ΟΣΤΟΥΝ

Έκδοση της Ελληνικής Εταιρείας Μελέτης Μεταβολισμού των Οστών (ΕΕΜΜΟ)

Joint Meeting of the

Hellenic Society for the Study of Bone Metabolism

Dutch Society for Calcium & Bone Metabolism

10-12
October 2019
MAICC
Megaron Athens International Conference Center
Athens
Greece

Τόμος 26
Τεύχος 3
Ιούλιος-Αύγουστος-Σεπτέμβριος 2019

ΠΕΡΙΕΧΟΜΕΝΑ

Τόμος 26, Τεύχος 3, Ιούλιος-Αύγουστος-Σεπτέμβριος 2019

Board Of Directors H.S.S.B.M. 2019-2020
Board Of Directors N.V.C.B.
Local Organizing Committee
Scientific Committee 90

Acknowledgements 91

Letter from the Editor 92

Scientific Program 93

Oral Presentations 99

E-Posters 112

Chairs - Speakers Index 120

Οδηγίες προς τους συγγραφείς 123

Board Of Directors H.S.S.B.M. 2019-2020

President:	Polyzois Makras
Vice President:	Efstathios Chronopoulos
Gen. Secretary:	Athanasios Anastasilakis
Treasurer:	Andreas Mavrogenis
Members:	Konstantinos Stathopoulos
	Themistoklis Temekonidis
	Symeon Tournis

Board Of Directors N.V.C.B.

President:	Natasha Appelman - Dijkstra
Treasurer:	Nathalie Bravenboer
Acting Secretary:	Sandrine Bours
Acting Secretary:	Astrid Bakker

Local Organizing Committee

Panagiotis Anagnostis
Georgios Antypas
Yannis Dionyssiotis
Dimitrios Hadjidakis
Alexios Iliopoulos
George Kapetanos
Dimitrios Karras
Evangelia Kaskani
Evangelia Kataxaki
Christos Kosmidis
George Lyritis
Aikaterini Matsouka
Konstantinos Mavroudis
Foteini Papadopoulou
Nikolaos Papaioannou
Dimos Patrikos
Michael Potoupnis
Grigorios Skarantavos
Konstantinos Stathopoulos
Themistoklis Temekonidis
Symeon Tournis
Nikolaos Tsakalakos
George Trovas

Scientific Committee

Chair: Socrates Papapoulos

Natasha Appelman-Dijkstra
Nathalie Bravenboer
Tijmen Münker
Sandrine Bours
Polyzois Makras
Efstathios Chronopoulos
Athanasios Anastasilakis
Andreas Mavrogenis

CME accreditation

The Joint meeting of the Hellenic Society for the Study of Bone Metabolism and the Dutch Society for Calcium and Bone Metabolism has been accredited by the European Accreditation Council for Continuing Medical Education (EACCME®) with 17 European CME credits (ECMEC®s).

Acknowledgements

The Organizing Committee wishes to thank the below-mentioned Companies:

PLATINUM SPONSOR

AMGEN

SPONSORS

ACTIVE LIFE SCIENTIFIC
the bone quality company

ALEXION

BIANEE A.E.
ΒΙΟΜΗΧΑΝΙΑ ΦΑΡΜΑΚΩΝ
ΕΤΑΙΡΕΙΑ ΤΟΥ ΟΜΙΛΟΥ ΓΙΑΝΝΑΚΟΠΟΥΛΟΥ

ELPEN

Galenica a.e.

IASIS PHARMA

INNOVIS
Future health today

ISOPLUS
for a healthyme

SOLGAR
Since 1947

ITF Hellas
Pharmaceuticals

KYOWA KIRIN

LEO

Lilly
PHARMASERVE

Medical
Pharmaquality

OSTEOSTRONG

PHARMANEL
PHARMACEUTICALS S.A.
MEMBER OF GIANNAKOPOULOS GROUP

RAFARM

Takeda

ucb
Inspired by patients.
Driven by science.

UNI-PHARMA
Pharmaceutical Laboratories S.A.

VivaPharm

Letter from the Editor

With a lot of commitment to their studies, sacrifices and stress, often faced with pessimism for the future the medical students graduate the School of Medicine and enter their desired residency program. Some decide to follow a career in orthopaedics, other decide to follow a career in rheumatology, endocrinology, internal medicine or other. During their residency program, some residents form strong bonds with consultants and professors; they start reviewing papers and medical writing, participate in meetings, seminars and summer schools, and join national and international committees. They finally achieve their specialty title and licensure; some decide to pursue a (fellowship) training in metabolic bone diseases.

Metabolic bone diseases include abnormalities of bones by a broad spectrum of disorders, most commonly caused by abnormalities of minerals such as calcium, phosphorus, magnesium, vitamin D, bone mass or bone structure. They are the third most common endocrine disorders after diabetes and thyroid diseases. They lead to dramatic clinical disorders that are commonly reversible once the underlying defect has been treated. The common metabolic bone diseases include osteoporosis, rickets/osteomalacia, flurosis and primary hyperparathyroidism, while the rare include Paget's disease of bone, tumor induced osteomalacia, fibrous dysplasia, osteogenesis imperfecta and others. It requires a case-based approach to the diagnosis and management of the patients with metabolic bones diseases. Bone pain and fractures are their hallmark manifestations. Combined treatment is always necessary.

A plethora of educational programs, symposia seminars and congresses, and prolific research in the field of metabolic bone diseases are currently available. In the present year, two European societies, the Hellenic Society for the Study of Bone Metabolism (HSSBM) and the Dutch Society for Calcium and Bone Metabolism (NVCB) have joint their annual meetings; a single meeting has been consented that will be held in Athens, Greece on October 10th-12th, 2019. The purpose was to improve the knowledge of participants regarding osteoporosis and other metabolic bone diseases, to provide important information for the recent advances in clinical and basic research as well as their interrelationship, to assess difficult tasks in the diagnosis and treatment of metabolic bone diseases, and to identify useful links between laboratory and clinical research. Participation is expected to be rewarded.

The faculty members and the participants will include endocrinologists, rheumatologists, orthopaedics, general practitioners, rehabilitation practitioners, internal medicine practitioners, pediatricians, nephrologists, researchers, and various health and allied health professionals in the field of molecular biology, musculoskeletal research, genetics, physiology and pharmacology. The presenters and lecturers are expected to present state-of-art lectures on the current research, clinical and laboratory diagnosis and treatment of the patients with metabolic bone diseases. Dedicated to continuous medical education, the presenters have provided a summary of their lectures in the form of abstracts to be included in the present issue of OSTOUN. We believe that the accumulation of these manuscripts in an issue would be useful for the readers of OSTOUN, and hopefully might lead to a change in practice.

The Editors of OSTOUN and the Board of HSSBM wish you a prolific meeting and a pleasant stay in Athens.

Andreas F. Mavrogenis
Editor-in-Chief OSTOUN

Polyzois Makras
President HSSBM

Scientific Program

Thursday, October 10th 2019

15:00 **Registrations**

17:00-18:30 **E-posters Discussion**

18:45-19:00 **Welcome Addresses**
N.M. Appelman-Dijkstra, P. Makras

19:00-20:30 **SESSION 1**
Chairs: **N.M. Appelman-Dijkstra, P. Makras**

19:00-19:45 Osteoporosis: where we have been
G. Lyritis

19:45-20:30 Osteoporosis: where are we going
S. Ferrari

20:30-21:00 **SESSION 2**
Chairs: **E. Kataxaki, E. Kaskani**

20:30-20:45 Educating physicians for osteoporosis
G. Kapetanos

20:45-21:00 Educating patients for osteoporosis
A. Kotsopoulou

21:00-21:15 **Discussion - Closing**
P. Makras

Friday, October 11th 2019

09:00-10:30 **SESSION 3**
Chairs: **T.J. de Vries, E. Kassi**

09:00-09:30 Molecular mechanisms of ion transport in metabolic bone diseases
B.C.J. van der Eerden

09:30-10:00 Non coding Rnas and bone metabolism
M. Yavropoulou

10:00-10:30 From mouse models to humans: the RANKL paradigm
E. Douni

10:30-10:45 **Coffee Break**

10:45-12:10 **ORAL PRESENTATIONS**
Chairs: **S. Polyzos, T.J.A.G. Münker**

O01 THE EFFECT OF DURATION OF VITAMIN D3 APPLICATION ON THE OSTEOGENIC DIFFERENTIATION OF HUMAN ADIPOSE STEM CELLS

Kelder C., Hogervorst J.M.A., Kleverlaan C.J., de Vries T.J., Wismeijer D., Bakker A.D.
Academic Centre for Dentistry Amsterdam (ACTA), University of Amsterdam and Vrije Universiteit Amsterdam, The Netherlands

O02 hMSC-TERTSCAS9: A VERSATILE TOOL TO STUDY OSTEOBLAST GENE FUNCTION

van de Peppel J.[1], Mies R.[1], Guo Y.[1], van der Eerden B.C.J.[1], Kassem M.[2], van der Oost J.[3], Mathijssen I.M.J.[4], van Leeuwen J.P.T.M.[1]
[1]Erasmus MC, Department of Internal Medicine, Rotterdam, The Netherlands, [2]Odense University Hospital, Department of Endocrinology and Metabolism, Odense, Denmark, [3]Wageningen University, Department of Microbiology, Wageningen, The Netherlands, [4]Erasmus MC, Department of Plastic and Reconstructive Surgery, Rotterdam, The Netherlands

O03 SURFACE CHARACTERISTICS OF AND CELLULAR RESPONSES TO COATED PERSONALIZED MEDICAL DEVICES

Münker T.J.A.G.[1], van Diemen E.[1], Zandieh Doulabi B.[1], Becking A.G.[2], Kleverlaan C.J.[1]
[1]Academic Centre for Dentistry Amsterdam (ACTA), Amsterdam NL, [2]Amsterdam University Medical Centers (Amsterdam UMC), Amsterdam NL

O04 HOMEODOMAIN TRANSCRIPTION FACTOR MEIS1 INHIBITS OSTEOGENIC DIFFERENTIATION AND ECM MINERALIZATION IN HMSC-TERTS

Guo Y.[1], Mies R.[1], Kassem M.[2], van Leeuwen H.[1], van de Peppel J.[1]
[1]Erasmus MC, Departments of Internal Medicine, Rotterdam, The Netherlands, [2]Department of Molecular Endocrinology, University of Southern Denmark and Odense University Hospital, Denmark

O05 ENDOTHELIAL CELL PHYSIOLOGY IN A MICROFLUIDIC DEVICE AND THEIR RESPONSE TO MESENCHYMAL STROMAL CELLS IN VITRO

Zhang S.[1], Tuk B.[2], van Neck J.W.[2], Koedam M.[1], van Leeuwen J.P.T.M.[1], van Steijn V.[3], van der Eerden B.C.J.[1]
[1]Department of Internal Medicine, Erasmus MC, Rotterdam, The Netherlands, [2]Department of Plastic and Reconstructive Surgery, Erasmus MC, Rotterdam, The Netherlands, [3] Department of Chemical Engineering, TU Delft, The Netherlands

O06 OCY454 AS A NOVEL OSTEOCYTE MODEL TO STUDY PHOSPHATE HOMEOSTASIS

Ratsma D.M.A.[1], Schreuders-Koedam M.[1], Zillikens M.C.[1], van der Eerden B.C.J.[1]
[1]Erasmus University Medical Center, Rotterdam, The Netherlands

O07 THE EFFECT OF VITAMIN D ON THE EXTRACELLULAR VESICLE COMMUNICATION IN BONE METASTASIS

Klazen J.A.Z.[1], Robbesom - van den Berge I.J.[1], Hartjes T.A.[1], Van Royen M.E.[1], Libregts S.[2], Van Wijnen A.[3], Zillikens M.C.[1], Van Leeuwen J.P.T.M., Van Driel M.J.J.E.[1]
[1]Erasmus Medical Center, Rotterdam, The Netherlands, [2]Utrecht University, Utrecht, The Netherlands, [3]Mayo Clinic, Rochester, Minnesota, USA

12:10-13:10 **Industry Sponsored Session**

13:10-13:40 **Lunch Break**

13:40-14:10 **FLS UPDATE**
Chairs: **E. Panagiotopoulos, C. Kosmidis**

13:40-13:55 Fracture Liaison Services: the Dutch experience
N.M. Appelman-Dijkstra

13:55-14:10 Fracture Liaison Services: the Greek experience
P. Makras

14:10-16:25 **SESSION 4**
Chairs: **M.C. Zillikens, G. Trovas**

14:10-14:40 Discontinuation of osteoporosis treatment
A. Anastasilakis

14:40 -15:10 Hip fractures: the winning patient
Th. Karachalios

15:10-16:25 **ORAL PRESENTATIONS**
Chairs: **M.C. Zillikens, G. Trovas**

O08 EFFECT OF CALCIUM AND VITAMIN D SUPPLEMENTATION WITH AND WITHOUT COLLAGEN PEPTIDES ON BONE MINERAL DENSITY AND BONE TURNOVER IN POSTMENOPAUSAL WOMEN WITH OSTEOPENIA - PRELIMINARY RESULTS

Karlafti E.[1], Lampropoulou-Adamidou K.[1], Argyrou Ch.[1], Tournis S.[1], Makris K.[2], Trovas G.[1], Dontas I.[1], Triantafyllopoulos I.K.[1]
[1]Laboratory for Research of the Musculoskeletal System "Th. Garofalidis", Medical School, National and Kapodistrian University of Athens, General Hospital of Athens KAT, Greece,
[2]Clinical Biochemistry Department, General Hospital of Athens KAT, Greece

O09 DIETARY INTAKE OF ADVANCED GLYCATION END PRODUCTS AND BONE MINERAL DENSITY AND PREVALENT FRACTURES: THE ROTTERDAM STUDY

Chen J.[1,2], Waqas K.[1], Trajanoska K.[1,2], Koromani F.[1,2], Uitterlinden A.G.[1,2], Rivadeneira F.[1,2], Zillikens M.C.[1]
[1]Department of Internal Medicine, Erasmus MC University Medical Center, Rotterdam, The Netherlands,
[2]Department of Epidemiology, Erasmus MC University Medical Center, Rotterdam, The Netherlands

O10 BONE MATERIAL STRENGTH INDEX AS MEASUERED BY IMPACT MICROINDENTATION IN VIVO IS NORMAL IN SUBJECTS WITH HIGH-ENERGY TRAUMA FRACTURES

Schoeb M., Winter E.M., Malgo F., Papapoulos S.E., Appelman-Dijkstra N.M.
Center for Bone Quality, Leiden University Medical Center, Department of Medicine, Division of Endocrinology, Leiden, The Netherlands

O11 TERIPARATIDE TREATMENT IN 16 PATIENTS WITH PREGNANCY- AND LACTATION-ASSOCIATED OSTEOPOROSIS

Lampropoulou-Adamidou K.[1], Trovas G.[1], Triantafyllopoulos I.K.[1], Yavropoulou M.P.[2], Anastasilakis A.D.[3], Anagnostis P.[4], Toulis K.A.[3], Makris K.[5], Balanika A.[6], Tournis S.[1]
[1]Laboratory for the Research of Musculoskeletal System "Th. Garofalidis", Medical School, National and Kapodistrian University of Athens, KAT Hospital, Greece, [2]1st Department of Propaedeutic Internal Medicine, National and Kapodistrian University of Athens, School of Medicine, Laikon General Hospital, Athens, Greece, [3]Department of Endocrinology, 424 General Military Hospital, Thessaloniki, Greece, [4]Unit of Reproductive Endocrinology, First Department of Obstetrics and Gynecology, Medical School, Aristotle University of Thessaloniki, Greece, [5]Biochemistry Departement, KAT Hospital, Athens, Greece, [6]Department of Computed Tomography, Asklepeion Voulas Hospital, Athens, Greece

O12 CLUSTERING OF HIP FRACTURE PATIENTS BY BONE METABOLISM MEASUREMENTS

Papakitsou E.[1], Giannikou P.[2], Andreopoulos A.[2], Giannakopoulos I.[2], Morakis A.[2], Sarantos K.[2], Sarras E.[2], Skagias K.[2], Tsagari A.[2], Dontas I.[3], Lyritis G.[4]
[1]Laiko General Hospital, Athens, [2]KAT Hospital, Kifissia, [3]Laboratory for the Research of Musculoskeletal System, Kapodistrian University, Kifissia, [4]Hellenic Osteoporosis Foundation, Kifissia

O13 PREVALENCE OF VERTEBRAL FRACTURES IN OSTEOPOROTIC PATIENTS OF THE GENERAL POPULATION IN GREECE: THE VERTEBRAL INTEGRITY ASSESSMENT (VERTINAS) STUDY

Stathopoulos K.D.[1], Chronopoulos E.[1,2], Kaskani E.[1], Drakopoulou T.[3], Ibro E.[3], Kosmidis C.[1]
[1]Hellenic Society for the Study of Bone Metabolism, [2]2nd Department of Orthopaedics, National and Kapodistrian University of Athens, School of Medicine, Greece, [3] Butterfly Bone Health Society, Athens, Greece

16:25-16:45 **Coffee Break**

16:45-18:15 **SESSION 5**
Chairs: **W.F. Lems, I. Yovos**

16:45-17:15 Stress and skeletal health
G. Chrousos

17:15-17:45 Osteoporosis and the vasculature
S.E. Papapoulos

17:45-18:15 Extraskeletal effects of bisphosphonates
I. Reid

18:15-18:30 **Break**

18:30-19:00 **Industry Sponsored Session**

19:00-19:30 **Industry Sponsored Session**

19:30-20:00 **Industry Sponsored Session**

Saturday, October 12th 2019

09:00-10:35 **SESSION 6**
Chairs: **B.C.J. van der Eerden, E. Chronopoulos**

09:00- 09:30 Molecular genetic diagnosis in early-onset osteoporosis
E. Tsourdi

09:30-10:00 Early detection, genetic background and management of atypical femoral fractures
M.C. Zillikens

10:00-10:35 **ORAL PRESENTATIONS**
Chairs: **B.C.J. van der Eerden, E. Chronopoulos**

O14 CIRCADIAN RHYTHM IS ESSENTIAL FOR BONE HEALTH
Schilperoort M.[1], Bravenboer N.[1,2], Kroon J.[1], Lim J.[1], Mletzko K.[3], Busse B.[3], van Ruijven L.[4], Rensen PCN.[1], Kooijman S.[1], Winter EM.[1]
[1]Leiden University Medical Center, Leiden, The Netherlands, [2]Amsterdam University Medical Centers, location VUMC, Amsterdam, The Netherlands, [3]University Medical Center Hamburg-Eppendorf, Hamburg, Germany, [4]Academic Centre for Dentistry Amsterdam, Amsterdam, The Netherlands

O15 SKIN AUTOFLUORESCENCE, A NONIVASIVE BIOMARKER FOR ADVANCED GLYCATION ENDPRODUCTS, IS ASSOCIATED WITH PREVALENT VERTEBRAL AND MAJOR OSTEOPOROTIC FRACTURES: THE ROTTERDAM STUDY
Waqas K.[1], Chen J.[1,2],Trajanoska K.[1,2], Koromani F.[1,2], Uitterlinden A.G.[1,2], Rivadeneira F.[1,2], Zillikens M.C.[1]
[1]Department of Internal Medicine, Erasmus Medical Center, Rotterdam, The Netherlands, [2]Department of Epidemiology, Erasmus Medical Center, Rotterdam, The Netherlands

O16 IDENTIFYING CAUSAL GENES FOR FAMILIES WITH HISTORY OF OSTEOPOROSIS AND/OR ATYPICAL FEMUR FRACTURES WITH EFFORT TO BUILD A COMMON WORKFLOW
Zhou W., van de Laarschot D.M., Verkerk J.M.H., Zillikens M.C.
Department of Internal Medicine, Erasmus Medical Center, Rotterdam, The Netherlands

10:35-10:45 **Coffee break**

10:45-12:45 **SESSION 7**
Chairs: **N. Bravenboer, E. Stathopoulos**

10:45-11:15 Analysis of in-vivo bone structure, adaptation and strength using high resolution peripheral quantitative CT
A. van Rietbergen

11:15-11:45 Radio-labelled analogues in the diagnosis of bone diseases
S. Chatziioannou

11:45-12:15 Bone material properties and fragility fractures
E.P. Paschalis

12:15-12:45 Implementation of microidentation in clinical practice
N.M. Appelman-Dijkstra

12:45- 13:45 **Industry Sponsored Session**

13:45-14:15 **Lunch Break**

14:15-16:15 **SESSION 8**
Chairs: **N.A.T. Hamdy, A. Mavrogenis**

14:15-14:45 Hematologic malignancies and bone metabolism: the multiple myeloma paradigm
E. Terpos

14:45-15:15 Animal and cell models to study periodontitis, the most common inflammatory bone disease
T.J. de Vries

15:15-16:15 **ORAL PRESENTATIONS**
Chairs: **N.A.T. Hamdy, A. Mavrogenis**

O17 IMPACT MICROINDENTATION ASSESSES PERIOSTEAL BONE MATERIAL PROPERTIES IN HUMANS
Rokidi S.[1], Bravenboer N.[2], Gamsjaeger S.[1], Chavassieux P.[3], Klaushofer K.[1], Paschalis E.[1], Papapoulos S.E.[2], Appelman-Dijkstra N.M.[2]
[1]Ludwig Boltzmann Institute of Osteology at Hanusch Hospital, Vienna, Austria
[2]Leiden Center for Bone Quality, Leiden University Medical Center, Leiden, The Netherlands,
[3]INSERM UMR 1033, University of Lyon, Lyon, France

O18 BONE MATERIAL STRENGTH INDEX AS MEASURED BY IMPACT MICROINDENTATION IN VIVO IS ALTERED IN PATIENTS WITH PRIMARY HYPERPARATHYROIDISM
Schoeb M.[1], Winter E.M.[1], Schepers A.[2], Snel M.[1], Appelman-Dijkstra N.M.[1]
[1]Center for Bone Quality and Center for Endocrine Tumours, Department of Internal Medicine, Leiden University Medical Center, Leiden, the Netherlands,
[2]Center for Bone Quality and Center for Endocrine Tumours, Department of Surgery, Leiden University Medical Center, Leiden, The Netherlands

O19 MAZABRAUD'S SYNDROME IS OFTEN ASSOCIATED WITH COMPLICATIONS OF FD/MAS; A MULTICENTER INTERNATIONAL COHORT STUDY
Hagelstein-Rotman M.[1,2], Boyce A.M.[3], Dur N.B.J.[2], Majoor B.C.J.[2], Gensburger D.[4], van de Sande M.A.J.[2], Dijkstra P.D.S.[2], Chapurlat R.[4], Appelman-Dijkstra N.M.[1]
[1]Department of Medicine: Division of Endocrinology, Centre for Bone Quality, Leiden University Medical Center, Leiden, the Netherlands,
[2]Department of Orthopaedic Surgery, Centre for Bone Quality, Leiden University Medical Center, Leiden, The Netherlands,
[3]Skeletal Disorders and Mineral Homeostasis Section, National Institute of Dental and Craniofacial Research, National Institutes of Health, Bethesda, Maryland,
[4]INSERM UMR 1033, University of Lyon, Hôpital Edouard Herriot, Lyon, France

O20 GORHAM STOUT SYNDROME OF THE PARIETAL BONE: A RARE CASE WITH A CHALLENGING TREATMENT APPROACH
De Keyser C.E.[1], Bos E.M.[2], Zillikens M.C.[1]
[1]Department of Internal Medicine, Erasmus Medical Center, Rotterdam, The Netherlands,
[2]Department of Neurosurgery, Erasmus Medical Center, Rotterdam, The Netherlands

O21 SPECIALIZED SURGICAL TREATMENT OF FIBROUS DYSPLASIA
Meier M., Majoor B., Appelman-Dijkstra N., Van de Sande M.
Leiden University Medical Center, Leiden, The Netherlands

16:15-16:30 **Coffee Break**

16:30-18:05 **SESSION 10**
Chairs: **N. Papaioannou, E.M. Winter**

16:30-17:00 Glucocortocoid induced Osteoporosis
W.F. Lems

17:00 -17:30 Chronic kidney disease mineral and bone disorder
N.A.T. Hamdy

17:30-18:05 **ORAL PRESENTATIONS**
Chairs: **N. Papaioannou, E.M. Winter**

O22 SERUM PHOSPHATE AND BMI IN THE ROTTERDAM STUDY: A BIDIRECTIONAL MENDELIAN RANDOMIZATION ANALYSIS
Bosman A., Campos-Obando N., Ligthart S., Voortman T., Ikram M.A., van der Eerden B.C.J., Uitterlinden A.G., Zillikens M.C.
Erasmus University Medical Center, Rotterdam, NL

O23 CHARACTERIZATION OF THE PATHOPHYSIOLOCIAL PROCESSES OF OSTEOARTHRITIS USING RNA SEQUENCING DATA OF SUBCHONDRAL BONE
Tuerlings M.[1], Coutinho De Almeida R.[1], Nelissen R.G.H.H.[2], Ramos Y.F.M.[1], Meulenbelt I.[1]
[1]Dept. of Biomedical Data Sciences, section Molecular Epidemiology, LUMC, Leiden NL,
[2]Dept. of Orthopaedics, LUMC, Leiden NL

O24 IS SOLUBLE CTLA-4 RELATED TO THE ONSET OF ACUTE PHASE RESPONSE (APR) IN PATIENTS WITH INFLAMMATORY RHEUMATIC DISEASES (IRD) RECEIVING INTRAVENOUS ZOLEDRONATE (ZOL)?

Giusti A.[1], Camellino D.[1,2], Saverino D.[2], Iervasi E.[2], Girasole G.[1], Bianchi G.[1], Papapoulos S.E.[1,3]

[1]Rheumatology Division, Musculoskeletal System Department, Local Health Trust 3, Genoa, Italy, [2]Autoimmunology Laboratory, Department of Internal Medicine, University of Genoa, Italy, [3]Center for Bone Quality, Leiden University Medical Center, Leiden, The Netherlands

18:05-18:30 **Break**

18:30-19:00 **Industry Sponsored Session**

19:00-20:00 **E-posters Discussion**

20:00 **Closing of the meeting**

Please cite as following:
Scientific Program of the Joint meeting of the HSSBM and the Dutch Society for Calcium and Bone Metabolism, MAICC, Athens, Greece, October 10-12, 2019. Ostoun 2019;26(3)

Oral Presentations

Friday, October 11th 2019, 10:45-12:10

O01. THE EFFECT OF DURATION OF VITAMIN D3 APPLICATION ON THE OSTEOGENIC DIFFERENTIATION OF HUMAN ADIPOSE STEM CELLS

Kelder C., Hogervorst J.M.A., Kleverlaan C.J., de Vries T.J., Wismeijer D., Bakker A.D.
Academic Centre for Dentistry Amsterdam (ACTA), University of Amsterdam and Vrije Universiteit Amsterdam, The Netherlands

Healing of critical sized defects might be aided by addition of 1,25(OH)2 vitamin D3 (vitD3) to bone tissue engineering scaffolds, as it can promote osteogenic differentiation of mesenchymal stem cells (MSCs). However, it is unknown what duration of application of vitD3 (short or sustained) leads to optimal osteogenic differentiation of MSCs. We hypothesize that sustained release of vitD3 leads to more osteogenic differentiation of MSCs than shorter applications.

Human adipose stem cells (hASCs), a clinically-relevant source of MSCs, were seeded at 105 cells per 20±1 mg calcium phosphate particles (day 0), cultured for 20 days, and treated with 124 ng vitD3. These 124 ng vitD3 was either provided during 30 min before seeding ([200 nM]), over the first 2 days of culture ([100 nM]), or over 20 days ([10 nM]). Alternatively, hASCs were treated for 2 days with 6.2 ng vitD3 ([10 nM]).

Live/dead staining showed that hASCs attached to the calcium phosphate particles and were viable (±75%) at day 2. VitD3 applied for any duration did not affect the proliferation or protein content of hASCS at day 7 and day 20, measured with alamar blue assay and BSA assay. VitD3 applied for the total culture duration of 20 days increased the release of active alkaline phosphatase (ALP) by an average of 2.7-fold at day 7 and 6.0-fold at day 20, compared to all the other conditions. These results show that sustained release of vitD3 may be beneficial for osteogenic differentiation of ASCs compared to a shorter application.

O02. hMSC-TERTS^{CAS9}: A VERSATILE TOOL TO STUDY OSTEOBLAST GENE FUNCTION

van de Peppel J.[1], Mies R.[1], Guo Y.[1], van der Eerden B.C.J.[1], Kassem M.[2], van der Oost J.[3], Mathijssen I.M.J.[4], van Leeuwen J.P.T.M.[1]
[1] Erasmus MC, Department of Internal Medicine, Rotterdam, The Netherlands,
[2] Odense University Hospital, Department of Endocrinology and Metabolism, Odense, Denmark,
[3] Wageningen University, Department of Microbiology, Wageningen, The Netherlands,
[4] Erasmus MC, Department of Plastic and Reconstructive Surgery, Rotterdam, The Netherlands

Investigation on primary human bone marrow stromal cells (BMSCs) is challenging due to inter-donor variations, their limited expansion capacity and the induction of cellular senescence. Although gene knockdown studies using siRNA/shRNA have been applied successfully in BMSCs, it may result in residual gene activity with heterogeneous effects between different knockdown constructs and individual cells. The aim of the current study is to generate Streptococcus pyogenes Cas9 (spCas9) expressing BMSCs that can be used to efficiently generate genomic gene disruptions using CRISPR-Cas and applied in functional studies of osteoblast differentiation.

Immortalized BMSCs (hMSC-TERTs) were transduced with a lentiviral construct expressing spCas9 in the absence of guideRNAs (gRNA). hMSC-TERTs^{Cas9} were transiently transfected with 1 or more gRNA constructs that target the genomic region of interest. Transfected cells were clonally expanded and gene disruptions were analysed by Sanger sequencing.

We have successfully applied hMSC-TERTs^{Cas9} to knockout transcription factors and a cell surface receptor by generating indels within coding regions. Complete removal of the VDR receptor illustrated that these cells do not respond anymore to vitamin D and were unable to differentiate into mineralizing osteoblasts. Additionally, we were able to generate homo- and heterozygous gene disruptions of FGFR2 and illustrate that the presence of 2 functionally intact alleles are essential for normal osteoblast differentiation in hMSC-TERTs^{Cas9}.

hMSC-TERTs^{Cas9} are an efficient tool to study the effects of gene disruptions in osteoblast differentiation. We are currently generating base-editing variants that allow single nucleotide modifications to generate hMSC-TERTs that mimic monogenetic bone diseases in vitro.

O03. SURFACE CHARACTERISTICS OF AND CELLULAR RESPONSES TO COATED PERSONALIZED MEDICAL DEVICES

Münker T.J.A.G.[1], van Diemen E.[1], Zandieh Doulabi B.[1], Becking A.G.[2], Kleverlaan C.J.[1] on behalf of the CranioSafe Group

[1] Academic Centre for Dentistry Amsterdam (ACTA), Amsterdam NL,

[2] Amsterdam University Medical Centers (Amsterdam UMC), Amsterdam NL

Background: Although functionalization of bone-replacing implants has led to the introduction of antibiotic eluting materials, sufficient control over the release dynamics to prevent long-term release below the minimum inhibitory concentration has not yet been achieved.

Aim: To aid in the development of functionalized bone-replacing implant surfaces, using polymer coatings that do not require the release of antibiotics, by determining the surface characteristics and cytotoxicity of these coatings.

Materials and Methods: Specimens were 3D printed using a photopolymerizable acrylate and coated with phosphonic acid or fluoride containing monomers. MC3T3-E1 pre-osteoblast-like mouse cells were tested for cellular viability, attachment, morphology, and DNA content in direct and indirect contact with these coatings.

Results: Although cellular attachment and metabolic activity was significantly lower in groups with high concentrations of monomer than in polystyrene controls, total metabolic activity increased when the coated specimens were incubated in full medium for 24 hours before cell-seeding. Combined with lower monomer concentrations this yielded viabilities above 70%, the cytotoxicity threshold under ISO 10993. Cellular DNA and indirect contact viabilities on coated specimens at day 4 were significantly lower than on polystyrene controls.

Conclusion: Personalized medical devices, such as bone-replacing implants, can be functionalized by using phosphonic acid or fluoride containing coatings which are not cytotoxic at low monomer concentrations on short timescales. However, as potentially harmful substances may elute from the coating, long-term cytotoxicity should be investigated and personalized medical devices should be pre-treated by elution before surgery.

O04. HOMEODOMAIN TRANSCRIPTION FACTOR MEIS1 INHIBITS OSTEOGENIC DIFFERENTIATION AND ECM MINERALIZATION IN HMSC-TERTS

Guo Y.[1], Mies R.[1], Kassem M.[2], van Leeuwen H.[1], van de Peppel J.[1]

[1] Erasmus MC, Departments of Internal Medicine, Rotterdam, the Netherlands,

[2] Department of Molecular Endocrinology, University of Southern Denmark and Odense University Hospital, Denmark

MEIS1 is an important transcriptional regulator in hematopoietic development. Previous studies illustrated that MEIS1 was silenced by DNA methylation during differentiation of hematopoietic progenitors, suggesting a critical role of MEIS1 in the maintenance of the undifferentiated state of HSCs. Gene expression studies from our lab indicated that MEIS1 was upregulated upon osteoblast and adipocyte differentiation of human BMSCs. Here, we investigated the role of MEIS1 during osteogenic differentiation and ECM mineralization of hMSC-TERTs.

Homozygous MEIS1 disruption mutants (MEIS1$^{-/-}$) were generated in hMSC-TERTs^{Cas9}. Cells were differentiated into osteoblasts and extracellular matrix (ECM) mineralization was determined using Alizarin Red Staining. Alkaline phosphatase activity (ALP), DNA-, protein- and calcium concentrations were measured at different time-point after osteogenic induction. Additionally, cell proliferation was analyzed by three different methods, population doubling time during 25 days expansion; KI67 FACS analyses and cell cycle analyses using EDU staining.

Our results indicated ALP activity in MEIS1$^{-/-}$ osteoblast differentiating cells was significantly increased (1.5-2 fold; $p<0.05$) at each timepoint compared to MEIS1$^{+/+}$ hMSC-TERTs^{Cas9} and ECM mineralization was enhanced. Passaging, KI67 and EDU labeling experiments did not show differences in cell proliferation between MEIS1$^{-/-}$ and MEIS1$^{+/+}$ hMSC-TERTs^{Cas9} cells. Interestingly, deletion of a single nucleotide (NM_002398:c.7533_7535delG) resulted in expression of 4 different transcripts (splice variants) with enhanced adipocyte differentiation.

Our findings suggest that the transcription factor MEIS1 is involved in the inhibition of osteogenic differentiation of hMSC-TERTs but did not affect cell proliferation. Further research will be necessary to elucidate the molecular function of MEIS1 in differentiating BMSCs.

O05. ENDOTHELIAL CELL PHYSIOLOGY IN A MICROFLUIDIC DEVICE AND THEIR RESPONSE TO MESENCHYMAL STROMAL CELLS IN VITRO

Zhang S.[1], Tuk B.[2], van Neck J.W.[2], Koedam M.[1], van Leeuwen J.P.T.M.[1], van Steijn V.[3], van der Eerden B.C.J[1]
[1] Department of Internal Medicine, Erasmus MC, Rotterdam, The Netherlands,
[2] Department of Plastic and Reconstructive Surgery, Erasmus MC, Rotterdam, The Netherlands,
[3] Department of Chemical Engineering, TU Delft, The Netherlands

Introduction: Fracture healing involves a complex sequence of physiological events. Adequate blood supply is the most critical step for healing as disturbed angiogenesis often causes nonunions. Recent studies suggest that the paracrine factors of human bone mesenchymal stromal cells (hBMSCs) have therapeutic effects on fracture healing. However, the current conventional cell culture models do not reflect the dynamic situation in vivo.

Objective: Develop a microfluidic device that provides a physiological context and compare it with static cell culture to explore the secretome of hBMSCs on endothelial cells.

Methods: Conditioned medium is collected from hBMSCs (hBMSC-CM). The effect of hBMSC-CM on human umbilical vein endothelial cell (HUVEC) adhesion and proliferation was evaluated by crystal violet staining and a Ki67 assay, respectively. The microfluidics device was fabricated using polydimethylsiloxane mixed with a curing agent; the single channel was coated with fibronectin. Cell viability was detected by the live/dead assay and cell morphology was monitored by fluorescent cell tracker.

Results: hBMSC-CM significantly accelerated HUVEC adhesion in the first 15 min following seeding compared to controls. hBMSC-CM increased Ki67-positive cell numbers (22.4% and 21.3%) compared to controls (5.4%) 48h post-seeding. For the dynamic cultures in microfluidics chips, live/dead assays showed that cell death was limited under physiological shear stress, which was mimicked by controlling flow rates (300μl h^{-1}).

Conclusion: The trophic factors released by hBMSCs are able to stimulate the angiogenetic response in static cultures. Our developed microfluidic device will help to investigate the paracrine effect of hBMSCs on skeletal angiogenesis under physiological situations.

O06. OCY454 AS A NOVEL OSTEOCYTE MODEL TO STUDY PHOSPHATE HOMEOSTASIS

Ratsma D.M.A.[1], Schreuders-Koedam M.[1], Zillikens M.C.[1], van der Eerden B.C.J.[1]
[1] Erasmus University Medical Center, Rotterdam, The Netherlands

Background: Phosphate (P) is essential for many processes including cellular signaling and skeletal mineralization. The main regulator is Fibroblast Growth Factor 23 (FGF23), which is secreted by osteocytes, but the exact mechanism underlying FGF23 regulation is poorly understood. Currently used cell models are inappropriate osteoblast lines or slowly differentiating osteocytes. Here, we propose the novel osteocyte cell line OCY454 as it expresses osteocyte differentiation markers already after one week of culturing.

Methods: The immortalized murine cell line OCY454 was kept at 33°C for three days to reach confluence, before being moved to 37°C for differentiation. At 37°C, cells were cultured with 0 or 4 mM β-glycerophosphate (β-GP; P donor). qPCR was used to study the expression of genes of interest at day 0 and 7.

Results: FGF23 was detectable in the first week of cell culture. Its regulators Dentin matrix acidic phosphoprotein 1 (DMP1) (36.1-fold, p=0.0002), Polypeptide N-acetylgalactosaminyl-transferase 3 (GalNt3) (2.65-fold, p=0.0002) and Phosphate Regulating Endopeptidase Homolog X-Linked (PHEX) (2.75-fold, p=0.029) were all upregulated at day 7 compared to day 0. Treatment with 4 mM β-GP significantly reduced the expression of DMP1 (3-fold, p=0.0094) and PHEX (7.5-fold, p=0.0031) at day 7 compared to 0 mM.

Conclusion: The osteocyte model OCY454 appears to be suitable to study P homeostasis because of its early expression of FGF23. Besides, the dynamic effects of β-GP on genes involved in FGF23 regulation suggests that the effect of P on this cell line may allow for mimicking the mechanisms of P homeostasis in vivo.

O07. THE EFFECT OF VITAMIN D ON THE EXTRACELLULAR VESICLE COMMUNICATION IN BONE METASTASIS

Klazen J.A.Z.[1], Robbesom - van den Berge I.J.[1], Hartjes T.A.[1], Van Royen M.E.[1], Libregts S.[2], Van Wijnen A.[3], Zillikens M.C.[1], Van Leeuwen J.P.T.M. and Van Driel M.J.J.E.[1]

[1] Erasmus Medical Center, Rotterdam, The Netherlands,

[2] Utrecht University, Utrecht, The Netherlands,

[3] Mayo Clinic, Rochester, Minnesota, USA

Background: Bone metastases, from for example prostate cancer (PCa), are currently incurable, resulting in death from bone-related events. Before primary cancer cells metastasize, they release nano-sized particles called extracellular vesicles (EVs), which transfer information from cell to cell. This communication mechanism is thought to be important for metastasis formation and outgrowth, which makes it a potential target for new therapies. A potentially promising therapeutic in bone metastasis that restores bone integrity and induces tumor cell death is vitamin D. However, the effect of vitamin D on the communication between PCa cells and bone cells via EVs is unknown.

Objective: Unravel the role of vitamin D in bone metastatic prostate cancer cell EV interaction with osteoblasts.

Methods: EVs from vitamin D treated and untreated GFP-expressing human PCa cells (PC-3) were isolated by differential ultracentrifugation and counted by high-resolution flowcytometry (BD influx) and microscopy-image-guided counting (EVQuant). mRNA content was analyzed by high throughput sequencing. EV uptake by human osteoblasts (SV-HFO) was measured by flowcytometry (BD Accuri C6).

Results: Treating bone metastatic PCa cells with vitamin D increased the number of EVs produced per cell, and also altered their mRNA content. Interestingly, the uptake of these EVs by osteoblasts was strongly reduced.

Conclusion: Vitamin D treatment of bone metastatic PCa cells affects their extracellular vesicle count, content and contact with bone. Our data identify new mechanisms by which vitamin D may alter how metastatic cancer cells communicate with bone cells, and thereby possibly reduce bone metastasis.

Friday, October 11th 2019, 15:10-16:25

O08. EFFECT OF CALCIUM AND VITAMIN D SUPPLEMENTATION WITH AND WITHOUT COLLAGEN PEPTIDES ON BONE MINERAL DENSITY AND BONE TURNOVER IN POSTMENOPAUSAL WOMEN WITH OSTEOPENIA – PRELIMINARY RESULTS

Karlafti E.[1], Lampropoulou-Adamidou K.[1], Argyrou Ch.[1], Tournis S.[1], Makris K.[2], Trovas G.[1], Dontas I.[1], Triantafyllopoulos I.K.[1]

[1] Laboratory for Research of the Musculoskeletal System "Th. Garofalidis", Medical School, National and Kapodistrian University of Athens, General Hospital of Athens KAT, Greece,

[2] Clinical Biochemistry Department, General Hospital of Athens KAT, Greece

Introduction: The mainstay of treatment of osteopenia and osteoporosis includes among others calcium and vitamin D supplementation. Collagen peptides (CPs) have been shown that may have a role as a treatment option. In the present randomized prospective study, we examined the efficacy, as expressed by changes in BMD and bone turnover markers, of supplementation of calcium, vitamin D with or without bioactive CPs.

Methods: Fifty-one female, postmenopausal women with osteopenia were allocated in: Group A who received a sachet containing 5 mg CPs, 500 mg calcium lactate and 400 IU vitamin D3 and group B who received a chewable tablet containing 500 mg calcium carbonate and 400 IU vitamin D3 per day.

Results: In group A and B, baseline mean BMD was 1.030 and 0.987 g/cm^2 at the lumbar spine (LS) (mean T-score -1.2 and -1.6, respectively), and 0.831 and 0.822 g/cm^2 at the total hip (TH) (mean T-score -1.4 and -1.4, respectively). After one year of supplementation, group A had a mean BMD slight increase of 0.97% at the LS and 0.52% at the TH and group B slight decrease of 0.83% and 0.37%, respectively. In group A, the P1NP significantly decreased by 17.3 % (p=0.019), and CTX increased by 9.7% (p=0.385) and in group B P1NP decreased by 4.1% (p=0.683) and CTX increased by 22% (p=0.244) within a year of supplementation.

Conclusions: These findings reflect that the addition of CPs in a calcium and vitamin D supplement may enhance its already known positive effect on bone metabolism.

O09. DIETARY INTAKE OF ADVANCED GLYCATION END PRODUCTS AND BONE MINERAL DENSITY AND PREVALENT FRACTURES: THE ROTTERDAM STUDY

Chen J.[1,2], Waqas K.[1], Trajanoska K.[1,2], Koromani F.[1,2], Uitterlinden A.G.[1,2], Rivadeneira F.[1,2], Zillikens M.C.[1]
[1] Department of Internal Medicine, Erasmus MC University Medical Center, Rotterdam, The Netherlands,
[2] Department of Epidemiology, Erasmus MC University Medical Center, Rotterdam, The Netherlands

Background: Advanced glycation end products (AGEs) are glycated proteins that accumulate in tissues with age and are involved in age-related diseases. Skin AGEs are a reflection of their tissue accumulation and diet is a major exogenous origin. Although AGEs are deposited in bone, the effect of dietary AGEs (dAGEs) on bone mineral density (BMD) and fractures is unclear.

Objectives: To study the association of dAGEs with skin AGEs, prevalent fractures and BMD in the population-based Rotterdam Study.

Methods: We included 2309 participants for dietary-skin AGEs and 3969 for dAGEs-bone analysis. Dietary intake of carboxymethyl-lysine (CML) was estimated as the most commonly investigated AGE using food frequency questionnaire and reference AGEs content in foods. Skin AGEs was measured 5 years later using skin autofluorescence (SAF). Prevalent major osteoporotic fractures (MOFs, n=338) and grade 2 and 3 vertebral fractures (VFs, n=300) assessed by Genant's classification were included. The associations were adjusted for age, sex, subcohorts, energy intake, physical activity, dietary quality, smoking status, diabetes status, and eGFR and additionally BMD, and stratified by subgroups when effect modification was present.

Results: CML intake was not associated with skin AGEs in the total population but was significantly associated after excluding diabetics and chronic kidney disease participants. CML intake was not associated with BMD and major osteoporotic fractures (ORs: 1.11 [95%CI 0.97-1.27] but there was a positive trend with vertebral fractures (ORs: 1.14 [95% CI 1.004-1.30].

Conclusions: Our results suggest that dAGEs can influence tissue AGEs accumulation and possibly fracture risk but longitudinal analysis is needed to confirm the findings.

O10. BONE MATERIAL STRENGTH INDEX AS MEASUERED BY IMPACT MICROINDENTATION IN VIVO IS NORMAL IN SUBJECTS WITH HIGH-ENERGY TRAUMA FRACTURES

Schoeb M.[1], Winter E.M.[1], Malgo F.[1], Papapoulos S.E.[1], Appelman-Dijkstra N.M.[1]
[1] Center for Bone Quality, Leiden University Medical Center, Department of Medicine, Division of Endocrinology, Leiden, the Netherlands

Background: Bone Material Strength index (BMSi), measured by Impact Microindentation (IMI) in the tibia, is a parameter to assess bone material properties at the tissue-level in vivo. BMSi is decreased in patients with low-energy fracture, independently of Bone Mineral Density (BMD) values, but it has not been measured in patients with high-energy (HET) fracture.

Objective: To evaluate tissue-level properties of bone with IMI in patients with HET.

Methods: We measured BMSi in 40 patients with HET and 40 age- and sex-matched controls with low-energy fracture by the OsteoProbe®.

Results: Mean age of HET patients and controls was 57.8±9.1 and 56.5±7.7 years, respectively. Fracture types were comparable and not significantly different between the two groups; vertebral 15 vs. 20, hip 4 vs. 4 and non-hip non-vertebral 30 vs. 25. Mean BMD T-Scores were in the osteopenic range in both groups but LS-BMD was higher in HET patients (0.95±0.13 vs. 0.88±0.12 g/cm^2, p=0.045), while FN-BMD values were not significantly different (0.76±0.09 vs. 0.72±0.10 g/cm^2, p=0.07). BMSi was significantly higher in the HET group (84.3±5.1vs. 78.2±4.8, p<0.001), also after adjusting for BMD (84.9±5.2 vs. 78.2±4.8, p<0.001), and within previously reported normal range.

Conclusion: Our data demonstrate that patients with fractures resulting from a high-energy trauma have significantly higher BMSi values compared to matched controls with similar fractures from a low-energy trauma. These findings illustrate that tissue-level material properties of bone are not impaired in HET patients and increased bone load rather than reduced strength is the main cause of such fractures.

O11. TERIPARATIDE TREATMENT IN 16 PATIENTS WITH PREGNANCY- AND LACTATION-ASSOCIATED OSTEOPOROSIS

Lampropoulou-Adamidou K.[1], Trovas G.[1], Triantafyllopoulos I.K.[1], Yavropoulou M.P.[2], Anastasilakis A.D.[3], Anagnostis P.[4], Toulis K.A.[3], Makris K.[5], Balanika A.[6], Tournis S.[1]

[1] Laboratory for the Research of Musculoskeletal System "Th. Garofalidis", Medical School, National and Kapodistrian University of Athens, KAT Hospital, Greece,

[2] 1st Department of Propaedeutic Internal Medicine, National and Kapodistrian University of Athens, School of Medicine, Laikon General Hospital, Athens, Greece,

[3] Department of Endocrinology, 424 General Military Hospital, Thessaloniki, Greece,

[4] Unit of Reproductive Endocrinology, First Department of Obstetrics and Gynecology, Medical School, Aristotle University of Thessaloniki, Greece,

[5] Biochemistry Departement, KAT Hospital, Athens, Greece,

[6] Department of Computed Tomography, Asklepeion Voulas Hospital, Athens, Greece

Objectives: Pregnancy- and lactation-associated osteoporosis (PLO) is a rare disease, often presenting with severe, prolonged and disabling back pain because of low energy or atraumatic vertebral fractures (VFs). Because of the rarity of the disease and the lack of controlled trials, there is no consensus to date on its optimal treatment.

Methods: We report a series of 16 cases with severe PLO treated with subcutaneous injection of 20μg/day teriparatide (TPTD) and calcium plus vitamin D3 supplements for a median period of 12 months (range, 2-24).

Results: Patients' mean age at the time of fracture was 34 years. The patients sustained an average of five VFs. Baseline mean BMD was 0.738 g/cm^2 at the lumbar spine (LS) and 0.652 g/cm^2 at the total hip (TH) (mean Z-score -3.5 and -2.8, respectively). Nine patients who completed one year of TPTD treatment achieved a mean BMD increase of 25.7% at the LS and 16.9% at the TH. Four patients who completed two years of TPTD treatment achieved a mean BMD increase of 38.3% at the LS and 25.3% at the TH. Six women had a positive family history of osteoporosis, and five had received low molecular weight heparin during pregnancy. No new fractures were observed while on-treatment. Back pain was relieved in all patients within 2-3 months.

Conclusions: TPTD treatment along with weaning and calcium plus vitamin D supplementation considerably increases BMD, ameliorates severe back pain, improves quality of life, and prevents further occurrence of VFs in women with PLO.

O12. CLUSTERING OF HIP FRACTURE PATIENTS BY BONE METABOLISM MEASUREMENTS

Papakitsou E.[1], Giannikou P.[2], Andreopoulos A.[2], Giannakopoulos I.[2], Morakis A.[2], Sarantos K.[2], Sarras E.[2], Skagias K.[2], Tsagari A.[2], Dontas I.[3], Lyritis G.[4]

[1] Laiko General Hospital, Athens,

[2] KAT Hospital, Kifissia,

[3] Laboratory for the Research of Musculoskeletal System, Kapodistrian University, Kifissia,

[4] Hellenic Osteoporosis Foundation, Kifissia

Functional hypoparathyroidism designates the combination of low Vitamin D without elevation of intact Parathyroid hormone (i-PTH) and is encountered in 34%-25% of hip fracture patients. This state may be related to parathyroid modulation or to definitions of normative values. It's relationship to bone metabolism is unknown. We used unsupervised learning k-means, to classify 255 hip fracture patients recruited in admission for an early Fracture Liaison protocol, by nine bone metabolism serum variables regardless of sex or age. Seventy five % of patients had 25(OH)Vitamin D lower than 14.2 ng/ml and mean i-PTH was 61.3 pg/ml. 192 patients (group A) clustered around a center with VitD 12.5 ng/ml and all other variables modestly lower (<-0,4 SD) than their means. Group B (n=57) had low VitD (8.4 ng/ml), normal Calcium(Ca), elevated i-PTH 78.6 pg/ml (+0,5 SD), N-terminal telopeptide of collagen I (NTx) 32.2 nMBCE (+0.63 SD) and Propeptide of Collagen I (PiNP) 90 ng/ml (+0,87 SD) and clearly elevated (>+1SD) total (ALP) and bone specific-Alkaline phosphatase (129.8 IU/L and 35.5 μg/L respectively). The most representative point of group C (n=16) had Cr 2.34 mg/dl, Ca 9.5 mg/dl, P 5.22 mg/dl, normal to high ALP and b-ALP and really high i-PTH (116.5 pg/ml), NTx (41 nMBCE) and PiNP (103.4 ng/ml). The analysis revealed a large group with all variables modestly lower than the means, an hyperparathyroid group with low Vitamin D, elevated bone markers and clearly high ALP and a small group with renal failure and findings of osteodystrophy, all vitamin D deficient and normocalcemic.

O13. PREVALENCE OF VERTEBRAL FRACTURES IN OSTEOPOROTIC PATIENTS OF THE GENERAL POPULATION IN GREECE: THE VERTEBRAL INTEGRITY ASSESSMENT (VERTINAS) STUDY

Stathopoulos K.D.[1], Chronopoulos E.[1'2], Kaskani E.[1], Drakopoulou T.[3], Ibro E.[3], Kosmidis C.[1]
[1] Hellenic Society for the Study of Bone Metabolism,
[2] 2nd Department of Orthopaedics, National and Kapodistrian University of Athens, School of Medicine, Greece,
[3] Butterfly Bone Health Society, Athens, Greece

Objective: To assess the prevalence of morphometric vertebral fractures in osteoporotic patients of the general population in Greece.

Methods: Patients receiving medication for osteoporosis were recruited via announcements by the Greek national media. Inclusion criteria: 1) age>50 y 2) postmenopausal status >2 y (women) 3) current (>1 y) use of medication for osteoporosis 4) lack of radiological vertebral assessment for >1 y. Exclusion criteria: 1) other bone metabolic diseases 2) secondary osteoporosis 3) inability to stand/walk 4) previous high-energy vertebral fractures. All patients completed short-form questionnaires including age, sex, current pharmaceutical treatment for osteoporosis including calcium/vitamin D supplementation, history of previous vertebral fractures, and signed informed consent to perform lateral x-rays of the thoracic and lumbar spine. Radiographs were evaluated according to the Genant method locally by radiologists and centrally through a specifically designed web database system by 3 orthopedic consultants, blinded for the patients' data. Statistical analysis was performed by a trained statistician.

Results: We report results of 1652 patients (1516 females, mean age 70.4±8.2 y and 136 males 74.8±8.1 y, all Caucasian). 85.7% of patients reported receiving bisphosphonates, 11.6% denosumab and 2.7% other agents. 38.6% and 40.6% of patients reported additional daily use of calcium and cholecalciferol supplements respectively. 419 of the patients (25,4%) were diagnosed from the orthopaedists as having at least one vertebral fracture. Of them, 98 (23.39%) reported knowledge of previous vertebral fracture, while 321 (76.61%) were unaware of having a vertebral fracture at all. Most common single fractures were Grade 1 T12, T11 and L1.

Conclusions: Our study indicated that the prevalence of morphometric vertebral fractures was ≥25% in patients under osteoporosis medication and more than 75% of them had already suffered ≥1 morphometric fractures without their knowledge. Our study highlights the importance of performing lateral x-rays in osteoporotic patients, especially those >60 y.

Saturday, October 12th 2019, 10:00-10:35

O14. CIRCADIAN RHYTHM IS ESSENTIAL FOR BONE HEALTH

Schilperoort M.[1], Bravenboer N.[1,2], Kroon J.[1], Lim J.[1], Mletzko K.[3], Busse B.[3], van Ruijven L.[4], Rensen PCN.[1], Kooijman S.[1], Winter EM.[1]
[1] Leiden University Medical Center, Leiden, the Netherlands,
[2] Amsterdam University Medical Centers, location VUMC, Amsterdam, the Netherlands,
[3] University Medical Center Hamburg-Eppendorf, Hamburg, Germany,
[4] Academic Centre for Dentistry Amsterdam, Amsterdam, the Netherlands

The past decade, it has become evident that circadian rhythms within metabolically active tissues are very important for physical health. However, although shift work has been associated with osteoporosis, circadian rhythmicity has not yet been extensively studied in bone tissue. In this study, we investigated which genes are rhythmically expressed in bone, and whether circadian disruption by weekly alternating light-dark cycles for 15 weeks affects bone turnover and structure in mice. Our results demonstrate diurnal expression patterns of clock genes (Rev-erbα, Bmal1, Per1, Per2, Cry1, Clock), as well as genes involved in osteoclastogenesis, osteoclast proliferation and function (Rankl, Opg, Ctsk) and osteocyte function (c-Fos) in bone. Alternating light-dark cycles disrupted rhythmic clock gene expression in bone (i.e. reversed rhythm of Rev-erbα and Cry1 (P≤0.01) and attenuated rhythm of Bmal1 and Clock (P≤0.05), three days after a light-dark shift). Furthermore, plasma levels of procollagen type 1 amino-terminal propeptide (P1NP) and tartrate-resistant acidic phosphatase (TRAP) were decreased (-22.4%, P<0.05 and -19.9%, P<0.01, respectively), indicating reduced bone turnover. These effects coincided with an altered trabecular bone structure and increased cortical mineralization (+1,8% in mean calcium content, P<0.05). Although mechanical properties were still adequate to maintain cortical bone strength (as determined by mechanical testing), the observed changes in mineralization could contribute to a decreased bone strength and increased fracture risk in the long term. Collectively, our results show that a physiological circadian rhythm is important to maintain bone health, which stresses the importance of further investigating the association between shift work and skeletal disorders.

O15. SKIN AUTOFLUORESCENCE, A NONIVASIVE BIOMARKER FOR ADVANCED GLYCATION ENDPRODUCTS, IS ASSOCIATED WITH PREVALENT VERTEBRAL AND MAJOR OSTEOPOROTIC FRACTURES: THE ROTTERDAM STUDY

Waqas K.[1], Chen J.[1,2], Trajanoska K.[1,2], Koromani F.[1,2], Uitterlinden A.G.[1,2], Rivadeneira F.[1,2], Zillikens M.C.[1]
[1] Department of Internal Medicine, Erasmus Medical Center, Rotterdam, The Netherlands,
[2] Department of Epidemiology, Erasmus Medical Center, Rotterdam, The Netherlands

Background: Advanced glycation end-products (AGEs) accumulation in bone has been implicated in reduced bone quality. Skin autofluorescence (SAF), measured by an AGE readerTM, is regarded as a marker of long-term AGEs accumulation in tissues. We aimed to investigate the association of SAF with bone mineral density (BMD) and fractures in the general population.

Methods: 2853 individuals with SAF measurements were included (mean age 74.1 years; 55.8% females). Prevalent major osteoporotic fractures (MOFs: hip, humerus, wrist, clinical vertebral) and prevalent vertebral fractures (VFs: clinical + radiographic) were used. Only moderate and severe radiographic VFs were included using Genant's classification which have been assessed 4-5 years before SAF measurement. Multivariate linear and logistic regression models were performed adjusted for confounders with and without BMD.

Results: The prevalence of MOFs was 8.5% and of VFs 7%. SAF had a curvilinear association with prevalent fractures and therefore, age-adjusted, sex stratified SAF quartiles were used. When we compared the top three quartiles of SAF combined with the first (lowest) quartile, the odds ratio for MOFs was 1.43 (95%CI:1.04-2.00, p=0.03) and for VFs 1.72 (95%CI:1.18-2.53, p=0.005) in fully adjusted models without BMD. Additional adjustment for BMD did not change the associations. We observed significant interaction of SAF with sex on BMD. Stratified analysis revealed negative association between SAF and BMD in females (β=-0.051; p=0.04), but not in males.

Conclusion: Higher skin AGEs are associated with prevalent vertebral and major osteoporotic fractures independent of BMD. Longitudinal analysis is needed to confirm our cross-sectional findings.

O16. IDENTIFYING CAUSAL GENES FOR FAMILIES WITH HISTORY OF OSTEOPOROSIS AND/OR ATYPICAL FEMUR FRACTURES WITH EFFORT TO BUILD A COMMON WORKFLOW

Zhou W., van de Laarschot D.M., Verkerk J.M.H., Zillikens M.C.
Department of Internal Medicine, Erasmus Medical Center, Rotterdam, the Netherlands

Object: To identify causal genes for families and sporadic cases with a history of osteoporosis and/or atypical femur fractures (AFF). To facilitate analyses, we are building a common workflow using a bioinformatics pipeline to select for genetic variants from whole exome sequencing data.

Methods: We performed whole exome sequencing on a family including seven members with osteoporosis, three of which have AFF. We hypothesize that 1) osteoporosis and AFF have separate causal genes, 2) a gene on top of an osteoporosis gene causes AFF and 3) more than one gene causes osteoporosis, and in combination predispose to AFF. In this regard, variants were filtered for rare (MAF <=0.001) exonic nonsynonymous variants and indels and splicing variants assuming a dominant mode of inheritance using a customized R package based on a model for the familial osteoporosis and a separate model for AFF. We used different in-house and publicly available databases to prioritize variants for the identification of candidate genes. Experiments were designed for further functional validation.

Results: We created an R package to customize the variants filtering. After filtering, 34 variants in 34 genes were left in the model for osteoporosis and 81 variants in 63 genes were left in the model for AFF. Prioritization was performed using gene and protein information from different resources, which resulted in several genes that require further experimental validation.

Conclusion: Our workflow facilitates the identification of causal genes for families with osteoporosis and/or AFF. Further experimental validation for selected candidate genes is needed.

Saturday, October 12th 2019, 15:15-16:15

O17. IMPACT MICROINDENTATION ASSESSES PERIOSTEAL BONE MATERIAL PROPERTIES IN HUMANS

Rokidi S.[1], Bravenboer N.[2], Gamsjaeger S.[1], Chavassieux P.[3], Klaushofer K.[1], Paschalis E.[1], Papapoulos S.[2], Appelman-Dijkstra N.[2]

[1] Ludwig Boltzmann Institute of Osteology at Hanusch Hospital, Vienna, Austria

[2] Leiden Center for Bone Quality, Leiden University Medical Center, Leiden, The Netherlands

3 INSERM UMR 1033, University of Lyon, Lyon, France

Impact microindentation (IMI) is a Reference Point Indentation technique measuring tissue level properties of cortical bone in humans in vivo. In the present study we examined bone material properties in transiliac bone biopsies obtained concurrently with measurements of Bone Material Strength index (BMSi) by IMI in 12 patients with different skeletal disorders and a wide range of BMD, with or without fractures. IMI was performed in the mid-shaft of the right tibia with a hand-held microindenter (OsteoProbe). Raman measurements were obtained at the outer edge of the cortex, and 5, 50, 100, 500 μm inwards. The calculated parameters were: i) Mineral content, organic matrix content and the mineral/matrix ratio. ii) Nanoporosity. iii) Glycosaminoglycan content. iv) Pyridinoline content. v) Maturity/crystallinity of the apatite crystallites. The results of this study showed no relationship between BMSi values with BMD. On the other hand, a positive correlation between BMSi and local mineral content, and an inverse correlation between BMSi and nanoporosity at the mineralized periosteal edge of the sample and at 5 μm inwards was found. A positive correlation was also observed between BMSi and pyridinoline content at the same locations. These results indicate that local mineral content, nanoporosity and pyridinoline content at the periosteal site in the transiliac bone biopsy are linked to the BMSi values measured in the tibia. As both high porosity at the nano level and low pyridinoline content of the bone matrix can negatively impact bone strength, our findings suggest that BMSi most likely assesses periosteal bone material properties.

O18. BONE MATERIAL STRENGTH INDEX AS MEASURED BY IMPACT MICROINDENTATION IN VIVO IS ALTERED IN PATIENTS WITH PRIMARY HYPERPARATHYROIDISM

Schoeb M.[1], Winter E.M.[1], Schepers A.[2], Snel M.[1], Appelman-Dijkstra N.M.[1]

[1] Center for Bone Quality and Center for Endocrine Tumours, Department of Internal Medicine, Leiden University Medical Center, Leiden, the Netherlands,

[2] Center for Bone Quality and Center for Endocrine Tumours, Department of Surgery, Leiden University Medical Center, Leiden, the Netherlands

Background: Parathyroid hormone (PTH) is important for bone mass maintenance and integrity. In primary hyperparathyroidism (PHPT), cortical bone remodelling increases resulting in reduction of Bone Mineral Density (BMD). Fracture rate is increased, although fractures occur at higher BMD values than expected. Therefore we hypothesised that factors other than bone mass such as tissue-level properties must also be affected.

Objective: To evaluate tissue-level properties of bone with Impact Microindentation (IMI) in the tibia in patients with PHPT.

Methods: We measured Bone Material Strength index (BMSi) by OsteoProbe® in 22 PHPT patients, 11 of whom had sustained one or more fragility fracture (FF), and 22 euparathyroid controls matched on age and FF status.

Results: Mean age of PHPT patients and controls was 64.7±11.7 and 64.1±10.9 years, respectively. PHPT patients were predominantly female (90.9% vs. 54.5%,p=0.01) and had higher calcium and PTH levels as expected. Five subjects had osteoporosis, 11 osteopenia and 5 normal BMD in both groups, and LS- and FN-BMD were not significantly different. However, BMSi was significantly lower in PHPT patients than in controls (75.9±6.3 vs. 82.6±4.6, p<0.001). In addition, BMSi was significantly lower in PHPT patients with FF than in PHPT patients without (73.6±5.3 vs. 78.6±6.8,p=0.04).

Conclusion: Our data demonstrate that PHPT patients have significantly lower BMSi compared to matched euparathyroid controls, with lowest values found in PHPT patients with FF. These findings suggest that tissue-level properties of bone are impaired in PHPT patients and that IMI is of additional value in the evaluation of bone fragility in PHPT.

O19. MAZABRAUD'S SYNDROME IS OFTEN ASSOCIATED WITH COMPLICATIONS OF FD/MAS; A MULTICENTER INTERNATIONAL COHORT STUDY

Hagelstein-Rotman M.[1,2], Boyce A.M.[3], Dur N.B.J.[2], Majoor B.C.J.[2], Gensburger D.[4], van de Sande M.A.J.[2], Dijkstra P.D.S.[2], Chapurlat R.[4] and Appelman-Dijkstra N.M.[1]

[1] Department of Medicine: Division of Endocrinology, Centre for Bone Quality, Leiden University Medical Center, Leiden, the Netherlands,

[2] Department of Orthopaedic Surgery, Centre for Bone Quality, Leiden University Medical Center, Leiden, the Netherlands,

[3] Skeletal Disorders and Mineral Homeostasis Section, National Institute of Dental and Craniofacial Research, National Institutes of Health, Bethesda, Maryland, 4INSERM UMR 1033, University of Lyon, Hôpital Edouard Herriot, Lyon, France

Mazabraud's syndrome (MZB) is a rare condition in which fibrous dysplasia (FD)/The McCune Albright syndrome (MAS) concur with intramuscular myxomas harboring the GNAS-mutation. Extra-skeletal, GNAS-related features might be associated with a more severe phenotype. MZB patients are often seen by orthopedic surgeons only and screening is usually not standard of care. We therefore evaluated MZB patients from the Netherlands (LUMC), USA (NIH) and France (INSERM).

All FD/MAS patients from these tertiary referral centers with an additional myxoma diagnosis were included. Demographics, disease extent and extra-skeletal manifestations of FD/MAS such as precocious puberty (PP) or café-au-lait patches (CAL) were retrieved from patient's medical records. Thirty MZB patients (30% female) were included. Average myxoma count was 1.4/patient. All patients were evaluated using skeletal scintigraphy. Twenty-six patients had polyostotic disease (87%). In 97% the myxoma was located adjacent to a skeletal FD lesion. MZB + "classical "MAS was present in 4 patients who all had PP+CAL with 3 of them having additional GH-excess. Because of thyroid involvement, 6 patients were later classified as MAS. Six other patients had CAL. Strikingly, we observed ductal carcinoma in situ of the breast in 3 patients(10%), breast cancer in 1 patient(3.3%), intra pancreatic mucinous neoplasms in 3 patients(10%) and giant liver-adenomas in 2 patients(6.6%).Thus, 43% of patients had other extra skeletal GNAS-features, 30% additional soft tissue tumors and 33% was classified as MAS.

In MZB, most patients suffer from polyostotic-FD. Almost 50% have extra-skeletal GNAS-related features of whom 30% had (pre-)malignant tumors. We therefore advocate MZB patients should undergo screening for the extent of bone disease and for additional FD/MAS-features, particularly other soft-tissue tumors.

O20. GORHAM STOUT SYNDROME OF THE PARIETAL BONE: A RARE CASE WITH A CHALLENGING TREATMENT APPROACH

De Keyser C.E.[1], Bos E.M.[2], Zillikens M.C.[1]

[1] Department of Internal Medicine, Erasmus Medical Center, Rotterdam, The Netherlands,

[2] Department of Neurosurgery, Erasmus Medical Center, Rotterdam, The Netherlands

A 24-years old man attended an academic hospital in the Netherlands with complaints of an asymptomatic growing defect of the parietal bone of the skull. The defect started at six years old, spontaneously without any trauma. Additional laboratory measurements showed no increased inflammation or bone turnover markers. CT-scans of the cerebrum showed an osteolytic region of the parietal bone, which was slowly progressive with two centimeters increase in diameter over nine years, with a maximum diameter of 54 millimeters. A MRI-scan confirmed the diagnosis Gorham Stout syndrome. We referred him to the neurosurgeon to investigate whether he could be treated with a graft, while we consider additional drug treatment to prevent further osteolysis.

Gorham Stout syndrome or vanishing bone disease is a rare entity characterized by progressive osteolysis with lymphatic and vascular proliferation. The underlying pathophysiology is unexplained yet. The disease usually affects persons younger than 40-years old. The upper part of the body is most frequently affected. Clinical presentation includes most frequently pain and functional impairment of the affected region but can be asymptomatic. Additional laboratory measurements are usually normal, and diagnosis is made based upon patient history, imaging and sometimes pathology. Current treatment is experimental and there is no guideline. Case reports describe treatment with bisphosphonates, interferon-alpha, anti-VEGF, mTOR inhibitors, radiotherapy and surgery with prosthetic or bone grafts.

We show the second case in literature with Gorham Stout syndrome of the parietal bone, and explain the challenge to determine an adequate treatment approach in this rare bone disease.

O21. SPECIALIZED SURGICAL TREATMENT OF FIBROUS DYSPLASIA

Meier M.[1], Majoor B.[1], Appelman-Dijkstra N.[1], Van de Sande M.[1]
[1] Leiden University Medical Center, Leiden, The Netherlands

Pain in fibrous dysplasia (FD) can be caused by several mechanisms, including abnormal bone turnover, pending fractures and/or deformities. For mechanical pain, surgery may be indicated. Allografts, intramedullary nails, (custom) plates and even prostheses have been used to stabilise lesions or treat fractures, osteotomies to correct deformities and joint reconstructions in joint degeneration or severe deformities. However, since pain is often multifactorial, multidisciplinary treatment is necessary, as the postoperative result may be unsatisfactory due to recurrent deformity or fractures in case of osteomalacia, or continuous abnormal bone turnover and pain. We would like to highlight the importance of specialized treatment of FD by demonstrating 2 patients.

Patient 1, a 21-year-old McCune-Albright syndrome patient, with FD-lesions in the femur, received a hip prothesis after failure of an intramedullary nail. After referral to our center, stem loosening was observed (figure 1), causing deteriorating mobility and pain. The uncemented prothesis and osteomalacia hampered stable fixation. Now treatment options are scarce due to poor remaining bone stock. Patient 2, 27-year-old, was referred for second opinion for severe hip pain from a FD-lesion. Prosthetic hip replacement was suggested elsewhere. Bisphosphonates were started, decreasing the pain score from 8/10 to 5/10. Since the pain disappeared only partially, a mechanical component was suspected and an intramedullary nail was implanted (figure 2). Postoperatively, she experienced no more pain and did not experience any limitations.

These cases illustrate the need for a multidisciplinary approach for FD, requiring specialized, personalized orthopaedic treatment with holistic and endocrinological expertise.

Figure 1

Figure 2

Saturday, October 12th 2019, 17:30-18:05

O22. SERUM PHOSPHATE AND BMI IN THE ROTTERDAM STUDY: A BIDIRECTIONAL MENDELIAN RANDOMIZATION ANALYSIS

Bosman A.[1], Campos-Obando N.[1], Ligthart S.[1], Voortman T.[1], Ikram M.A.[1], van der Eerden B.C.J.[1], Uitterlinden A.G.[1], Zillikens M.C.[1]

[1] Erasmus University Medical Center, Rotterdam, NL

Objectives: Observational studies have reported associations between serum phosphate (P) and body mass index (BMI) in specific settings but the nature of this relation in the general population is unclear. This study aimed to investigate whether P and BMI and body composition are related and to explore evidence of causality through bidirectional one-sample Mendelian Randomization (MR).

Methods: 9633 subjects from three cohorts from the population-based Rotterdam Study were included. Age-adjusted results were meta-analyzed. Outcome measures were BMI, waist-to-hip ratio, fat mass, lean mass and fat%, estimated by DXA. Subgroup analysis adjusted for leptin levels was performed. For MR, allele scores with 5 single nucleotide polymorphisms (SNPs) for P and 941 SNPs for BMI were constructed. Results: An inverse association between P (mg/dL) and BMI was found (β (95% CI): men: 0.41 (-0.76 to -0.05), p =0.02; women: -1.98 (-2.26 to -1.71), p <0.001), with a significant sexinteraction.

Results were not explained by potential confounders (serum calcium, 25hydroxyvitamin D, glomerular filtration rate or smoking). Adjustment for leptin attenuated but did not abolish this relation in women. There was a negative relation with fat mass and fat% in both sexes. Sex-adjusted MR analyses strongly suggests a borderline causal effect of genetically determined BMI on phosphate (β (95% CI):-0.01 (-0.02 to 0.00), p =0.05).

Conclusion: P was negatively associated with BMI and body fatness with a stronger effect in women compared to men. In women leptin explained part of this relation. MR analysis suggests a causal effect of BMI on P, potentially in part through leptin.

O23. CHARACTERIZATION OF THE PATHOPHYSIOLOCIAL PROCESSES OF OSTEOARTHRITIS USING RNA SEQUENCING DATA OF SUBCHONDRAL BONE

Tuerlings M.[1], Coutinho De Almeida R.[1], Nelissen R.G.H.H.[2], Ramos Y.F.M.[1], Meulenbelt I.[1]

[1] Dept. of Biomedical Data Sciences, section Molecular Epidemiology, LUMC, Leiden NL,

[2] Dept. of Orthopaedics, LUMC, Leiden NL

Objective: To characterize the pathophysiological processes of osteoarthritis (OA) in subchondral bone by RNA sequencing.

Methods: We performed RNA sequencing on macroscopically preserved and lesioned OA subchondral bone of patients that underwent a joint replacement surgery due to OA (N=24 pairs; 6 hips, 18 knees, RAAK-study). Unsupervised hierarchical clustering and differential expression analysis were performed on the data.

Results: Upon performing cluster analysis we identified two clusters; one representing hips and the other representing knees. Due to the low hip sample size, differential expression analysis was performed on knee samples only. We identified 1757 significantly differentially expressed (DE) genes between lesioned and preserved subchondral bone. The most significant gene was FRZB (FDR=5.13x10-8), encoding the frizzled receptor protein and is a well-known gene in OA in cartilage. The highest upregulated gene in lesioned compared to preserved bone was STMN2 (FC=23.0, FDR=1.8x10-4), which is involved in osteo- and neurogenesis. The most downregulated gene was CHRDL2 (FC=0.09, FDR=4.13x10-6), which is involved in BMP signalling. Notable other genes were IL11 (FC=4.07, FDR=7.0x10-3), WNT16 (FC=5.23, FDR=1.3x10-4), and TNFAIP6 (FC=2.26, FDR=3.6x10-4).

Conclusion: To our knowledge, we are the first to report on the DE pattern of OA subchondral bone using RNA sequencing on a large sample size. Despite the fact that the OA process in cartilage is similar between hips and knees, we here show the hip and knee samples clustering apart from each other, indicating distinct pathophysiological OA processes between the two joint sites regarding the subchondral bone.

O24. IS SOLUBLE CTLA-4 RELATED TO THE ONSET OF ACUTE PHASE RESPONSE (APR) IN PATIENTS WITH INFLAMMATORY RHEUMATIC DISEASES (IRD) RECEIVING INTRAVENOUS ZOLEDRONATE (ZOL)?

Giusti A.[1], Camellino D.[1,2], Saverino D.[2], Iervasi E.[2], Girasole G.[1], Bianchi G.[1], Papapoulos S.E.[1,3]
[1] Rheumatology Division, Musculoskeletal System Department, Local Health Trust 3, Genoa, Italy,
[2] Autoimmunology Laboratory, Department of Internal Medicine, University of Genoa, Italy,
[3] Center for Bone Quality, Leiden University Medical Center, Leiden, The Netherlands

Objective: APR is a transient, flu-like reaction to first exposure to intravenous nitrogen-containing bisphosphonate (NBP) thought to be due to activation and increased proliferation of γδ T cells related to the molecular mechanism of action of NBP. Cytotoxic T-Lymphocyte Antigen-4 (CTLA-4), is involved in the downregulation of T cell proliferation, and its role as inhibitor of the immune response has been proposed. The aim of this study was to evaluate the potential relationship between soluble CTLA-4 and the development of acute phase response (APR) in patients with IRD treated with ZOL.

Methods: Included in the study were patients with IRD treated with a single intravenous ZOL infusion 5 mg. APR was defined as a rise in axillary temperature above 38°C at any time during the first 48 hours and an increase in musculoskeletal pain by more than 10 mm in a visual analogue scale.

Results: We studied 10 women, mean age 73±9.4 years, with IRD, 8 of whom were receiving glucocorticoids. Five patients experienced APR (APR+), associated with the expected increases in serum CRP and IL-6. In all patients, baseline levels of sCTLA-4 decreased significantly from 27.92±11.97 ng/ml to 18.15±11.47 ng/ml at 24 hr, and to 3.64±4.56 at 72 hr and were not statistically different between APR+ and APR- patients (p=0.63, p=0.88 and p=0.47, respectively).

Conclusions: Contrary to our hypothesis, sCTLA-4 was not related to the occurrence of APR after ZOL. The significance of the substantial decrease of sCTLA-4 levels after ZOL in all studied patients warrants further investigation.

E-Posters

P01. SICKLE CELL ANAEMIA MAY ADVERSELY AFFECT THE SKELETON, REGARDLESS OF SEVERITY. PRESENTATION OF AN INTERESTING FAMILY

Doulgeraki A.[1], Drakaki K.[2], Polyzois G.[1], Fragodimitri C.[2]
[1] Department of Bone and Mineral Metabolism, Institute of Child Health, Athens, Greece,
[2] Thalassaemia Unit, "Aghia Sophia" Children's Hospital, Athens, Greece

Objective: To describe bone status in four siblings of African origin, presenting with sickle cell disease of different severity.

Patients and methods: The patients underwent dual-energy X-ray absorptiometry (DXA) for bone mineral density assessment and laboratory basic bone profile. Physical activity, dietary calcium intake and number of fractures were also recorded.

Results: Each patient's profile was as follows:

Patient 1: male, 8.5y, occasionally transfused during painful crises, on no medications, with low back pain.

Patient 2: male, 10y, transfused since infancy due to splenic sequestration and also with a history of autoimmune haemolysis for the last year, on desferioxamine and methylprednisolone.

Patient 3: female, 13.5y, asymptomatic, no transfusions or medications.

Patient 4: male, 16.5y, regularly transfused for the last 18 months, because of acute chest syndrome, not on any chelation therapy as yet.

All siblings reported very low calcium intake, no extracurricular physical activity and no fractures. Yet, all presented with severe vitamin D deficiency and secondary hyperparathyroidism. They did not have hypercalciuria. Of note, all patients had low bone mineral density Z-score of the lumbar spine. This finding prompted further investigation with lateral spine X-ray, which revealed diffuse osteopenia and platyspondyly. Patient 2 also had biconcave shape of L1, L3 and L5 vertebral bodies.

Conclusion: These sickle cell anaemia cases justify a low threshold for investigating bone status, regardless of clinical profile and highlight the importance of establishing detailed and updated guidelines for diagnosis and treatment of skeletal complications of the disease.

P02. ONE-YEAR SKELETAL FOLLOW UP OF CHILDREN WITH ACUTE LYMPHOBLASTIC LEUKAEMIA AND OSTEONECROSIS. A CASE SERIES.

Doulgeraki A.[1], Nikita M.[2], Kanaka-Gantenbein C.[3], Servitzoglou M.[2], Karavanaki K.[4], Zambakidis C.[5], Athanasopoulou H.[1], Polyzois G.[1], Tsentidis C.[6], Baka M.[1], Kossiva L.[4]
[1] Department of Bone and Mineral Metabolism, Institute of Child Health, Athens, Greece,
[2] Oncology Department, "P. & A. Kyriakou" Children's Hospital, Athens, Greece,
[3] Division of Endocrinology, Diabetes and Metabolism, 1st Department of Paediatrics, Medical School, National and Kapodistrian University of Athens, "Aghia Sophia" Children's Hospital, Athens, Greece,
[4] 2nd Department of Paediatrics, Medical School, National and Kapodistrian University of Athens, "P. & A. Kyriakou" Children's Hospital, Athens, Greece,
[5] Department of Orthopaedics, «P. & A. Kyriakou,» Children's Hospital, Athens, Greece,
[6] Department of Endocrinology, Metabolism and Diabetes Mellitus, Nikaea-Piraeus General Hospital "Agios Panteleimon", Greece

Objectives: To present the skeletal status of children with acute lymphoblastic leukaemia (ALL) and osteonecrosis (ON) over a one-year period.

Methods: All children diagnosed with ALL in our centre during a two-year period underwent bone turnover evaluation and dual-energy X-ray absorptiometry at the time of diagnosis and after one year. Those with severe, persistent bone pain were further investigated with MRI, to detect possible ON.

Results: Six ALL patients had ON (21% of the cohort), aged 10.8±2.22 years; five were girls. Median time from ALL diagnosis was eleven months. Fifteen joints were affected in total, mostly hips and knees. The patients were treated as per BFM 2009 protocol. Four subjects were of intermediate risk. The remaining two were classified as high risk and they had received extra dexamethasone. At ALL diagnosis, four out of six ON patients were vitamin D insufficient and were given cholecalciferol. Bone turnover had an increasing trend over time in all ON cases, with both bone formation and resorption markers showing longitudinal increase. The opposite was true for bone mineral density (BMD); there was a gradual decline of BMD Z-scores for all patients at all sites.

Conclusion: In our cohort, ON occurred mainly in peripubertal girls during maintenance ALL therapy. BMD was adversely affected and bone turnover was increased, possibly as a compensating mechanism for bone necrosis. These observations could justify the use of bisphosphonates at an early stage, before bone necrosis becomes extensive, therefore inhibiting their action.

P03. OVERGROWTH DISORDERS AND SKELETAL HEALTH: PRESENTATION OF A GREEK PAEDIATRIC COHORT WITH SOTOS SYNDROME

Doulgeraki A.[1], Kapogiannis C.[2], Polyzois G.[1], Papaggelopoulos P.[3], Athanasopoulou H.[1], Frisira E.[4], Savidou O.[3]
[1] Department of Bone and Mineral Metabolism, Institute of Child Health, Athens, Greece,
[2] Department of Paediatrics, University Hospital of Heraklion, Crete, Greece,
[3] Department of Orthopaedics, Attikon University Hospital, Athens, Greece,
[4] Department of Genetics, National and Kapodistrian University of Athens, "Aghia Sophia" Children's Hospital, Athens, Greece

Objective: Sotos syndrome is a rare overgrowth disorder (1-9/100,000, NSD1 mutation). Bone mineral density (BMD) and turnover data in these patients are scarce. We describe the skeletal status of a Greek cohort and also pursue the best method to adjust BMD for their tall stature (Ht-age vs bone age (BA)). Patients and methods: BMD (with dual-energy X-ray absorptiometry) and bone turnover markers were measured in children with diagnosis of Sotos syndrome. Also, dietary and fracture history, deformities and pain were recorded.

Results: Nine patients were assessed; seven had scoliosis. No fracture or significant pain was recorded. However, they all had suboptimal dietary calcium intake. Median, unadjusted BMD Z-scores of lumbar spine (LS) and total body less head (TBLH) were normal. However, the Z-scores obtained through Ht-age correction were lower, compared to those calculated with BA correction, especially at the LS site. All patients were vitamin D sufficient (median 25-OH-D: 30.5ng/ml). Regarding bone turnover, bTRAP (bone tartrate-resistant acid phosphatase, osteoclast product) was positively correlated to ALP and osteocalcin (markers of bone formation), i.e. bone turnover appeared coupled. Also, it was negatively correlated with daily calcium intake and BMD Z-scores (LH, TBLH), adjusted for Ht-age ($p<0.05$).

Conclusion: There was no evidence of osteoporosis in our cohort. BMD adjustment with Ht-age reflected their bone profile more effectively than with BA, as it was correlated significantly with bTRAP and calcium intake. Therefore, bTRAP could potentially have a prognostic value for skeletal health.

P04. CLINICAL AND RADIOLOGICAL OUTCOMES OF TERIPARATIDE ADMINISTRATION IN PATIENTS WITH OSTEOPOROTIC SACRAL FRACTURES

Begkas D.[1], Chatzopoulos S.[1], Lymaxis E.[1], Panagopoulos P.[1], Iliadis I.[1], Papageorgiou A.[1], Pastroudis A.[1]
[1] 6th Orthopaedic Department, Asclepieion Voulas General Hospital, Athens, Greece

Objective: To evaluate the clinical and radiological outcomes of teriparatide administration in patients with osteoporotic sacral fractures (OSF).

Materials and methods: Between 2015 and 2017, 8 female patients with OSF were hospitalized in our clinic. In all cases, treatment included bed rest (and progressive mobilization within 3 months), analgesics, vitamin D and subcutaneous administration of teriparatide 20 μg/day. Patients' follow-up was performed at 1, 3, 6 and 12-month time intervals, and the evaluation of their treatment outcomes was based on clinical (visual analogue scale pain score - VASPS) and radiographic (x-rays - Rö and computerized tomography - CT) criteria, on bone mineral density (BMD) and bone turnover markers (BTM) measurements before and after initiation of the treatment, as well as on the occurrence of complications.

Results: The mean patients' age was 72.6 (68-76) years. All of them presented significant pain reduction 1 month after therapy onset and spectacular improvement of their mobility within the following 6 months. The mean VASPS was significantly reduced (12.8mm) as compared to pre-treatment (87.6mm) score ($p<0.0001$). Rö and CT revealed healing of all fractures and further sclerotic lesions at the fracture site in 2 cases, 6 to 12 months after treatment onset, while BMD and BTM values showed a small increase. There were no complications.

Conclusions: Despite the fact that there is no significant increase in BMD and BTM values, the use of teriparatide in the treatment of OSF results in a significant increase of their healing process, rapid pain relief, quick mobilization of patients, and in minimizing the likelihood of complications.

P05. EFFECT OF EARLY POSTOPERATIVE ADMINISTRATION OF BISPHOSPHONATES ON HEALING OF OSTEOPOROTIC FRACTURES OF THE DISTAL RADIUS

Begkas D.[1], Panagopoulos P.[1], Chatzopoulos S.[1], Iliadis I.[1], Lymaxis E.[1], Papageorgiou A.[1], Pastroudis A.[1]
[1] 6th Orthopaedic Department, Asclepieion Voulas General Hospital, Athens, Greece

Objective: To evaluate the effect of early postoperative administration of bisphosphonates on healing of osteoporotic fractures of the distal radius.

Materials and methods: Between 2011 and 2017, 120 patients (87 females and 33 males) with a mean age of 68.4 (57-82) who suffered from osteoporotic fractures of the distal radius, were surgically treated in our clinic using open reduction and internal fixation (locking plates and screws). All of them received postoperative treatment with bisphosphonates (Alendronate 70 mg/week or Risedronate 35 mg/week). In 62 patients (group A) the bisphosphonate treatment was administered immediately (within 2-3 days postoperatively), while in the remaining 58 patients (group B) was delayed (3 months postoperatively). Treatment results on fracture healing for each group were based on clinical/functional (pain or tenderness, grip strength, wrist range of motion, Quick-Disabilities of the Arm, Shoulder and Hand Score – QDASHS) and radiographic (anteroposterior and lateral X-rays - radiological fracture healing time) criteria.

Results: The mean follow-up duration was 38.4 (24-60) months. Radiologically, the mean fracture healing time for group A was 3.1 (2.5-4.5) months and for group B 2.9 (2.5-4) months ($p = 0.07$). After the sixth post-operative month, there was no significant difference between the two groups in improving pain or tenderness in the fracture area, grip strength, range of motion and QDASHS.

Conclusions: Early administration of bisphosphonates after surgically treated osteoporotic radial fractures does not appear to significantly affect.

P06. ZOLEDRONATE FOR THE PREVENTION OF BONE LOSS IN WOMEN DISCONTINUING DENOSUMAB TREATMENT. A PROSPECTIVE 2-YEAR CLINICAL TRIAL

Anastasilakis, A.D.[1], Papapoulos, S.E.[2], Polyzos, S.A.[3], Appelman-Dijkstra, N.M.[2], Makras, P.[4]
[1] Department of Endocrinology, 424 General Military Hospital, Thessaloniki, Greece;
[2] Center for Bone Quality, Department of Internal Medicine, section Endocrinology, Leiden University Medical Center, Leiden, The Netherlands;
[3] First Department of Pharmacology, Faculty of Medicine, Aristotle University of Thessaloniki, Thessaloniki, Greece;
[4] Department of Endocrinology and Diabetes and Department of Medical Research, 251 Hellenic Air Force & VA General Hospital, Athens, Greece

Objective: Cessation of denosumab treatment is associated with increases in bone turnover above baseline values and rapid bone loss. We investigated the efficacy of zoledronate to prevent this bone loss in women with postmenopausal osteoporosis who were treated with denosumab and discontinued treatment after achieving osteopenia.

Methods: We investigated the efficacy of zoledronate to prevent this bone loss in women with postmenopausal osteoporosis who were treated with denosumab (mean duration 2.2 years) and discontinued treatment after achieving osteopenia. Women were randomized to receive a single zoledronate 5 mg infusion (n=27) or two additional denosumab 60 mg injections (n=30). Both groups were followed for a total period of 24 months.

Results. At 24 months LS-BMD was not different from baseline in the ZOL group, but decreased in the Dmab group by $4.82 \pm 0.7\%$ ($p<0.001$) from the 12-month value; the difference in BMD changes between the two groups, the primary endpoint of the study, was statistically significant ($p=0.025$). Results of FN-BMD changes were similar. Zoledronate infusion was followed by small but significant increases in serum Procollagen type 1 N-terminal propeptide (P1NP) and C-terminal telopeptide of type 1 collagen (CTX) during the first year and stabilization thereafter. In the denosumab group, bone turnover marker values did not change during the first 12 months but increased significantly at 15 months and in the majority of women these remained elevated at 24 months. Neither baseline nor 12-month bone turnover marker values were associated with BMD changes in either group of women. In the denosumab group, 3 patients sustained vertebral fractures (2 patients multiple clinical, 1 patient morphometric) while 1 patient in the zoledronate group sustained clinical vertebral fractures 12 months after the infusion.

Conclusion: A single intravenous infusion of zoledronate given 6 months after the last Dmab injection prevents bone loss for at least two years independently of the rate of bone turnover. Follow-up is recommended, as in a few patients ZOL treatment might not have the expected effect at 2 years.

P07. LONG-TERM PERSISTENCE WITH DENOSUMAB IN POSTMENOPAUSAL WOMEN WITH OSTEOPOROSIS: RESULTS FROM A GREEK TERTIARY HOSPITAL

Mole E.[1], Moschou D.[1], Koutsantoni E.[1], Krikelis M.[1], Zoupidou K.[1], Donta I.[2], Gazi S.[1]
[1] Department of Rheumatology, KAT General Hospital of Attica, Athens, Greece
[2] Researce Center of Myoskeletal System Disorders, Th. Garofalidis, KAT General Hospital of Attica, Athens, Greece

Objectives: Long-term persistence with prescribed medications for osteoporosis is poor. The aim of the study was to evaluate the 60-month persistence with Denosumab (DNS) administered subcutaneously every 6 months in postmenopausal women with osteoporosis.

Methods: Retrospective study of 155 postmenopausal women with osteoporosis, aged 66.9±9 years and postmenopausal years 19±10, who received DNS (60mg/6months) for 5 years. Among them 106 patients were previously treated with bisphosphonates (BIS) for 1-13 years (mean: 5.8±3.3). Endpoints included: the percentage of patients who persisted with DNS at 12, 24, 36, 48 and 60 months (greater than or equal to 10 injections with a gap between injections of no more than 6 months plus 12 weeks), the changes in BMD in persistent patients and the incidence of adverse events.

Results: Among them, 12, 24, 36, 48 and 60 months persistence was 83.87%, 61.3%, 47.1%, 21.93% and 7.1% respectively. At the end of 5th year among persistent patients, mean BMD increased from baseline by 10.8% at the lumbar spine (LS) and 9.94% at the femoral neck (FN). As far as it concerns the adverse events, 3 patients with previous BIS uptake developed osteonecrosis of jaw and 1 patient developed a new vertebral fracture.

Conclusion: Persistence with DNS treatment was excellent in the first year and gradually deteriorated in the fifth year of follow-up. On the other hand BMD of persisted patients was significantly improved.

P08. DETECTING STRUCTURAL CHANGES OF THE BONE TISSUE USING RAMAN SPECTROSOPY

Gialama L.
Undergraduate student, Department of Physics, National and Kapodistrian University of Athens, Athens, Greece

Objective: Review of the Raman spectroscopy technique and its usefulness in detecting structural abnormalities of the bones.

Materials and methods: A review of the scientific literature was conducted accesing the electronic databases Pubmed and Google Scholar without chronological limitations. Finally, 11 articles in English and Greek language were included in this review.

Results: Raman spectroscopy is a technique based on the phenomenon of the same name. In this phenomenon, the frequency of the radiation passing through the sample varies partially. This is an inelastic scattering that accounts for 0.001% of the scattered radiation and is observed in vertical directions of the incident radiation. Raman spectroscopy has become an important tool for assessing bone quality because it can help us understand how the changes in bone composition and structure affect the mechanical characteristics of the bone. The technique is also associated with a lower signal/noise ratio than the one achieved in Fourier Transformation (FTIR) Infrared Spectroscopy, which provides the same information. The Raman technique is still applied experimentally and potentially could be used to diagnose osteoporosis but also to screen patients with osteoporosis if the necessary safety conditions are met.

Conclusion: Raman spectroscopy is a non-invasive technique useful for diagnosing changes in tissue composition. This technique is currently being used for ex-vivo bone analysis. The non-invasive in-vivo application of Raman spectroscopy is still under study.

P09. INCREASED BONE MARROW ADIPOSITY IN HUMANIZED RANKL TRANSGENIC MOUSE MODELS OF OSTEOPOROSIS

Rinotas V.[1,2], Kritikos K.[1,2], Nikolaou P.[1,2], Papadopoulos A.[1,2], Kolokotroni A.[1,2], Douni E.[1,2]
[1] Laboratory of Genetics, Department of Biotechnology, Agricultural University of Athens, Athens, Greece,
[2] Biomedical Sciences Research Center "Alexander Fleming", Vari, Greece

Bone Marrow Adiposity (BMA) increases during aging and is further enhanced in osteoporosis, whereas its pathophysiological significance remains insufficiently understood. We have recently established two novel genetic osteoporosis models, Tg5516 and Tg5519, by expression of human RANKL (Receptor activator of nuclear factor-κB ligand), the main inducer of osteoclastogenesis, in transgenic mice (TgRANKL). A common characteristic in both transgenic lines is the progressive development of BMA. To understand the mechanisms that promote BMA expansion in osteoporosis, we analyzed its progression in both TgRANKL osteoporosis models and explored the adipogenic potential of bone marrow mesenchymal stromal cells (BMSCs). Histological analysis and micro-computed tomography demonstrated that BMA development in the Tg5516 line was restricted at the distal femural metaphysis, while in the Tg5519 model BMA expanded progressively throughout the marrow cavity and correlated with increased bone resorption, indicating a close interaction between BMA and osteoclastogenesis. E x vivo analysis of BMSCs from TgRANKL mice showed a dramatically altered adipogenic differentiation profile that strongly correlated with increased expression of adipogenic markers, including PPARγ and C/EBPα as well as RANKL as shown by qPCR. Furthermore, the effectiveness of an anti-osteoporosis treatment in BMA development was investigated upon treatment of TgRANKL models with the bisphosphonate alendronate. Notably, alendronate effectively improved bone mass and attenuated BMA expansion at metaphysis, indicating a possible involvement of osteoclasts and bone resorption in BMA development. Our results demonstrate that TgRANKL mice constitute unique genetic models for investigating the pathogenic mechanisms that regulate development and expansion of BMA in osteoporosis.

P10. MAMMARY GLAND DEVELOPMENT IN HUMANIZED TgRANKL MOUSE MODELS OF OSTEOPOROSIS

Kolokotroni A.[1,2], Rinotas V.[1,2], Gkikopoulou E.[1,2], Dermitzaki E.[1,2], Efstathiou E.[1,2], Rentis T.[1,2], Samiotaki M.[1], Panayotou G.[1], Douni E.[1,2]
[1] Institute for Bioinnovation, B.S.R.C. Alexander Fleming, Athens, Greece,
[2] Department of Biotechnology, Agricultural University of Athens, Athens, Greece

Receptor activator of nuclear factor-κB ligand (RANKL) is one of the central regulators in bone remodeling by inducing osteoclast formation and bone resorption. Apart from its fundamental role in the skeletal system, recent studies have highlighted the key role in the formation of lactating mammary glands during pregnancy, as well as in the initiation of breast cancer. Given that RANKL mediates the paracrine effect of progesterone in the proliferation of mammary epithelial cells, RANKL is considered as a highly promising therapeutic target for the prevention and treatment of various breast cancer subtypes. In the current study, we demonstrated that both endogenous mouse and human RANKL were expressed in the mammary glands of virgin TgRANKL females and were further upregulated during pregnancy or upon exogenous progesterone administration. Moreover, a specific localization of RANKL was identified at the luminal epithelial cells in ductal and alveolar structures. As regards the mammary structure, we identified a widespread epithelial expansion in TgRANKL mice compared to wild-type mice through whole mount carmine staining, histological and microCT analysis. Ductal epithelial expansion in the mammary glands was analogous to the levels of RANKL expression and osteoporosis severity in TgRANKL lines. Notably, immunocytochemical analysis revealed increased proliferation in epithelial cells, as shown by the proliferative markers Ki67, Cyclin D1 and BrdU. Proteomic and RNAseq analysis also supported increased cell proliferation, adhesion and inflammation. Collectively, our results demonstrate that increased expression of RANKL in the mammary glands of TgRANKL osteoporotic mice is correlated with enhanced proliferation of mammary epithelial cells.

P11. SPONTANEOUS INSUFFICIENCY FRACTURES OF THE KNEE: A RETROSPECTIVE ANALYSIS BY USING MRI IN THE EMERGENCY DEPARTMENT

Gklara P., Perdikakis E.
424 GMTH General Military Hospital

Objective: Subchondral insufficiency knee fractures are associated with osteoporosis and can be reversible or progress to spontaneous osteonecrosis and rapidly destructive osteoarthritis. The purpose of our study was to examine the use of MRI in the emergency setting for osteoporotic patients affected with subchondral insufficiency knee fractures.

Materials & Methods: This was a retrospective study that was carried out in the emergency department and only patients with known osteoporosis and MRI-verified subchondral insufficiency knee fractures were included. Between 2009 and 2019, twelve consecutive patients were studied. Patient demographics and MRI findings were recorded. Measurements of the subchondral fracture line in MRI were performed and Fischer's exact test was used for statistical analysis ($p<0.05$).

Results: 8 female and 4 male patients (mean age 72.1yrs) were examined. Medial femoral condyle was affected in 4 cases and the medial tibial plateau in 8 cases. MRI showed bone marrow edema in all cases (100%), verified a subchondral fracture line measuring from 7 to 32mm in all patients (100%) and depicted articular collapse in 4 cases (33.3%). According to the modified Ficat-Arlet classification lesions were classified as following: Stage II (4 patients), Stage III (4 patients), Stage IV (2 patients) and Stage V (1 patient). 3 patients were treated surgically and 9 conservatively. The grade of the lesions and the magnitude of the fracture line did not show any statistical significant difference ($p= 0.17$).

Conclusion: The role of MRI in the emergency setting is highly recommended in osteoporotic patients to identify subchondral insufficiency knee fractures.

P12. MICRORNA-21-5p IS DIFFERENTIALLY EXPRESSED IN HIV-INFECTED PATIENTS WITH OSTEOPOROSIS

Yavropoulou MP.[1,2], Kolinou A.[3], Tsave O.[2], Tsachouridou O.[4], Skoura L.[3], Chatzidimitriou D.[5], Metallidis S.[4], Makras P.[2]

[1] 1st Department of Propaedeutic Internal Medicine, National and Kapodistrian University of Athens, School of Medicine, LAIKO General Hospital of Athens, Greece,
[2] Laboratory of Biomedical Research, 251 Hellenic Air Force & VA General Hospital, Athens, Greece,
[3] Department of Microbiology, Medical School, Aristotle University of Thessaloniki, Thessaloniki, Greece,
[4] 1st Internal Medicine Department, Infectious Diseases Division, Medical School, Aristotle University of Thessaloniki,
[5] National AIDS Reference Centre of Northern Greece, Medical School, Aristotle University of Thessaloniki, Greece

Objective: Human immunodeficiency virus (HIV)-infected patients demonstrate an increased risk of osteoporosis and fractures. The pathophysiology of HIV-induced bone loss is complex and remains largely unknown. Recent studies have identified a molecular signature of small non-coding RNAs (microRNAS) in patients with osteoporosis, but data are lacking in HIV-infected patients. The aim of the present study was to investigate the expression profile of microRNAs in osteoporotic patients with HIV – infection.

Methods: One hundred and 26 HIV-infected males on anti-retroviral treatment (ART) were included in the study. Measurement of bone mineral density, vertebral fracture assessment and complete biochemical work up were performed in all. MicroRNA extraction from the serum was performed with microRNEasy kit (Qiagen).

Results: Mean age of the enrolled patients and mean duration of ART were 55 ± 8 years and 11 ± 7 years, respectively. Sixty % of the patients had low bone mass (51 were osteopenic and 25 osteoporotic). None of the patients had a fragility fracture. We investigated the microRNA profile in the serum of a subgroup of 60 patients: 30 with osteoporosis and osteopenia and 30 matched for age and ART-duration patients with normal bone mass. From the 12 microRNAs that were selected for analysis miR21-5p was found significantly decreased in the serum of HIV-infected patients with osteoporosis compared with normal bone mass counterparts.

Conclusion: Serum expression of MicroRNA-21-5p is significantly decreased in osteoporotic HIV infected patients compared with normal bone mass HIV-patients, in line with what has been shown in non-HIV-infected osteoporotic patients.

P13. PREVALENCE OF OSTEOPOROSIS, SARCOPENIA AND LIPODYSTROPHIA IN MALE HIVINFECTED PATIENTS ON ANTI-RETROVIRAL TREATMENT

Yavropoulou MP.[1,2], Kolinou A.[3], Tsachouridou O.[4], Skoura L.[3], Chatzidimitriou D.[5], Makras P.[2], Metallidis S.[4]

[1] 1st Department of Propaedeutic Internal Medicine, National and Kapodistrian University of Athens, School of Medicine, LAIKO General Hospital of Athens, Greece,

[2] Laboratory of Biomedical Research, 251 Hellenic Air Force & VA General Hospital, Athens, Greece,

[3] Department of Microbiology, Medical School, Aristotle University of Thessaloniki, Thessaloniki, Greece,

[4] 1st Internal Medicine Department, Infectious Diseases Division, Medical School, Aristotle University of Thessaloniki,

[5] National AIDS Reference Centre of Northern Greece, Medical School, Aristotle University of Thessaloniki, Thessaloniki, Greece

Objective: Human immunodeficiency virus (HIV)-infection and the need for chronic anti-retroviral therapy (ART) are associated with increased rate and earlier onset of degenerative –aging related disorders such as osteoporosis, sarcopenia and lipodystrophy despite adequate control of the HIV infection. The aim of the present study was to investigate the prevalence of osteoporosis, sarcopenia and lipodystrophy in HIV –infected males in Greece and their association with the ART, duration of the disease and status of the viral load.

Methods: For the purposes of this cross-sectional case-control study one hundred and twenty six male HIV – infected patients and 50 non-HIV infected age and gender matched controls were included in the study. Measurement of bone mineral density (BMD), body composition assessed with whole-body dual–energy X-ray absorptiometry, vertebral fracture assessment, complete biochemical profile, CD4 lymphocytes blood count and viral load were performed in all. Relative skeletal muscle mass index (RSMI) and fat mass ratio (FMR) were calculated. RSMI <7.26 kg/m was classified as sarcopenia and FMR <1.961 was classified as lipodystrophy.

Results: Mean age of patients and mean duration of HIV infection and ART treatment was 55 ± 8 years and 11 ± 7 years, respectively. All the parameters tested with DXA scan [bone mass, total body fat %, fat free mass (g), fat mass ratio (%) and RSMI] were significantly lower in HIV-infected patients compared to controls. Forty three % of the patients were osteopenic, 16% were osteoporotic, 91% had lipodystrophy and 37% presented with sarcopenia, according to pre-classified thresholds. None of the tested parameters were associated with, CD4 count, viral load, duration of HIV infection or the duration of ART.

Conclusion: HIV infected males have a high prevalence of low bone mass, lipodystrophy, and sarcopenia independently of the viral load or duration of the ART.

P14. POLYPHARMACY AND FALLS OF ELDERLY WITH HIP FRACURE-A RETROSPECTIVE STUDY AND LITERATURE REVIEW

Papaioannou I.[1], Pantazidou G.[2], Kostoglou-Athanassiou I.[3], Repantis T.[1], Korovessis P.[1]

[1] Orthopaedic Department of General Hospital of Patras, Greece,

[2] Public Health Unit, University of Patras, Greece,

[3] Endocrinology Department of General Hospital Asklepeio of Voula, Greece

Object of the study: Polypharmacy is closely related with elderly's falls, while falls are associated with increased morbidity, mortality, undesirable events, unplanned admissions to emergency departments, whereas fear of falling leads to isolation and resignation. The aim of the study is to investigate the possible association of polypharmacy and falling among older patients.

Material and Method: We randomly selected 61 elderly patients (51 women, 10 men) with an average age of 83,39 years who were hospitalized in our clinic for hip fracture due to falling. As a control group, we randomly selected 60 patients (38 women and 22 men) with an average age of 72,98 years who were hospitalized in our department for degenerative diseases.

Results: In the hip fracture group we had 4,77 ± 2,9 drugs per day per patient, while in the control group the average was 3,6 ± 1,85. It is worth noting that only 3,11% of patients with hip fracture received less than four medications.

Conclusions: Several studies have linked polypharmacy with falls and for this reason polypharmacy until 2000 was considered as an independent risk factor for falls. However, more important seems to be the type of drugs that potentially can cause falls like anticholinergics or sedatives. Our study also shows the increased use of drugs in the group of patients with falls and hip fractures. Elderly people who receive more than three drugs or drugs that induce falls should be considered as «candidates» for fall and should be properly recognized and consulted.

P15. THE DIAGNOSIS OF PRIMARY HYPERPARATHYROIDISM IN THE SETTING OF AN OSTEOPOROSIS CLINIC

Kostoglou-Athanassiou I.[1], Athanassiou L.[2], Manta E.[1], Giannakopoulos A.[1], Pastroudis A.[1], Athanassiou P.[3]
[1] Osteoporosis Clinic, Asclepeion General Hospital, Voula, Athens, Greece,
[2] First Department of Medicine, Asclepeion General Hospital, Voula, Athens, Greece,
[3] Department of Rheumatology and Osteoporosis Clinic, St. Paul's General Hospital, Thessaloniki, Greece

Primary hyperparathyroidism may remain undiagnosed for a significant amount of time if the diagnosis is unsuspected. In many cases the diagnosis of osteoporosis is made before the diagnosis of primary hyperparathyroidism. The aim of the study was to present primary hyperparathyroidism as a cause of attendance to the osteoporosis clinic.

Methods: A cohort of 45 patients attending to the osteoporosis clinic during the second trimester (April – June) of 2019 is presented. In all patients a bone mineral density measurement by DEXA for the diagnosis of osteoporosis was made. Serum levels of Ca, P, urea and creatinine were measured as well as 24h Ca urinary levels. Serum levels of PTH and 25(OH)D_3 were also measured.

Results: Within the cohort of 45 patients examined in the osteoporosis clinic during the second trimester of 2019 8 were diagnosed with primary hyperparathyroidism. In these patients increased levels of serum PTH, increased blood Ca and increased urinary Ca were observed. Bone mineral density measurement revealed either osteoporosis or osteopenia. In patients diagnosed with primary hyperparathyroidism investigation was performed for the localization of the adenoma with thyroid-parathyroid ultrasound and scintigraphy with ^{99m}Tc SESTAMIBI. In 5 patients a parathyroid adenoma was revealed. Surgery was recommended. In 1 patient, female aged 65, the presence of primary hyperparathyroidism was already known. A parathyroid adenoma had been excised 10 years earlier. However, the disease recurred. The diagnosis of parathyroid hyperplasia was made. Alendronate was administered for the management of osteoporosis and cinacalcet 30 mg/day for the management of hypercalcemia. In 2 patients a parathyroid adenoma was not found. For the management of osteoporosis in the cohort of patients with primary hyperparathyroidism alendronate was administered.

Conclusions: Primary hyperparathyroidism is a disease with mild or very mild symptoms. Therefore, the diagnosis may not be made promptly if the disease is not suspected. Patients present with osteoporosis. Knowledge of the disease may lead to its diagnosis, when patients present in the osteoporosis clinic, leading to the proper management of the problem.

P16. CLINICAL TREATMENT EFFECTS OF BISPHOSPHONATE ADMINISTRATION IN DENTAL PATIENTS WITHOUT SYSTEMIC DISORDERS: A SYSTEMATIC REVIEW AND NETWORK META-ANALYSIS

Zymperdikas V.F.[1,2], Yavropoulou M.P.[3], Kaklamanos E.G.[4], Papadopoulos M.A.[1]
[1] Department of Orthodontics, Faculty of Dentistry, School of Health Sciences, Aristotle University of Thessaloniki, Greece,
[2] 424 Military Hospital of Thessaloniki, Greece,
[3] 1st Propaedeutic Department of Internal Medicine, National and Kapodistrian University of Athens, Greece,
[4] Hamdan Bin Mohammed College of Dental Medicine, Mohammed Bin Rashid University of Medicine and Health Sciences, Dubai, United Arab Emirates

Objective: To investigate the treatment effects of bisphosphonate (BP) use on dental patients free of systemic diseases through clinical measurements.

Methods: Sixteen electronic databases were systematically and unrestrictedly searched up to July 2019, complemented by additional manual searches. Only randomized controlled trials (RCTs) providing dental clinical measurements on human patients treated with BPs compared with controls that were untreated or treated with placebo or with other BP type. Measurements until 12 months of treatment were pooled according to time of evaluation in effects. After appropriate risk of bias assessment, a random-effects model was used to calculate mean differences (MDs) and the respective 95% confidence intervals (95% CIs), in order to take into consideration the existing heterogeneity.

Results: Nine RCTs (10 datasets) were finally included in the network meta-analysis including 528 subjects reporting on treatment effects after 2-12 months of BP administration. BP treatment seems to be associated with significant improvement of most assessed measurements, compared with BP-naive controls. According to the network ranking, zoledronate was found to be more efficient in improving probing depth and clinical attachment gain, while alendronate seems better in control of bleeding and plaque scores. No differences were found between patient- and drug-related factors. The long-term analysis of the pharmaceutical effects on dental tissues could not be performed due to inadequate pertinent data.

Conclusions: BP administration seems to be effective in improving the clinical measurements of periodontal disorders in the short-term, mainly through control of periodontal inflammation.

Chairs - Speakers Index / Ευρετήριο Ομιλητών & Προέδρων

A

Anastasilakis Ath.
Endocrinologist, Consultant of Endocrinology, 424 General Military Hospital, Thessaloniki, Greece

Appelman-Dijkstra N.M.
Endocrinologist, Chair Center for Bone Quality: Department of Medical Medicine, Chair Academic Training Program Endocrinology, Leiden University Medical Center, The Netherlands

B

Boutzios G.
Senior Consultant in Endocrinology, Endocrine Unit, Department of Pathophysiology Laiko General Hospital, Athens, Greece

Bravenboer N.
Associate Professor, Head Lab for Bone Metabolism, Department Clinical Chemistry, Amsterdam University Medical Centers, Location VUMC, Amsterdam, The Netherlands, Leiden University Medical Center for Bone Quality: Department of Internal Medicine, The Netherlands

C

Chatziioannou S.
Professor of Nuclear Medicine, National Kapodistrian University Athens, Director PET/CT, Foundation for Biomedical Research of the Academy of Athens, Greece

Chronopoulos E.
Associate Professor in Orthopedics, Athens Medical School, National & Kapodistrian University Athens, Greece, 2nd Orthopaedic Department Konstantopoulio General Hospital, Athens, Greece

Chrousos G.
Emeritus Professor of Pediatrics and Endocrinology, Holder, UNESCO Chair on Adolescent Health Care, Director, University Research Institute of Maternal and Child Health and Precision Medicine, National and Kapodistrian University of Athens, Medical School, Aghia Sophia Children's Hospital, Athens, Greece

D

De Vries T.J.
Department of Periodontology, Academic Centre of Dentistry Amsterdam (ACTA), University of Amsterdam and Free University of Amsterdam, Amsterdam, The Netherlands

Douni E.
Associate Researcher, Biomedical Sciences Research Center Alexander Fleming, Athens, Greece

F

Ferrari S.
Professor MD, Head, Service and Laboratory of Bone Diseases, Chairman, Academic Department of Medicine, Geneva University Hospital and Faculty of Medicine, Switzerland

G

Giustina A.
Member, Italian Superior Health Council Prorector for Institutional and International Relations, Full Professor and Chair of Endocrinology and Metabolism Director, Postgraduate School of Endocrinology and Metabolic Diseases, San Raffaele Vita- Salute University, Head, Division of Endocrinology IRCCS San Raffaele Hospital, Milan, Italy

H

Hamdy N.A.T.
Associate Professor Emeritus and Medical and Scientific Advisors, Leiden University Medical Center for Bone Quality: Department of Internal Medicine, The Netherlands

J

Johnston S.
Chief Medical Officer AXIOM SPACE, Inc Flight Surgeon, NASA Johnson Space Center, USA

K

Kapetanos G.
Emeritus Professor of Orthopaedics, Aristotle University of Thessaloniki, Greece

Karachalios T.
Professor of Orthopaedics, University of Thessaly, Greece

Kaskani E.
Reumatologist, Athens, Greece

Kassi E.
Endocrinologist, Associate Professor Medical School, National and Kapodistrian University, Athens, Greece

Kataxaki E.
Director Rheumatologist, Thriassio Hospital of Elefsina, Greece

Kosmidis C.
Orthopedic Surgeon, Athens, Greece

Kotsopoulou A.
Phychologist, Scientific Collaborator of Butterfly Bone Health Society, Athens, Greece

Chairs - Speakers Index / Ευρετήριο Ομιλητών & Προέδρων

L

Lems W.F.
Professor in Rheumatology, Amsterdam University Medical Centre, The Netherlands

Lyritis G.
Emeritus Professor of Orthopedics, National and Kapodistrian University of Athens, Greece

M

Makras P.
Endocrinologist, Dep. Director of Department of Endocrinology, Head of Department of Medical Research, 251 Hellenic Air Force & VA General Hospital, Athens, Greece

Mavrogenis A.
Associate Professor of Orthopaedics, Medical School, National and Kapodistrian University of Athens, Greece

Mavroudis K.
Endocrinologist, Ex Consultant of Endocrinology, Diabetes and Metabolism, Asklepieion Voulas General Hospital, Athens, Greece

Münker T.J.A.G.
PhD Candidate, Academic Centre for Dentistry Amsterdam (ACTA), Department of Dental Material Sciences, Amsterdam, The Netherlands

P

Panagiotopoulos E.
Professor of Orthopaedics, University of Patras, President of FFN Greece

Papaioannou N.
Associate Professor of Orthopaedics, National and Kapodistrian University of Athens, Greece

Papapoulos S.E.
Professor Emeritus, Leiden Center for Bone Quality, Leiden University Medical Center, The Netherlands, Consultant, Department of Musculoskeletal Diseases, Division of Rheumatology, Genoa Health Trust, Italy

Paschalis E.P.
Senior Scientist, Ludwig Boltzmann Institute of Osteology, Austria

Polyzos S.
Assistant Professor of Pharmacology, Medical Research Methodology, School of Medicine, Aristotle University of Thessaloniki, Greece

R

Reid I.
Professor, Faculty of Medical and Health Sciences University of Auckland, Auckland, New Zealand

S

Stathopoulos K.
Orthopaedic Surgeon, Senior Scientific Associate University of Athens, School of Medicine, Postgraduate Course on Bone Metabolic Diseases, Athens, Greece

T

Terpos E.
Professor of Hematology, Plasma Cell Dyscrasias Unit, Department of Clinical Therapeutics, School of Medicine, National and Kapodistrian University of Athens Alexandra General Hospital, Greece

Tournis S.
Research Fellow, Laboratory for Research of the Musculoskeletal System Th. Garofalidis, Medical School, National and Kapodistrian University of Athens, KAT Hospital, Athens, Greece

Trovas G.
Endocrinologist, Laboratory for the Research of Musculoskeletal System Th. Garofalodis, Medical School, National and Kapodistrian University of Athens, Greece

Tsourdi E.
Endocrinologist, University Clinic Dresden Medical Center, Dresden, Germany

V

Van der Eerden B.C.J.
Assistant Professor, Groupleader Internal Medicine Calcium and Bone Metabolism Erasmus University Medical Center, Department of Internal Medicine Rotterdam, The Netherlands

Van Rietbergen B.
Associate Professor of Orthopaedic Biomechanics, Department of Biomedical Engineering, Eindhoven University of Technology, Eindhoven, The Netherlands

W

Winter E.-M.
Endocrinologist, Leiden University Medical Center for Bone Quality: Department of Internal Medicine, The Netherlands

Chairs - Speakers Index / Ευρετήριο Ομιλητών & Προέδρων

Y

Yavropoulou M.
Endocrinologist, Endocrinology Division, 1st Propaedeutic Department of Internal Medicine, National and Kapodistrian University of Athens, Laiko General Hospital of Athens, Greece

Yovos I.
Emeritus Professor of Medicine - Endocrinology, Aristotle University of Thessaloniki, Greece

Z

Zillikens M.C.
Professor, Internist-Endocrinologist, Head of Bone Center, Department of Internal Medicine, Erasmus University Medical Center Rotterdam, The Netherlands

Θράκης 2, 151 24 Μαρούσι
Τηλ./FAX: 210-6128606
E-mail: eemmo@otenet.gr

Οδηγίες προς τους συγγραφείς

Το «ΟΣΤΟΥΝ», επιστημονικό όργανο της Ελληνικής Εταιρείας Μελέτης Μεταβολισμού των Οστών, έχει σκοπό την ενημέρωση και επιμόρφωση των ιατρών πάνω στον τομέα της φυσιολογίας και παθολογίας του μυοσκελετικού συστήματος και ειδικότερα των Μεταβολικών Νοσημάτων των Οστών. Για την πραγμάτωση του σκοπού αυτού το περιοδικό δημοσιεύει:

- Άρθρα του εκδότη.
- Ξένες δημοσιεύσεις.
- Ανασκοπήσεις. Ολοκληρωμένες αναλύσεις ιατρικών θεμάτων στις οποίες θα υπογραμμίζονται ιδιαίτερα οι σύγχρονες απόψεις.
- Πρωτότυπες εργασίες.
- Ενδιαφέρουσες περιπτώσεις (Case Reports).
- Γράμματα προς τον Εκδότη.
- Επίκαιρα θέματα. Σύντομη περιγραφή των τελευταίων απόψεων σε συγκεκριμένο θέμα.
- Ενδιαφέρουσες δημοσιεύσεις.
- Σεμινάρια, στρογγύλες τράπεζες, συμπόσια.

ΕΙΔΗ ΑΡΘΡΩΝ ΠΟΥ ΔΗΜΟΣΙΕΥΟΝΤΑΙ ΣΤΟ ΠΕΡΙΟΔΙΚΟ

Άρθρα προς τον Εκδότη: Γράφονται από τον διευθυντή σύνταξης του περιοδικού ή από άλλο πρόσωπο μετά από σχετική ανάθεση από τον διευθυντής σύνταξης ή τον πρόεδρο του ΔΣ της Ελληνικής Εταιρείας Μελέτης Μεταβολισμού των Οστών. Δεν πρέπει να υπερβαίνουν τις δυο σελίδες

Ξένες δημοσιεύσεις: Γράφονται από ξένο, διαπρεπή συγγραφέα κατόπιν συνεννοήσεως με τη συντακτική επιτροπή. Μεταφράζονται με ευθύνη της συντακτικής επιτροπής.

Ανασκοπήσεις: Ολοκληρωμένες αναλύσεις ιατρικών θεμάτων με έμφαση στις σύγχρονες απόψεις. Γράφονται κατά προτίμηση από έναν/μια συγγραφέα, κατ εξαίρεση από δύο ή τρείς, ιδίως όταν το θέμα απαιτεί συγγραφείς διαφόρων ειδικοτήτων. **Η έκταση του άρθρου πρέπει να είναι 15-20 σελίδες στις οποίες περιλαμβάνονται η εικονογράφηση, η βιβλιογραφία και στα Ελληνικά και Αγγλικά , η περίληψη, οι λέξεις κλειδιά, οι συγγραφείς και ο τίτλος του άρθρου.**

Πρωτότυπες εργασίες: έχουν κλινικό ή εργαστηριακό ή κλινικοεργαστηριακό περιεχόμενο. Το κείμενο περιλαμβάνει βραχεία εισαγωγή, στην οποία αναφέρεται ο σκοπός της εργασίας, περιγραφή του υλικού και των μεθόδων, έκθεση των αποτελεσμάτων, συζήτηση στην οποία περιλαμβάνονται και τα τελικά συμπεράσματα. Η περίληψη πρέπει να είναι αυτοτελής και να περιέχει το σκοπό της εργασίας, τις βασικές μεθόδους που χρησιμοποιήθηκαν, τα κύρια ευρήματα και τα σημαντικότερα συμπεράσματα. **Η έκταση του άρθρου δεν πρέπει να υπερβαίνει τις 14 σελίδες, μαζί με τη βιβλιογραφία.**

Ενδιαφέρουσες περιπτώσεις (Case Reports): Σε αυτές παρουσιάζονται ενδιαφέρουσες ή σπάνιες περιπτώσεις με κλινικές εκδηλώσεις που περιγράφονται για πρώτη φορά, ή περιπτώσεις με ιδιαίτερη επιστημονική αξία, καθώς και περιπτώσεις στις οποίες χρησιμοποιήθηκαν νέες διαγνωστικές ή θεραπευτικές μέθοδοι , ή διατυπώνονται νέες απόψεις για την παθογένεια τους. Πρέπει να έχουν έκταση έως 5 σελίδες και περιλαμβάνουν σύντομη εισαγωγή, περιγραφή της περίπτωσης, πίνακες ή εικόνες (έως 4), τα κύρια εργαστηριακά ευρήματα, βραχύ σχόλιο- συζήτηση, και περιορισμένη βιβλιογραφία (10-15 παραπομπές).

Γράμματα προς τον Εκδότη: Σε αυτά περιγράφονται κρίσεις για δημοσιευμένα άρθρα (στο περιοδικό ΟΣΤΟΥΝ ή ακόμα και σε άλλα επιστημονικά περιοδικά) παρατηρήσεις για ανεπιθύμητες ενέργειες φαρμάκων, κρίσεις για το περιοδικό κ.λπ. **Η έκτασή τους δεν υπερβαίνει τις 400 λέξεις. Ο αριθμός των βιβλιογραφικών παραπομπών δεν πρέπει να υπερβαίνει τις 8.**

Επίκαιρα θέματα: Πρόκειται για σύντομα άρθρα 4-5 σελίδων που αποσκοπούν στη περιγραφή των τελευταίων απόψεων σε συγκεκριμένο θέμα.

Ενδιαφέρουσες δημοσιεύσεις: Κατόπιν προσκλήσεως ανατίθεται σε μέλος της εταιρείας να παρουσιάσει τα αποτελέσματα σημαντικών ερευνών, τα οποία έχουν πρόσφατα δημοσιευτεί σε έγκριτα περιοδικά ή ανακοινώθηκαν σε διεθνή συνέδρια.

Σεμινάρια, στρογγύλες τράπεζες, συμπόσια: Περιλήψεις, ενδιαφέρουσες ανακοινώσεις, προγράμματα συνεδρίων.

ΤΡΟΠΟΣ ΥΠΟΒΟΛΗΣ

Όλα τα άρθρα υποβάλλονται στο ηλεκτρονικό ταχυδρομείο της Εταιρείας ostoun@eemmo.gr ως συνημμένα αρχεία (κείμενο, πίνακες, εικόνες).

ΒΑΣΙΚΕΣ ΟΔΗΓΙΕΣ

Η γραμματοσειρά του άρθρου πρέπει να είναι Times New Roman, το μέγεθος της γραμματοσειράς δώδεκα (12) και η απόσταση των σειρών (διάστιχο) πρέπει να είναι 1,5. Η αρίθμηση των σελίδων αρχίζει από τη σελίδα με τον τίτλο. Οι αριθμοί αναγράφονται στο άνω δεξιό μέρος κάθε σελίδας.

Πρώτη σελίδα - Σελίδα του τίτλου: Στη σελίδα αυτή αναγράφονται:

1) ο τίτλος του άρθρου, ο οποίος πρέπει να είναι κατά το δυνατόν σύντομος (όχι περισσότερες από 20 λέξεις) αλλά κατατοπιστικός.
2) το πρώτο όνομα, τα αρχικά του πατρικού και το επίθετο κάθε συγγραφέα.
3) το όνομα των κλινικών, εργαστηρίων, τμημάτων στα οποία πραγματοποιήθηκε η εργασία.
4) το όνομα και η διεύθυνση (φυσική και ηλεκτρονική) και το τηλέφωνο του συγγραφέα που είναι υπεύθυνος για την αλληλογραφία σχετικά με την εργασία.

Δεύτερη σελίδα: Περιέχει την περίληψη στα Ελληνικά και **όρους του ευρετηρίου** (λέξεις κλειδιά): Η περίληψη πρέπει να είναι ουσιαστική και κατατοπιστική και **να μην υπερβαίνει τις 300 λέξεις**. Μετά την περίληψη παρατίθενται 3-10 λέξεις (όροι ή μικρές φράσεις) ευρετηριασμού, απαραίτητες για τη σύνταξη των ευρετηρίων του περιοδικού. Οι λέξεις αυτές πρέπει να αντιστοιχούν στους διεθνείς όρους λεξικογράφησης που χρησιμοποιεί το Index Medicus.

Οι ακόλουθες σελίδες περιέχουν το κείμενο της εργασίας.

Τελευταία σελίδα: περιέχει τον τίτλο και τα ονόματα του/των συγγραφέων, την Περίληψη στην Αγγλική γλώσσα και τους πρόσθετους όρους ευρετηρίου στην ελληνική και αγγλική γλώσσα. Η περίληψη δεν πρέπει να υπερβαίνει τις 300 λέξεις και πρέπει να αναφέρει τον σκοπό της εργασίας, τη βασική μεθοδολογία και τα κύρια ευρήματα και τα κύρια συμπεράσματα. Την αγγλική περίληψη συνοδεύουν οι όροι ευρετηριασμού επίσης στα Αγγλικά.

Ακολουθεί η Βιβλιογραφία (λίστα βιβλιογραφικών αναφορών) και ακλουθούν οι λεζάντες των εικόνων και πινάκων του άρθρου.

ΒΙΒΛΙΟΓΡΑΦΙΑ

Παραδείγματα τρόπου γραφής των βιβλιογραφιών (κατά το σύστημα Vancouver):

Αριθμήστε τις βιβλιογραφικές παραπομπές διαδοχικά, με τη σειρά με την οποία αναφέρονται στο κείμενο. Χρησιμοποιείστε για τις βιβλιογραφίες στο κείμενο, στους πίνακες και στις λεζάντες, αραβικούς αριθμούς σε εκθέτες (1,2,3 κ.λπ.) μετά την τελεία της πρότασης (π.χ.....διαβητικής κετοξέωσης.[1]). Αν μια βιβλιογραφία επαναλαμβάνεται ισχύει ο αριθμός της πρώτης αναφοράς. Όταν σε ένα σημείο του κειμένου χρειάζονται πολλές παραπομπές, τότε αναφέρονται με χρονολογική σειρά.

Οι τίτλοι των περιοδικών πρέπει να γράφονται κατά τον καθιερωμένο τρόπο για κάθε περιοδικό, σε συντομογραφία αν πρόκειται για λέξεις περισσότερες από μία (σύμφωνα με τον Index Medicus), π.χ., Diabet Med. Προκειμένου για βιβλίο θα αναφέρεται το όνομα του συγγραφέα, η χρονολογία εκδόσεως, ο τίτλος, ο εκδοτικός οίκος και η πόλη που εκδόθηκε το βιβλίο.

Η αναφορά σε περιλήψεις συνεδρίων (abstracts), «αδημοσίευτες παρατηρήσεις» (unpublished data), και «προσωπικής επικοινωνίας» (personal communication) θα πρέπει να αποφεύγεται καθώς δε μπορεί να ελεγχθεί η εγκυρότητά τους.). Οι εργασίες οι οποίες έχουν γίνει δεκτές προς δημοσίευση, αλλά δε δημοσιεύτηκαν ακόμη, μπορεί να αναφερθούν στη βιβλιογραφία. Στην περίπτωση αυτή σημειώστε το περιοδικό και τη φράση “in press”- «υπό δημοσίευση» (σε παρένθεση). Η παράθεση των βιβλιογραφικών αναφορών στη λίστα στο τέλος του κειμένου θα πρέπει να είναι όπως ακριβώς αυτές αποδίδονται στο PubMed.

Άρθρα: Τυπικό άρθρο περιοδικού (Γράψτε όλους τους συγγραφείς, εφόσον είναι έξι ή λιγότεροι. Όταν είναι επτά ή περισσότεροι, αναφέρετε μόνο τους πρώτους τρεις και προσθέστε «et al» ή «και συν.» αν πρόκειται για ελληνική δημοσίευση).

Παράδειγμα βιβλιογραφικής αναφοράς σε άρθρο:

Rupp T, Butscheidt S, Vettorazzi E, Oheim R, Barvencik F, Amling M, Rolvien T. High FGF23 levels are associated with impaired trabecular bone microarchitecture in patients with osteoporosis. Osteoporos Int. 2019; May 1. [Epub ahead of print]

Παράδειγμα βιβλιογραφικής αναφοράς σε άρθρο:

Wong RMY, Wong H, Zhang N, Chow SKH, Chau WW, Wang J, Chim YN, Leung KS, Cheung WH. The relationship between sarcopenia and fragility fracture-a systematic review. Osteoporos Int. 2019; 30(3):541-553.

Παράδειγμα βιβλιογραφικής αναφοράς σε βιβλίο:

Mihalko MJ. Amputations of the hip and pelvis. In: Canale TS, Beaty J (Eds). Campbell’s operative orthopaedics. 12th ed. Philadelphia: Mosby. 2013: 651- 658.

Πίνακες: Δακτυλογραφούνται με διπλό διάστημα σε χωριστή σελίδα ο καθένας. Αναφέρονται στο κείμενο και αριθμούνται με αραβικούς αριθμούς. Πρέπει να συνοδεύονται από περιεκτική, σύντομη λεζάντα, ώστε για την κατανόησή τους να μην είναι απαραίτητη η αναφορά του αναγνώστη στο κείμενο.

Εικόνες (σχήματα, φωτογραφίες): Οι εικόνες μπορεί να είναι ασπρόμαυρες ή έγχρωμες και υψηλής ανάλυσης >150 dpi) ώστε να είναι δυνατή η ικανοποιητική απόδοσή τους σε ηλεκτρονική μορφή. Εάν χρησιμοποιηθούν εικόνες ασθενών θα πρέπει τα πρόσωπά τους να μην διακρίνονται, αλλιώς θα πρέπει να υποβληθεί στη Σύνταξη έγγραφη συγκατάθεση του ασθενούς για τη δημοσίευση των φωτογραφιών. Εάν μία φωτογραφία έχει δημοσιευθεί αλλού πρέπει να συνοδεύεται από γραπτή άδεια του εκδότη που έχει το copyright αναδημοσίευσης της φωτογραφίας. Στη λεζάντα της φωτογραφίας θα πρέπει να αναφέρεται η πηγή προέλευσής της. Οι λεζάντες των σχημάτων και των φωτογραφιών δακτυλογραφούνται με διπλό διάστημα, σε ξεχωριστή σελίδα και αριθμούνται με αραβικούς αριθμούς.

ΑΞΙΟΛΟΓΗΣΗ ΓΙΑ ΔΗΜΟΣΙΕΥΣΗ - ΠΝΕΥΜΑΤΙΚΑ ΔΙΚΑΙΩΜΑΤΑ (copyright)

Τα άρθρα που υποβάλλονται στο ΟΣΤΟΥΝ θα αξιολογούνται για δημοσίευση από Επιτροπή Αξιολόγησης και θα δημοσιεύονται εφόσον ισχύουν οι ανωτέρω προϋποθέσεις και εφόσον τα αποτελέσματα ή το ίδιο το κείμενο δεν έχουν δημοσιευθεί και δεν έχουν υποβληθεί για δημοσίευση σε άλλο ελληνικό περιοδικό. Οποιαδήποτε εργασία δημοσιευθεί στο ΟΣΤΟΥΝ δεν μπορεί να αναδημοσιευθεί χωρίς τη γραπτή έγκριση του Διευθυντή Σύνταξης.