

**UNIVERSITY OF MEDICINE AND PHARMACY *CAROL DAVILA* BUCHAREST**

**FACULTY OF MEDICINE**

**CLINICAL DEPARTMENT 5**

**Internal Medicine (Cardiology, Gastroenterology, Hepatology, Rheumatology, Geriatrics, Family Medicine, Occupational Health)**

 **“Sfânta Maria” Clinical Hospital**

**Methods of bone metabolism assessment and therapeutic implications in musculoskeletal pathology
SUMMARY**

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 The thesis entitled "**Methods of bone metabolism assessment and therapeutic implications in musculoskeletal pathology"** is structured in three sections andincludes brief exposure of professional career, teaching skills and scientific research. The work alludes to the most important scientific contributions made after becoming doctor of medicine.

The first part includes identification information, then professional, academic and scientific accomplishments, with separate subsections for each of the areas. The last part includes development directions and relevant personal bibliographic titles.

Education and training:

1981- High School Diploma – “Andrei Şaguna” National College, Braşov, Romania

1988 – MD Degree, University of Medicine and Pharmacy “Carol Davila”, Bucharest, Romania

1994 – National Specialist Certificate in Internal Medicine (after full training)

1997 – National Specialist Certificate in Rheumatology (after full training)

1998 – Certificate of Consultant in Internal Medicine

2002 – Certificate of Consultant in Rheumatology

1998 – 2003: Assistant Professor, Consultant in Internal Medicine and Rheumatology, “Sf. Maria” Hospital, Bucharest, Romania

**From 2003 – Lecturer** at the University of Medicine and Pharmacy „Carol Davila”, Bucharest, **Internal Medicine: d**iagnostic and therapeutical decisions for chronic and emergency cases and teaching students in General Medicine.

**Rheumatology: d**iagnostic and therapeutical decisions for chronic and emergency cases, teaching students in general medicine in daily bed-teaching and course, courses for postgraduate doctors, bone ultrasound measurements, research studies (I participated as a principal investigator in 29 international and 3 national trials and as sub-investigator in 28 international trials).

**National and International Postgraduate Courses**

* I graduated densitometry and ultrasonography courses and became **Certified Clinical Densitometrist (CCD)** San Diego, February 2006 and **Full Faculty of ISCD** – International Society of Clinical Densitometry – from 2006,
* Mediterranean musculosculoscheletal ultrasound course, Naples, 4-6 oct. 2011
* Second International Coures of Musculoscheletal Ultrasound, Bucharest 8-10 martie 2012
* Third International Course of Musculoscheletal Ultrasound – intermediate level, Bucharest 7-9 martie 2013
* 22nd EULAR Sonography Course – advanced Musculoskeletal Ultrasound in Rheumatology 2015
* EULAR on-line introductory ultrasound course sept.2015-may 2016
* Certified in musculoscheletal ultrasonography 5 dec. 2015

 Training projects: author of e-learning module concerning osteoporosis, author of e-learning module concerning abarticular rheumatism, courses for of young rheumatologists (summer school 2015- 2019), courses for medical doctors (osteoporosis, gout, psoriatic arthritis (2 international courses)

* + ISCD Bone Densitometry Course, Banja Niska, Serbia, May 22-23, 2010,
	+ ISCD Bone Densitometry Course, Sofia, Bulgaria, October 11-13, 2011,
	+ ISCD Bone Densitometry Course, Velingrad, Bulgaria, October 3-5, 2012,
	+ International Society for Clinical Densitometry - ISCD Bone Densitometry Course, *Clinicians*, 7 courses between 2006 and 2019,
	+ International Society for Clinical Densitometry - ISCD Bone Densitometry Course, *Technologists*, 3 courses between 2010 and 2012
	+ International Society for Clinical Densitometry - ISCD Course, *DXA Body Composition Analysis,* 2019

 I coordinated graduation thesis of students from the Rheumatology modules including papers with osteoporosis subject (***Difficulty of diagnosis and the evaluation of DXA artifacts in patients with osteoporosis, Osteoporosis in inflammatory rheumatic diseases***).

 I wrote over 30 book chapters and I realized a monograph entitled “***Osteoporosis from* a *multidisciplinary perspective”*** *2017,* and one as a co-author “***Actualities in diagnosis and treatment of osteoporosis”*** *2006*

            I was a member of the research team of an international project grant /Advanced Romanian Mobilization Scheme (ARMS) 2005-2009 FP6 and member of the research team for 3 national grants/projects.

 I contributed to 25 ISI papers (14 as first author, author of correspondence or equal) and as co-author for11 ISI articles.

 One of the main scientific fields of interest is the assessment of bone metabolism and therapeutic implications in pathology. These have been addressed from several perspectives:

1. ***Densitometric and biologic bone mass evaluation in patients with prostate adenocarcinoma and treated by ADT - androgen deprivation therapy***
2. ***Densitometric “whole body” bone mass evaluation in patients with rheumatoid arthritis***
3. ***Densitometric “whole body” adipose tissue evaluation in patients with rheumatoid arthritis***
4. ***A novel quantitative method for estimating bone mineral density using B‑mode ultrasound and radiofrequency signals in patients with rheumatoid arthritis***
5. These have been addressed from the PhD degree thesis “Clinical, osteodensitometric and biologic assessment of bone mineral density in patients with prostate cancer treated with estrogen agonists or antiandrogens”. Osteoporosis was considered as a disease of old women, though it is frequently present also in men. Data from the literature were obtained from studies of osteoporosis in women. There are three main causes of osteoporosis in men: hypogonadism, alcohol abuse, prolonged cortisone therapy. One of the most frequent cancers in men – prostate cancer – has as treatment androgen deprivation (surgical or by using antiandrogen/estrogenic therapy). Osteoporosis develops quickly in that type of patients. This study wants to investigate some aspects of bone metabolism using dual-X-ray absorptiometry (DXA) and calcaneus quantitative ultrasound (QUS) and also to evaluate bone turnover (by determination of osteoprotegerin, osteocalcin and urinary deoxypyridinoline) in a group of patients with prostate cancer treated with androgen deprivation (antiandrogen/estrogenic therapy) and compare the values with those obtained in a control group (group M). I continued the study of this group of patients and I published the paper: ***Osteoporosis and bone metabolism in treatment-naïve primary prostate adenocarcinoma patients.*** REV.CHIM. (Bucharest), 69, No. 5 2018. The objectives of the study were to evaluate bone metabolism in primary prostate cancer (PCa) patients prior to any treatment and to compare estrogens and anti-androgens in terms of bone metabolism. The study prospectively included consecutive patients with primary PCa who were proposed for radical prostatectomy and androgen deprivation therapy (ADT; either estrogens or anti-androgens) and age-matched controls. Bone markers (osteoprotegerin – OPG; osteocalcin; deoxypyridinoline) were measured before treatment and after 6 months. Bone mineral density (BMD) was measured by DXA before treatment and after 12 months. Osteoporosis was found to be prevalent among hormone-naïve PCa patients. Estrogens are associated with an increase of serum OPG, while anti-androgens with a decrease of serum OPG. Irrespective of ADT type, BMD still decreases in primary PCa patients.
6. ***Dual X-Ray Absorptiometry Whole Body Composition of Bone Tissue in Rheumatoid Arthritis - a Cross-Sectional Study. Maedica (Buchar). 2015 Mar;10(1):19-26. PubMed PMID: 26225145; PubMed Central PMCID: PMC4496760.***

 Previous studies of bone tissue in rheumatoid arthritis (RA) using dual X-ray absorptiometry (DXA) concentrated on regions of interest that were used to diagnose osteoporosis. This study was cross-sectionally aimed to compare the whole body bone tissue (wbBT) of RA patients with healthy subjects and to identify the RA variables which significantly predict wbBT. **A**ll RA patients and controls underwent clinical examination, laboratory tests and whole body DXA composition, which recorded total and regional bone indices.Compared to controls, RA patients had significantly lower whole body and regional bone mass Disease duration, C-reactive protein and inflammation, radiographic damage, disease activity scores are significantly correlated/associated with lower wbBT. Clinical structural damage is associated with lower wbBT and it can significantly predict them, while glucocorticoid treatment,

even in low doses, was associated with lower wbBT percent. Treatment with biologics was associated with a lower rate of whole body osteoporosis.The main associated factors with the generalized bone loss in female RA patients are disease duration and disease activity. Clinical structural damage is the most powerful predictor of the whole body bone loss. These results suggest a general disturbance of skeletal bone metabolism in RA and could explain a greater risk of fragility fractures of non-central sites (e.g. ribs, tibia, ankles etc.) compared to post-menopause osteoporosis.

1. ***Dual X-ray Absorptiometry Whole Body Composition of Adipose Tissue in Rheumatoid Arthritis. Rom J Intern Med. 2015 Jul-Sep;53(3):237-47. PubMed PMID: 26710499*.** Rheumatoid arthritis may influence not only abdominal fat, but also whole body adiposity, since it is associated with chronic inflammation and disability. The study aims to evaluate the whole body adiposity of RA patients and to assess potential influences of disease specific measures. We included Caucasian postmenopausal female RA patients and age-matched postmenopausal female controls. Each subject underwent on the same day clinical examination, laboratory tests, whole body dual X-ray absorptiometry (DXA) composition and physical activity estimation using a self-administered questionnaire. A total of 107 RA women and 104 matched controls were included. Compared to controls, the RA group had less physical activity and a higher prevalence of normal weight obesity. Overfat RA women had a significantly higher toll of inflammation, disease activity, glucocorticoid treatment and sedentary behavior. RA women with inflammation, glucocorticoid treatment and higher disease activity class had higher whole body and trunk adipose tissue indices and higher prevalence of overfat status. Glucocorticoid treatment, inflammation, disease duration and severity correlated with whole body adipose tissue and significantly predicted high adiposity content and overfat phenotypes. RA disease duration and severity are associated with higher whole body and regional adiposity. Low-dose glucocorticoid treatment seems to contribute to adiposity gain and redistribution. Clinicians may need to assess body composition and physical activity in RA patients in order to fully manage cardiovascular outcomes and quality of life.
2. ***A novel quantitative method for estimating bone mineral density using B‑mode ultrasound and radiofrequency signals‑a pilot study on patients with rheumatoid arthritis – Experimental ant Therapeutic Medicine.* *July 2019 DOI: 10.3892/etm.2019.7746***The objective was to observe if an innovative quantitative ultrasound (QUS) technique, which combines B mode ultrasound and radiofrequency signals (REMS - Radiofrequency Echographic Multi Spectrometry), is reliable compared to previous dual-energy X-ray absorptiometry (DXA) results in typical Romanian patients. The study prospectively included unscreened post-menopausal women with rheumatoid arthritis (RA) and age-matched healthy controls. Bone mineral density (BMD) measurements were done with an EchoS machine (Echolight®) which combines B mode ultrasound and radiofrequency signals. Non-normally distributed continuous variables are reported as “median (interquartile range)”. The study included 106 RA patients 119 controls. RA patients had significantly less weight and lower body mass index (BMI) and basal metabolic rate (BMR) than controls, although the prevalence of obesity and body fat differed insignificantly. RA patients had significantly lower spine and hip BMD, higher fracture risks and higher prevalence of osteoporosis. RA patients with osteoporosis, compared to non-osteoporosis RA patients, were significantly older and with a longer menopause duration, but they had significantly lower BMI, body fat, obesity prevalence and BMR. Among both controls and RA patients, median spine and hip BMD were significantly higher as BMI increased from under-weight to obesity. In conclusion, osteoporosis is prevalent among RA patients, as a part of a more complex of body mass composition transformation, involving BMI and fat mass. The new QUS scanning technique replicates the findings of the established DXA measurements of BMD and is potentially suitable for wide population screening of osteoporosis.

 **Other research was realized with the collaboration of**  “Cantacuzino’’ National Medico‑Military Institute for Research and Development and was published in Experimental and Therapeutic Medicine 17.5 (2019): 3465-3476 - ***Usefulness of complex bacteriological and serological analysis in patients with spondyloarthritis*** Spondyloarthritis (SpA) is a group of associated chronic systemic inflammatory immune‑mediated rheumatic diseases affecting axial and peripheral joints and entheses. The aim of the study was to identify what param­eters are useful to determine in order to better understand the correlation between the disease activity/severity and the microbiological results/immune status against intestinal and/or urogenital pathogens. Microorganisms known to trigger SpA, including *Klebsiella spp., Yersinia spp., Salmonella spp., Campylobacter spp*. and *Chlamydia spp.*, were analyzed in various specimens (stool, urine, synovial fluid and serum) collected from 27 randomly selected SpA patients and 26 healthy controls using a combined direct and indirect approach relying on conventional culture technique and nucleic acid‑based assays together with serological testing by ELISA. Although *Escherichia coli* derived from phylogroup A prevailed in the gut microflora of the patients and controls, differences were observed regarding the representatives of the other phylogroups with a higher prevalence of *E.coli* members of phylogenetic group B1 in the stool specimens of patients. Antibodies against the targeted species were detected in SpA patients and controls, and the serological profiles of the former were more diverse and complex. In conclusion, the detection of anti‑bacterial antibodies combined with other specific labora­tory investigations should be more extensively used to monitor SpA patients in association with their symptoms and in order to determine and administer more effective therapeutics.

***Directions of future career development on research, teaching activity and health care***

 We must aim to increase the quality of the didactic process at the university and postuniversity level. Various didactic activities, including the organization of DXA lectures for registrars and consultants for the proper DEXA technique and image evaluation is an important point in development.

I want to continue in my future research activity the two main fields of interest: osteoporosis and microbiota in rheumatic diseases. It is important to increase the clinical database with patients with rheumatologic diseases that are assessed for osteoporosis and fracture risk (we want to address patients with ankylosing spondylitis, systemic lupus erythematosus, systemic sclerosis, polymyositis, psoriatic arthritis/psoriasis, diabetes mellitus). We will try to assess bone mass with the new quantitative ultrasound (QUS) technique and implement trabecular bone score (TBS) for the fracture risk in these patients. We aim to have a multidisciplinary approach, with qualified research team. We want to continue the collaboration with “Cantacuzino’’ National Medico‑Military Institute for Research and Development

 In the end the there is an extremely important need for communication and greater visibility, with increased number of studies and scientific papers with impact factor.