GRAFT SUBSTITUTE IN OSTEOPOROTIC UNSTABLE INTERTROCHANTERIC FRACTURES OF FEMUR TREATED WITH GAMMA NAIL

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Aims: Compare gamma nail with bone substitute and only gamma nail to evaluate the effectiveness of synthetic bone graft substitute in osteoporotic unstable intertrochanteric fractures treated with gamma nail.
Methods: All of the 60 patients admitted to the hospital between June 2012 and June 2015 who underwent gamma nail for unstable intertrochanteric fractures were evaluated. The mean age was 72(65–80), there were evaluated BMD and diagnosed osteoporosis, radiologic comparison was done between 60 patients of unstable intertrochanteric fracture (AO type A2) during 1 y. The patients were divided into two groups, a group treated with gamma nail with synthetic bone graft substitute (calcium sulfate /tricalcium phosphate) group (30 patients) and another group treated only with gamma nail (30 patients). Postoperative Tip-apex distance, lag screw slippage and femoral neck-shaft angle change were measured between two groups. Complications during the follow-up period was compared by VAS score and Harris hip score.
Results: In two group, Vas score and HSS were improved better than pre-operation state. No significant difference of Tip-apex distance, lag screw slippage and femoral neck-shaft angle was found. Treated only gamma nail group was 2 case of cutting-out of the lag screw, but also there was a significant difference.
Conclusion: As there are lesser lag screw slippage and neck-shaft angle change, synthetic bone graft substitute applied in osteoporotic unstable intertrochanteric fractures seems to be useful in maintaining reduction and preventing failure of internal fixation when proper reduction and screw insertion is performed.

P208
EFFECTS OF SESAME OIL ON OSTEOPOROSIS IN RATS

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Aims: To investigate the effects of sesame oil on experimental postmenopausal osteoporosis among rats.
Methods: Bilateral ovariectomy was performed on sexually mature female rats to simulate postmenopausal osteoporosis model in rats. Nineteen ovariectomized Sprague Dawley rats (SD rats) were divided into three groups: sesame oil was given orally 0, 0.25, or 0.5 ml/kg/d in each group for 4 months after ovariectomy. Control group was set up by five SD rats without ovariectomy nor oil feeding. Assessment was done at 4 months after ovariectomy. BMD and four kinds of serum bone turnover markers were surveyed in this study. BMD was assessed by using DXA. Bone turnover markers including two bone formation markers: alkaline phosphatase (BAP) and procollagen I C-terminal propeptide (PICP) and two bone resorption markers: crosslinked N-telopeptide (NTX) and pyridinoline (PYD) were measured by enzyme-linked immunosorbent assay.
Results: Sesame oil feeding significantly increased BMD in postmenopausal osteoporosis rat. BAP and PICP levels were significant higher in sesame oil-treated rats compared with that in ovariectomy only rats. In addition, sesame oil feeding significantly decreased bone resorption marker NTX levels in serum in postmenopausal osteoporosis rat. With the more amount of sesame oil given, the more osteoprotective effect of sesame oil was observed in this study.
Conclusion: The most important finding of our study was that by orally given sesame oil for four months, the osteoprotective effects of sesame oil on ovariectomized rats were obviously noted. Estrogen deficiency arising after the menopause leads to acceleration of bone turnover, the rate of bone resorption exceeding the rate of bone formation. Oxidative stress was closely related with differentiation of osteoblast and osteoclast. Prior study also suggested that sesame ingestion can improve antioxidant status and sex hormone status in postmenopausal women [1]. In conclusion, the present study indicated that estrogen deficiency caused by bilateral ovariectomy could lead to change in bone metabolism. In ovariectomized rats, feeding them with sesame oil could have beneficial effect on bone turnover marker and bone mineral density. In other word, sesame oil ingestion has an osteoprotective effect on ovariectomy-caused estrogen deficiency rats. Thus, sesame oil, as the food supplement, has the potential to play an important role in postmenopausal osteoporosis.
References: 1. Wu WH et al. J Nutr 2006;136:1270.

P209
INTRA-ARTICULAR PARATHYROID HORMONE (1–34) IMPROVED KNEE OSTEOARTHRITIS AND FUNCTION IN RATS BY DECREASING CHONDROCYTE TERMINAL DIFFERENTIATION AND APOPTOSIS VIA AUTOPHAGY

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Aims: Joint trauma leads to post-traumatic osteoarthritis (PTOA) as a long-term complication. Anterior cruciate

ligament (ACL) tears are among the most common knee injuries in young athletes usually leads to OA. Previous study showed PTH(1–34) can alleviate OA progression in papain-induced OA model. Autophagy is a protective mechanism in normal cartilage, and its aging-related loss is linked with chondrocyte death and OA. These led us to evaluate whether autophagy plays roles in PTH treating OA after ACL transection (ACLT).

Methods: 36 male rats were randomized into 3 groups: control group, OA group induced by ACLT and treatment group, OA with intra-articular PTH(1–34) for 5 weeks. Pain and knee function was assayed by weight bearing and treadmill test. Matrix was assayed by histology with OARSI score and TUNEL stain, histomorphometric study for glycosaminoglycan stain and immunohistochemistry for collagen type II (COLII) and X (COLX), Ihh and autophagy-related proteins.

Results: PTH(1–34) significantly improved the rats to bear weight and endurance in treadmill. Terminal differentiation of chondrocyte aggravated after ACLT. PTH(1–34) preserved glycosaminoglycan and decreased OARSI score. PTH(1–34) preserved COLII and decreased terminal differentiation by decreasing Ihh and COLX protein expression. Autophagy decreased after ACLT. PTH(1–34) ameliorated chondrocyte apoptosis via regulating the expressions of autophagy related proteins including by reducing mTOR and p62 and enhancing LC3 and Beclin-1.

Conclusion: The development of OA after an ACL rupture and reconstructive surgery remains an unsolved problem. Chondral injury is also associated with acute traumatic ACL rupture in most patients. To resolve this unmet need, we study the effect of PTH in ACLT animal model. Chondrocyte apoptosis is an important mechanism of PTOA. Autophagy may be a protective mechanism in normal cartilage and compromised autophagy participates in the development of OA. mTOR is a negative regulator of autophagy. Suppression of autophagy is always accompanied by massive accumulation of a selective substrate for autophagy; p62. In this study, we found intra-articular PTH(1–34) injection can reduce knee pain by increasing the weight bearing of lower limb and increase knee function by increasing the endurance in treadmill test. Besides, PTH(1–34) can maintain GAG and COLII and decrease OARSI score, the expression of COLX and chondrocyte apoptosis. The possible mechanisms are reducing chondrocyte terminal differentiation and apoptosis. Higher levels of Ihh signaling in chondrocytes cause a more severe OA phenotype in human and mouse OA. Suppression of Ihh expression by PTH(1–34) with subsequent suppression of terminal differentiation may be one mechanism. Increased autophagy with subsequent decrease apoptosis may be another mechanism of the effect of PTH(1–34) in alleviating OA. Increasing autophagy by LC3 and Beclin-1 via mTOR suppression with reduced p62 may play important roles.

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SPECIALIZED HIP SURGEON DECREASES ONE-YEAR MORTALITY IN ELDERLY PATIENTS WITH FRAGILE HIP FRACTURE

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Aims: Hip fractures cause acute pain and loss of function, and often lead to hospitalization. After acute hip surgery, in-hospital mortality may be as high as 9.5 % and one-year mortality as high as 14-36 %. This study evaluated the risk factors related to one-year mortality in a medical center by analyzing the demographic, clinical, and surgical characteristics of the patients, as well as data on the medical provider.

Methods: From January 2009 to December 2010, the records of 313 patients who received surgery for hip fracture were reviewed. Those with multiple fractures or combined trauma were excluded. Aside from descriptive statistics analyses were done using independent *t* test, analysis of variance, chi-square test, linear regression, and logistic regression.

Results: The total complication rate was 53.7 %. The most common complication was anemia. The one-year mortality rate was 12.1 %, which was associated with comorbidity, complication, and surgical care quality, particularly a specialized high volume hip surgeon acting as an orthogeriatrician. Despite the longer hospital stay and higher medical costs, the presence of a high volume specialized hip surgeon had a one-year mortality rate of 4.7 % and a 67 % reduction in mortality. One-year mortality was also related to more than three comorbidities. Postoperative complications increased the one-year mortality.

Conclusion: A high volume hip surgeon specializing in hip fracture patient care and acting as an orthogeriatrician can significantly reduce mortality. Nonetheless, combined care of these patients with geriatric specialists is strongly recommended, especially for those with more than three comorbidities.

P211

THERAPEUTICAL PROBLEMS IN A PATIENT WITH OSTEOGENESIS IMPERFECTA AND MULTIPLE COMORBIDITIES

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Aims: We present the case of a female patient, 57 y old, who is hospitalized in the Rheumatology Clinic in February 2016 for tenderness and swollen joints.
Methods: This is the first presentation in our clinic and from patient history we note osteogenesis imperfecta (diagnosed in childhood), seropositive rheumatoid arthritis (2007), osteoporosis with multiple vertebral compressions, repeated episodes of fracture (in 2015 right ankle and right hip fractures). From the time of diagnosis with rheumatoid arthritis she followed initial treatment with leflunomide, then associated methotrexate and adalimumab from 2010. In the 2010–2014 period, there were no pain or swollen joints. After 4 y, symptoms reappeared and she switched adalimumab treatment with rituximab. Also, in 2014 her physician started treatment with corticosteroids (methylprednisolone 8 mg/d) and introduced bisphosphonate therapy, along with calcium and alpha D3. On this background, joint symptoms are controlled, but the patient had two episodes of spontaneous fractures (right ankle, then right hip). We recommend stopping methylprednisolone and changing biological treatment, but the patient refused.
Results: At this patient, there are multiple causes of osteoporosis: postmenopausal osteoporosis, osteogenesis imperfecta, prolonged immobilization due to fractures, rheumatoid arthritis, corticosteroid treatment.
Conclusion: In a case of noncompliant patient, who refuse stopping corticosteroids, under important immunosuppressive therapy (leflunomide, methotrexate and mabthera), denosumab represents a safe alternative? Do we have other therapeutic options?

P212
ROLE OF WITHAFERIN A IN LONGITUDINAL BONE GROWTH AND ITS CHONDROPROTECTIVE EFFECT IN CARTILAGE DEGENERATIVE DISEASE

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Aims: We investigate the chondrogenic effect of constituent of Herb *Withania somnifera* leaf (WFA) in bone growth, achievement of greater peak bone mass and its chondroprotective effect in autoimmune disease and cartilage degenerative disease.
Methods: For in vitro study we culture rat articular chondrocytes (RAC) to study cytotoxicity assay, antioxidant, anti-inflammatory activity, cell cycle progression, transcription and translation of chondrogenic markers. In vivo studies WFA at 10 mg/kg/d dose used for osteochondrogenic activity in growing rat, dexamethasone induced growth retardation in growth plate and secondary osteoporosis in growing rats, and intra-articular injection of monosodium iodoacetate induced osteoarthritis study in adult rats with μCT.
Results: Cytotoxicity study by MTT and apoptosis showed that 1 μM and below WFA concentration were safe. WFA at 100 nM significantly reduced ROS generation and restored mitochondrial membrane potential that are altered by inflammatory cytokines (IL-1β and TNF-α) finally WFA reduced inflammation induced cell death. Cell cycle analysis showed that WFA 100 nM induced statistically significant ($P < 0.01$) increase chondrocyte cells proliferation and bone length in metatarsal organ culture. Alizarin staining and osteogenic genes study showed that WFA maintained chondrocytes population by lagging dedifferentiation into hypertrophic direction. WFA enhanced extracellular matrix synthesis like increase in GAG, alcian blue content and up regulating the expression of chondrogenic genes aggrecan ($P < 0.01$), collagen II ($P < 0.001$) and Sox9 ($P < 0.01$) as compared to control. In vivo study showed that WFA significantly increased the length of femur 11.1 % ($P < 0.05$) and tibia 8.74 % ($P < 0.01$) compared to vehicle. Histomorphometric analysis demonstrated that WFA increased the growth plate height by increasing cells in proliferating and hypertrophic zone. WFA supplementation results in significantly improved trabecular architecture by increased bone volume ($P < 0.05$) and trabecular number ($P < 0.01$) of isolated femur and tibia that help in achievement of greater peak bone mass. We found WFA treatment reduced glucocorticoid prompted growth retardation and cartilage loss in MIA-treated animals.
Conclusion: Here, we demonstrate that WFA increased bone length and trabecular micro-architecture of long bones in growing female rats and its therapeutic potential in osteoarthritis induced cartilage destruction and glucocorticoid induced growth arrest.
Acknowledgement: CSIR and ASTHI (BSC0201) Government of India.

P213
DENOSUMAB IS THE MANAGEMENT OF OSTEOPOROSIS IN CHINESE: THE LARGEST CASE SERIES TO DATE

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Aims: To investigate the effect of denosumab on changes in BMD; as well as adverse events and drug compliance in Hong Kong Chinese postmenopausal women.
Methods: 365 postmenopausal Hong Kong Chinese women were recruited from Sep 2011 to May 2016. The criteria of entry were a T-score of −2.5 at either the Femoral Neck or total spine; or a T-score of −2.0, with one or more risk factor for osteoporosis. BMD at the total hip and spine was measured by a dual x-ray densitometer (Lunar Prodigy models, Madison, WI, USA) and expressed as BMD (g/cm^2) at baseline; and every 12 months. Subcutaneous denosumab injection was

performed every 6 months. During the clinic visit, all adverse events were recorded. In addition, subjects were told to report to the investigators any adverse events/episodes of illness in between clinic visit. Reasons for termination of denosumab treatment were also recorded.

Results: 365 subjects were recruited from Sep 2011 to May 2016. The mean duration of follow-up was 6 months. Of the 365 subjects, 13.6 % defaulted from the denosumab treatment. In 2.7 %, the investigator stopped the denosumab treatment due to adverse events as follows: the 5 most common non-skin adverse events are tiredness (n = 22); URTI (n = 12); joint pain (n = 10); dizziness (n = 8); discomfort (n = 5); chest discomfort (n = 5). The skin adverse events are as follows: Mild eczematous skin reaction (n = 7); maculopapular rash (n = 1); psoriasiform dermatitis (n = 1); this was severe and led to drug discontinuation. Other significant adverse events are as follows: osteonecrosis of jaw (n = 1); decreased WBC count (n = 1) and pneumonia (n = 1). No deaths occurred in the treatment period and no multiple vertebral fracture has been observed after drug treatment was stopped.

The following are mean changes in BMD:

	Baseline (g/cm^2)	%Change 12 months (n = 200)	%Change 24 months (n = 110)
Femoral neck	0.660	2.5	3.7
Total spine	0.786	5.0	6.0

Conclusion: Denosumab injection was associated with significant increase in BMD in postmenopausal Hong Kong Chinese women. Mild skin reaction was common. Continuous documentation of adverse events is critical for further understanding of the safety and risk-benefit of this drug.

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ASSOCIATIONS OF DIETARY PATTERNS WITH BONE MASS, MUSCLE STRENGTH AND BALANCE IN A COHORT OF AUSTRALIAN MIDDLE-AGED WOMEN

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Aims: To examine associations between dietary patterns and musculoskeletal health outcomes in middle-aged women.

Methods: This study was a cross-sectional analysis from a cohort of 347 women (aged 36–57 y). Food intakes were measured by the Cancer Council of Victoria food frequency questionnaire. Total body bone mineral content, femoral neck and lumbar spine BMD (DXA), lower limbs muscle strength (LMS), dynamic and static balance (timed up and go test, step test, functional reach test (FRT) and lateral reach test were also measured. Foods were grouped as grams eaten/day and exploratory factor analysis was used to identify dietary patterns. Associations were assessed using multivariable linear regression.

Results: Three dietary patterns were identified: 'Healthy' (high consumption of vegetables, legumes, fruit, tomatoes, nuts, snacks, garlic, whole grains and low intake of high-fat dairy), 'high protein, high fat' (red meats, poultry, processed meats, potatoes, cruciferous and dark-yellow vegetables, fish, chips, spirits and high-fat dairy) and 'Western' (high intakes of meat pies, hamburgers, beer, sweets, fruit juice, processed meats, snacks, spirits, pizza and low intake of cruciferous vegetables). After adjustment for confounders, 'Healthy' pattern was positively associated with LMS. The 'Western' pattern was inversely associated with FRT. There were no other associations with 'Healthy' or 'Western' patterns and none with 'high protein, high fat' pattern.

Conclusion: Maintaining a healthy diet may be important for muscle strength and balance in adult life, providing support for dietary strategies for prevention of age-related loss in muscle and balance.

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MUSCULOSKELETAL FORM AND FUNCTION IN CHINESE POSTMENOPAUSAL WOMEN ARE INFLUENCED BY BOTH CALCIUM INTAKE AND VITAMIN D STATUS

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Aims: The interaction of calcium intake and vitamin D status on fracture propensity remains controversial; however some studies have identified a role for both in improving bone structure and muscle strength and balance, important factors for falls. This cross-sectional study of a population with lower calcium intake and vitamin D status than that now encountered in many Western studies aimed to examine firstly whether thresholds exist for the association of 25(OH)D with these bone and neuromuscular outcomes and secondly examine potential interactions between serum 25-hydroxvitamin D (25(OH)D) and calcium intake on these variables.

Methods: Study participants were 441 community-dwelling Chinese women aged 60–88 y. Bone structure was examined by DXA BMD of total body, lumber spine (LS), total hip and femoral neck (FN). Neuromuscular functions examined were handgrip and lower limb muscle strength, one-leg standing time with eyes closed and time completing the timed up and go test (TUG). The data was examined by linear and by locally weighted smoothing (LOWESS) plots and piecewise regressions for 25OHD and calcium intake separately and together before and after adjustment for age, season and body weight. To evaluate the size of the effects tertiles of calcium intake (127–695, 695–982, 87–2436 mg/d) and tertiles of 25(OH)D (<29, 29–42, and 42+ nmol/L) were examined in a cross tabulation analysis.
Results: Mean age was 68.2 (5.6) y, mean 25OHD was 38.9 (17.4 nmol/L) and mean calcium intake was 861 (352) mg/day. In regression analysis before and after adjustment serum 25(OH)D was significantly associated with BMD at all sites and one leg standing times ($p < 0.05$) but there were no thresholds i.e. relations were linear across the range. Higher calcium intake was significantly associated with higher LS and FN BMD, TUG, and both muscle strength tests ($p < 0.05$)[RP1] [FW2]. Crosstabs identified benefit of a high calcium intake in participants in the lowest tertile of serum 25(OH)D for hip and FN BMD. High calcium intake also speeded TUG in all tertiles of 25(OH)D. High calcium intake improved handgrip strength only in the highest tertile of serum 25(OH)D (p for trend = 0.040) and LMS only in the middle tertile (p for trend = 0.005). No other additive effects were identified in these analyses.
Conclusion: Chinese postmenopausal women living in Beijing may benefit from increases in calcium intake and vitamin D to improve factors known to reduce fracture risk in other populations. These hypotheses are now being studied in an RCT.

P216
USE OF DENOSUMAB IN A RHEUMATOLOGY CENTRE

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Aims: 1) To describe the demographic of patients treated with denosumab. 2) To investigate the incidence of hypocalcemia after the first administration of denosumab. 3) To investigate the association between calcium level post denosumab with creatinine clearance and the use of activated vitamin D, respectively.
Methods: We collected data on demographic details, patients' weight, laboratory investigations (creatinine, albumin and calcium level post denosumab injection), fracture prevalence, previous treatment of osteoporosis and use of vitamin D. Only patients who were more than 55 y old were included in this study. Pearson correlation coefficient was computed to assess the relationship between calcium level post denosumab and creatinine clearance. To assess the association between the mean of calcium level and the use of vitamin D, student's t-test was used.
Results: 28 patients, 27 (94.4 %) of whom were females, received their first injections of denosumab. They consisted of 19 (67.9 %) Chinese and 9 (32.1 %) Malay patients, whose mean age was 77.32 ± 9.28 y (range 60–90 y). There were 13 (46.4 %) patients with rheumatoid arthritis and 9 (32.1 %) patients with primary osteoarthritis. The mean duration of osteoporosis was 8.36 ± 3.84 months and previous osteoporosis treatment included bisphosphonate and strontium, used by 23 (82.1 %) and 12 (42.9 %) patients, respectively. Nine (32.1 %) patients had an episode of fracture (6 vertebral, 2 Colles' and 1 neck of femur), while 2 (7.1 %) patients had 2 episodes of fractures (bilateral neck of femur) prior to denosumab use. The mean duration of denosumab use was 11.96 ± 5.75 months. The mean calcium level was 2.35 ± 0.16 mmol/L (range 2.0-2.7 mmol/L) in 22 (78 %) patients who had their calcium levels checked post denosumab. There was no significant difference in the mean calcium levels between those who were on vitamin D (n = 18) and not on vitamin D (n = 4), (2.36 ± 0.17 mmol/L vs. 2.30 ± 0.08, p = 0.13). There was no significant correlation between calcium level post denosumab and creatinine clearance, r = −0.23, p = 0.30. One of 22 patients (8.3 %) with a creatinine clearance of 43 ml/min developed hypocalcemia of 0.20 mmol/L. All except one patient who defaulted follow up, are still undergoing treatment with denosumab.
Conclusion: Denosumab was well tolerated among our patients who were mostly Chinese. We found no significant association between calcium level post denosumab with creatinine clearance and the use of vitamin D, which may be due to the small sample size. Hypocalcemia was mild and it occurred in one patient, who was at stage 3 chronic kidney disease. Most importantly, we need to improve our practice by ensuring that calcium levels before and after administration of denosumab are done for all patients.
Acknowledgement: We would like to thank the Director General of Health Malaysia for his permission to present this abstract.

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CHALCONE 4-HYDROXYDERRICIN INHIBITS OSTEOCLAST FORMATION AND ACCELERATES OSTEOBLAST DIFFERENTIATION

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Aims: 4-Hydroxyderricine (4-HD) is a major polyphenol of *Angelica keiskei* (Ashitaba), exhibiting antiallergic, antidiabetic, antioxidant, antitumor effects. The present study was designed to evaluate the effects of 4-HD on bone formation and maintenance by using cultured osteoclasts and osteoblasts.
Methods: We used the formation system of multinucleated osteoclasts from mouse splenic cells, and we identified a molecular pathway of osteoclast differentiation mediated by 4-HD with real-time PCR method. We used preosteoblast MC3T3-E1 cells for osteoblast differentiation as alkaline phosphatase activity and deposition of calcium.
Results: 4-HD did not affect cell proliferation of stromal ST2 cells and preosteoblast MC3T3-E1 cells at concentration of 1 μM to 10 μM. This compound inhibited the formation of multinucleated osteoclasts. 4-HD also inhibited the expression of receptor activator of nuclear factor-kB ligand and macrophage-colony stimulating factor in ST2 cells. By contrast, 4-HD enhanced indices of osteoblast differentiation by MC3T3-E1 cells.
Conclusion: Our findings indicate that 4-HD has critical effects on bone metabolism.

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MONTHLY ORAL IBANDRONATE (IBN) 100MG IS AS EFFECTIVE AS MONTHLY INTRAVENOUS (IV) IBN 1MG: SUBGROUP ANALYSES OF THE MOVEST STUDY

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Aims: We present subgroup analyses of the phase III MOVEST study [Nakamura T, et al. Osteoporos Int 2015], which compared the efficacy and safety of monthly oral IBN with monthly IV IBN in Japanese patients (pts) with primary osteoporosis.
Methods: In total, 422 ambulatory pts aged ≥55 y with primary osteoporosis were randomized to receive monthly oral IBN 100 mg plus monthly IV placebo, or monthly IV IBN 1 mg plus monthly oral placebo. BMD gains at the lumbar spine (LS; L2−L4) were examined in the following patient subgroups: LS BMD T-score at screening (≥−3.0 or <−3.0), prevalent vertebral fractures (yes or no), age (<75 or ≥75 y), baseline vitamin D (25OHD) levels (<20 or ≥20 ng/mL), bisphosphonate (BP) treatment history (yes or no) and prior osteoporosis drug treatment other than BP (yes or no).
Results: The per-protocol set comprised 183 and 189 pts in the oral and IV IBN groups, respectively. At 12 months, mean relative changes from baseline in LS BMD were 5.22 % (95%CI 4.65–5.80) with oral IBN and 5.34 % (95%CI 4.78–5.90) with IV IBN. In pts with LS BMD T-score at screening ≥−3 or <−3, BMD gains were 4.42 % and 5.79 %, respectively, with oral IBN and 4.60 % and 5.83 %, respectively, with IV IBN. In pts with or without prevalent vertebral fractures, BMD gains were 5.21 % and 5.23 %, respectively, with oral IBN and 5.01 % and 5.49 %, respectively, with IV IBN. In pts aged <75 or ≥75 y, BMD gains were 5.46 % and 4.51 %, respectively, with oral IBN and 5.25 % and 5.77 %, respectively, with IV IBN. In pts with baseline 25OHD levels <20 or ≥20 ng/mL, BMD gains were 4.76 % and 5.35 %, respectively, with oral IBN and 6.57 % and 5.05 %, respectively, with IV IBN. In pts with or without BP pretreatment, BMD gains were 4.33 % and 5.47 %, respectively, with oral IBN and 4.22 % and 5.70 %, respectively, with IV IBN. In pts receiving prior osteoporosis drug treatment other than a BP, BMD gains were similar to the above mentioned results.
Conclusion: Monthly oral IBN 100 mg, which has been licensed in Japan, demonstrated the same BMD gains as monthly IV IBN 1 mg in Japanese pts with osteoporosis. IV IBN and oral IBN increased BMD levels to the same extent in patient subgroups defined by LS BMD T-score at screening, prevalent vertebral fractures, age, baseline 25OHD levels, and prior osteoporosis treatment (BP or non-BP treatment). Both formulations of IBN are expected to show beneficial efficacy in osteoporotic pts.
Disclosure of Interest: H. Hagino Consultant/speaker's bureau/advisory activities: Asahi Kasei Pharma Corp., Astellas Pharma Inc., Chugai Pharmaceutical Co. Ltd., Eisai Co. Ltd., Eli Lilly Japan K.K., Mitsubishi Tanabe Pharma Corp., Ono Pharmaceutical Co. Ltd., Pfizer Inc., Takeda Pharmaceutical Co. Ltd., MSD K.K. and Teijin Pharma Ltd., T. Nakamura Consultant/speaker's bureau/advisory activities: Asahi Kasei Pharma Corp., Chugai Pharmaceutical Co. Ltd., Daiichi Sankyo Inc., Eli Lilly Japan K.K., Takeda Pharmaceutical Co. Ltd., MSD K.K. and Teijin Pharma Ltd., M. Ito Consultant/speaker's bureau/advisory activities: Chugai Pharmaceutical Co. Ltd., Asahi Kasei Pharma Corp., Astellas Pharma Inc., Daiichi Sankyo Inc., Ono Pharmaceutical Co. Ltd., and Taisho Pharmaceutical Co. Ltd., J. Hashimoto Company employee of: Chugai Pharmaceutical Co. Ltd., Y. Asao Company employee of: Chugai Pharmaceutical Co. Ltd., M. Yamamoto Company employee of: Chugai Pharmaceutical Co. Ltd., K. Endo Company employee of: Chugai Pharmaceutical Co. Ltd., K. Katsumata Company employee of: Chugai Pharmaceutical Co. Ltd., R. Matsumoto Company employee of: Taisho Pharmaceutical Co., Ltd., T. Nakano Consultant/speaker's bureau/advisory activities: Asahi Kasei Pharma Corp., Chugai Pharmaceutical Co. Ltd., Daiichi Sankyo Inc., and Teijin Pharma Ltd., H. Mizunuma Consultant/speaker's bureau/advisory activities: Chugai Pharmaceutical Co. Ltd. and Serono Japan Co. Ltd.

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PF708, A THERAPEUTIC EQUIVALENT CANDIDATE TO BRANDED TERIPARATIDE, DEMONSTRATES CLINICAL PHARMACOKINETIC AND PHARMACODYNAMIC EQUIVALENCE TO THE REFERENCE PRODUCT

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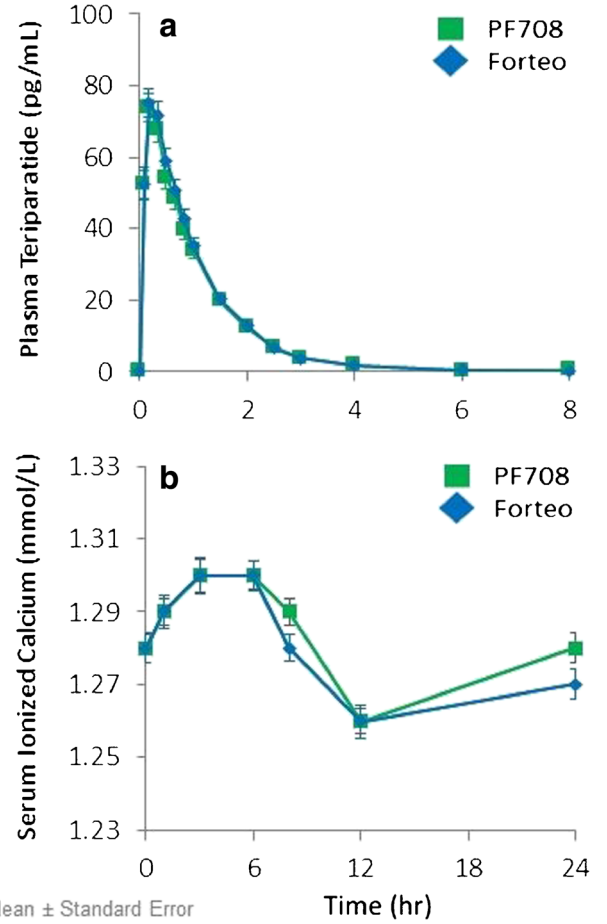
Aims: PF708 is a 34-amino acid recombinant analog of human PTH and has the same route of administration, dosage form, formulation, and delivery device functionality as the reference product, branded teriparatide, which has been approved as an anabolic treatment for osteoporosis since 2002. PF708 is being developed as a therapeutic equivalent in the USA and as a biosimilar outside the USA to provide a treatment option that is equally safe, pure, and potent as the reference product, at a potentially lower cost.

Methods: PF708 was investigated in a randomized, double-blind, crossover study that compared the pharmacokinetic (PK) and pharmacodynamic (PD) parameters of PF708 and branded teriparatide (20 μg) in 70 healthy subjects. Half of the subjects were randomized to receive PF708 first and Forteo second, and the other half were randomized to receive the drugs in reverse sequence. Each study participant completed two 1-day study periods, separated by a 3-day washout period. Key PK endpoints were plasma area-under-the-curve (AUC), maximum concentration (C_{max}), time to maximum concentration, and half-life of teriparatide after subcutaneous injection of PF708 or the reference product.

Results: There were no statistically significant differences in any of PK parameters. The plasma teriparatide concentration-time profiles after PF708 and reference product administration were equivalent (Figure 1A). The geometric mean ratios for $AUC_{0\text{-inf}}$, $AUC_{0\text{-last}}$ and C_{max} were all near 100 %, and the 90 % confidence intervals were entirely within the 80-125 % interval required for concluding bioequivalence. There were also no significant differences between PF708 and the reference product in the key PD endpoint – serum ionized Ca^{2+} (Figure 1B). The safety and tolerability profiles of PF708 and the reference product were comparable, and there were no significant findings in clinical laboratory evaluations, vital sign measurements, electrocardiogram readings, physical examinations or injection site assessments after either PF708 or reference product administration. Additionally, antidrug antibodies were not detected four days after single-dose administrations of PF708 or the reference product.



Conclusion: Overall, these results indicate that PF708 is equivalent to the reference product in PK, PD and safety profiles and support the continued development of PF708 as a therapeutic equivalent in the USA and a biosimilar product outside the USA.

Disclosure of Interest: H. Chen Company employee of: Current employee, Stock ownership or royalties: Stock owner, H. Jin Company employee of: Current employee, J. Lee Consultant/speaker's bureau/advisory activities: consultant, R. Stoltz Grant/research support from: research support

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FREEDOM FROM HYPOCALCEMIA? REVIEW OF A PROTOCOLIZED NURSE LED INJECTABLE OSTEOPOROSIS MEDICATION SERVICE AT A TERTIARY TEACHING HOSPITAL IN SOUTH EAST ASIA

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Aims: Though the incidence of hypocalcemia with denosumab (DMB) in the Freedom Trial has been reported

to be only <0.05 %[1], the incidence in patients seen in clinical practice is likely much higher. The incidence of DMB associated hypocalcemia (DAH) during osteoporosis treatment has not been elucidated in Asia. Our hospital has a nurse led Osteoporosis Medication Service (OMS) that provides counselling services for patients prescribed osteoporosis medications. The DMB Protocol requires that 25(OH)D, corrected calcium and serum creatinine levels be checked in all patients prescribed DMB. Serum corrected calcium and creatinine are checked in all patients 2 weeks after the DMB administration. We investigated the incidence and clinical features if any of DAH through an audit of patients who received DMB through the OMS.

Methods: Retrospective review of 52 consecutive postmenopausal women with osteoporosis administered DMB (60 mg) through the OMS. Biochemical hypocalcemia was defined as albumin-corrected serum calcium level of ≤2.09 mmol/l. Logistic regression analysis was done to identify characteristics associated with DAH.

Results: 10 of 52 (19.2 %) patients became hypocalcemic as defined above after the 1st dose of DMB. The mean age of the 52 patients was 75.8 ± 10.2 y. The mean corrected serum calcium, eGFR and 25 (OH)D levels pre-DMB administration were 2.26 ± 0.14 mmol/L, 69 ± 24 ml/min/m^2 and 30 ± 8.8 ng/ml, respectively. All 52 patients were on 360 mg of elemental calcium and 400 IU of vitamin D prior to DMB administration. No particular clinical or biochemical feature was significantly associated with the development of DAH. No patient required hospitalization and all the patients were asymptomatic. 45 of the 52 patients received a 2nd dose of denosumab 6 months later. A protocol had been instituted in place by then in which patients with pre-injection 25(OH)D level less than 20 ng/ml were replaced with 2000 IU/d or 50,000 IU/week of oral cholecalciferol or ergocalciferol respectively for 8–10 weeks. Those with levels between 20–30 ng/ml were replaced with similar doses for 4–6 weeks prior to injection. Elemental calcium supplements up to 1200 mg/d was given depending on pre-injection corrected calcium levels. Only 2 (4.4 %) of these patients became hypocalcemic with no patient who became hypocalcemic after the 1st dose becoming so after the 2nd dose.

Conclusion: Clinicians should be aware that the incidence of hypocalcemia following DMB administration in real life clinical settings is much higher than what is reported in clinical trials. Though no particular clinical or biochemical characteristic could predict the development of hypocalcemia in our cohort of postmenopausal women receiving DMB for osteoporosis, the dramatic decrease in hypocalcemia incidence after the second dose can be attributed to the interim institution of the protocolized pre-injection vitamin D and calcium replacement.

References: [1]Cummings SR et al. NEJM 2009

P221
THE PROPHYLACTIC POTENTIAL OF VITAMIN E AGAINST GLUCOCORTICOID-INDUCED OSTEOPOROSIS

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Aims: Long-term glucocorticoid treatment induces oxidative stress and free radical formation causing changes in bone leading to osteoporosis. Vitamin E is a potent antioxidant which exists in two forms: tocopherol and tocotrienol. It has the ability to inhibit the production of free radicals and has protective effects against free radical associated diseases. A rich, natural source of tocotrienols is the annatto bean. The objective of this study was to compare the effects of annatto-derived tocotrienol and alpha-tocopherol acetate on glucocorticoid-induced osteoporosis.

Methods: Thirty adult male Sprague Dawley rats were adrenalectomized and replaced with 120 μg/kg/d intramuscular dexamethasone injection. Ten of these rats were supplemented with annatto tocotrienol 60 mg/kg/d and the other 10 were supplemented with alpha tocopherol 60 mg/kg/d. The control group of 10 rats was given vehicle palm olein 0.1 ml/kg/d by oral gavage. An additional 10 rats were sham operated and given vehicle palm olein 0.05 ml/kg/d by intramuscular injection and 0.1 ml/kg/d orally. The treatments were given for eight weeks and rats were sacrificed. The right femoral bones were used for bone histomorphometric analysis and the left femoral bones were analyzed for malondialdehyde (MDA) a marker of lipid peroxidation.

Results: The results showed that long-term glucocorticoid treatment increased MDA level in the bone and was associated with significant reduction in bone volume/tissue volume and trabecular number. Supplementation of annatto tocotrienol or alpha tocopherol significantly prevented the rise in MDA levels and maintained bone structure

Conclusion: The results of this study suggested that both annatto tocotrienol and alpha tocopherol have protective effect on glucocorticoid-induced bone loss and may be used as a supplement to prevent osteoporosis in patients taking long term glucocorticoid therapy.

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REGULATION OF THE ACTIVE COMPOUNDS FROM EUCHEUMA COTTONII ON THE NUCLEAR FACTOR-ERYTHROID 2-RELATED FACTOR-2 (NRF2): IN SILICO STUDY

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Aims: Nuclear factor-erythroid 2-related factor 2 (Nrf2) is a redox-sensitive transcription factor that regulates the expression of a variety of antioxidant and detoxification genes through an antioxidant response element. Previous studies demonstrated that there were decrease in antioxidants and antioxidant cofactors in osteoporosis. This study aimed to evaluate the active compounds of *Eucheuma cottonii* on the Nrf2 as an antioxidant producer in osteoporosis.
Methods: Three dimensional structure of the (−)- catechin and phloroglucinol was obtained from NCBI's PubChem. (−) – catechin ID was CID73160 and phloroglucinol ID was CID359. Analysis was performed in silico using the primary method of docking by the use of Hex 8.0 software and Haddock web server. Analysis of interactions was then performed to determine the interactions between the ligand and its receptors by using the software Discovery Studio Client 3.5.
Results: Ligand docking energy show that catechin have lowest binding energy with Nrf2 (−226.9 kJ/mol), while phloroglucinol have highest binding energy (−141.2 kJ/mol). A lower binding energy means that the catechin is easier to interact with the Nrf2.
Conclusion: Catechin was more likely to bind with the Nrf2 for antioxidant expression in osteoporosis.

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THE RESULT OF THE TREATMENT IN OSTEOPOROTIC ANKLE FRACTURES WITH SMALL FRAGMENT USING CLAW PLATE IN ELDERLY

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Aims: Osteoporotic fractures in ankle have often included small bone fragments and were very unstable. There had been tried to fix them for anatomical reduction, using variable methods. However, it was not easy to keep the reduction, especially in elderly. The purpose of this study was to evaluate the results of the treatment in ankle fractures with small fragment using claw plate in elderly.
Methods: The 19 patients with ankle fractures, which included the small fragments, from January to July 2012 were evaluated retrospectively. All patients were more than 65 y and had osteoporosis. The authors have been tried to fix it using claw plate in all cases. The mean follow up period was 15 months (range 12–18 months). The claw plate was designed to catch the small fragment and made of tubular plate or locking tubular plate with bending it after cutting the distal end of them. It had two different hooks to keep the reduction and the fragment. Functional outcome scores were obtained using Olerud Molander Ankle score (OMA), VAS, and American Orthopedic Foot and Ankle Society (AOFAS) score at 2, 3, 6, 9, 12 months after the operation, when each patient underwent a physical examination and radiography. There was evaluated statistically by SPSS 19.0, p value was defined by <0.05.
Results: There were no complication, such as metal failure and loss of reduction. AOFAS score improved from 56.4 ± 3.1 at 2 months to 93 ± 1.5 at 12 months ($p = 0.01$). The VAS improved from 6.2 ± 0.9 at 2 months to 1.2 ± 0.8 at 12 months ($p = 0.001$). OMA score improved from 15.5 ± 0.2 at 2 months to 75 ± 2.5 at 12 months ($p = 0.001$). There was significant difference statistically. There was obtained the bony union in 3 months after the operation in all cases.
Conclusion: We suggested that the claw plate is the alternative method to fix the osteoporotic ankle fracture with small fragments in elderly, without complications.

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OSTEOPOROSIS CARE GAP IN BRUNEI DARUSSALAM

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Aims: Osteoporotic fractures are a major cause of morbidity and mortality across the world. Patients who sustain an osteoporotic fracture are at increased risk of sustaining another fracture hence efforts are directed towards secondary fracture prevention. Guidelines from various learned societies are now available in this area. The aim of this study was to identify osteoporosis care gap in Bruneian patients admitted with hip fracture and to compare it with regional and international studies.
Methods: Patients admitted to a tertiary care hospital with hip fracture were identified from the Medical Records Unit using the ICD code from January 2014 to December 2015. The demographic data, referral for BMD assessment, medications at discharge, occupational

therapists / geriatrician referral and medications at latest outpatient review were obtained.

Results: A total of 80 patients were recruited (M:F 24:56; average age 79.5 ± 9.1 y). Surgery was performed on 64 patients. The average follow up after discharge was 3.5 months (1–13 months). Only 1 patient underwent BMD assessment. About 50 % of patients were discharged with calcium and vitamin D supplements and 75 % of these continued with their medication at last review. Bisphosphonate was prescribed to only 14 (18.4 %) patients. The number of patients referred for occupational therapy and geriatrician was low in 2014 (42 % and nil, respectively) but showed considerable improvement in 2015 (80 % and 46 %, respectively).

Conclusion: There is considerable care gap in osteoporosis treatment for patients with hip fracture in Brunei Darussalam. It is expected that findings of this study would help in improving the standard of care for patients admitted with hip fracture in future.

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A STUDY OF SERUM ELECTROLYTE AND BONE TURNOVER MARKER LEVELS AFTER DENOSUMAB ADMINISTRATION

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Aims: Denosumab is a fully human monoclonal antibody that targets RANKL and blocks its binding to RANK, preventing osteoclasts from resorbing bone mass and significantly reducing the risk of vertebral, nonvertebral, and proximal femoral fractures. One of the major and critical adverse events of denosumab injection is hypocalcemia, which is most often observed in the one-week period following administration. Examination of albumin-adjusted calcium (Ca) level after one week is recommended to exclude the presence of hypocalcemia. Although hypophosphatemia has been reported to be an adverse event with a frequency of more than 1 % in patients subcutaneously administered 120 mg of denosumab for tumor treatment, there have been no reported data regarding its frequency in patients administered 60 mg for osteoporosis. The purpose of the present study was to evaluate the occurrence of denosumab adverse events focusing on serum electrolyte levels soon after administration, as well as to confirm its efficacy.

Methods: Thirty-five women between the ages of 55–91 y with postmenopausal osteoporosis were enrolled and treated with a 60 mg subcutaneous injection of denosumab and an oral Ca tablet combined with native vitamin D and magnesium. Serum Ca and phosphorus (P) were measured at baseline and at 1,2,3,and 4 weeks after administration. The bone formation marker intact serum procollagen type I N-terminal propeptide (P1NP) and bone resorption marker tartrate-resistant acid phosphatase-5b (TRACP-5b) were also evaluated at baseline and 4 weeks after administration. Laboratory investigations after a second injection were performed in 29 patients in the same manner.

Results: Both serum Ca and P electrolyte levels significantly decreased soon after administration. Hypocalcemia was detected in 2 patients: one patient 1 week after administration, and the other 2 weeks after. Hypophosphatemia was observed in 9 patients: 7 patients 1 week after administration and 2 patients after 2 weeks. Hypocalcemia was observed 1 week after the second administration in 1 of the 29 patients. Hypophosphatemia was detected in 1 patient 1 week after. There were no patients who discontinued the treatment due to adverse events in the present study. All serum electrolyte levels recovered within 4 weeks of each administration. At 4 weeks, P1NP level was decreased by 22.7 % and TRACP-5b was decreased by 66.3 %.

Conclusion: Adverse events were not observed clinically throughout the duration of the study period. However, hypocalcemia and hypophosphatemia were observed within 1 or 2 weeks after the first and/or second administration of denosumab. Therefore, measuring serum electrolyte levels of Ca and P within in 1 or 2 weeks is strongly recommended for the detection of hypocalcemia and hypophosphatemia. Furthermore, denosumab administration resulted in a low bone remodeling ratio reflected by decreases in both P1NP and TRACP-5b levels which may reduce fracture risk.

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DID THE ORTHOPAEDIC ARTICLES ABOUT SURGICAL TREATMENT FOR OSTEOPOROTIC FRACTURES DESCRIBE POSTOPERATIVE MEDICAL MANAGEMENTS?

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Aims: To report the proportion of description about T-score and postoperative medical managements for osteoporosis among the orthopaedic articles about surgical treatment for osteoporotic fractures.

Methods: A systematic search for Korean articles about the osteoporotic fracture and published between January 2006 and December 2015 was done. 89 articles were identified from the title or keywords search and 54 articles were excluded because the articles included 1) nonclinical study; 2) conservative treatment or arthroplasty after osteoporotic fracture; 3) study about BMD or imaging study; 4) study about medication; 5) review articles or case report. The remaining 35 articles were evaluated for full review and all articles were included the surgical treatments for the osteoporotic fractures. The authors checked whether the articles described the

detailed T-score, period of follow-up after surgical treatment and the medical management.

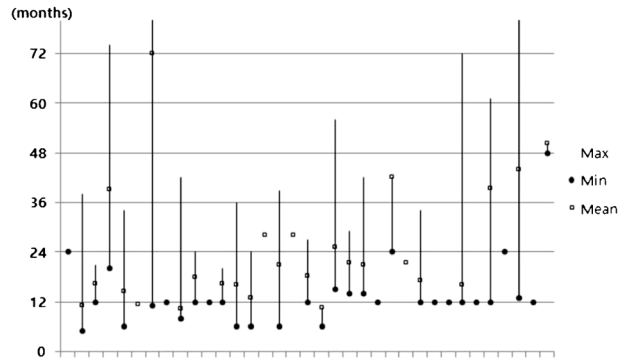
Results: Among the 35 articles, the articles showed the detailed T-score were 22 articles and the articles showed the detailed T-score or upper limit were 32 articles (91.4 %). 31 articles except 4 articles describing only the average follow-up period described that they had a minimum follow-up period of 5 months, and 23 articles of them had a minimum follow-up period of 12 months. Total 9 articles (25.7 %) described the medical management and among 9 articles, only 4 articles included the detailed contents about the treatment period and medication.

Table

Author	Year	Treatment initiation or duration	Prescribed pharmacologic drug	Remarks
Park et al.	2006	at discharge ~	Alendronate	
Min et al.	2006	for more 2 years	medicine	
Kim et al.	2007	PO 3 months ~	Alendronate or Risedronate	
Kim et al.	2007	for follow-up periods	medicine	
Ahn et al.	2009	-	Bisphosphonate	Drug compliance rate at PO 6 /12 months
Oh et al.	2010	-	Bisphosphonate	
Ahn et al.	2010	-	medicine	
Yim et al.	2012	for more 1 year	Risedronate or Alendronate or Ibandronate	Treatment compliance rate
Min et al.	2014	for more 2 years	medicine	

PO: postoperative

Figure



Conclusion: The present analysis indicates that the proportion (25.7 %) of the articles introducing postoperative medical management was lower than the proportion (91.4 %) of the articles introducing the T-score. It is considered that description for osteoporosis management after surgery in the articles about the osteoporotic fractures will make the orthopaedic surgeons to have the focus of the osteoporosis treatment as well as surgical treatment of osteoporotic fractures.

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EFFECTS OF A 24 MONTHS TREATMENT WITH DENOSUMAB IN A GROUP OF PEOPLE SUFFERING FROM OSTEOPOROSIS: OUR EXPERIENCE

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Aims: Osteoporosis is a systemic disease of the skeleton characterized by a reduced bone mass and by an alteration of the bone microarchitecture, both factors are determinant of an increase of the fracture risk. The fractures constitute the most relevant clinical event and they affect with much frequency the wrist, vertebra and femur. The aim of our study has been that of evaluating the effects of denosumab on 372 patients with average age of 72.7 y old ±8.9 SD affected by osteoporosis.

Methods: The subjects enrolled on this study have been examined with DXA L1-L4 and femur districts, calculation of the fracture risk through FRAX algorithm and questionnaires to evaluate the occurring of fractures at the beginning of the treatment (t0) and after 24 months of therapy (t1). To compare the results registered before and after 24 months of treatment have been used chi square and the Wilcoxon signed rank test.

Results: From the study that we performed emerged that the 372 subjects enrolled, 146 proved to be adherent to therapy in a very good way, 6 adhered in a good way while poor adherence has been shown by 15 subjects. Finally 205 subjects at the moment under treatment with denosumab have not been added in the study because they have not reached yet the

number of four subministrations. 2 of the 6 patients we spoke above have quit after the 4th subministrations the treatment (for causes not depending from the drug) therefore they have been added in the study. After 24 months of therapy with denosumab the patients have shown a significant recovery of mineral bone density on the spine ($p < 0.001$) and on the femur ($p < 0.001$) in terms of t-score, z-score and BMD with a considerable reduction of the fractures risk of the hip ($p < 0.01$) through the calculation of the FRAX algorithm, while such calculation regarding the reduction of the fracture risk apart from the hip fracture, even though there was a positive trend it did not reach a significant statistical difference ($p = 0.076$).

Conclusion: From the date obtained by our experience, we can see that the drug used resulted in great relevance effects over patients affected by osteoporosis and in general it was well tolerated and produced a significant improvement of the adherence levels. In this way from what we have studied we can affirm that denosumab drug represents an important progress on the osteoporosis treatment.

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CALCIUM AND VITAMIN D FORTIFIED MILK REDUCES BONE TURNOVER AND IMPROVES BONE DENSITY IN POSTMENOPAUSAL WOMEN OVER ONE YEAR

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Aims: To compare the effects of a high calcium vitamin D fortified milk with added FOS-Inulin vs. regular milk on serum PTH, bone turnover markers as well as bone density in Chinese postmenopausal (PM) women living in Malaysia, over one year.

Methods: Postmenopausal women ($n = 121$, mean age 59 (±4) y) were recruited, and were randomized into two groups: control ($n = 60$; regular milk at 500 mg calcium per day) or intervention ($n = 61$; fortified milk at 1200 mg calcium, 96 mg magnesium, 2.4 mg zinc, 15 μg vitamin D and 4 g FOS-inulin per day). Exclusion criteria included having diagnosed osteoporosis, endocrine disease or being on any drugs that can affect bone health. The volunteers were assessed at baseline, months 3, 6 and 12 for bone biomarkers, C-telopeptide of type I collagen (CTx-1), propeptide of type I collagen (PINP), as well as for changes in vitamin D status and levels of PTH. Bone density measurements were taken at baseline and month 12 using GE Lunar iDEXA (GE Healthcare, USA). 117 women completed the trial.

Results: At baseline, mean body weight and BMI did not differ between the two groups (57.2 kg vs. 60.1 kg and 23.4 kg/m^2 vs. 24.5 kg/m^2). Lumbar spine (1.021 vs. 1.079 g/cm^2, $P = 0.065$) and femoral neck (0.803 vs. 0.857 g/cm^2, $P = 0.162$) bone density were not different between the groups. Mean dietary calcium intake assessed by Food Frequency Questionnaire was 527 and 547 mg/d for the control and intervention groups, respectively. Mean 25(OH)vitamin D3 levels among groups were between 62.3 and 64.8 nmol/L ($P > 0.99$). Over the 12 months of supplementation, mean plasma 25 (OH) D3 levels increased to 74.8 nmol/L in the intervention group and remained relatively stable in the control group at 63.1 nmol/L ($P < 0.001$ between groups). Bone turnover markers CTx-1 and PINP reduced significantly over the 52 weeks, with the changes being significantly different between control and the intervention group ($P = 0.018$ and $P = 0.004$). PTH levels remained stable in the intervention group and increased in the control group ($P = 0.001$ between groups). Bone density of the femoral neck remained stable in the intervention group while it decreased over time in the control group ($P = 0.07$ between groups and $P = 0.009$ within control).

Conclusion: These results indicate that while both regular milk and fortified milk reduced bone resorption in older women, the fortified milk was measurably more effective and was able to maintain bone density at the femoral neck over one year.

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GLUCOSAMINE AND COLLAGEN IN A CALCIUM FORTIFIED MILK AFFECT MARKERS OF JOINT TURNOVER IN ACTIVE YOUNG WOMEN

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Aims: To assess whether the use of cartilage and bone biomarkers in a small group of active women is an effective way to assess joint health, and to compare the effects of glucosamine and collagen on cartilage and bone biomarkers.

Methods: 45 physically active young women aged between 30–45 y, were recruited for the study. Exclusion criteria included having osteoporosis, metabolic bone disease, a bone fracture in the last 12 months, and use of drugs or supplements that will affect bone or joint health. Subjects were randomised into three groups and each received two servings of calcium and vitamin D fortified milk/day containing either 750 mg or

250 mg glucosamine HCl or 1 g collagen/serve. The trial had a four week run-in time with blood and urine samples at week −4, −2 and at week 0, to calculate baseline and assess variation over time. At week 0, supplementation started for 12 weeks, and blood as well as urine samples were taken at week 4, 8 and 12. C-telopeptide of type II collagen (CTx-II), collagen type II cleavage (C2C), cartilage oligomeric matrix protein (COMP), CP II and human aggrecan were measured. Vitamin D status and dietary intake of calcium were also recorded. Outcome variables were analysed as difference from baseline using repeated measures Linear Mixed Model ANOVA.

Results: There were no significant differences at baseline for any measure between the three groups. The average BMI was 25.2 ± 4.1. Daily calcium intake was reported as 518 ± 239 mg/d. Vitamin D status improved significantly over 12 weeks in all groups. CTx-II reduced over the 12 weeks in response to both glucosamine and collagen. The response was significant ($P < 0.05$) at weeks 4 and 12 with a dose of 500 mg glucosamine per day, but at no time point there were significant differences between groups. For CPII, the change from baseline in response to 1500 mg glucosamine at week 8 and 12 and 500 mg glucosamine at week 12 were significant ($P < 0.05$). C2C decreased from baseline over time with the response at week 4 to collagen being significant. The levels of aggrecan as well as COMP remained relatively unchanged over the 12 weeks of supplementation.

Conclusion: The measured markers were all highly variable within and between participants. All treatments affected cartilage degradation but not to similar degrees. CTx-II reduced in response to all treatments and seemed to best reflect changes in cartilage degradation. CP-II seemed to respond to Glucosamine but not collagen while COMP and aggrecan showed no response. CTx-II seems to be a marker of choice but further research on variability and sensitivity are required.

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Disclosure of Interest: C. Norris Company employee of: Fonterra Co-operative Group Ltd, L. Schollum Company employee of: Fonterra Co-operative Group Ltd,

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EFFECT OF DENOSUMAB ON BONE MINERAL DENSITIES IN POSTMENOPAUSAL WOMEN IN KKH

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Aims: Denosumab is a new antiresorptive agent used for the treatment of osteoporosis. It is a human monoclonal antibody that binds to cytokine RANKL. RANKL inhibition results in decreased osteoblast maturation and function, leading to reduced bone resorption due to osteoblasts. Continued denosumab treatments (up to 6 y) have showed sustained bone turnover reduction, resulting in low fracture incidence[1] and improved bone mineral density in patients. Since 2012, KK Women's and Children's Hospital has treated 253 patients with denosumab for osteoporosis. We intend to analyze the changes in BMD using DXA scan for patients on denosumab after 3 y of therapy. Objective: Pilot Study to evaluate the BMDs of postmenopausal women before and after denosumab treatment for osteoporosis in KKH.

Methods: 18 postmenopausal patients with osteoporosis (BMD T-score < −2.5) were recruited in this study. These patients ranged between 57–83 y old. 17 were Chinese, 1 was Indian. These patients received subcutaneous denosumab 60 mg once every 6 months for 3 y. BMD readings before and after therapy are compared.

Results: There were improvements in BMD scores in all patients. Mean BMDs of the spine increased between 3.4 % to 18.4 % and hip increased between 5.7 % to 29 %, respectively. There were no new vertebral or hip fractures reported during therapy. We were unable to analyze the BMD results of 1 patient, as this was done overseas using a different BMD machine.

Conclusion: Denosumab improved patients' bone mineral densities after 3 y of treatment. More patients can be recruited to further validate the study.

References: [1]Papapoulos et al. Osteoporos Int 2015;26:2773.

P231

IL-18BP PREVENTS NLRP3 INFLAMMASOME MEDIATED IL-18 ACTIVATION IN ESTROGEN DEFICIENT MICE AND DECREASES IN OSTEOPOROTIC WOMEN

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Aims: To study the role of IL-18BP in postmenopausal osteoporosis.IL-18BP is a natural antagonist of pro-inflammatory IL-18 cytokine which is known as IFN-γ inducing factor and linked with autoimmune disorders like rheumatoid arthritis.

Methods: Adult 8–10 weeks old mice were ovariectomized (Ovx) and 0.5 mg/kg of IL-18BPd was exogenously supplemented in Ovx mice. In this study four groups were incorporated vehicle, vehicle + IL-18BPd, Ovx and Ovx + IL-18BPd. Long bones were collected for μCT, peripheral blood mononuclear cells (PBMCs) for FACS analysis. Serum was collected

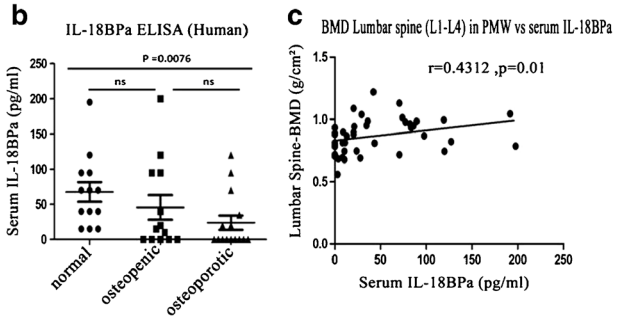
for CBA and ELISA assays. Coculture experiment of osteoblasts with CD4-T cells and Cd11b + cells were performed for in vitro study. Blood was also collected from postmenopausal women for ELISA and BMD was done using DXA.

Results: We found that mRNA level of mice IL-18BPd and human IL-18BPa was decreased in PBMCs of Ovx mice and osteoporotic women respectively. mIL-18BPd enhances osteoblast differentiation and inhibits the activation of NLRP3 inflammasome and caspase-1 which process IL-18 to its active form. Using ovx mice model we also determined the effect of mIL-18BP on various immune and skeletal parameters. Ovx mice treated with mIL-18BPd exhibited decrease in Th17/Treg ratio and pro-inflammatory cytokines. mIL-18BPd treatment restored trabecular micro architecture, preserved cortical bone parameters likely attributed to increased number of bone lining cells and reduced osteoclastogenesis. These results were corroborated in female osteoporotic subjects where decreased serum IL-18BP levels were observed. Also the level of IL-18 was increased in osteoporotic subjects.

Demographic data of post menopausal women (PMW) divided into normal, osteopenic and osteoporotic according to WHO classification by T-score.

a

	NORMAL	OSTEOPENIC	OSTEOPOROSIS
Post menopausal women(n)	15	15	15
Height (in cm)	153.9±1.44	152.13±1.44	151.74±1.34
Weight(in Kg)	69.36±2.52	67.43±2.63	59.48±2.43*,a
AGE (in years)	63.86±2.68	61.46±1.99	64.23±1.23



Conclusion: Our study forms a strong basis for using humanized IL-18BP towards the treatment of postmenopausal osteoporosis.

Acknowledgement: We acknowledge Dr. A L Vishwakarma for helping in the FACS analysis and SAIF instrumentation facility.

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PREVENTIVE EFFECT OF QUERCETIN-SOLID LIPID NANOPARTICLES (QSLNS) IS MORE POTENT THAN QUERCETIN (Q) IN AN OVARIECTOMIZED RAT MODEL OF POSTMENOPAUSAL OSTEOPOROSIS

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Aims: To evaluate the skeletal effects of quercetin loaded solid lipid nanoparticles (QSLNs) in ovariectomized rats.

Methods: Fifty adult female Sprague Dawley rats were submitted to ovariectomy or sham surgery. The groups (10 animals each) were as follows: Sham + vehicle, OVx + vehicle, OVx + Q, OVx + QSLNs and OVx + 17β-estradiol. Q, QSLNs (5.0 mg/kg/d) and 17β-estradiol administered orally for 12 weeks. After treatment, animals were euthanized and samples (bone and uterus) were collected for further analysis. Bone microarchitecture, bone turnover marker (C-telopeptide fragment of collagen type I), biomechanical strength, and skeletal expression of osteoclastogenic gene markers were studied. Uterine histomorphometry was used to assess estrogenicity. One-way ANOVA was used to test the significance of effects.

Results: Single oral dose of QSLNs (5.0 mg/kg/d) significantly increased bioavailability compared to plain quercetin. Oral administration of QSLNs to ovariectomized rats increased serum quercetin levels by 3.5-fold compared to plain quercetin. BMD of OVx group for distal femur, proximal tibia metaphysis and L5 vertebra compared with the sham, it showed significant decrease by ~49 %, ~55 % and ~30 %, respectively ($p < 0.001$). QSLNs and 17β-estradiol groups showed significant higher BMD at trabecular sites by ~47 % and ~59 % (femur), by ~70 % and ~53 % (tibia) and by ~54 % and ~49 % (L5), respectively, compared to OVx group($p < 0.001$). However, on the other hand, Q group had maintained the gain in BMD achieved during 12 weeks of treatment to a certain extent, such that it has significantly higher BMD at trabecular sites of femur, tibia and L5 by ~22 %, ~29 %, and ~26 % respectively when compared to OVx group ($p < 0.05$). Moreover, BMD at trabecular sites of femur, tibia and L5 was comparable between 17β-estradiol. μCT analysis showed that the QSLNs group improved trabecular microarchitecture in distal femoral, proximal tibial and lumbar spine cancellous bone. QSLNs treatment recovers bone loss (BV/TV; in femur by ~21 %, $p < 0.01$, in tibia by ~26 %, $p < 0.05$ and in vertebrae by ~12 %, $p < 0.05$) over Q treatment group. The developed quercetin formulation based on solid lipid nanoparticles inhibited bone loss in osteopenic rats. Q and QSLNs inhibited RANKL-induced osteoclast cells differentiation and expression of osteoclast specific genes in

in vitro experiments using bone marrow cells treated with RANKL and M-CSF. QSLNs had no effect on adipogenesis and uterine weight in OVx rats.

Conclusion: We have shown that QSLNs at an oral dose of 5.0 mg/kg/d alleviates estrogen deficiency induced loss of bone mass, bone strength and micro-architecture of long bones and vertebrae. The bone loss preventing effect of QSLNs is significantly better than Q. Application of this QSLNs strategy to deliver other phytoestrogens/drugs needs to be examined further to treat osteoporosis.

P233

INTERACTION OF CATECHIN AND PHLOROGLUCINOL FROM EUCHEUMA COTTONII WITH NUCLEAR FACTOR KAPPA B (NF-kB): IN SILICO STUDY

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Aims: Targeting NF-kB and MAPK signalling may be better alternative strategy for the treatment of bone destructive diseases by inhibiting the osteoclastogenesis. This study aimed to evaluate the active compounds from *Eucheuma cottonii* on NF-kB as inflammatory pathway in osteoporosis.

Methods: Three dimensional structure of the (−)- catechin and phloroglucinol was obtained from NCBI's PubChem. (−) – catechin ID was CID73160 and phloroglucinol ID was CID359. Analysis was performed in silico using the primary method of docking by the use of Hex 8.0 software and Haddock web server. Analysis of interactions was then performed to determine the interactions between the ligand and its receptors by using the software Discovery Studio Client 3.5.

Results: Ligand docking energy we found that catechin have lowest binding energy with the NF-kB (−256.1 kJ/mol), while phloroglucinol have highest binding energy (−129.6 kJ/mol). A lower binding energy means that the catechin is easier to interact with the NF-kB.

Conclusion: Catechin was more likely to bind with the NF-kB as inflammatory transcription factor in osteoporosis.

P234

OSTEOBLASTIC DIFFERENTIATION REQUIRES ESTROGEN RECEPTOR ALPHA (ER-A 66) AND IS ACCELERATED BY ESTROGEN AND RESVERATROL

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Aims: Bone remodeling, a multistep process is regulated by many factors and estrogen is known to have a critical role. Deficiency of estrogen in postmenopausal women leads to the development of osteoporosis. Estrogen (E2) treatment could offer osteoprotection concomitant with the restoration of ER-α level implying a role for ER-α in bone remodeling. Hormonal replacement therapy could alleviate the postmenopausal osteoporosis but it has other undesirable side effects. Alternative therapy with a naturally occurring phytoestrogen resveratrol (3, 4, 5-trihydroxystilbene) has been shown to have osteoprotective effects in animal model. Resveratrol is known for its multiple benefits and works by signaling through estrogen receptors (α and β).Thus the aim of the study is to elucidate the role of ER-α 66 in the differentiation of precursor osteoblasts in response to estrogen and resveratrol using two fetal osteoblastic cell lines of which one is deficient in ER-α 66 isoform.

Methods: The fetal osteoblastic cell lines hFOB/ER9 (expressing ER-α 66) and hFOB1.19 (deficient in ER-α 66) were grown in DMEM up to about 80 % confluence after which the cells were treated in the presence of either 1 μM resveratrol or 10 nM estradiol for 48 h for use in the following assays. The osteogenic differentiation was evaluated by alizarin staining to assess the mineralization process in both the cell lines. The osteoblastic activity was assessed by determining the activity of alkaline phosphatase (ALP). The promoter occupancy of the candidate osteogenic genes by ER-α was assessed by chromatin immunoprecipitation (ChIP) assay using ER-α antibody and validated by analysing the expression of the candidate genes by quantitative real-time PCR.

Results: Cellular viability of ER-α deficient and proficient cell was not affected by estradiol and resveratrol. Osteoblastic activity (ALP activity) and osteogenesis marker (mineralization) was found to be significantly modulated by estradiol and Resveratrol in ER-α proficient cells only. Promoter occupancy of ER-α on osteogenic genes (RUNX2, ER, osterix, AhR, B-catenin, cyclin D1, B-actin, BMP7, TGF, Col1A1, ALP, OSP, OSN, OCN, GREB-1 and GAPDH) is shown by PCR performed from ChIP pull down DNA. Expression of RUNX2 is suppressed in presence of over expressed ER-α in hFOB1.19 cells. Resveratrol in presence of estradiol has dual effect as agonist in normal media and antagonist in the cells grown in osteogenic media.

Conclusion: ER-α66 has the potential to activate the osteoblastic differentiation in ligand independent manner but when bound to its ligands (estrogen or resveratrol) the process is accelerated. RunX2, a master regulator of osteoblastic differentiation, is effective only when ER-α 66 coexists.

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AZADIRACHTIN A INTERACTS WITH ER ALPHA DOMAIN AND REGULATES BONE FORMATION

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Aims: To assess the molecular mechanism of azadirachtin A in osteoblast cells and check their ability to prevent bone loss in osteoporotic mice model.

Methods: In this study, we checked expression of genes which involved in BMP2/ERα pathway time dependently. We performed in silico study for the confirmation of interaction of azadirachtin A with ERα. For In vivo study, we divided the five groups, Sham, OVx, OVx ± 1 mg/kg/d, OVx ±5 mg/kg/d and OVx ± E2 (5 μg/kg/d). We orally administrated azadirachtin A for 6 weeks. At the end of termination, we collected bone, serum and uterus from the different groups for analysis of different parameters.

Results: Recently, we have reported that azadirachtin A, a terpenoids isolated from *Azadirachta indica* has osteogenic activity in osteoblast cells. We investigated that azadirachtin A induced BMP2 pathway genes time dependently. Interestingly, azadirachtin A enhanced ERα expression there were confirmed by treatment of MPP antagonist and siRNA at transcript and translational level. There were no significant effects observed by treatment of ER antagonists, including ICI 182,780 and ERβ THC. In silico molecular docking confirmed that azadirachtin A bound to ERα with maximum energy compare to ERβ. In this study, we have demonstrated that azadirachtin A functions through activation of the genomic ERE pathway which was confirmed by ERE promoter activation luciferase assay. Meanwhile, we have also found that azadirachtin A induced activation of ERK signaling (nongenomic action) in osteoblast cells. Overall, azadirachtin A acts on osteoblastic cells by triggering activation of Ras/ERK/ MEK/ Raf signaling pathway. In vivo, azadirachtin A enhanced bone formation, microarchitectural parameters, osteogenic gene expression and simultaneously reduced osteoclast gene expression in bone at 1 mg/kg dose in osteoporotic model. Interestingly, azadirachtin A reduced osteocalcin levels in serum.

Conclusion: Azadirachtin A exerts antiosteoporotic response via BMP2/ERα pathway and it could be positioned as a potential drug for postmenopausal osteoporosis.

P236

IL-27 PREVENT BONE LOSS IN ESTROGEN DEFICIENT CONDITIONS BY INDUCING THE EXPRESSION OF EARLY GROWTH RESPONSE GENE-2

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Aims: Estrogen withdrawal after menopause is associated with a rapid and sustained increase in the rate of bone loss. T cells and various cytokines contribute majorly to the estrogen deficiency induced bone loss. Recent studies have identified IL-12 cytokine family comprising of pro-inflammatory IL-12 and IL-23 and the anti-inflammatory IL-27 and IL-35 cytokines. IL-27 has been reported to provide protection against collagen induced arthritis. However, this cytokine has not been studied in estrogen deficiency induced bone loss conditions. Hence, the main objective of this study is to investigate the role of IL-27 in estrogen deficient Ovx mice model and its role in various immune and skeletal parameters.

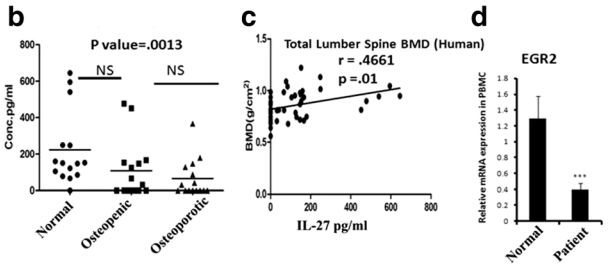
Methods: Adult Balb/c mice (N = 8/group) were treated with IL-27 subcutaneously postovariectomy (Ovx) twice in a week for one month. Animals were autopsied and long bones were harvested to study bone microarchitecture. Peripheral blood mononuclear cells were isolated for fluorescence-activated cell sorting and RNA analysis. Serum was collected for cytokine bead array.

Results: Treatment of IL-27 to ovx mice induce the expression of early growth response 2 gene (EGR2) in T cells, osteoblast and osteoclast. EGR2 play a very important role in autoimmunity by suppressing Th17 cell differentiation by inhibiting transcription factor RORγt and augmenting SOCS3. Supplementation of IL-27 activates Egr-2 to induce IL-10 producing Tr1 cells. IL-27 treatment restored trabecular microarchitecture and preserved cortical bone parameters. IL-27 treatment also promotes osteoblast survival by inducing Egr-2 expression and suppression of IL-17 mediated osteoblast apoptosis by inducing anti apoptotic factor like MCL-1. The overall effect leads to enhanced osteoblast proliferation and differentiation. IL-27 also directly suppresses osteoclast functions in an Egr-2 mediated Id2 up regulation which is a repressor of RANKL induced osteoclastogenesis. The net result is reduced osteoclastogenesis and enhanced osteoblastogenesis which inhibits Ovx induced bone loss. We also evaluated serum IL-27 levels in postmenopausal women. Our

results show significant decrease in serum IL-27 levels in postmenopausal women with osteoporosis as compared to normal or osteopenic postmenopausal women. Corroborating these observations was the decreased Egr-2 mRNA expression in osteoporotic patients.

a

	Normal	Osteopenic	Osteoporotic
Post menopausal females (n)	15	15	15
Sex	Female	Female	Female
Height (cm)	153.9 ± 1.44	152.13 ± 1.44	151.74 ± 1.34
Weight (Kg)	69.36 ± 2.52	67.43 ± 2.63	59.48 ± 2.43
Age (years)	63.86 ± 2.68	61.46 ± 1.33	64.23 ± 1.23



Conclusion: Our study demonstrates the immunomodulatory effect of IL-27 and forms a strong basis for using humanized IL-27 towards the treatment of postmenopausal osteoporosis.

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IMPACT OF THREE DIFFERENT DAILY DOSES OF VITAMIN D3 SUPPLEMENTATION IN HEALTHY PREPUBERTAL SCHOOL GIRLS FROM NORTH INDIA

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Aims: Vitamin D deficiency is a widely recognised public health problem world over including India. Information with regard to daily doses of vitamin D_3 supplementation in prepubertal children is lacking. In view of the above, we undertook this study to compare the efficacy of daily supplementation of 600 IU, 1000 IU and 2000 IU vitamin D_3 in prepubertal girls.
Methods: We recruited 240 prepubertal school girls in the age group of 6.1-11.8 y with minimal sun exposure and negligible dietary intake of vitamin D_3. These children were randomised into three groups A (n = 74), B (n = 69) and C (n = 77) with a mean baseline serum 25(OH)D of 10.13, 10.18 and 9.68 ng/ml, respectively, and supplemented with daily 600 IU (A), 1000 IU (B) and 2000 IU (C) of vitamin D_3 under supervision for 6 months. Serum 25(OH)D, PTH, calcium (Ca^{+2}), phosphate (PO_4), alkaline phosphatase (ALP), bone markers PINP and CTX and urinary calcium/creatinine ratio were evaluated before and after supplementation.
Results: Of 240 recruited girls, 216 completed the study. As per Lips criteria, all were vitamin D deficient (<20 ng/ml), with mild, moderate, and severe deficiency in 44.09 %, 52.27 % and 3.64 % children, respectively. Secondary hyperparathyroidism (PTH > 65 pg/mL) was seen in 14.5 % children. Using IOM (Institute of Medicine) criteria to define vitamin D deficiency in children (<12.5 ng/ml), 74.55 % girls were vitamin D deficient at baseline. Following 6 months of supplementation, there was a significant overall increase in serum 25(OH)D of 18.78 ng/ml ($p = 0.007$) with significant reduction in mean PTH levels of 15.42 pg/ml ($p = 0.00$) and appreciable reduction in the prevalence of secondary hyperparathyroidism from 14.5 to 4.5 % ($p = 0.00$). The increase in the serum 25(OH)D levels following supplementation was maximum with 2000 IU (23.22 ng/ml), followed by 1000 IU (17.36 ng/ml) and 600 IU (15.48 ng/ml) and the difference in rise of serum 25(OH)D levels was statistically significant between groups A and C ($p = 0.00$) and groups B and C ($p = 0.00$). Postsupplementation serum 25(OH)D levels of 20 ng/ml or more were seen in 91 % in group A, 97 % in group B and 100 % group C. This difference was also statistically significant ($p = 0.08$), while 25(OH)D levels more than 12.5 ng/ml were observed in 100 % girls in all three groups. An important observation was a significant rise in serum PINP (537.9 ± 199.35 to 654.9 ± 217.54 ng/ml, $p < 0.0001$) and a significant reduction in serum CTX (0.745 ± 0.234 to 0.382 ± 0.227 ng/ml, $p < 0.0001$) postsupplementation.
Conclusion: High prevalence of vitamin D deficiency was observed in pre-pubertal girls. Supplementation with all three doses resulted in significant increase in the serum 25(OH)D levels, with maximum impact using 2000 IU/d. More than 90 % of vitamin D deficient girls achieved desired target (20 ng/ml) of serum 25(OH)D in all three groups. Significant decrease in serum CTX and increase in PINP following vitamin D supplementation suggests reduction in bone turnover.

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ADDRESSING GAPS IN OSTEOPOROSIS MANAGEMENT IN THE VALUEDCARE HIP FRACTURE PROGRAMME

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Aims: The ValuedCare (VC) hip fracture programme is a quality improvement (QI) programme launched by

Changi General Hospital (CGH), a major public hospital in Singapore, in collaboration with Geisinger Health System (GHS) USA to provide comprehensive care for patients with hip fracture. This programme incorporates multiple best practice elements (BPEs) comprising process indicators, evidence based management protocols and key outcome measures over one year. Various studies worldwide have demonstrated gaps in secondary prevention after hip fracture. This study aims to identify existing gaps in osteoporosis management and develop osteoporosis-related BPEs in the VC programme.

Methods: A retrospective study was conducted on 126 consecutive patients aged ≥65 y admitted from 1 July to 30 November 2014 with a fragility hip fracture and underwent surgical fixation. We obtained records of BMD scanning, calcium/vitamin D (Vit D) supplementation and antiresorptive drug treatment within 3 months postoperatively. Gaps identified were analysed via a series of QI sessions with GHS and our multidisciplinary team, leading to the development of related BPEs and protocols.

Results: 57.1 % of the patients had BMD testing done. Patients >80 y old were less likely to have BMD testing (42.4 % vs. 73.3 %; $p < 0.001$). Combined calcium/Vit D supplementation was prescribed in 95 % of the patients. Specific Vit D supplementation such as cholecalciferol (1000 IU) or ergocalciferol (50000 IU) was prescribed in 63 % of the patients depending on their serum 25-hydroxyVit D level. Antiresorptives such as alendronate or risedronate were prescribed in 21.4 % of the patients. None were prescribed parenteral antiresorptives. Patients with chronic kidney disease (CKD) were less likely to receive antiresorptive treatment (10.3 % vs. 26.4 %; OR 3.41; $p = 0.041$)

Conclusion: Secondary prevention of falls and fractures is critical in hip fracture patients. Whilst supplementation was widely practised, clear gaps in BMD testing and antiresorptive treatment initiation were identified. Osteoporosis-related BPEs have since been implemented in the VC programme, including BMD and serum Vit D testing, supplementation, community rehabilitation as well as bisphosphonate initiation within 4 weeks postoperatively. Case managers and telecarers will educate patients, monitor compliance to osteoporosis management and track falls and fractures over one year. Complex cases are referred to the bone clinic for consideration of parenteral therapy. Challenges remain in enforcing long-term compliance and initiation of anti-resorptive treatment, particularly in patients with CKD and the oldest, frail elderly population.

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ESTABLISHING A FRACTURE LIAISON SERVICE NETWORK FOR ELDERLY POPULATION IN TAIWAN

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Aims: To establish a fracture liaison service (FLS) network in Taiwan, and evaluate the effects of FLS on the assessments of bone health and osteoporosis treatments.

Methods: The FLS network includes 4 healthcare systems: National Taiwan University Hospital (NTUH) and its Beihu Branch (BB) since 2014, Linkou Chang Gung Memorial Hospital (LCGH), China Medical University Hospital (CMUH), and Kaohsiung Medical University Hospital (KMUH) since 2015. Fracture patients were managed following the 13 Capture the Fracture Best Practice Standards. Patients were eligible to be enrolled into FLS if they had new hip fracture in orthopedic ward, newly identified radiographic vertebral fractures from radio-images in medicine ward or clinical vertebral fractures in outpatient clinics. They were excluded from the service if they had life expectancy shorter than 2 y of life or not be able to complete study assessments for communication or cognitive problems. Core strategies include BMD, FRAX estimation, lifestyle consultations, screening for secondary osteoporosis, medications, and fall assessments (high risk only) provided mainly by coordinators. The FLS system is set up to remind patients to take their medications at home or to return to clinic for regular injections of medications. Major outcomes included the completion rates of BMD, vertebral fracture examination, secondary causes of osteoporosis, treatment initiation rate, and medication review. Each patient would be assessed at baseline, and every 3–4 months for 1–2 y.

Results: We screened 1130 patients to enrol 981 of them (545 from NTUH and its BB branch, 107 from LCGH, 100 from CMUH and 229 from KMUH). Mean age was 76.51 ± 9.92 y, 72.0 % were women. 68.0 % and 12.8 % reported having had previous falls and osteoporosis medications, respectively. All hospitals have 99.8 % completion rate for fall prevention services and 100 % completion rates of both life style assessments and medication review. There was no difference among groups. The average completion rate of the five hospitals for patient evaluation, postfracture assessment timing, vertebral

fracture examination, secondary causes of osteoporosis, and medication initiation were, 97.6 %, 98.0 %, 95.4 %, and 95.4 %, respectively. Between group variations were detected for the above 5 indicators (all $p < 0.001$). Female patients were more likely to receive osteoporosis medications than male patients (85.1 % vs. 76.7 %) ($p = 0.002$). In addition, we were accredited as gold medals (NTUH and KMUH), and silver medal (NTUH-BB) for best practice programs of the Capture the Fracture campaign from the International Osteoporosis Foundation.

Conclusion: This FLS network was able to increase the rates of assessment of BMD for bone health and the rates of osteoporosis treatments in elderly with high fracture risks in Taiwan.

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ARE FRACTURE LIAISON SERVICES A WORTHWHILE VENTURE? COST-EFFECTIVENESS OF THE AUSTIN HOSPITAL FRACTURE CAPTURE PROGRAM

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Aims: To determine the cost-effectiveness of the Austin Hospital Fracture Liaison Service (Fracture Capture).

Methods: Patients over 50 y of age who presented to the emergency department from the general community with a minimal trauma fracture were identified, referred for investigation and clinic review, and treated when appropriate. For cost-effectiveness analysis, input costs included program personnel, investigations, medications for one year and two clinic appointments. Baseline fracture risk was calculated using the Garvan Institute Fracture Risk Calculator and published risk reductions for specific medications applied to calculate risk and expected number of subsequent fractures after treatment. QALYs (quality adjusted life years) gained were calculated by application of published utility values to expected number of fractures saved in proportions observed in our cohort. Cost avoided from prevention of fractures was similarly calculated using the acute and subacute costs of specific fracture sites. Cost-effectiveness was considered over a 5-y time period using an incremental cost-effectiveness ratio (ICER). ICER = net cost of service minus the costs averted from prevention of fracture events, divided by the QALYs gained.

Results: 209 patients were included in the cost-effectiveness analysis. 146 patients were treated ($n = 17$ strontium, $n = 34$ alendronate, $n = 53$ risedronate, $n = 13$ denosumab, $n = 4$ teriparatide), 12 were not treated and 51 were inappropriately captured and seen in clinic. The calculated ICER was AUD $30,727 per QALY gained, below the cost-effectiveness cutoff of AUD$50,000.

Conclusion: This type of fracture liaison service is cost effective, and supports the advocacy for widespread implementation in order to facilitate closure of the osteoporosis care gap.

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CAN PRALIA ELIMINATE STEROID INDUCED OSTEOPOROSIS IN THE PULMONARY DISEASES?

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Aims: Respiratory physicians encounter numerous situations where oral steroids are prescribed to treat or control pulmonary diseases, and are often faced with the dilemma that long-term steroid use will deteriorate BMD and quality.

Methods: In our respiratory center, the first preventative measure used to combat a steroid-induced state of osteoporosis is the prescription of oral bisphosphonates. According to the diagnostic criteria of the Japan Orthopaedic Association, 14 patients diagnosed with steroid induced osteoporosis were judged to be in need of more drastic treatment measures than what is usually prescribed. All 14 of these patients had a prior history of receiving oral bisphosphonates, and their treatment courses were changed from oral bisphosphonate, to the subcutaneous injection of Pralia® via 60 mg syringe (INN: denosumab; genetic recombination) every 6 months, combined with a daily oral intake of Denotas® chewable combination tablets (a tablet form mixture of CaCO3 and cholecalciferol, which is sold only in Japan). Denosumab (developed by the biotechnology company Amgen, USA) is the first fully human monoclonal antibody to inhibit RANKL; a protein that acts as the primary signal for bone removal.

Results: BMD in the lumbar spine area of these patients increased significantly, while BMD in the hip area showed no significant increase. None of these patients presented hypocalcemia or other serum electrolyte imbalance in routine blood analysis.

Conclusion: Pralia is the only drug which has shown evidence that it can help prevent hip fracture in elderly patients, although our data did not show a statistical difference in the hips of the steroid-taking population. Our data, however, did indicate a significant improvement in bone density of the lumbar spine region. To our knowledge, no data regarding active prevention measures for combating steroid induced osteoporosis have been ever reported. Our data indicates that Pralia can play a promising role in the treatment of steroid induced osteoporosis.

P242

FINDING OUT VERTEBRAL FRACTURE AS SCREENING FOR OSTEOPOROSIS USING ROUTINE THORACIC AND ABDOMINAL CT SCAN OF INPATIENTS

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Aims: There are 135,00 inpatients of our hospital on one year, so we think there are also many inpatients of all departments except orthopaedic who need treatment for osteoporosis. We evaluated routine thoracic or abdominal CT scans of inpatients, except orthopaedic, obtained for other purposes and found out patients who had vertebral fracture and need treatment of osteoporosis.
Methods: We analyzed retrospectively 459 inpatients' thoracic or abdominal CT scans obtained for other purpose on our hospital between March and April 2016, patients were in hospital of all departments except orthopaedics and were over 50 y old. The sagittal reconstruction was analyzed for mild-to-severe vertebral compression fractures (more than 20 % vertebral compression) using the visual semiquantitative method. Likely osteoporosis was defined by more than 20 % vertebral compression fracture. And more we checked out the rate of having history of osteoporosis or fragility fracture (hip and vertebral fracture) and also the rate of having treatment for osteoporosis in the patients who had vertebral fracture analyzed from our research.
Results: The rate of vertebral fracture was 32 % (147/459 cases), especially female 43.4 % (75/173 cases). The rate of having history of fragility fracture was 27.2 % (40/147 cases) and having treatment for osteoporosis was 13.6 % (20/147 cases).
Conclusion: Without additional radiation exposure and cost, we could found out 147 patients who had likely osteoporosis for 2 months using routine thoracic or abdominal CT scans obtained for other purposes that included spine. Only 13.6 % of these patients had treatment for osteoporosis. We think this analysis of sagittal reconstruction CT scans provides the effective and easy opportunistic screening for patients of osteoporosis and having the risk for secondary fragility fractures.

P243

EFFECT OF MONTHLY MINODRONATE TREATMENT OVER TWO YEARS IN JAPANESE PATIENTS WITH OSTEOPOROSIS

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Aims: (1) To determine the efficacy of two-year minodronate (MIN) treatment in Japanese patients with osteoporosis, and (2) to detect the influencing factors for the responder of MIN treatment.

Methods: A retrospective chart review was conducted of 190 Japanese patients (40 males and 150 females, mean age; 79.5 ± 8.7 y) with osteoporosis. Patients were administrated oral monthly MIN (50 mg/tablet) over 2 y, and were measured BMD and bone turnover markers (TRACP5b, P1NP and ucOC) every 6 months. We divided the patients into 2 groups; responder (percent change of lumbar spine BMD (L-BMD) >2 % at 6 months after MIN treatment or femoral neck BMD (F-BMD) >1 % at 24 months after MIN treatment) and nonresponder (percent change of L-BMD <2 % at 6 months or F-BMD < 1 % at 24 months), and clarify the influencing factors for the responder of MIN treatment used by statistical analysis.
Results: After MIN treatment, the L-BMD significantly increased by 2.8 ± 4.6 % ($P < 0.01$) change from baseline, 4.0 ± 5.1 % ($P < 0.01$), 5.5 ± 5.9 % ($P < 0.01$) and 4.9 ± 13.5 % ($P < 0.01$) at 6, 12, 18 and 24 months, respectively. On the other hand, the F-BMD was delayed in increase by −0.7 ± 6.9 %, −0.6 ± 7.7 %, 0.5 ± 7.3 % and 1.1 ± 7.8 % ($P < 0.05$) at 6, 12, 18 and 24 months, respectively. The bone turnover markers were rapidly reduced at 6 months after MIN treatment (TRACP5b; −31.3 ± 39.3 % ($P < 0.01$) change from baseline, P1NP; −43.5 ± 59.3 % ($P < 0.01$) and ucOC; −19.6 ± 66.4 % ($P < 0.01$)). The responders of L-BMD were 92 cases (48 %), and the influencing factors were previous vertebral fracture, diabetes mellitus, and baseline percentage of lumbar YAM < 70 %. Comorbidity of chronic pulmonary disease affected the nonresponder of L-BMD. The responders of F-BMD were 44 cases (23 %), and the influencing factors were walking ability, low baseline serum Ca value, low ucOC and low P1NP at 6 months, and low TRACP5b at 12 months. Comorbidity of rheumatoid arthritis affected the nonresponder of F-BMD.
Conclusion: Oral monthly MIN treatment was rapidly effective in increase of L-BMD. However, we need to continue the MIN treatment over 2 years to ameliorate the F-BMD. There is a difference in the influencing factor between L-BMD and F-BMD.

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EVALUATION OF POLICE GENERAL HOSPITAL'S FRACTURE LIAISON SERVICE (PGH'S FLS): THE FIRST PROSPECTIVE COHORT STUDY IN THAILAND

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Aims: To assess the fracture liaison service's effectiveness in osteoporotic hip fracture treatment, secondary fracture and 1st year mortality rate in Police General Hospital, Bangkok, Thailand.

Methods: A prospective cohort study was conducted. We studied male and female patients, 50 y of age and older, who presented with fragility fracture around the hip due

to low energy trauma that were admitted to Police General Hospital and participated in PGH's Liaison service from April 1, 2014 - March 30, 2015. The sample size was 75 patients, with a follow up time 1 year. The data from this study was compared with that of a previous study (Tanawat A et. al, 2015).

Results: After a follow up period of 1 year, the mortality rate was measured to be 10.7 % and there was no evidence of secondary fragility fracture. Postinjury BMD checking and osteoporotic medication treatment were 48 % and 80 %, respectively. Patients who participated in the project were found to have a decreasing rate of secondary fracture from 30 % to 0 % ($P < 0.0001$), an increasing postinjury BMD follow up rate from 28.33 % to 48 % ($P = 0.0053$), and a postinjury osteoporotic medication administration rate increase from 40.8 % to 80 % ($P = 0.0148$), all with statistical significance. However, the 1-y mortality rate was not significant ($P = 0.731$) when compared to the previous study.

Conclusion: Fracture liaison service improves the treatment of osteoporosis and secondary osteoporotic fracture for fragility hip fracture in Police General Hospital.

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A PROPOSITION: THE BRAND-NEW STYLE OF "REGIONAL LIAISON TREATMENT OF OSTEOPOROSIS" DEVELOPED BY THE EFFECTIVE UTILIZATION OF CT DATA

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Aims: Effective utilization of CT data scanned for disease of internal organs enables us to pick the numerous target patients of osteoporosis treatment out from inpatients in regional central hospitals. In Japan, "Osteoporosis Liaison Service" is becoming popular gradually. The authors propose a new style of Regional Liaison Service.

Methods: We have some backgrounds. 1. There are some regions where hospitals with DXA device and practitioners cooperate in treatment of osteoporosis. 2. In Japan, most acute care hospitals are under DPC/PDPS (diagnosis procedure combination / per-diem payment system). These hospitals are in disadvantageous condition for osteoporosis treatment. 3. Some hospitals have developed OLS for the hip fracture patient. But the target of OLS is limited to the fracture patients. 4. DPC hospitals almost forcibly make reverse introduction letters to family doctors at discharge of patients. 5. There are approximately 3200 DXA devices for trunk in Japan (2013), and 45 devices in Kagawa prefecture. 6. By the fixed point survey for all inpatients in our hospital 40 y or older, the author found that 38 % of male and 47 % of female patients had vertebral or hip fractures. 8. Approximately 80 % of them received CT of the trunk, but the vertebral fracture was not evaluated positively.

Results: By analysis of CT data, numerous patients are proved in need of medicine for osteoporosis. We have the opportunity to extract approximately 5000 target patients from the 13,500 inpatients each year at our hospital. Then we propose the new Regional Liaison Service. Family doctors and private facilities with DXA devices are responsible for the osteoporosis treatment. The following details are below.

1. Extraction of the target patients and launch of making request form. Radiographer, doctor in charge, orthopedist or radiologist make CT sagittal section image. A doctor judges the presence of vertebral fractures and makes a request form. It is better if the key image of vertebral fracture is printed on the request form. Developing a software which automates this procedure is expected.
2. Action of OLS member in DPC hospitals. (1) Radiological technologist; Cooperation in the first process.(2) Nurse; Introduction of OLS. Inform the physiotherapist about patients at high risk of falls. (3) Physiotherapist; Guidance of exercise.(4) Nutritionist; Meal guidance.(5) Pharmacist; Guidance of medicine. Explanation of the pharmacotherapy according to the patient's condition.(6) Medical clerk; Writing down about the action of OLS on request form and attach it to the reverse introduction letter.
3. Treatment of osteoporosis. Practitioners perform treatment of osteoporosis cooperating facilities with DXA.

Conclusion: To develop this act, the OLS staff training and regional workshops are needed. We can expand this target extraction method by effective utilization of CT data for outpatients if the procedure is automated. Authors expect this act to be one of the standard methods of treatment of osteoporosis.

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IMPLEMENTATION OF A CLINICAL PATHWAY INVOLVING HOSPITAL AND GENERAL PRACTITIONERS FOR OSTEOPOROTIC VERTEBRAL FRACTURES: COMBINATION OF BALLOON KYPHOPLASTY AND WEEKLY TERIPARATIDE INJECTIONS

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Aims: We launched a new clinical pathway involving hospital and general practitioners for osteoporotic vertebral fractures with a combination of balloon kyphoplasty (BKP) and weekly teriparatide injections. The purpose of the present study was to determine the clinical efficacy of the clinical pathway.

Methods: Forty-six patients with osteoporotic vertebral fractures who underwent BKP between October 2012 and

October 2013 and were followed using the pathway were included. All of the patients were treated according to the clinical pathway and had a minimum follow-up of 1 year. The first teriparatide injection was administered during hospitalization following BKP. General practitioners administered subsequent weekly teriparatide injections. The pathway consists of BKP during hospitalization and outpatient osteoporosis therapy with weekly teriparatide injections by general practitioners to prevent subsequent fractures. Hospital and general practitioners shared patient information via a clinical pathway notebook. The visual analogue scale (VAS) and EuroQol five dimensions questionnaire (EQ-5D) were used to measure pain and health status. We also assessed the refracture rate and dropout rate of osteoporosis therapy.

Results: The average age at BKP was 77.2 ± 6.6 y (range, 66–92 y); the mean duration of follow-up was 21.3 ± 7.4 months (range, 12.1-35.8 months). The average VAS decreased from 75.1 before BKP to 26.2 and 26.2 one week and 2 y after BKP, respectively. The average EQ-5D was also significantly improved from 0.32 before BKP to 0.67 and 0.74 two years after BKP, respectively. The refracture rate was 26.2 % (11/42). The dropout rate was 67.9 % at 72 weeks.

Conclusion: Our study suggests that BKP improves pain and health status, and the clinical pathway involving BKP and the weekly injection of teriparatide by hospital and general practitioners can reduce subsequent fractures.

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EVALUATION OF BONE METABOLISM AND QOL IN PATIENTS WITH OSTEOPOROSIS AFTER TREATMENT WITH THE ANTI-RANKL ANTIBODY DENOSUMAB

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Aims: To investigate the effects of denosumab in patients with osteoporosis based on the evaluation of changes in bone density, bone metabolism markers, and health-related quality of life (QOL).

Methods: The study included 400 patients with osteoporosis who received denosumab treatment (80.4 ± 7.7 y; including 82 patients switched from the other medications). The exclusion criteria were: serum calcium (Ca) level <8.0 mg/dL; moderate to severe renal insufficiency; dementia and psychiatric disorders; and undergoing dental treatment and/or having recurrent gingivitis. The following clinical evaluations were performed before the first administration of denosumab and after 6 and 12 months of the treatment: bone mineral assay in the distal end of the radius using DXA; serum levels of P1NP and TRACP-5b. A questionnaire survey employing visual analogue scale (VAS) scores for low back pain and patients' QOL using the MOS Short-Form 36-Item Health Survey (SF-36) was also carried out.

Results: The bone density relative to the young adult mean (YAM) ratio was significantly increased at both 6 and 12 months after the treatment with denosumab as compared to that determined before the first administration (51.6 ± 10.6 % pretreatment, 52.1 ± 10.8 % [$P < 0.05$] after 6 months, and 52.6 ± 10.8 % [$P < 0.001$] after 12 months). The serum levels of P1NP and TRACP-5b were significantly decreased (P1NP: 55.9 ± 30.1 μg/L, 24.5 ± 17.4 μg/L [$P < 0.001$] and 26.1 ± 15.0 μg/L [$P < 0.001$]; TRACP-5b: 545 ± 246 mU/dL, 290 ± 145 mU/dL [$P < 0.001$] and 288 ± 159 mU/dL [$P < 0.001$], respectively). The VAS scores for low back pain showed significant improvement (41.4 ± 30.0 mm, 26.8 ± 27.2 mm [$P < 0.05$] and 23.1 ± 21.8 mm [$P < 0.001$], respectively). The SF-36 scores at 6 months after administration of denosumab, as compared to those before the treatment, improved in three categories including physical functioning (77.9 points pre-treatment, 82.7 points [$P < 0.05$] after 6 months), role physical (78.7 points, 82.5 points [$P < 0.05$], respectively) and bodily pain (68.0 points, 75.6 points [$P < 0.05$], respectively). Moreover, there were no adverse events of hypocalcemia or osteonecrosis of the jaw during the observation period of this study.

Conclusion: This study demonstrated that denosumab suppressed bone turnover and increased bone strength in patients with osteoporosis. The SF-36 scores showed significant improvement in the physical dimension categories including physical functioning, role physical and bodily pain, suggesting that denosumab can potentially contribute to QOL improvement as well as increasing of bone strength.

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TRIAGE IN THE MANAGEMENT OF OSTEOARTHRITIS OF KNEE

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Aims: To triage the osteoarthritis into 3 groups for the better assessment and management of osteoarthritis of knee.

Methods: A total of 500 patients of osteoarthritis were assessed and were triaged and labelled into 3 groups. This was done with the help of WOMAC scoring and Kellgren Lawrence grading. Patients coming with WOMAC score >50 but with KL grade 1 were placed in Group 1- reversible.

Patients coming with WOMAC score <50 but with KL grading 2/3 were placed in Group 2- irreversible. Whereas, patients with WOMAC score >50 and KL grading 3/4 were placed in Group 3 - in crisis. These patients were followed up and the best mode of management was evaluated in all the groups.

Results: In Group 1 the patients benefitted from NSAIDs, oral SYSDOA drugs and physiotherapy. In Group 2 the patients benefitted from NSAIDs, joint alignment surgeries and procedures like arthroscopic debridement. Whereas, in Group 3 the patients did not benefit from any other procedure but total knee replacement.

Conclusion: This triaging of the osteoarthritis was found to be really useful in deciding the method of management of OA knee.

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SERUM VITAMIN D CONCENTRATION ASSOCIATED WITH BONE MINERAL DENSITY BUT NOT VERTEBRAL FRACTURE PREVENTION IN OLD MALES

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Aims: Lower serum vitamin D concentration was known to be associated with osteoporosis and vertebral fracture risk in postmenopausal women. However the relationship between serum vitamin D concentration and BMD with fracture risk in old Chinese males remains limitedly addressed, especially in rural community. The aim of this study is to clarify the impact of serum vitamin D status on BMD and vertebral fracture risk in old males.

Methods: Through systemically whole village sampling, this cross-section study enrolled 414 males older than 65 y old who lived in Tianliao Township, a sunny rural community in Southern Taiwan in 2010. The response rate was 60.8 % and the statistical power was 0.80. A total of 403 subjects (mean age 74.6 ± 6.2 y old) with completed data were included for final analysis. Serum 25-hydroxyvitamin D concentration was measured by a competitive radioimmunoassay kit (Cobas®, Roche Diagnostics). Lumbar (L1-4) and hip (total and neck) BMD was obtained by mobile DXA (Hologic Explorer QDR). A vertebral compression fracture, tested by mobile thoracolumbar X-ray lateral view from T3 to L5 (Daeyoung DC325-R), is defined as a reduction in vertebral body height of at least 20 % or 4 mm.

Results: A total of 32 % participants (n = 129) had serum 25-hydroxyvitamin D concentration <30 ng/mL. The prevalence of vertebral compression fracture was 58.4 % (n = 232). After adjusting for age, gender, BMI, current smoking, excessive alcohol consumption, history of previous fracture, parent fractured hip history and glucocorticoid using, multivariate regression analysis demonstrated that 25-hydroxyvitamin D concentration were independently correlated with hip neck (standardized $\beta = 0.139$, $P = 0.006$) and total hip BMD (standardized $\beta = 0.130$, $P = 0.007$). However 25-hydroxyvitamin D concentration was not associated to lumbar BMD (standardized $\beta = 0.039$, $P = 0.442$) and vertebral fracture (odds ratio = 1.002, 95CI: 0.987-1.017, $P = 0.791$).

Conclusion: The higher the serum 25-hydroxyvitamin D concentration, the better the total hip and hip neck BMD in older Chinese males was found in this study. However, serum 25-hydroxyvitamin D concentration showed no significant impact on lumbar BMD and vertebral fracture prevention. Although serum vitamin D concentration seems play a beneficial role for hip BMD, further studies are needed to investigate the effect of vitamin D on hip fracture prevention.

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IS VITAMIN D SUPPLEMENT OF 800–1200 IU/D ENOUGH IN THE BISPHOSPHONATES THERAPY FOR OSTEOPOROSIS?

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Aims: To study that the daily supplement of 800–1200 IU of vitamin D is enough or not to obtaining optimal 25OHD levels in the bisphosphonate therapy for osteoporosis.

Methods: 112 female patients with osteoporosis were included in our study. Inclusion criteria were 1) the patients' age ≥50 y; 2) the T-score of BMD at the femoral neck or total lumbar spine ≤ −2.5; 3) initial treatment of bisphosphonates; 4) no vitamin D supplement before treatment. The patients received oral vitamin D at 800–1200 IU/d in bisphosphonate therapy. Serum 25OHD was checked before and 16 weeks after vitamin D supplement. The 25OHD ≥30 ng/ml was considered as the optimal 25OHD level.

Results: The serum 25OHD was 4–41.65 ng/ml (24.26 ±7.98 ng/ml) in 112 patients and 88 (78.6 %) patients had vitamin D deficiency (serum 25OHD <30 ng/ml) before the therapy. 25OHD was 9.9-57.32 ng/ml (32.04±8.12 ng/ml) in 112 patients and only 65 (58 %) patients had 25OHD ≥30 ng/ml 16 weeks after the therapy.
Conclusion: Vitamin D deficiency is common in the patients with osteoporosis. 78.6 % patients had vitamin D deficiency in our study. The supplement of vitamin D was needed for osteoporotic patients receiving bisphosphonate therapy. NOF recommends an intake of 800–1000 IU of vitamin D per day for adults aged 50 and older. IOF recommends intake of 2000 IU/d in individuals who are obese, and in those with osteoporosis, limited sun exposure and malabsorption. The daily supplements of vitamin D 800–1200 IU significantly improved the 25OHD level in our study. But 47 of 112 (42 %) patients still did not achieve the ideal 25OHD levels. The higher doses of vitamin supplements may be required to achieve and maintain optimal vitamin D levels.

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IN SILICO STUDY OF ACTIVE COMPOUNDS FROM LABISIA PUMILA ON RANK/RANKL/OPG SYSTEM

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Aims: *Labisia pumila* is a plant with very high phenolic and flavonoid levels. Both of these compounds in the plant are believed to have varied pharmacological activities. Numerous studies have evaluated the benefits of *L. pumila* in rat model of osteoporosis, but no researcher has investigated the RANK/RANKL/OPG system. This study aimed to evaluate the active compounds from *L. pumila* to the RANK/RANKL/OPG pathway.
Methods: Analysis was performed in silico using the primary method of docking by the use of Hex 8.0 software and Haddock web server. Analysis of interactions was then performed to determine the interactions between the ligand and its receptors by using the software Discovery Studio Client 3.5.
Results: RANK-RANKL complex has the lowest interaction with pyrogallol (−136.3 kJ/mol) and has the highest interaction with rutin (−313.0 kJ/mol). Similar results were shown by the complex interaction of RANK-OPG with the active compounds, wherein the complex RANKL-OPG has the lowest interaction with pyrogallol (−136.3 kJ/mol) and has the highest interaction with rutin (−322.0 kJ/mol).
Conclusion: Flavonoids (kaempferol, rutin, apigenin) and isoflavonoids (caffeic acid, pyrogallol, gallic acid) contained in *L. pumila* have a complex interaction with the RANK-RANKL and RANKL-OPG. This proves that *L. pumila* can be used as antiosteoporosis agents through the modulation in RANK/RANKL/OPG signalling pathway.

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OSTEOPOROSIS RISK ASSESSMENT IN A RESOURCE POOR ENVIRONMENT

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Aims: To determine and classify osteoporosis risk into mild, moderate and severe among adults in Enugu Southeast Nigeria and identify those who need further investigation and treatment.
Methods: A cross-sectional descriptive study was conducted among adult respondents. An interviewer administered questionnaire was utilized by research assistants trained to administer the questionnaire. There were 15 nonmodifiable risk factors common to males and females, an extra 3 for the females by virtue of their disposition and 2 for males. The modifiable risk factors were 5 and common to each gender. Thus a total of 23 risk factors were assessed for females and 22 for males. The presence or absence of a risk factor was determined during the interview and coded '1' when present and '0' when absent. Those with a total score of 1-7 risk factors were classified as mild osteoporosis risk, score of 8-16 was classified moderate risk while a score of >17 meant severe risk. The parameters for osteoporosis risk were adapted from the 'One Minute Osteoporosis Risk Test' of the International Osteoporosis Foundation (IOF). This was modified.
Results: Respondents were 937 of 1000, a response rate of 93.7%. Most were aged >56 y. Mean age was 48.02±13.2 y. There were more females 567 (60.5%), than males 370 (39.5%). Majority (35.4%) had attained managerial levels in their professions and some had retired (18.2%). The total

mean BMI was found to be 26.96 kg/m^2, 27.51 kg/m^2 among females and 25.74 kg/m^2 among males as most respondents were overweight. Among females, 83.8% were assessed to have mild osteoporosis risk, 2.1% with moderate risk. Among the males, 87.6% were assessed to have mild osteoporosis risk and 1.1% moderate risk.

Conclusion: Mild to moderate risk of osteoporosis was predominant in the study population. There is therefore need for public enlightenment, early diagnosis and treatment, to reduce the incidence of osteoporosis related fractures and its complications bearing in mind the stringent financial situation availing.