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DEFINING SARCOPENIA: THE IMPACT OF DIFFERENT DIAGNOSTIC CRITERIA ON THE PREVALENCE OF SARCOPENIA IN A LARGE MIDDLE AGED COHORT. A.Y. Bijlsma, C.G.M. Meskers, C.H.Y. Ling, S.E. Kurrle, I.D. Cameron, R.G.J. Westendorp, A.B. Maier *(Leiden, The Netherlands)*

Introduction: Low muscle mass at older age is an increasing problem in our ageing society. Annual loss of muscle mass has been reported as 1-2% from the age of 50 years onwards and it may be over 50% among those aged 80 years and older when compared to muscle mass in younger adults. Decline of muscle mass implies decline of muscle strength amongst others. Reduced handgrip strength was found to be associated with functional impairments, increased morbidity and mortality. Since the coining of the term "sarcopenia", a variety of definitions using different diagnostic criteria have been formulated and applied, in absence of a general consensus. Little is known about the degree of agreement between the diagnostic criteria and their effects on estimates of the prevalence of sarcopenia, which appears to vary extremely between different cohorts ranging from 7 to over 50% in the elderly. The use of different diagnostic criteria may lead to different conclusions and may have different implications for treatment. Objectives: To the best of our knowledge, we are the first to assess the degree of agreement and the effect on estimates of the prevalence of sarcopenia according to commonly used diagnostic criteria in one cohort. Furthermore, we assessed the degree of concordance within individuals using the different criteria. By this, we aim to show the impact of the failure to reach a definition of sarcopenia. Material and methods: Body composition values as measured by bioimpedance analysis (BIA) and handgrip strength measurements were obtained in 654 subjects (329 women and 325 men) of the Leiden Longevity Study (LLS). The LLS consists of middle-aged offspring of nonagenarian Caucasian siblings together with their partners, representatives of the general population. We investigated the prevalence of sarcopenia, stratified by gender, emerging from seven diagnostic criteria described in the literature. Definitions including either muscle mass or handgrip strength were used and muscle mass had to be measured by BIA or dual-energy x-ray absorptiometry. Diagnostic criteria differed regarding correction factors and reference populations. Applied correction factors included height, body mass and a combination of body height and body fat. Reference populations differed regarding age and ethnicity. Additionally, the prevalence of sarcopenia was analyzed in age categories (below 60 years, 60-69 years and 70 years and above). Finally, the degree of concordance within individuals applying the diagnostic criteria was assessed. Results: The mean age of the subjects was 61.8 years and 64.5 years and mean whole body lean mass 43.7 kg and 59.6 kg for females and males respectively. The prevalence of sarcopenia differed widely using the different diagnostic criteria for sarcopenia. In males, the prevalence ranged from 0% to 28.6% in the lowest age category, from 0% to 17.7% in the middle and from 0% to 19.4% in the highest age category. In females the prevalence ranged from 0% to 18.8% (lowest age category), 0% to 21.2% (middle age category) and 0 to 19.4% (highest age category). Only two subjects (0.3%) were identified as sarcopenic according to all diagnostic criteria that marked prevalence above 0%. Discussion: In this large middle aged Dutch cohort, the prevalence of sarcopenia varied widely when different diagnostic criteria were applied. Furthermore, no increase in the prevalence of sarcopenia with increasing age was found. Therefore, studies using different diagnostic criteria are not comparable. Regarding sarcopenia, the question arises as to which aspect of muscle function is represented by the term. Besides the production of force, muscle tissue is also an important regulator of biological processes. For instance, as a protein store, it provides a homeostatic reserve to recover from disease. Furthermore, skeletal muscle has been identified as the major tissue involved in glucose metabolism, accounting for approximately 75% of whole-body insulin-stimulated uptake. Muscle strength is not only determined by the amount of muscle tissue, but also by the quality of the force producing proteins and the connective tissue transmitting the generated force to the bones, the muscle energy supply and neural control. To circumvent the confusion that may arise from intermingling underlying pathophysiological processes and clinical outcomes, we suggest to define sarcopenia in a simple way as "low muscle mass". Regarding the diagnostic criteria it seems unavoidable to compare subjects to young reference populations that are comparable in ethnicity. Conclusion: The prevalence of sarcopenia varies widely depending on diagnostic criteria. It is necessary to reach a consensus definition in order to make studies comparable and for implementation in clinical care. Defining sarcopenia as "low muscle mass" keeps the terminology clear and does justice to the multifunctionality of muscle and the complex interrelationships with other factors that are responsible for its function.

REPORT OF THE EUROPEAN WORKING GROUP ON SARCOPENIA IN OLDER PEOPLE. J.-P. Michel, J.-P. Baeyens, J. Bauer, Y. Boirie, T. Cederholm, F. Landi, F.C. Martin, Y. Rolland, S.M. Schneider, E. Topinkova, M. Vandewoude, M. Zamboni, A.J. Cruz-Jentoft *(Genève, Switzerland)*

Introduction: The objectives of the European Working Group on Sarcopenia in Older People (EWGSOP) were to propose a working definition of sarcopenia, and reviews techniques for measuring variables of sarcopenia. Objectives: This EWGSOP paper proposes guidelines for use of these tools as a way to identify sarcopenia and evaluate treatment effectiveness, and offers advice about which tools may be best-suited for clinical practice and for research studies. Material and methods: Several European scientific organizations working in nutrition and geriatric medicine created a joint European Working Group on Sarcopenia in Older People (EWGSOP). Results: This final EWGSOP document offers a working definition of sarcopenia, and reviews techniques for measuring variables of sarcopenia. Discussion: Further, examples of currently-used cut points for the diagnosis of sarcopenia are discussed. Based on increased awareness of sarcopenia in older people and widespread use of tools for screening and assessment, the ultimate goal is to identify dietary strategies, lifestyle changes, and treatments that can prevent or delay the onset of sarcopenia. Conclusion: The testing of the proposed tools is now in progress using a multicentric European prospective study.

ANALYSIS OF MOLECULAR MECHANISMS INVOLVED IN AGE-RELATED MUSCLE MASS DECREASE: A STUDY ON BIOPSIES OF MUSCLE VASTUS LATERALIS FROM PATIENTS OF DIFFERENT AGE. M. Conte, C. Lanzarini, L. Bucci, G. Trisolino, G. Bracci, E. Martucci, M. Capri, S. Salvioli, M.V. Narici, G. Butler-Browne, C. Franceschi *(Bologne, Italy)*

Introduction: Aging is a complex process characterized by changes in body composition, in particular with a relative decline of muscle mass and strength and with an associated increase in fat mass. This decline is termed sarcopenia and represents an important risk factor for disability, loss of autonomy, morbidity and mortality in the elderly. Many factors are involved in the etiology of sarcopenia, among which key-players are represented by physical inactivity (muscle disuse), malnutrition, increased level of pro-inflammatory cytokines such as IL-6 and tumor necrosis factor alpha, production of free radicals and decrease in aerobic energetic metabolism in mitochondria and hormonal changes (age-dependent decline of GH/IGF-1 promotes loss of muscle mass). However, the relationships between physical activity, aging and the molecular mechanisms of sarcopenia remain unclear. Many studies indicate that several molecular signalling pathways are involved in the development of sarcopenia, among which the IGF-1/p53 pathway seems to be crucial and both p53 and IGF-1 are affected by inflammation. Objectives: In the present study, we hypothesized that chronic inflammation, a condition typical of old age, impacts on sarcopenia through the IGF-1/p53 pathway. To verify this hypothesis, in the framework of the ongoing EU 7th Program Project MYOAGE. Understanding data from patients aged 20 to over 80 years, undergoing programmed hip surgery. The study obtained ethical clearance by the Ethics Committees of the S. Orsola Hospital and IOR, Bologna, Italy. Material and methods: Upon obtaining the informed consent from each patient, we collected a comprehensive Case Report Form (CRF) including data on life style (physical activity, diet, smoking habits and alcohol consumption), anthropometric measures (height, mass, BMI, thigh length and width) and clinical history. Hematological parameters, quadriceps strength, and muscle thickness measured by ultrasound were also assessed. Muscle biopsy from vastus lateralis muscle samples were collected and stored. On muscle biopsies, we measured the expression of some key genes involved IGF-1/p53 loop, such as IGF-1, p53, AKT, PTEN, MDM2, IGF-BP3 by Real time RT-PCR technique; expression of NF-kappaB and Mortalin (GRP75) as well as activation of p53 by Western blotting were also assessed. All these results were analyzed in comparison with CRF data to understand the correlation between aging, inflammation and loss of muscle mass and strength and to identify potential biological markers of sarcopenia. Further investigations will regard the balance between protein synthesis and degradation analyzed by the expression analysis of genes involved in the initiation step of mRNA translation. Results: The expression of genes such as IGF-1 and AKT seems to decrease with aging, with a gender difference (males have higher levels than females). Other genes such as p53 and its downstream IGF-BP3 and PTEN seem to be affected by gender in old people, being more expressed in women than men. Phosphorylation of p53 at serine 20 and 46 is necessary for its stabilization and activation. Western blot analysis indicated that these modifications are particularly evident in old subjects (60-80 years old) as compared with young people (30-40 years old) and very old people (>80 years old). A similar result is found when analyzing Mortalin expression, which appears to be strongly activated in the same group of subjects. Analysis of the expression of NF-kappaB subunit p65 revealed that it is mostly present in patients

belonging to group of subjects aged 60-80 years. Discussion: It is well known that NF-kappaB is the key regulator of inflammation that represents one of the major risk factor characterizing the aging process and underlying many aging-related diseases, such as sarcopenia. Sarcopenia is indeed considered an inflammation-based phenomenon driven by elevated levels of IL-6 and up-regulated by NF-kappaB. On the basis of our data it can be suggested that the patients with the higher level of inflammation is that of 60-80 years of age. These data shall be confirmed with other measurements such as the assessment proinflammatory cytokines levels. IGF-1 is a direct candidate to protect against muscle weakness. Literature data demonstrate that IGF-1 has a strong feed-back loop with p53, a well-known inducer of apoptosis and cell senescence. For these reasons, it is important to evaluate the effects that these factors could have on sarcopenia. Our results revealed that patients aged 60-80 years show a strong expression and stabilization of p53 suggesting a major susceptibility of this age category to inhibition of IGF-1 axis and consequently loss of muscle mass and strength. This hypothesis is further supported by the analysis of Mortalin, a stress protein belonging to HSP70 family, which is particularly expressed in the 60-80 years patients, thus indicating a strong activation of stress response in these subjects. Conclusion: These preliminary results suggest that the IGF-1/p53 pathway and inflammation play a crucial role in the onset of sarcopenia in the elderly. As in many other studies on human aging and longevity, we observed a non monotonic trend of gene expression, being the age group of 60-80 years the one with more pronounced alterations with respect to young people, while the very old one (>80 years) seems to be more preserved. It is not clear whether this is a positive remodeling towards an efficient response to stress and inflammation or rather a loss of the capacity to cope with these stresses. Further studies are still ongoing to extend and confirm these observations.

ACCELERATED SKELETAL MUSCLE AGING IS A MOLECULAR SIGNATURE IN OPMD. A. Venema, Y. Anvar, P.A.C. Hoen, S. van der Maarel, V. Raz *(Leiden, The Netherlands)*

Introduction: Muscle weakness is a common clinical feature in neuromuscular diseases and aging. The molecular mechanisms that are associated with muscle weakness are poorly understood. Oculopharyngeal muscular dystrophy (OPMD) is a dominant late-onset muscle disorder. Patients with OPMD carry an expansion mutation that leads to a poly-alanine expansion in PABPN1. Although the mutant protein is ubiquitously expressed, symptoms appear above the age of 40. The molecular mechanisms that underlie OPMD late onset and progression OPMD are mostly unknown. Objectives: We set to identify the molecular mechanisms that are associated with onset and progressiveness in affected muscles. Materials and methods: Whole genome expression profiling was performed on RNA from quadriceps of mutant PABPN1 carriers, which were subgrouped into presymptomatic and symptomatic (N=8). The dataset was complemented with age-matching controls (N=38).Three statistical analyses were preformed to indentify deregulated genes and molecular pathways. Results: We identified a molecular switch in muscle aging around age of 42, where aging pathways became deregulated. We found that transcriptome changes in OPMD are significantly similar to changes observed in normal ageing of skeletal muscles, but they occur at an earlier age than in healthy controls. Under 42 years only minor transcriptome changes were found in pre-symptomatic and in OPMD. The ubiquitin-proteasome system and protein aggregation are ranked with the highest association of deregulation in OPMD and in muscle aging. Discussion: We suggest that in OPMD muscle weakness onset is triggered by naturally occurring aging-associated transcriptional changes. We indicate specific gene targets as molecular regulators for muscle weakness. Conclusion: Our study revealed significant molecular similarities between OPMD and muscle aging with a temporal shift. Since onset of muscle weakness in OPMD is relatively synchronized as compared with healthy individuals, we suggest that muscle weakness in OPMD can be used as a model to study muscle weakness.

ANIMAL MODEL FOR AGRIN-DEPENDENT SARCOPENIA: THE SARCO MOUSE. J.W. Vrijbloed, S. Hettwer, S. Kucsera, R. G. Fariello *(Schlieren, Switzerland)*

Introduction: Sarcopenia is an emerging medical problem and imposing an increasing burden to health care costs in the Western world. The causes of sarcopenia are subject of intensive research but largely poorly understood. An essential prerequisite to properly address diagnosis and treatment of pathological conditions is the availability of suitable animal models. These models should reproduce the pivotal behavioural and pathological features of the condition they are supposed to mimic. Human sarcopenia is characterized by loss of muscle mass and strength causing altered gait and weakness. It is accompanied by pathological changes in the muscle, including reduction in number and variation of size of the muscle fibers, type II fiber atrophy, and the occurrence of hybrid fibers. We have recently found that levels of a c-terminal agrin fragment (CAF), exclusively generated from agrin's cleavage by neurotrypsin (CAF is absent in neurotrypsin KO mice), are significantly augmented in more than 1/3 of the Sarcopenia patients. Agrin, a synaptically located protein, is a key player during initial formation and maintenance of neuromuscular junctions (NMJs) by inducing acetylcholine receptor (AChR) assembly and aggregation. Once cleaved by neurotrypsin agrin is inactive leading to a dispersal of NMJs. In the cleavage process, a soluble, 22 kD CAF fragment is freed and circulates in body fluids. Objectives: To: 1.) provide an animal model of sarcopenia for advancing knowledge of the pathogenic mechanisms and that is suitable for testing potential therapeutic interventions; 2.) test the assumption that there is an agrin-dependent form of sarcopenia casually linked to an unbalance of the agrin/neurotrypsin system. Material and methods: The hsnt transgenic mouse (termed SARCO) was generated as described by Bolliger et al. 2010. (J Cell Sci 123:3944-3955). In brief, the cDNA of human neurotrypsin was inserted downstream of a loxP-STOP-loxP cassette consisting of a false ATG codon, a splice donor site and a SV40 poly-A signal into a pBS302 plasmid. This construct was then cloned into the Thy-1.2 expression cassette excised and the resulting fragment was used for transgenesis by injection into fertilized mouse oocytes from hybrid donor mice (C57/B6 x C3A). To achieve germline transmission this conditional hNT transgenic line was crossed with a CMV-Cre deleter line. The resulting mice harbouring a constitutively active hsnt insert were backcrossed for 10 generation to C57/Bl6 mice. The neurotrypsin gene was shown to be inserted as a single copy and did not insert into any open reading frame. Results: The generated transgenic mice (termed SARCO mice) are fertile and breed normally. As expected CAF levels in SARCO mice are elevated by a factor of 1.5 compared to the WT. Furthermore they share all the essential pathological features of sarcopenia patients which include reduction of muscle mass, irregular fiber size with central nuclei, increase in hybrid fibers, selective fiber type loss and altered morphology of the NMJs. In addition, SARCO mice show significant motor impairment, exhibit a crooked posture with a pronounced kyphosis which became obvious around day 30 (P30) and aggravated with aging. These phenotypes prefigure a pathologically altered neuromuscular system. Starting at postnatal day 8 (P8), SARCO mice lose weight in comparison to their wild type (WT) littermates. Juvenile SARCO mice exhibited a weight loss of 20 % at P30 with partial recovery in adulthood (P60). Senescent SARCO mice of P480 have only approximately 70 % of WT weight. Discussion: The neurotrypsin-overexpressing transgenic mice generated in this study were shown to represent an accurate model for agrin-dependent sarcopenia. They show all the essential pathological features of sarcopenia patients. In comparison to the widely used aged rats, they have several advantages, which are: sarcopenia-related effects can be seen within days (rather than months) making the use of SARCO mice more cost and time-effective; the signal (the sarcopenic phenotype) is much stronger than in aged rats and can be more easily distinguished from healthy mice or rats, respectively. At the onset of the sarcopenia symptoms the mice have a body weight of approximately 10 grams which reduces the amounts of compound needed for testing, often a critical parameter in the early discovery phase, when the model is used to test new potential treatments. Taken together, the SARCO mouse is a valuable tool to study agrin-dependent sarcopenia and to test possible treatments in vivo. Conclusion: The SARCO mouse represents a valuable model for Sarcopenia and offer an ideal in vivo approach to test and evaluate possible pharmaceutical treatments such as small-molecule inhibitors of neurotrypsin in order to significantly improve the muscular performance of sarcopenic patients thereby ameliorating their quality of life.

TEMPORAL RELATIONSHIP BETWEEN COGNITIVE PERFORMANCE AND MUSCLE STRENGTH IN OLDEST OLD PEOPLE. D.G. Taekema, C.H.Y. Ling, S. Kurrle, I.D. Cameron, C.G. Meskers, G.J. Blauw, R.G.J. Westendorp, A.J.M. de Craen, A.B. Maier *(Leiden, The Netherlands)*

Introduction: Cognitive decline and sarcopenia are highly prevalent health problems in elderly and are mutually affecting and potentiating each other. Both predict detrimental outcomes in elderly, such as functional impairment and mortality.The temporal relationship between decline of muscle strength and cognitive performance is still unclear. We hypothesized that cognitive decline precedes muscle weakness based on the knowledge that motor skill learning and motor output depend on activity of frontal and parietal brain regions. Objectives: To study the temporal relationship between cognitive performance and muscle strength in a population based cohort of oldest old people. Material and methods: Leiden 85-plus Study, a prospective population based four year follow-up study of 555 subjects, all aged 85 years at baseline. A neuropsychological test battery was used to assess global cognitive performance attention, processing speed and memory. Subjects were followed up over a four year period with repeated cognitive tests. Handgrip strength was measured at age 85 and 89 years as a proxy for muscle strength. Cross-sectional and prospective associations between cognitive performance and handgrip strength were analyzed by linear regression analysis adjusted for anthropometry, income, education, comorbidity, and physical activity. Results: At age 85 and 89 years, better cognitive performance was associated with higher handgrip strength (all, $P < .03$), except for attention. In the longitudinal analysis, better cognitive performance at age 85 years was associated with slower decline in handgrip strength in the following four years after adjustment for possible confounders (all, $P < .01$). There was no longitudinal association between baseline handgrip strength and cognitive decline (all, $P > .10$), except for global cognitive performance ($P = .007$). Discussion: Baseline cognitive performance was associated with subsequent change in handgrip strength, whereas baseline handgrip strength was not associated with cognitive decline. It seems likely that in elderly subjects cognitive control of movement and muscle strength are affected by cerebral neuropathology. Conclusion: Our results suggest that cognitive decline precedes the onset of muscle weakness and not vice versa. Cognitive decline in elderly subjects should make clinicians vigilant for muscle weakness in the near future. Further clinical research is needed to assess suitable interventions.

THE PROGNOSTIC VALUE OF MUSCLE STRENGTH IN SPORADIC AND FAMILIAL LONGEVITY. C.H.Y. Ling, D. Taekema, A.J.M. de Craen, R.G.J. Westendorp, A.B. Maier *(Leiden, The Netherlands)*

Introduction: Low muscle strength has been shown to be associated with increased morbidity and mortality in diverse samples of middle-aged and elderly people. However, the oldest old population (i.e., over 85 years) is underrepresented in such studies and the value of muscle strength as marker of exceptional familial human longevity has not been previously explored. We postulated that the genetic influence on exceptional survival might also be involved in muscle strength determination pathways. Objectives: Our objective was to assess the association between muscle strength and mortality in the oldest old population, representing sporadic longevity and to assess muscle strength and mass in a sample of middle-aged adults who are genetically enriched for exceptional familial

longevity and comparing them to age and environmentally matched controls. Material and methods: To study the association between muscle strength and sporadic longevity we included 555 participants (65% women) from the Leiden 85-plus Study, a prospective population-based study of all 85-year-old inhabitants of Leiden, Netherlands. We measured handgrip strength of participants at baseline and again at age 89 years. We collected baseline data on comorbidities, functional status, levels of physical activity and adjusted for potential confounders. All participants were followed for survival. To investigate the value of muscle strength as marker for exceptional familial longevity we included 336 offspring of nonagenarian siblings from the Leiden Longevity Study who were enriched for heritable exceptional longevity, and 336 of their partners were used as controls. The Leiden Longevity Study is a prospective follow up study of long-living nonagenarian sibling pairs together with their offspring and their partners. Though of the same chronological age these offspring have previously been observed to be of a younger biological age than their partners. This is reflected by their lower mortality, beneficial glucose and lipid metabolism, preservation of insulin sensitivity and resistance to cellular stress. Handgrip strength was used as a proxy for overall muscle strength. Results: During a follow-up period of 9.5 years (range 8.5-10.5 years), 444 (80%) participants died. Risk for all-cause mortality was elevated among participants in the lowest tertile of handgrip strength at age 85 years (hazard ratio [HR] 1.35, 95% confidence interval [CI] 1.00-1.82, p = 0.047) and the lowest two tertiles of handgrip strength at age 89 years (HR 2.04, CI 1.24-3.35, p = 0.005 and HR 1.73, CI 1.11-2.70, p = 0.016). We also observed significantly increased mortality among participants in the tertile with the highest relative loss of handgrip strength over four years (HR 1.72, CI 1.07-2.77, p = 0.026). No significant difference in handgrip strength was seen between the offspring of the nonagenarian siblings and their partners after adjustment for potential confounders including body composition, sum score of comorbidities, medication use, smoking and alcohol history. The main determinants of midlife handgrip strength were age, gender, total body percentage fat and relative appendicular lean mass. Discussion: Our results show that low muscle strength and a greater decline in strength over time in the oldest old, representing sporadic longevity, are associated with increased all cause mortality. Future studies of interventions like resistance training, which has been shown to be efficacious in preserving muscle strength, could show whether maintenance of muscle strength translates into a reduction in mortality among weak elderly people. The value of muscle strength as a functional marker of life span in middle aged adults with exceptional familial longevity was not found. We postulated that offspring who have previously been shown to have a survival advantage compared to their birth cohort, would have superior muscle properties that would manifest as stronger muscle strength. Consequently, this would provide these individuals with a greater safety margin of muscle strength above the survival threshold later in life which contributes to their exceptional longevity. However, the findings of our study suggest that the genetic component of susceptibility to extreme survival is likely to be separated from that of muscle strength and mass. Conclusion: Handgrip strength, a surrogate measurement of overall muscle strength, is a predictor of all-cause mortality in the oldest old population. Application of handgrip dynamometry as a screenings tool in a multidimensional geriatric assessment may help identify older people at risk for disability and holds potential for use in prognostication of survival among elderly people. Although midlife handgrip strength has previously been shown to be an important prognostic indicator of survival, it is not a marker of exceptional familial longevity in middle-aged adults.

THE EFFECT OF DISUSE ON THE ELECTRICAL PROPERTIES OF MUSCLE: IMPLICATIONS FOR USING ELECTRICAL IMPEDANCE TECHNIQUES IN THE EVALUATION OF SACROPENIA. M. Sung, R. Ellman, J. Spatz, A. Cloutier, M. Bouxsein, S. Rutkove *(Brookline, USA)*

Introduction: Convenient, cost-effective and reliable methods for quantifying sarcopenia are needed. One approach, electrical impedance myography (EIM), a technique that is based on the localized application and measurement of high-frequency, low-intensity electrical current over a small area of muscle, may fulfill these requirements. Previous studies have demonstrated age-dependent change in the surface-measured electrical impedance properties of muscle. However, the mechanism underlying these changes remains uncertain. One approach to better understand these effects is to measure directly the electrical properties of excised senescent tissue. Since disuse atrophy bears similarities to and may a play a role in the development of sarcopenia, in this study we sought to assess disuse-induced changes in muscle's electrical properties. Objectives: To evaluate the effect of muscle disuse induced by partial and complete hind limb unloading on the electrical properties of muscle. Material and methods: Approximately 25 female C57/Bl6J mice underwent various degrees of hind limb unloading for a period of 2 weeks. A control group of 20 animals was allowed to walk normally. At the completion of the unloading period, the animals were sacrificed and the left gastrocnemius of each animal removed and placed in an electrical impedance-measuring cell. Electrical impedance measurements were completed using a commercially available bioimpedance device across a frequency range of 3kHz to 1 MHz. From the obtained raw resistance and reactance data, and by knowing the size of tissue, the muscleâ€™s inherent conductivity (ability to pass electrical charge) and permittivity (ability to store electrical charge). were calculated. Results: Conductivity had a median value of approximately 0.39 S/m in the control animals versus 0.71 S/m in the fully unloaded animals at 20 kHz and 0.49 S/m in the control animals versus 0.69 in the fully unloaded animals at 50 kHz. Changes in the partially unloaded animals were intermediate to those that were fully loaded and the control animals. Changes in conductivity inversely correlated with the muscle mass across the groups of animals, with R2 values of 0.61 at 20 kHz and R2 values of 0.54 at 50 kHz, suggesting that the greater the degree of disuse, the greater the increase in muscle conductivity. Subtler and less consistent changes in muscle permittivity were observed with full and partial unloading. Discussion: These results show that disuse induces a major increase in the conductivity of muscle. This change is of unclear origin but could relate to increased interstitial water, Type 2 fiber atrophy, or intrinsic changes to the actual conductivity of the sarcomere itself. Additional electrical studies of senescent muscle, both loaded and unloaded, may provide new insights into the mechanisms underlying the previously observed changes in the muscles of older individuals with electrical impedance techniques. Conclusion: Disuse induces major changes in the inherent electrical properties of muscle that could help explain in part the previously observed alterations in the impedance parameters of older individuals. Future planned studies on senescent muscle will likely provide important additional insights into the mechanism underlying these changes.

SARCOPENIA IN A TAIWANESE METROPOLITAN ELDERLY POPULATION. C.-C. Lin, T.-C. Li, C.-S. Liu, N.-H. Meng, C.-H. Lin, C.-K. Chang, W.-Y. Lin, C.-I. Li, C.-W. Yang *(Taichung, Taiwan)*

Introduction: Sarcopenia is a condition with multidimensional causes and confers a high risk for adverse health outcomes. Little information exists on the prevalence of sarcopenia in a general elderly population in Taiwan. Objectives: This study aimed to report the prevalence of sarcopenia in a Taiwanese metropolitan elderly population. Material and methods: We did a cross-sectional survey of a sample consisting of 1,347 ethnic Taiwanese elders aged 65 years and over who lived in 8 administrative units of the North District of Taichung City, Taiwan in 2009. Sarcopenia was defined according to the criteria proposed by European Working Group on Sarcopenia in Older People (EWGSOP) in 2010. Elders with sarcopenia were characterized by low muscle mass, plus at least one of low muscle strength or low physical performance. Low muscle mass was defined as sex-specific lowest 20% of skeletal muscle mass index measured by dual energy X-ray absorptiometry in our study sample. Low muscle strength was measured as low handgrip strength and low physical performance as low gait speed based on frail criteria proposed by Fried et al. Results: The age- and gender-weighted prevalence of sarcopenia was 15.4%. The prevalence of sarcopenia was 7.0%, 16.4% and 43.2% in men aged 65-74, 75-84 years and 85 years and over, and 7.9%, 22.1% and 26.3% in women aged 65-74, 75-84 years and 85 years and over, respectively. For sociodemographic characteristics, only older age was associated with an increased likelihood of sarcopenia after adjusted for gender, educational attainment and marital status. Discussion: The prevalence of sarcopenia in elders aged 60-70 years was ranged among previous studies from 5% to 13% due to various definitions. The overall prevalence was 13.4% in our study. The prevalence was higher than that in a France study (9.5% in elders aged 70 years and above, Rolland et al, 2003) and in a USA study (7% in older man and 10% in older female, Janssen et al, 2002). Conclusion: Sarcopenia was present in 15.4% of the Taiwanese elderly population aged 65 years and over in a metropolitan area; there were substantial variations by age.

NUTRITIONAL SUPPORT & SARCOPENIA: BY CONTRAST TO WHEY OR HIGH PROTEIN DIETS, THE LACK OF RECOVERY OF MUSCLE MASS DURING AGING CANNOT BE OVERCOME BY A DIETARY FREE LEUCINE SUPPLEMENTATION AFTER PROLONGED IMMOBILIZATION. H. Magne, I. Savary-Auzeloux, C. Sornet, C. Migné, L. Combaret, D. Dardevet (Saint-Genès-Champanelle, France)

Introduction: Sarcopenia is the progressive loss of muscle mass and strength associated with normal ageing. This phenomenon is a highly predictive factor of frailty, of limited mobility, of increased susceptibility to injury and of impaired recovery. Many mechanisms have been proposed to explain sarcopenia. One of them could be periods of immobilization or acute inactivity, which increase with age and may contribute by themselves to muscle atrophy. However, the effect of disuse by itself on skeletal muscle in elderly individuals has not been extensively investigated and the subsequent recovery ability has been even less studied despite the fact that an impaired recovery prevailed in old animals and elderly humans after immobilization-induced muscle atrophy. Even if knowledge of the cellular and molecular mechanisms underlying this lack of recovery is limited during ageing, an imbalance of muscle protein metabolism, apoptosis and cellular regeneration/differentiation is certainly involved. Some studies have described a decrease of the regenerative potential of satellite cells after immobilization in aged rodents (Zarzhevsky et al. 2001; Conboy et al. 2003). However, muscle recovery after unloading is also dependent from the generation of a sustained positive nitrogen balance which results from and increased muscle protein synthesis, decreased proteolysis, or simultaneous changes in both process. We previously showed that muscle proteolysis and apoptosis increased during immobilisation in old rats during plastering but these metabolic pathways were rapidly normalized with reloading (Magne et al. 2011). Then, following immobilization, an alteration in the response of muscle protein synthesis has been hypothesized to explain the absence of a positive nitrogen balance and subsequently the lack of recovery of muscle mass we observed during aging. During the recovery period, the postprandial phase is playing a critical role since it is during this period that the major anabolic factors regarding protein metabolism are elevated. Amino acids and particularly leucine play an important role in the stimulation of the muscle postprand of protein synthesis and inhibition of proteolysis. The lack of stimulation of protein synthesis during aging after immobilization may then result from a leucine resistance of muscle protein metabolism that may be overcome by increasing dietary leucine supply. Objectives: Aims of this study were (1) to determine if a lack of muscle protein response to food intake in old rats after an immobilization-induced atrophy took place during the recovery period, and (2) to test the effect of dietary leucine supplementation with free leucine or leucine rich protein diets on muscle mass recovery. Material and methods: Rats aged 22-24 months were subjected to unilateral hind limb casting immobilization for 8 days (I8). Casts were

then removed and animals were allowed to recover for 10 to 40 days (R10 to R40) with either a control diet (C: 13% casein), a free leucine supplemented control diet (LEU: 4.5% leucine), a leucine rich protein diet (PRO: 13% Prolacta®) or a leucine rich high protein diet (HP: 13% Prolacta® + 13% casein). Muscle atrophy, apoptotic pathways (apoptosome, caspase-3 and -8 activities), regeneration/differentiation processes (myogenic factor: Myf5), ubiquitine-proteasome-dependent proteolysis (amount of polyubiquitinated proteins, chymotrypsin-like activity and FOXO3a-phosphorylation), were measured in the same rat on both non-immobilized and immobilized (I) gastrocnemius muscles. Muscle protein synthesis and protein S6 phosphorylation were also measured at both the postabsorptive (PA) and postprandial (PP) state. Intramuscular markers of oxidative stress (carbonyls content and total glutathione content) and inflammation (amount of MCP-1) were also measured. Results: At I8, a significant muscle atrophy (-21%, P<;0.05) occurred in the immobilized gastrocnemius muscle and recovery was absent even at R40. Muscle atrophy was explained by (1) an increased amount of polyubiquitinated proteins and chymotrypsin-like proteasome activity (+53% and +33% respectively, P<;0.05), (2) a large decreased in protein synthesis at the PP state (-30%, P<;0.05), (3) an increased of apoptosome, caspase-3 and -8 activities (+60%, +48% and +26% respectively, P<0.05) and (4) a decrease amount in Myf5 (-50%, P<;0.05). An increase of carbonyls, total glutathione and MCP-1 (+14%, +37% and +68% respectively, P<;0.05) content were associated to these phenomenons. Inflammation, apoptosis and protein synthesis were normalized as soon as R10, but proteolysis was still elevated at R10 before its complete normalization when animals were fed the control diet. With the LEU diet, proteolysis was normalized earlier (-30% at R10, P<0.05 vs C diet) and protein synthesis was 30% higher in PP than in controls (as soon as R10, P<0.05 vs C diet). These observations were correlated with an increased phospho-FOXO3a/FOXO3a ratio (+80% at R30, P<0.05 C diet) and a sustained increase of phospho-S6 amount (+30%). However, despite this improvement of muscle anabolism, leucine failed to improve muscle mass recovery. When rats were fed with either the PRO or the HP diets, a significant improvement of muscle recovery was nevertheless observed when compared to the C and LEU diets. Discussion: We demonstrated here that 8 days of immobilization in old rats resulted in skeletal muscle atrophy associated with a co-activation of the ubiquitine-proteasome-dependent proteolysis and the caspase-dependent-apoptotic pathways and a large decreased of protein synthesis. During the subsequent recovery, these pathways were rapidly but only normalized which explained that skeletal muscle mass did not recover even 40 days after cast removal. However, muscle recovery after unloading has to result, not only from normalization of protein metabolism but also from an increased protein synthesis to positive the nitrogen balance. We hypothesized that this unability of protein synthesis to respond accurately in order to initiate a positive nitrogen balance is due to an ed (Magne et al. 2011). Indeed, we previously showed that these phenomenon altered muscle protein synthesis response to amino acids during aging (Marzani et al. 2008, Rieu et al. 2009, Balage et al. 2010). A supplementation with free leucine was sufficient to stimulate muscle protein anabolism but failed in muscle mass gain over time. However when an excess of leucine was given through leucine rich proteins or associated with a high protein diet, a beneficial effect on muscle mass during the recovery period could be observed. These results are in favour of a more prolonged and sustained positive nitrogen balance compared to free leucine intake alone. Conclusion: Our results showed that a short immobilization period during aging initiated muscle atrophy that was not recovered after 40 days and may then contribute to initiate sarcopenia. The lack of recovery is not due to a defect in proteolysis or apoptosis down-regulation during the recovery period but by a lack of a significant response of muscle protein synthesis to food intake. A free leucine supplementation, despite its beneficial effect on muscle protein synthesis and associated signalling pathways also failed in muscle mass recovery whereas a leucine-rich-protein diet (whey proteins) or a high protein diet were found to be efficient. These discrepancies need to be further studied but they underline the importance of the quality of dietary proteins ingested and the kinetic of appearance of leucine in generating sustained postprandial positive nitrogen balance translating into muscle mass gain during aging.

CHRONIC DIETARY OMEGA 3 INTAKE IMPROVES MUSCLE MASS IN AGED RAT BY SENSITIZING MUSCLE PROTEIN SYNTHESIS TO INSULIN BUT NOT TO AMINO ACIDS. I. Savary-Auzeloux, I. Mothe-Satney, C. Sorne, C. Gladine, B. Morio, S. Polakof, B. Comt, D. Dardevet *(Saint-Genès-Champanelle, France)*

Introduction: Sarcopenia is the progressive loss of muscle mass and strength associated with normal ageing. This phenomenon is a highly predictive factor of frailty, of limited mobility, of increased susceptibility to injury and of impaired recovery. Among the various causes leading to sarcopenia, a decreased sensitivity of protein metabolism to anabolic stimuli has been demonstrated. The anabolic stimuli whose action have been shown to be blunted during ageing include meal (Mosoni et al, 1995; Arnal et al, 1999), amino acids (Katsanos et al, 2005), leucine (Dardevet et al, 2000; Rieu et al, 2006) and insulin (Rassmussen et al, 2006). In this context, increasing research has been focussed recently on the strategies capable to restore the muscle protein metabolism sensitivity to the anabolic stimuli (mainly amino acids and insulin) during ageing. Among those potentially efficient strategies, some specific nutrients such as long-chain n-3 polyunsaturated fatty acids (LCn-3 PUFA) may be promising candidates. Indeed, these molecules, when incorporated into the cell membrane, up regulate skeletal muscle insulin sensitivity of glucose metabolism in various physiopathological (and insulin resistant) states such as obesity, type 2 diabetes and high fat feeding (Storlien et al, 1987; 1991; Liu et al, 1994). Concerning protein metabolism sensitivity to insulin and/or amino acids in LCn-3 PUFA supplemented subjects, the data are scarcer. Yet, Gingras et al (2007) have shown an increased whole body protein metabolism sensitivity to insulin in LCn-3 PUFA supplemented steers using hyper insulinemic euglycemic euaminoacidemic clamp. However, in this study, no direct measurement of protein synthesis in the muscle has been undertaken. More recently, in LCn-3 PUFA supplemented elderly subjects, Smith et al (2011) have demonstrated an increased response of muscle protein synthesis to insulin and/or amino acids (hyper insulinic, hyperaminoacidemic euglycemic clamp). Both studies also demonstrate that this increased protein metabolism sensitivity to insulin and/or amino acids at the muscle level could be mediated via the mTOR pathway (increased phosphorylation of mTOR and p70S6k). However, it is not known yet if such suplementation will be effective in preserving muscle mass during aging. Objectives: In light of the previous presented data, the aim of the present work is to first answer the very simple question: Are LCn-3 PUFA enriched diets capable to prevent and/or delay muscle loss with age? Indeed, the published data obtained in old subjects (Smith et al, 2011) have not measured lean body mass due to the relatively short period of LCn-3 PUFA supplementation (8 weeks) and the too low precision of the DXA method. The lower inter individual variability as well as the difference in life span between the rat model compared to humans led us to consider the rat as a good model to address this issue in this pilot study. Furthermore, several studies have shown that old rats develop sarcopenia with similar alterations found in humans. The second question is more related to the mechanisms of action of the LCn-3 PUFA involved in the potential increased sensitivity of muscle protein metabolism to insulin and amino acids in supplemented subjects. Indeed the data from Smith et al (2011) could not discriminate if the target of LCn-3 PUFA was the improvement in the stimulation of muscle protein metabolism by insulin or aminoacids or both. Additionally, the data from Gingras et al (2007) show a crucial role of insulin in the stimulation of amino acid fluxes at the whole body level but no direct measurement of protein metabolism has been done at the muscle level. So, the second question we raised was to assess the differential impact of LCn-3PUFA on insulin and amino acids stimulated muscle protein metabolism when given chronically during aging. In addition, the impact of such supplementation was also assessed on muscle proteolysis which, beside protein synthesis, is the other metabolic pathway controlling muscle mass and that has never been studied yet. Material and methods: 30 Wistar rats (16 month-old) were housed individually under controlled environmental conditions and were submitted to a control diet (C) or a LC n-3PUFA (N3) enriched diet (ad libitum) for 4 months. The food intake and animals weight were recorded weekly. The animals were euthanized at the end of the experimental period in the fasted state, hindlimb muscles (gastrocnemius, tibialis anterior, extensor digitorum longus and soleus muscles) were rapidly excised, weighed and frozen in liquid nitrogen for further analysis. The response of muscle protein synthesis and proteolysis to various concentrations of insulin (0,1,5,75nM) or leucine (0,100,200 μM) was measured in vitro on epitrochlearis muscles. Values are expressed as means ± SEM. Data were analysed using a one way (group : control or LCn-3 PUFA enriched diet) or two way (group : control or LCn-3 PUFA enriched diet; Dose of insulin or leucine employed in the incubation medium) variance ANOVA. Significance was defined at the P<0.05 level. Results: No significant difference between the C and N3 diets was observed for food intake. Animals weight was also similar in both groups (532 ± 10 g at slaughter). The hindlimb muscle weight was significantly increased by 6.3 % in N3 animals compared to C animals (Gastrocnemius: + 5.7% (P<0.05); Tibialis: 7.9% (P=0.06); EDL: +6.5 % (P=0.1); Soleus: NS). Concerning the in vitro epitrochlearis incubation, our results showed that protein synthesis stimulation or proteolysis inhibition by leucine were not improved in N3 animals relatively to C. Contrarily, insulin stimulation of protein synthesis was significantly increased by 22% (P<0.05) in N3 animals compared to C. Discussion: Our results show that the N3 diet was capable to allow the muscle mass to remain significantly above the value of the C animals after 4 months supplementation. Since both experimental diets were iso-nitrogenous, iso-engergetic and iso-lipidic, it is highly probable that this anabolic effect on muscle mass is due to the lipid composition of the diet and particularly the n-6/n-3 ratio which is divided by 10 (n-6/n-3 ratio: 5.5 and 0.4 for C and N3 diets respectively) in our study. This is the first time that a positive impact of a LC-n-3 PUFA enriched diet is observed on muscle mass. What can be the mechanisms responsible to this increased muscle mass in N3 compared to C animals? The data obtained in vitro on epitrochlearis muscle show that leucine may not be involved whereas insulin sensitivity of protein synthesis was increased in N3 animals. Our data confirm but also sharpen the data obtained on elderly subjects (Smith et al, 2011) since we confirmed an anabolic effect of LC n-3 PUFA on muscle protein metabolism and also demonstrated an impact on mass. In addition, we clarified that insulin more than leucine was the target and the relay of the anabolic effect of LC n-3 PUFA in regulating muscle protein metabolism. These data need to be reinforced by an investigation of the impact of the C and N3 diets on the intracellular signalling pathways leading to the stimulation of protein synthesis. Our data showed that only a specific signalling pathway for insulin is targeted by the LC n-3 PUFA. Because both insulin and leucine are known to share mTOR/S6K1 signalling pathway to stimulate muscle protein synthesis, the impact of LC n-3 PUFA was then upstream from mTOR and independent of leucine such as Insulin Receptor/IRS1/Akt kinases.

EFFECTS OF A COMBINED NUTRITIONAL AND RESISTANCE EXERCISE INTERVENTION ON BODY COMPOSITION, MUSCULAR STRENGTH, PHYSICAL FUNCTION AND QUALITY OF LIFE IN INDEPENDENTLY LIVING ELDERLY ICELANDERS. A. Ramel, O.G. Geirsdottir, A. Arnarson, K. Briem, P.V. Jonsson, L. Thorsdottir *(Reykjavik, Iceland)*

Introduction: The decrease in muscle mass and strength associated with ageing can have adverse consequences such as functional impairment, loss of independence and frailty. There is evidence that resistance exercise can increase muscle mass and -strength and thus improve physical function in elderly. Good nutrition, e.g., appropriate energy- and protein intakse, is necessary to maintain or even increase muscle mass and -strength. Although strength gains experienced after a period of resistance exercise can be maintained

for short periods after training ceases, it is important to gain insight into determinants which influence adherence to a physically active lifestyle which is important to maintain strength over longer periods. Objectives: The effects of a combined nutritional and resistance exercise intervention on body composition, muscular strength, physical function and quality of life were investigated in independently living elderly Icelanders. After the intervention, the elderly were followed up 6 - 18 months and adherence to physical activity as well as changes in physical outcomes were measured. Materials and methods: Subjects (N = 237, 73.7 ± 5.7 yrs, 58.2% female) participated in a 12-week resistance exercise program (3 times/week; 3 sets, 6-8 repetitions at 75-80% of the 1-repetition maximum) designed to increase strength and muscle mass of major muscle groups. They were randomized into 3 groups receiving different drinks after each training session to promote muscle strength or mass: group 1: 20 g whey protein + 20 g carbohydrates; group 2: 20 g milk protein + 20 g carbohydrates; group 3: 40 g carbohydrates. Body composition (DXA), quadriceps- and grip strength, timed up and go test (TUG), six minute walk for distance (6MW) and health related quality of life (HRQL) were measured at baseline and endpoint. A follow up investigation was conducted 6 - 18 months after the intervention. Results: At baseline 237 participants started the 12-week program, 204 participants (86%) completed the intervention and 149 participants (73%) completed the follow-up. Although the increase in lean mass was small (+0.8 kg, P<0.01), quadriceps strength (+53.5 N), grip strength (+3.0 lb), TUG (-0.6 sec), 6MW (+33.6 m) and HRQL (+1.2 t-score) improved significantly (all P <; 0.01) after the intervention. Changes in 6MW predicted improvement in HRQL after 12 weeks. The nutrtional intervention did not significantly affect the outcomes. At follow-up, quadriceps strength was significantly lower than endpoint strength (P < 0.001) however, both quadriceps strength and TUG-time were significantly better than at baseline. At follow-up 41.9% of participants continued unsupervised resistance exercise, 24.4% three times or more per week. No significant differences in age, gender, social or economical factors were found between those who continued resistance exercise after endpoint and those who quit. The only factor which predicted minutes of daily physical activity at follow-up was daily physical activity at baseline. Sex, education, job, age, time from intervention endpoint or physical improvement during the 12-week resistance exercise program did not predict daily physical activity. Time from intervention endpoint, frequency of resistance exercise and amount of daily physical activity predicted quadriceps strength at follow-up. Discussion: Our study shows that a 12-week resistance exercise program significantly improves lean mass, muscle strength, physical function and HRQL in elderly individuals, and that improvements in physical function predict improvements in HRQL. Our study also indicates that mainly former lifestyle affect physical activity among elderly Icelanders during follow up and that gains and improvements experienced during a 12-week resistance exercise program do not predict future physical activity. Strength declines after cessation of a resistance exercise program and the decline is associated to length of follow-up period. However, after 18 months with habitual physical activity and unsupervised resistance exercise, quadriceps strength remains higher than pre-training values. Conclusion: Physical activity and resistance exercise can postpone the loss of muscle strength and are likely an important factor in maintaining independence of the elderly and prolonging healthy aging.

LONG TERM DIETARY LEUCINE EXCESS IN OLD RATS ALTERS INSULIN SIGNALING PATHWAYS IN ADIPOSE TISSUE BUT NOT IN MUSCLE; IT DOES NOT LEAD TO OVERALL GLUCOSE INTOLERANCE. G. Zeanandin, M. Balage, C. Sornet, J. Dupont, S.M. Schneider, I. Mothe-Satney, D. Dardevet *(Saint-Genès-Champanelle, France)*

Introduction: Aging is frequently associated with major quantitative changes in body composition characterized by a decrease in lean body mass (i.e muscle mass) and an increase in body fat mass. The clinical and functional consequences of muscle mass loss (known as sarcopenia) are decreased physical performance and autonomy of elderly people. The consequences of fat mass accumulation are less obvious but may play a major role in the metabolic changes observed with aging, especially the development of insulin resistance. The origin of age-related sarcopenia is multifactorial but it has become obvious that muscle protein loss during aging may be partly explained by a decreased response and/or sensitivity of protein synthesis and degradation to physiologic concentrations of amino acids, especially leucine. Leucine acts as a signal nutrient in promoting protein synthesis in skeletal muscle and adipose tissue via mTOR/S6K1 pathway activation, and may be of interest to prevent age-related sarcopenia. However, hyper-activation of mTOR/S6K1 has been suggested to inhibit the first steps of insulin signaling and finally promote insulin resistance. Objectives: This study was thus conducted to examine the impact of a sustained dietary leucine excess (6 months ad libitum) on overall glucose tolerance, insulin response on muscle glucose transport in vitro and body composition in old rats. A special focus was put on studying the signaling pathway in skeletal muscle and adipose tissue. Material and methods: Old Wistar rats (18-month) were fed ad libitum a 15% protein diet supplemented (LEU group) or not (C group) with 4.45 % leucine for 6 months. Overall insulin sensitivity was estimated through an oral glucose tolerance test at baseline (before starting the experimental period) and at the end of the nutritional experiment. Muscle insulin sensitivity of glucose transport was assessed in vitro using isolated epitrochlearis muscles incubated with increasing insulin concentrations in presence of 5.0 mmol/L of 2-deoxy-D-[3H] glucose (DOG: 0.5 μCi/mL). Insulin signaling was assessed on gastrocnemius muscle and perirenal adipose tissue at the postabsorptive state and 30 min after the rats were fed by gavage with a nutrient bolus. Results: Muscle mass was not changed by leucine supplementation whereas perirenal adipose tissue weight was dramatically increased (+ 45%, P < 0.0001). mTOR/S6K1 signaling pathway was not significantly altered in muscle from old rats subjected to long-term dietary leucine excess compared to control rats whereas it was increased in adipose tissue in response to acute food intake. Phosphorylation of IRS1 on serine 635/636 was increased in adipose tissue (+ 67 %, P < 0.05) and was associated with decreased Akt phosphorylation in leucine-supplemented rats. Unlike in adipose tissue, phosphorylation of IRS1 on serine 635/636 was unchanged in muscle. Long-term leucine supplementation did not induce alteration of overall glucose tolerance. However, insulin-stimulated glucose transport was improved in muscles from leucine-supplemented rats compared to controls; it was related to improvement in Akt expression and phosphorylation in response to food intake. Discussion: Previously, a defect in postprandial anabolism with age has been proposed to be one of the mechanisms responsible for the loss of muscle mass during aging. This anabolic resistance has been attributed to a decrease in leucine sensitivity and may be counteracted by increasing leucine proportion in the diet in both rodents and humans (Dardevet et al. 2002; Rieu et al. 2003, 2006; Katsanos et al. 2006). Consequently, it has been suggested that long-term dietary leucine supplementation may be necessary to counteract or prevent muscle loss during aging. In the present study, we did not observe any significant increase in skeletal muscle mass in old rats supplemented ad libitum with free leucine for 6 months, despite a significant increase in plasma leucine. Lack of muscle mass gain after chronic leucine supplementation could be explained by a loss of leucine efficiency to stimulate postprandial muscle protein synthesis when given ad libitum after a long-term period compared to short-term supplementations through a leucine-enriched meal, as demonstrated previously (Rieu et al. 2003, 2006). The lack of major activation of the mTOR pathway observed in skeletal muscle from leucine-supplemented rats is consistent with such a hypothesis. It has been suggested that acute overactivation of the mTORC1'S6K1 pathway by amino acids may alter early steps of insulin signaling and promote insulin resistance . The present study showed that chronic leucine supplementation did not induce similar effect in skeletal muscle. Indeed, S6K1 phosphorylation was similar in control and leucine-supplemented rats both in the basal state and after administration of the nutrient bolus, suggesting that chronic exposure to leucine excess has not induced sustained activation of S6K1. In agreement, phosphorylation of IRS1 on S636/639 was not altered in muscles from leucine-supplemented rats. Akt expression and phosphorylation was rather improved inducing a better insulin response of glucose transport assessed in vitro. Conversely, we observed that long-term leucine supplementation induced an increase in perirenal tissue mass. Increased activation of the mTOR pathway in adipose tissue from leucine-supplemented rats, as assessed by increased phosphorylation of both mTOR and S6K1 is consistent with a protein synthesis-induced hypertrophy. Previously, Lynch et al. (2002) showed that an acute or a 12-day leucine administration significantly increased adipose tissue protein synthesis in young rats. Over-activation of mTOR/S6K1 in adipose tissue from leucine-supplemented rats was related to increased phosphorylation of IRS1 on S636/639 and a trend to a decreased Akt phosphorylation suggesting a negative feed-back toward the first steps of insulin signaling in adipose tissue. We recently showed that short-term (5 weeks) leucine supplementation impaired whole-body glucose tolerance in young adult rats that correlated with perirenal adipose tissue accumulation (Balage et al 2011). Surprisingly, in the present study, 6-month leucine supplementation did not change overall glucose tolerance in old rats despite a significant increase in perirenal adipose tissue content suggesting an age-related effect of leucine supplementation. Dardevet D et al (2002) J Nutr 132:95-100. Rieu I et al (2003) J Nutr 133:1198-1205. Rieu I et al (2006) J Physiol 575:305-315. Katsanos CS et al (2006) Am J Physiol - Endocrinol Metab 291:E381-E387. Lynch, CJ et al (2002) Am J Physiol - Endocrinol Metab 283:E503-E513. Balage M et al (2011). J Nutr Biochem 22:219-226. Conclusion: A prolonged leucine supplementation in old rats differently modulates IR/IRS/Akt and mTOR/S6K pathways in muscle and adipose tissue. It does not increase muscle mass but seems to promote hypertrophy and hyperplasia of adipose tissue that did not result in insulin resistance. Further studies are needed for a better comprehension of the cross-talk between muscle and adipose tissue in a critical situation such as aging and to determine the optimum nutritional design to prevent age-related sarcopenia using dietary leucine.

LOSS OF MUSCLE STRENGTH, MASS (SARCOPENIA) AND QUALITY (SPECIFIC FORCE) AND ITS RELATIONSHIP WITH PHYSICAL DISABILITY AND FUNCTIONAL LIMITATION- THE CHAMP STUDY. N.N. Hairi, R.G. Cumming, V. Naganathan, D.J. Handelsman, D.G. Le Couteur, H. Creasey, L.M. Waite, M.J. Seibel, P. N. Sambrook *(Kuala Lumpur, Malaysia)*

Introduction: Aging results in physical and biological changes in the structure and function of muscle. Wilth less muscle mass, muscle strength and function are greatly reduced. Objectives: To determine the association between loss of muscle strength, mass (sarcopenia) and quality (specific force) with physical disability and functional limitation among older men. Material and methods: This is a cross-sectional analysis of 1705 community-dwelling men aged 70 years or more who participated in the baseline assessments of the Concord Health and Ageing in Men Project (CHAMP) study. Upper and lower extremity strength was measured using dynamometers for grip and quadriceps strength. Appendicular skeletal lean mass was assessed using dual energy x-ray absorptiometry (DEXA). Muscle quality was defined as the ratio of strength to mass in upper and lower extremities. For each parameter, subjects in the lowest 20% of the distribution were defined as below normal. Physical disability was measured by self report questionnaire. Functional limitation was assessed according to self report and objective lower extremity performance measures. Results: After adjusting for important confounders, the prevalence ratio (PR) for poor quadriceps strength and self reported functional limitation was 1.91 (95% CI 1.10 - 2.40); for performance based functional limitation the PR was 1.81 (95% CI 1.45 - 2.24). The adjusted PR for poor grip strength and physical disability in IADL was 1.37 (95 % CI 1.20- 1.56). The adjusted PR for low skeletal lean mass (adjusted for fat mass) and physical disability in ADL was 2.08 (95% CI 1.37 - 3.15).

For muscle quality, the PR for lower extremity specific force and functional limitation and physical disability was stronger than upper extremity specific force. Discussion: We found loss of muscle strength, loss of muscle mass (sarcopenia) and loss of muscle quality (specific force) are associated with different types of impairment in physical function among older people. Our results supports our hypothesis that muscle quality is more strongly associated with physical function than muscle mass alone, however we found muscle strength alone to be even more strongly associated with physical function. Stronger associations were found between loss of muscle strength, mass and quality with functional limitation than with physical disability. Conclusion: Muscle strength is the single best measure of age related muscle change and is associated with physical disability in IADLs, mobility disability and functional limitation.

MYOSTATIN SERUM CONCENTRATIONS IN MEN "AGE-RELATED CHANGES AND CORRELATES" THE STRAMBO STUDY. P. Szulc, C. Goettsch, M. Schoppet, L.C. Hofbauer, R. Chapurlat *(Lyon, France)*

Introduction: Myostatin is an autocrine muscle-derived inhibitor of muscle growth and function. The potential determinants of serum myostatin levels in men have not been defined. Objectives: The objective of this study was to assess age-related changes in the circulating concentration of myostatin in men and its associations with lifestyle factors, hormones and cytokines involved in the regulation of the metabolism of muscle and bone as well as with the calcifications in the lumbar aorta. Material and methods: We measured serum myostatin in 1,153 men aged 20 to 87 (STRAMBO cohort) using an ELISA that detects the dimeric full-length protein and its C-terminal fragment (Immundiagnostik AG, Bensheim, Germany). We assessed aortic calcification (AC) at the lumbar aorta on the Vertebral Fracture Assessment scans and relative appendicular muscle mass (RASM, kg/m2) using the HOLOGIC Discovery device. Lifestyle factors were assessed by epidemiological questionnaire. High sensitivity C-reative protein was measured using the immunoturbidimetric assay (CRPHS, Cobas). Results: Between 20 and 60 years of age, circulating myostatin increased by 28% (n=353, r=0.16, p<0.005), whereas RASM was stable. After 60 years, serum myostatin and RASM decreased (n=800, r= -0.12 and r= -0.21, p<0.001). We analyzed data in 780 men aged 60, who did not take vitamin D or calcium supplements, using the multivariate analysis of covariance. Men having aortic calcifications had lower myostatin levels (3.3%, 0.23 SD, p<0.005). Men in the highest myostatin quartile (>39.5 mg/L) had lower average AC score compared with the three lower quartiles combined (p<0.005 adjusted for confounders). In multivariate models, prevalence of AC decreased with increasing myostatin levels (OR=0.76 per 1SD decrease, 95%CI: 0.64-0.91, p<0.001). AC prevalence was lower (OR=0.48, 95%CI: 0.33-0.68, p<0.001) in the highest quartile vs three lower quartiles combined. Serum levels of myostatin and 25-hydroxyvitamin D (25OHD) were positively correlated (partial r=0.20, p<0.001). Serum myostatin levels were 12% higher (0.76 SD, p<0.001) in 45 men with 25OHD>40 ng/mL compared with 369 men with 25OHD<20 ng/mL. In multivariate models, low calcium intake (<590 mg/day, lowest quartile) was associated with 11% lower (0.37 SD, p<0.01) serum myostatin vs three higher quartiles combined. Elevated concentration of C-reactive protein (CRP, >3.27 mg/L, highest quartile) was associated with 4.3% lower (0.30 SD, p<0.001) serum myostatin levels compared with the three lower quartiles combined. Serum myostatin levels were 5% lower (0.43 SD, p<0.05) in 45 current mild smokers (median: 8 cigarettes/day) compared with non-smokers. Men who drank >110 g alcohol/week (median) had 12% lower (0.41 SD, p<0.001) myostatin level compared with men who drank less. Discussion: The mechanisms of these associations need to be defined. Lower myostatin levels may reflect some adaptive anti-catabolic reaction of the muscular tissue to harmful factors. As myostatin is synthesized mainly by specific muscle cells, these results may also reflect lower mass of these cells due to action of these factors. Conclusion: Thus, in men serum myostatin concentrations increased until the age of 60, then decreased. In older men, aortic calcification, lower 25OHD level, low calcium intake, higher CRP level, current smoking, and higher alcohol intake were all independently associated with lower myostatin levels.

LOW MUSCLE MASS AND CURRENT SMOKING ARE THE MAIN DETERMINANTS OF AORTIC CALCIFICATIONS PROGRESSION IN OLDER MEN THE PROSPECTIVE MINOS STUDY. P. Szulc, R. Chapurlat *(Lyon, France)*

Introduction: Extended abdominal aortic calcifications are predictive of cardiovascular morbidity and mortality as well as of fragility fracture in older men and in postmenopausal women. However, the analysis of the determinants of the aortic calcifications was focused on the cross-sectional studies and only limited prospective data are available. Objectives: Our aim was to analyze determinants of the progression of aortic calcifications in a large cohort of men during a long term prospective follow-up. Material and methods: The study was performed in 621 men aged 50 and over who were followed up prospectively for 7.5 years. Bone composition was assessed by dual energy X-ray absorptiometry (HOLOGIC 1000W, Hologic, USA). Lateral spine radiographies were performed at baseline as well as after 36 and 90 months of follow-up. Aortic calcifications were assessed on lateral X-rays of lumbar spine using the 24-point aortic calcification score (ACS) (Kauppila, 1997). Lifestyle factors were assessed using an epidemiological questionnaire. Blood was collected in the fasting state at baseline. Serum concentrations of hormones as well as of glucose, cholesterol, HDL-cholesterol and triglycerides were measured using standard laboratory methods. Results: Median ACS progression was 0.27 point/year (IQ range: 0-0.67 point/year). Accelerated (faster) ACS progression was defined as the highest quartile (more than 0.67 point/yr, n=167). In multivariate models, age predicted faster ACS progression (OR =1.05 per year, 95%CI: 1.02-1.09, p<0.001). Secondary hyperparathyroidism and current smoking were each associated with accelerated ACS progression (OR=2.06, 95%CI: 1.34-4.10, p<0.01 and OR=4.34, 95%CI: 2.04-9.24, p<0.001, respectively). Also in multivariate models, abdominal obesity was predictive of faster ACS progression (highest vs lowest tertile: central fat mass OR =2.32, 95%CI: 1.28-4.21, p<0.005; waist OR=2.13, 95%CI: 1.10-4.13, p<0.01). Low relative appendicular skeletal muscle mass (RASM, kg/m**2.3) predicted the accelerated ACS progression (OR= 1.55 per 1 SD decrease, 95%CI: 1.17-2.05, p<0.005). Similarly, the lowest tertile of RASM (<6.58 kg/m**2.3) was associated with higher risk of accelerated progression of aortic calcifications in comparison with the highest tertile (>7.13 kg/m**2.3) (OR=2.46, 95%CI: 1.39-4.34, p<0.005). After further adjustment for baseline ACS, only low RASM (OR=2.56, p<0.005)and current smoking (OR=3.21, p<0.05) remained significant predictors of the accelerated ACS progression. Other variables (self reported ischemic heart disease, hypertension, diabetes; serum fasting glucose, cholesterol, HDL-cholesterol, triglycerides, 25OH-vitamin D as well as bioavailable and total 17beta-estradiol and testosterone) did not predict the accelerated ACS progression in the multivariate models regardless of the presentation of these variables (continuous, various thresholds). Discussion: Our data confirm the importance of several factors as determinants of the aortic calcifications: age, smoking, abdominal obesity. In addition, we show that low muscle mass is predictive of accelerated progression of the aortic calcifications. From the pathophysiological point of view, it suggests that sarcopenia and aortic calcification (and more generally, cardiovascular diseases) share common risk factors. From the practical point of view, these results indicate the necessity of the study of parameters which may be helpful to identify the group of elderly men at high risk of sarcopenia and cardiovascular diseases. Conclusion: Thus, in older men, current smoking and low RASM as well as, to a lesser extent, age, abdominal obesity, and secondary hyperparathyroidism were each predictive of the prospectively assessed accelerated ACS progression independent of one another and of other confounding variables.

CHANGES IN MUSCLE ARCHITECTURE WITH OLD AGE : A SIGNATURE OF SARCOPENIA. M.V. Narici, G. Trisolino, G. Bracci, O.R. Seynnes, E.L. Campbell, M. Conte, C. Lanzarini, L. Bucci, M. Capri, S. Salvioli, J. McPhee, G. Butler-Browne, C. Franceschi *(Manchester, United Kingdom)*

Introduction: Sarcopenia is a main cause of the loss of mobility and independence and of the increased risk of falls in the elderly, affecting 42% of men and 57% of women over 70 years of age (Janssen et al. 2000). Early detection of sarcopenia is thus of primary importance for the introduction of preventive countermeasures. So far, diagnosis of sarcopenia has been based on appendicular skeletal muscle mass (ASM) assessed either by DEXA, bioelectrical impedance analysis, MRI or CT and expressed relative to ASM values of young controls. Although the use of these indexes may be practical for clinical purposes, their accuracy and/or cost, have been questioned (Pahor et al. 2009). Using ultrasound imaging, we previously reported that sarcopenia is associated with changes in muscle architecture, as muscle fibre fascicle length and pennation angle are significantly smaller in older individuals (Narici et al. 2003). In the present study, by applying this technique to populations of young and older individuals of different physical activity levels, we investigated whether these changes in muscle architecture could be used as new biomarkers of sarcopenia. Objectives: To identify a biomarker of sarcopenia based on changes in muscle architecture using ultrasonography. Material and methods: This ongoing investigation, part of the EU Framework 7th project Myoage ("Understanding and combating human age-related muscle weakness"), has so far been performed on a total of 115 subjects of both sexes, distributed in the following groups: 24 active young (AY) adults aged 18-35 yr, 27 active older (AO) individuals aged 67-82 yr, 24 master athletes (MA) aged 67-96 yr and 31 frail older (FO) individuals, awaiting hip surgery, aged 65-94 yr. In each subject we measured fascicle length (Lf) and muscle thickness (t) of the vastus lateralis muscle using B-mode ultrasound (Esaote Mylab 25) fitted with a 10-15 MHz linear probe. Since both Lf and t tend to increase with hypertrophy and decrease with atrophy (Narici and Maganaris, 2006), the ratio of Lf/t was calculated for each individual to assess whether the geometric proportionality between fascicle length and muscle thickness changed with age. Statistical significance of differences in Lf , t, and in the Lf/t ratio between the AY, AO, MA and FO groups were assessed using a one-way ANOVA followed by a Tukey post-hoc analysis. Significance was set at P<0.05. Results: Fascicle length: Values of Lf were: 8.12±1.05 cm in AY, 7.23±0.89 cm in AO, 7.57±1.08 cm in MA and 5.72± 1.23 cm in FO. Compared to AY, Lf was 10.9 % lower in AO (<0.038) and 29.5% lower in FO (P<0.001). Instead, no significant difference in Lf existed between MA and AY. Muscle thickness: Values of t were 2.12±0.37 cm in AY, 1.61±0.31cm in AO, 1.75±0.29 cm in MA and 1.03±0.31 cm in FO. Values of t were 24% lower in AO (P<0.001) and 51.4% lower in FO (P<0.001) than in AY. Smaller differences were found in the MA, for t values were 17.4 % lower than in the AY (P<0.002). Fascicle length to muscle thickness ratio: The Lf/t ratio was 3.92±0.67 in AY, 4.58±0.64 in AO, 4.38±0.63 in MA and 5.8±1.27 in FO. Compared to the AY, this ratio was 17% higher in the AO (<0.01) and 47.7% higher in the FO (P<;0.001). Instead no significant differences in Lf/t ratio were present between AY and MA. Discussion: These data show that the age-related loss of muscle mass i s associated with marked changes in muscle architecture, represented by a decrease of muscle thickness and also of fascicle length. A decrease in t is indicative of a loss of sarcomeres in-parallel while a decrease in Lf is most likely due to a loss of sarcomeres in "series (Narici & Maganaris 2006). The finding of an increase in the Lf/t ratio with old age suggests that the larger is the degree of sarcopenia, the greater is the disproportion between the loss sarcomeres in parallel and those in series. Since this phenomenon is not found in the older athletes (MA), it suggests that regular high-intensity physical activity is effective for maintaining skeletal muscle geometric proportionality, a feature that is instead lost in sarcopenia associated with reduced physical activity. The potential functional implications of this observation are noteworthy. Since force depends on the number of sarcomeres in-parallel (and thus from t), while velocity depends on the number of sarcomeres in-series (and thus from Lf), the observed increase in Lf/t suggests

that the loss of muscle power in old age (power being the product of force and velocity) is mostly due to a decrease in muscle force rather than in shortening velocity. Conclusion: We report here for the first time a new biomarker of sarcopenia based on ultrasound measures. This biomarker, represented by the ratio of muscle fibre fascicle length to muscle thickness (Lf/t) significantly increases in old age, particularly so when sarcopenia is associated with inactivity. We believe that a change in the LF/t ratio represents a specific signature of sarcopenia which could be useful for the diagnosis of this condition. Funding by EU Framework 7th Program, Project MYOAGE, grant No 223576 is acknowledged. (1) Janssen I, Heymsfield SB, Wang ZM et al. (2000) Skeletal muscle mass and distribution in 468 men and women aged 18-88 yr. J Appl Physiol 89:81-8; (2) Narici MV, Maganaris CN, Reeves ND & Capodaglio P. (2003). Effect of aging on human muscle architecture. J Appl Physiol 95, 2229-2234; (3) Narici MV and Maganaris CN (2006) Muscle architecture and adaptations to functional requirements. In Skeletal Muscle Plasticity in Health and Disease: From Genes to Muscle. R. Bottinelli and C. Reggiani (Eds), GJM Stienen (series Ed), Springer (publ), Dordrecht, pp265-288; (4) Pahor M, Manini T and Cisari M. (2009) Sarcopenia: clinical evaluation, biological markers and other evaluation tools. J Nutr, Health & Aging, 13, 724-728.

HOW FAR IS IT POSSIBLE TO COUNTERACT SARCOPENIA? THE BIRKEBEINER AGING STUDY OF OLDER CROSS-COUNTRY SKIERS. A.H. Ranhoff, M. Myrstad *(Bergen, Norway)*

Introduction: Physical activity, and particularly endurance training from middle age, is as a modifiable life style factor with great potential in preventing sarcopenia and contributing to a better life for older people. Training and exercise are subsets of physical activity that is planned, structured and repetitive and has as a final or an intermediate objective the improvement or maintenance of physical fitness. The goal of endurance training is to improve physical endurance and capacity by increasing the maximal oxygen consumption. Endurance training includes exercise bouts on a wide range of intensity levels and durations, but to improve capacity the endurance training has to be performed regular over a longer time-span. A few studies have assessed mortality or morbidity in larger cohorts of still active athletes such as participants in marathon runs, long-distance bike runs or long-distance ski races. In many countries this is a growing group in the middle-aged population and studies of these athletes might give us more information about health effects of long-term strenuous endurance training. Age-related loss of skeletal muscle (sarcopenia) is an integral component of frailty, and it is the most studied of all contributing physiological systems that decline in frailty. The maintenance of skeletal muscle mass is dependent on hormonal, inflammatory, neurological, nutritional, and activity components. There are reasons to believe that endurance training can counteract sarcopenia and frailty in the same way as resistance training, which is better studied. Frailty has been associated with both overweight and underweight and the role of long-term endurance training in keeping people at a normal weight is probably important. The effect of endurance training on physical capacity is strongly related to the effect on muscle mass and strength. Peak endurance performance is maintained until 35 years of age, followed by modest decrease until 50?60 years of age, with progressively steeper decline thereafter. In a review of 1841 papers on physical activity and ageing from 1978, it was concluded that even moderate exercise can delay age-related decline in physical capacity with as much as 8-10 years. The reduction of physical capacity by age has previously been demonstrated in male participants of The Birkebeiner cross-country ski race. The athletes between 60 and 70 years performed at the same level as 25-years old men in the general population. Running speed and speed in cross-country skiing correlate well with VO2max and has been shown to decrease in marathon runners from the age of 50 to 60. The Birkebeiner cross-country ski race of 54 km has been arranged almost yearly since 1932, and is known as one of the worlds most challenging cross-country ski races. Completing the Birkebeiner cross-country ski race requires systematic and long-term endurance training. Objectives: The aim of the Birkebeiner Aging Study is to study somatic and mental health, as well as life style factors, coping and health-related well-being among these older athletes and compare with age-matched participants in health surveys. In a longitudinal follow up we will study the changes in physical activity, health, function, well-being, as well as mortality. The objective of this presentation is to give baseline results and answer the question "how far is it possible to counteract sarcopenia on an individual level?". Material and methods: The Birkebeiner Aging study is a prospective study of health and life style self-reported by postal questionnaire. It has a cross-sectional as well as longitudinal design. Participants in the Birkebeiner cross-country ski race who are 65 years or older and live in Norway are subjects for inclusion. After the 2009 race, 440 men and 43 women were invited to answer a postal questionnaire. The questionnaire includes the subjects' self report of bodyweight and height, the Modified Health Assessment Questionnaire (MHAQ) to assess disability and the SF-12 to assess health-related well-being. Since VO2max correlates well with average racing speed and ranking, we use average racing speed obtained from the race results as a surrogate measure for physical capacity. This paper only gives results from baseline for the participants in the 2009 race and from scrutinising the race results from previous races for some selected participants. Results: Of the 483 invited, 420 (87.0%) responded to the questionnaires, 32 (7.5%) were female. Median age for men and women was 68 (range 65-90) and 67 (range 65-74) years respectively. Almost all reported normal weight and only seven had BMI <20, while 11 had BMI ?28. Hundred-and-ten (23%) had experienced disease-related interruptions in the exercise of more than three months and 146 (35.0%) reported to have stayed in hospital. Most (405, 96.4%) reported their health to be good or very good. Health-related well-being, measured by the SF-12 questionnaire, was higher than normative values. The Physical Summary Score (PSC) and the Mental Summary Score (MSC) of the SF-12-score were (mean (±SD)) 57.1 (5.7) and 53.9 (4.6) respectively. A majority (388, 80%) reported that participation in the Birkebeiner race improved their quality of life and 353 (73%) reported that they feel younger than others at same age. Finishing time, as a surrogate for physical capacity, reveal variation among the participants. In the 2009 race average finishing time for the study participants was 4:37:02 (SD 0:51:00), range 3:16:18 ? 9:00:08). Average speed at different ages for five selected subjects; one healthy woman and four men, of which three are healthy and one underwent cardiac surgery with valve implantation and coronary bypass at the age of 61 years, show only small variations in average speed from year to year for each of the five participants. For the male with the best physical capacity (highest speed), a decline started when he was 70 years old, while a decline is seen from between 75 and 80 years for the two oldest males. For the female participant and the male who had cardiac surgery, average speeds are stable over time, but they are still not over the age of 70 years. Discussion: The role of long-term endurance training in the prevention of frailty and sarcopenia is poorly studied. Some few previous studies show reduced mortality and disability, and the first base-line results of the Birkebeiner Aging Study show that still active older athletes report good health. Almost all have normal BMI, which is an important resilience factor against frailty and many age-related diseases. However, they are not a disease-free population since as many as 43% reported chronic health problems. The participants are a heterogeneous group, with variation in age from 65 to 90 years of age, in experience with disease, and in physical capacity based on the race results. This gives us the opportunity to compare age groups, the healthy with those with chronic health problems, and groups with different physical capacity. The examples show that endurance training, and even to participate in a strenuous competition, are possible at very high age and after serious health problems. The strength of this study is a high respondent rate (87%), which gives us a representative study population. The study subjects have been doing endurance training at a high level for decades and are a unique group of older persons according to their training experience, and then suitable for a study of long-term endurance training in preventive gerontology. Conclusion: In the first base-line results of the Birkebeiner Aging Study, older cross-country skiers report generally good health, health-related well-being, and they are almost free from disabilities and have normal BMI. Also participants who report health problems are able to restore and preserve physical capacity and counteract sarcopenia. Up to 90 years of age it is possible to counteract sarcopenia and participate in a skirace of 54 km, although for these athletes there seems to be decline in physical capacity starting from the age of 70-80 years.

AN ISOCALORIC LOW PROTEIN DIET IN RODENTS: AN EXPERIMENTAL MODEL OF FRAILTY AND/OR SARCOPENIA. R. Rizzoli, P. Ammann *(Geneva, Switzerland)*

Introduction: Frailty and sarcopenia are very frequent in the oldest old. Even if clinical diagnosis criteria are becoming recognized for both conditions, these disorders are still missing an operational definition. In addition, experimental models of acquired frailty or sarcopenia are insufficiently developed. Objectives: To set up an experimental model of frailty and/or sarcopenia. Material and methods: We developed a model of frailty and/or sarcopenia in adult rats or mice by pair feeding the animals with an isocaloric low protein diet, as compared with a normal amount of protein containing diet. Both diets differ only by the casein content as the source of protein, the same amount of calories being provided by carbohydrate addition. Results: Animals receiving an isocaloric low protein diet display the following features : a rapid, within 2 weeks, decrease in bone mineral mass, alterations in bone microstructure and material level properties, a reduction in bone strength, and a marked decrease in muscle mass. These changes, which are observed in both sexes, are accompanied by reduced IGF-I and calcitriol levels, lower sex hormones concentration or function, decreased growth hormone secretion, and higher circulating PTH. An isocaloric low protein diet blunts the response to exogenous IGF-I, growth hormone or PTH. All the bone, muscle and hormones abnormalities are corrected by essential amino acids supplements. Discussion: These features in rodents fed such a diet are quite reminiscent of the situation in the frail oldest old. Conclusion: This model should be of help to further study the pathophysiology of frailty and/or sarcopenia, and to explore preventive or curative measures.

DENERVATION CAUSES MYOSIN HEAVY CHAIN CO-EXPRESSION AND MYOFIBER ATROPHY IN SENESCENT RAT GASTROCNEMIUS MUSCLE. R. Hepple, S.L. Rowan, F.M. Purves-Smith, K. Rygiel, N.M. Solbak, D.M. Turnbull *(Montreal, Canada)*

Introduction: Aging of muscle is associated with progressive atrophy that accelerates in advanced age. This whole muscle atrophy is characterized by marked heterogeneity in myofiber size within the muscle, and a progressive accumulation of very small myofibers (1000 m2 in size) that frequently express multiple myosin heavy chain (MHC) isoforms (MHC co-expression). Interestingly, we recently showed that the accumulation of these severely atrophied myofibers tracks the trajectory of sarcopenia in both a prototypical fast and a prototypical slow twitch muscle (Rowan et al., Exp Gerontol. DOI 10.1016/j.exger.2011.03.005). In seeking to the explain the reason for the accumulation of these small fibers, although there is abundant evidence of denervation in aging muscles, the extent to which denervation causes myofiber atrophy in aging muscle has not been quantified previously. Furthermore, although MHC co-expression is a well-known consequence of experimental denervation, the extent to which denervation in aging muscle is responsible for myofiber MHC co-expression has also not been examined previously. Objectives: The objectives of our study were to quantify (i) the extent of motoneuron depeletion in lumbar spinal cord with aging; (ii) the contribution of denervation to myofiber atrophy in aging muscle; (iii) the contribution of denervation to myofiber MHC

co-expression in aging muscle; and (iv) to gain insight into the mechanisms driving myofiber atrophy following denervation in aging muscle. Material and methods: We examined motoneuron (MN) soma counts in the lumbar spinal cord using immunolabeling for choline acetyl transferase. We also examined the in situ myofiber expression of the denervation-specific (in adult muscle) sodium channel, Nav1.5, in relation to fiber size and MHC expression pattern, in young adult (YA) and senescent (SEN) rat gastrocnemius muscle using immunofluorescence labeling in muscle cross-sections. To gain insight into the mechanisms driving atrophy of denervated myofibers, we also characterized ubiquitin ligase (MAFbx, MuRF1) expression by immunofluorescence labeling in Nav1.5 positive versus Nav1.5 negative fibers in serial sections of the same muscles. Results: Gastrocnemius muscle mass declined 38% between YA (2054 ± 41 mg) and SEN (1277 ± 36 mg; P<0.05). The number of MN soma in the lumbar spinal cord declined 27% between YA (638 ± 34 MNs x mm-1) and SEN (469 ± 13 MNs x mm-1). Nav1.5 positive fibers (1548 ± 70 m2) were 35% smaller than Nav1.5 negative fibers (2367 ± 78 m2; P<0.05) in SEN muscle, whereas Nav1.5 negative fibers in SEN muscle were only 7% smaller than fibers in YA muscle (2553 ± 33 m2; P<0.05). No Nav1.5 positive fibers were seen in YA. In contrast, approximately 90% of fibers 1000 m2 were Nav1.5 positive, a myofiber size we have shown previously is unique to SEN muscle and the abundance of which tracks the trajectory of sarcopenia. Nav1.5 positive MHC slow fibers showed up-regulation of MAFbx and MuRF1 but were, on average, not smaller than Nav1.5 negative MHC slow fibers. Conversely, MHC fast fibers had much higher constitutive levels of MAFbx than MHC slow and, when expressing Nav1.5, MHC fast fibers had elevated MuRF1 and were 23-50% smaller than Nav1.5 negative fibers. More than 70% of MHC co-expressing fibers were Nav1.5 positive, and these Nav1.5 positive fibers not only showed elevations of both MAFbx and MuRF1, but they were markedly smaller than either MHC slow or MHC fast Nav1.5 negative fibers. Discussion: The decline in motoneuron soma in the lumbar spinal cord of the rat with aging parallels that shown previously in human lumbar spinal cord with aging (Tomlinson and Irving, J Neurol Sci. 34: 213-319, 1977), and demonstrates a significant loss in motoneuron number in association with sarcopenia. The observation that Nav1.5 positive fibers were significantly smaller than Nav1.5 negative fibers in SEN muscle, whereas Nav1.5 negative fibers in SEN were <7% smaller than myofibers in YA muscle where no Nav1.5 labeling was seen, implicates denervation as the primary cause of myofiber atrophy in aging muscle. Similarly, the vast majority of the smallest myofibers in SEN muscle were Nav1.5 positive, implicating denervation as the cause of their progressive accumulation as sarcopenia progresses with advancing age. As >70% of MHC co-expressing fibers were Nav1.5 positive, our results are consistent with denervation also being the primary cause of MHC co-expression and the well-known shift in fiber type expression seen in aging muscle. In general, our results suggest that denervation causes more atrophy in MHC slow fibers than MHC fast fibers. Our results further show that the patterns of myofiber atrophy within each MHC class following denervation were associated with fiber-type specific patterns of up-regulation of ubiquitin ligases that are essential to drive muscle atrophy under a variety of conditions, including denervation. We saw a much higher constitutive expression of MAFbx in fast twitch myofibers, which may help explain their apparently greater atrophy susceptibility in response to denervation in aging muscle. However, assuming that denervated MHC slow fibers also contribute to the appearance of MHC co-expressing fibers, which were the smallest fibers seen in aging muscle, denervation is likely also a significant cause of atrophy in MHC slow fibers with aging, but this point is easily missed if one does not account for the origins of the MHC co-expressing fibers. Conclusion: Our results suggest that denervation is a significant cause of myofiber atrophy and MHC co-expression in aging muscles. Atrophy of denervated myofibers in aging muscle occurs in part through activation of the proteasome machinery, where distinct fiber-type expression patterns of the ubiquitin ligase MAFbx relates to the differences in degree of atrophy seen between fiber types following denervation. Collectively, therefore, our results implicate denervation as the primary cause of myofiber atrophy in aging muscle, suggesting renewed focus on the causes of denervation in aging muscle will be key to identifying therapeutically effective treatments for sarcopenia.

MYOSTEATOSIS AND MYOFIBROSIS: RELATIONSHIP WITH AGING, INFLAMMATION AND INSULIN RESISTANCE. E. Zoico, A. Rossi, F. Corzato, D. Olioso, C. Bambace, F. Fantin, M. Zamboni *(Verona, Italy)*

Introduction: Sarcopenia, the age-associated loss of skeletal muscle mass and function, is characterized not only by quantitative changes in skeletal mass, but also by qualitative changes determining an increased risk of functional impairment, physical disability and frailty. The mechanisms impairing muscle quality and contributing to Sarcopenia are still incompletely known. Aging of skeletal muscle is associated with an increase in fibrous connective tissue and an impairment of muscle regenerative potential. Even though functional consequences of muscle fibrosis seem relevant in geriatric research this phenomenon of myofibrosis (MF) is not so well known and only a few papers described a clear association between fibrosis and aging. The increase in muscle fat infiltration with aging, also called myosteatosis (MS) has been object of intense investigation but its relation with MF is not known. Objectives: The aim of this paper was to investigate the main predictors of muscle quality, evaluated as the degree of MF and MS, in healthy aging. To test this hypothesis we selected a sample of healthy elderly men undergoing elective vertebral surgery and we studied samples of paraspinous muscle (PM) and subcutaneous adipose tissue (SAT) near the muscle. Material and methods: A total of 14 men, aged between 60 and 80 years (70.9 ± 6.8 years, mean Â± SD) with BMI ranging from 25.3 to 44 Kg/m2 (30.6 ± 4.9 Kg/m2 , mean ± SD) were studied. In biopsies of paraspinous muscle (PM) we histologically determined the area of MF and MS. Muscle quality index (MQI) was calculated as the mean percentage of MF and MS area in three sections. The intramuscular adipose tissue (IMAT) within the PM area was evaluated by MRI and total body composition was studied by DXA in all subjects. Circulating fasting glucose, insulin, hs-CRP, leptin, adiponectin and IL-6 were measured and a HOMA index calculated. Quantification of gene expression in PM and in subcutaneous adipose tissue (SAT) near the muscle was performed by Real time-PCR. Results: Subjects with a worse muscle quality presented higher values of MQI and had significantly higher values of BMI, waist circumference, fat mass and fat mass percentage. Moreover, subjects with higher values of MQI presented higher values of IMAT compared to men with lower values of this index. Elderly men with higher degrees of MF and MS had higher values of circulating leptin levels, insulin and HOMA index, but no more significantly after adjustment for FM. The expression of IL-6 in SAT was significantly higher in subjects with higher values of MQI compared to those with lower values of the index. In PM we found significant higher expression of Wnt-10b and a trend toward higher expression of myostatin, SOCS-3 and SREBP-a, in elderly subjects with higher degrees of MF and MS. Discussion: The main finding of this study is that not only the degree of MS but also the degree of MF is associated with a pattern of increased adiposity, with central fat distribution and a worse metabolic profile. Only a few studies were specifically designed in humans to investigate the molecular mechanisms contributing to sarcopenia. Aging of skeletal muscle is associated not only with muscle atrophy and replacement of muscle by adipose tissue, but also with an increase in fibrous connective tissue. Muscle fibrosis has been shown to be related to a decrease in muscle strength, elasticity as well as to reduced blood supply of muscle fibers, further increasing muscle fiber atrophy. Conclusion: Not only the degree of MS but also the degree of MF may be related to a pattern of increased adiposity with central fat distribution and worse insulin sensitivity.

NEURAL COMPENSATION IN SARCOPENIA. C.G.M. Meskers, A.B. Maier, A.C. Schouten, J.H. Arendzen, J.H. de Groot *(Leiden, The Netherlands)*

Introduction: Sarcopenia i.e. low muscle mass is of increasing interest because of high prevalence in old age and its relation with detrimental outcome, i.e. functional impairment and loss of ADL dependency. Muscle mass, i.e. the number of force generating sarcomeres is a major determinant of muscle function, in combination with energy supply and nervous control. Functions of the muscle or motor and its controller, i.e. the peripheral and central nervous system are strongly intermingled. Muscle contraction and relaxation are constantly monitored by sensory organs which detect changes in either position and velocity: muscle spindles and force: golgi tendon organs. This information is fed back to the spinal cord, where is its processed under supervision and tuning by higher areas of the central nervous system and referred to the muscles by the alpha-motor neurons. Muscle and nervous system are thus within a closed loop and cause and effect are undefined. This allows for several scenarios regarding the muscle-nervous interaction in sarcopenia. The nervous system might be the primary cause for sarcopenia and subsequent functional decline; the nervous system might degenerate synchronously with muscle or the nervous system may compensate for muscular degeneration. Identification of aforementioned scenarios in sarcopenia may have consequences for therapy. Because of their narrow relation within a closed loop, function of muscle and nervous system are hard to separate. Novel control engineering techniques based on quantification and parameterization of a system's reaction to precise perturbations may be the appropriate tool. Objectives: The aim of the study was to separate and quantify muscle from neural function simultaneously during a functional task and assess its outcome as a function of age and history of falls. We were particularly interested to find evidence for the existence of different scenarios regarding muscle and nervous system functional decline in old age and clinical evident pathology: primary nervous function decline (scenario 1); simultaneous decline (scenario 2) or compensation by the nervous system for primary muscle dysfunction (scenario 3). Material and methods: Continuous random force perturbations were applied to the hand by a haptic wrist rotational manipulator and had to be actively resisted. Environmental conditions, i.e. viscosity of the manipulator were varied. The relations between input perturbation and output joint angle and muscle activity as assessed by electromyography of the mm. flexor and extensor carpi radialis were quantified. Muscular and neural contributors to aforementioned relations were discerned by neuromuscular modeling. Main outcome parameters were active muscle stiffness, i.e. passive elastic muscle properties modulated by (co) contraction, reflex gain, reflex gain modulation to the different environmental conditions applied and reflex loop time. Aforementioned outcome parameters were assessed in a cohort of 50 subjects with an age range of 9 to 84 years divided over five bins of increasing mean age. A sixth group was formed by seven elderly patients with a history of falls. Results: Active muscle stiffness declined with age above 50 years with a further decline in the group of patients ($F=3.1$, $p=0.018$), representing loss of muscle function. In contrast, both reflex gain and modulation were higher in healthy elderly aged over 75 years of age and patients ($F=2.66$, $p=0.03$). Discussion: It was possible to disentangle and quantify discern muscular from neural contributions to joint stiffness during active task performance by using external perturbations and a system identification and parameter estimation approach. Active intrinsic stiffness as a representative of muscle function was found to decrease with age as expected. Evidence was found for enhanced activity of the neural system at older age and in patients with a history of falls, i.e. higher reflex gains and a tendency to enhanced reflex modulation to provoking external conditions. By adding viscosity to the environment, i.e. the manipulator, reflex gains can be tuned up without the penalty of becoming instable. Previous research by our group showed that this tuning up of reflex gains is mechanically optimal. Thus, evidence was found for the third scenario as previously postulated. Tuning up of reflex gains may be compensatory for decline of active muscle stiffness. This is important for understanding the relation between low muscle mass and functional decline at old age and may have therapeutic consequences. It should be noted that the level at which the up regulation is powered remains undefined and may originate from changes in sensory organ function up to the higher brain areas. The role of

cognition in this respect remains to be elaborated. Interventions, such as dedicated strength training may be required to make a further distinction between different scenarios of muscle-nervous interplay in sarcopenia and functional decline. Conclusion: Evidence was found for increased neural function in combination with declined active muscle stiffness as a function of age and in patients with a history of falls. This underlines the necessity to assess neural function in combination with muscle properties in understanding and treating sarcopenia and functional decline in old age.

SELECTIVE ACTIVATORS OF FAST SKELETAL MUSCLE TROPONIN: A NOVEL APPROACH TO TREATMENT OF NEUROMUSCULAR DISORDERS. J.M. Cedarbaum, M.M. Chen, J. Lee, D. Morgans, A. Wolff, F. Malik *(San Francisco, USA)*

Introduction: CK-2017357 is a novel activator of the fast skeletal muscle troponin complex, the first of a novel therapeutic class intended to improve skeletal muscle function. Objectives: To reveiw preclinical and clinical studies of CK-2017357 completed to date. Material and methods: Data from animal models, a Phase 1 study in healthy volunteer subjects, and and a Phase 2 Evidence-of-Effect study in ALS patients will be reviewed. Results: CK-2017357 slows the rate of calcium release from the regulatory troponin complex, thus sensitizing fast skeletal muscle fibers to calcium in vitro. In an in-situ nerve-muscle preparation CK-2017357 increased the force of muscle contraction at physiologically-relevant rates of nerve stimulation, increased the power of muscle contraction, and diminished the rate of development and degree of fatigue of both normal and ischemic muscle. CK-2017357 increased the force of contraction of the anterior tibialis muscle following stimulation of the peroneal nerve in healthy volunteers in a similar fashion to what was observed pre-clinically, confirming translation of mechanism into humans. Single-dose, Phase 2a Evidence of Effect (EoE) clinical trials have been completed or are underway in patients with Amyotrophic Lateral Sclerosis (ALS), lower limb claudication due to peripheral artery disease, and Myasthenia Gravis. In patients with ALS treated with single doses of CK-2017357 or placebo, we observed dose-related decreases in sub-maximal handgrip fatigue, small but significant increases in isometric strength, and a significant increase in maximal voluntary ventilation (MVV). Both patient and investigator global assessments also improved. The most frequent adverse events associated with CK-2017357 administration included dizziness, fatigue, headache, somnolence and euphoric mood. Discussion: The effects of CK-2017357 in ALS patients are consistent with and reflective of preclinical findings. Conclusion: The unique mechanism of action of skeletal muscle troponin activators may have applicability to treatment of a wide variety of conditions with impaired muscle function including neuromuscular disorders, primary muscle diseases and age-related muscle loss.

IS GLUTAMINE THE CORNERSTONE OF SARCOPENIA IN VERY OLD INDIVIDUALS? D. Meynial-Denis, A.M. Beaufrère, L. Cynober, P. Patureau Mirand *(Clermont-Ferrand, France)*

Introduction: Glutamine is the most abundant free amino acid in the body and has its primary source in skeletal muscle, from where it is released into the bloodstream and transported to a variety of tissues such the gut. The size of the muscle glutamine pool may be related to lean body mass and so, to sarcopenia. Objectives: Because glutamine is known to have a specific role in very old rats (up to 25 months of age), the aim of this study is to demonstrate that glutamine is the cornerstone of sarcopenia with advanced age. For this reason, we have orally supplemented female rats (27 months) with glutamine (20% of diet protein) intermittently, before animals became very old (named long-term treatment with glutamine). Rats were studied after the last glutamine cure. Material and methods: Skeletal muscle (tibialis anterior) and gut were dissected and weighed. A 2-cm length of the proximal part of the jejunum was removed for measurements of intestinal histomorphometry. Results: Muscle mass decreased by ~ 20 % with advanced age. No difference was observed in skeletal muscle mass with glutamine supplementation. However, glutamine synthesis was enhanced in skeletal muscle from very old female rat as previously reported. Glutamine played a role in maintaining mass of splanchnic tissues. Total intestine mass was significantly higher in glutamine supplemented very old rats than in controls (~15%). By histomorphometry, we demonstrated that villus height increased with glutamine supplementation in very old female rats; this increase was similar to that measured in gut mass. Discussion: Long-term treatment with glutamine had positive effects on very old rats: 1) it prevented the loss of body weight, but, 2) it did not prevent the inevitable sarcopenia because of its inefficiency to limit the loss of muscle mass due to aging and, 3) it maintained or improved the gut mass. Long-term treatment with glutamine essentially played a role in maintaining intestine integrity and intestinal immune function. Indeed, villus height was improved by this treatment. Consequently, the observed increase in glutamine requirements can be explained by the increased use of glutamine by the gut. Glutamine may play a role in repairing possible gut mucosal deterioration due to aging by increasing mucosal protein synthesis and decreasing ubiquitin-dependent proteolysis, as previously reported in healthy humans. Conclusion: Glutamine is not the cornerstone of sarcopenia in very old individuals even if a very high synthesis capacity is maintained in aging atrophied-muscle.

AGRIN-DEPENDENT SARCOPENIA. J.W. Vrijbloed, S. Hettwer, A. Shaheen, P. Dahinden, R. G. Fariello *(Schlieren, Switzerland)*

Introduction: Sarcopenia is characterized by reduced lean muscle mass associated with diminished functionality at old age leading to frailty, disability and increased mortality. Sarcopenia is imposing a heavy burden, not only on the affected individual but also on our rapidly aging society. Various causes for sarcopenia have been suggested, among which, on the basis of recent data in aged animals, a crucial role of the neuromuscular junction (NMJ), the sole link between motor neurons and muscle fibers, has emerged. As a consequence sarcopenia is commonly referred to as a syndrome of the NMJ. The extracellular matrix protein agrin is essential for the formation and stabilization of NMJs. Agrin forms a complex with LRP4, a low-density lipoprotein receptor (LDLR)-related protein and MuSK, a transmembrane tyrosine kinase. Agrin is cleaved by the pre-synaptic protease neurotrypsin at two sites thereby losing its NMJ stabilizing function. Agrin cleavage by neurotrypsin frees a soluble 22 kDa C-terminal Agrin Fragment (CAF) detectable in blood. Transgenic mice over-expressing neurotrypsin in motoneurons (SARCO mice) exhibit a sarcopenia-like phenotype. In these mice CAF is elevated in the serum. Conversely, in neurotrypsin knockout mice CAF is undetectable. SARCO mice exhibit reduced muscular mass, abnormal gait and diminished limb strength. Histopathology of SARCO mice muscles reproduces all the key features of the pathology found in muscles of sarcopenia patients. Objectives: To test the hypothesis that over-activity of neurotrypsin as revealed by elevated levels of CAF in serum, may play a pathogenic role in the genesis of sarcopenia. Material and methods: Previous pilot studies demonstrated that in a healthy population of Swiss blood donors CAF is measurable in blood where it shows a narrow range of values that do not vary with aging. Based on these observations, a pilot multi-center, non-randomized, open-label, vertical clinical study was designed. Briefly, 133 informed and consenting elderly (> 65 y.o.a) were recruited and assigned to a sarcopenia patients (SP) group defined according to up to date diagnostic criteria and an aged matched control (AMC). The SP group was characterized by a DXA scan value below -1. People with DXA values between -1 and 0 were assigned to the SP group if presenting weakness in their grip and knee strength and/or reported difficulties in daily living as to walking and lifting objects, with frequent falls. People with DXA values >0 were assigned to the AMC group. The SP group comprised 73 subjects (34 women and 39 men, aged 65 to 87), the AMC group comprised 60 subjects (28 women and 32 men, aged 65 to 88 years). Anthropometric data, DXA, blood levels of inflammatory and other markers (IL-1, hs-CRP, TNF-alpha, glucose, etc.) as well as grip and knee strength were assessed. As a further reference CAF values of a healthy population, serum from Swiss blood donors (BD; n = 169; 86 women and 83 men, age 19 to 74 years) were analyzed. The serum CAF values were determined using Western blot and assays were performed in blind. Results: The mean CAF level in the BD group was about 3 ng/ml without gender specific differences or age correlation and was indistinguishable from the AMC group. The SP group showed a 1.5-2 fold increased mean CAF level which was statistically highly significant. Detailed analysis of the CAF levels showed that approximately 40% of the sarcopenia patients had non-overlapping values with the normal range. Interestingly, the CAF levels of the males in the SP group were significantly more elevated then the females indicating that males are probably more affected by agrin-dependent sarcopenia. Discussion: The results of this study confirmed a role of the neurotrypsin/agrin axis in sarcopenia stressing the clinical relevance of our original animal data. CAF levels in the sarcopenic test group as a whole were significantly higher compared to both the age-matched controls and the healthy blood donors. None of the variables under observation that might have influenced the significance of the results (diabetes, renal function, vitamin D levels and inflammation markers) correlated to the CAF values. These results indicate that excessive agrin inactivation at the NMJ may be an important event in the development of sarcopenia. Thus, CAF detection in serum may be of diagnostic value. Measuring CAF blood levels in sarcopenia patients lead to the first causal classification of sarcopenia in an agrin-dependent form that is distinguishable from natural muscle aging. Further work needs to be performed in order to establish the selectivity and specificity of this test and to detect possible variations of CAF levels according to the evolution of sarcopenia. Some of these activities will be performed within the EU-funded project DISARCO during which an ELISA immunoassay will be developed for clinical use. Within this project Neurotune will provide the scientific background, Microcoat GmbH the ELISA technology and the Friedrich-Alexander University Erlangen-Nürnberg (Prof. Sieber), will perform a clinical trial. Conclusion: Elevated agrin degradation occurs in a substantial subset of sarcopenia patients and can be used to identify those patients in whom a novel pathogenic target may be therapeutically exploited. Excessive degradation of agrin by neurotrypsin leading to fragmentation of the NMJs appears to be an important process in the pathogenesis of sarcopenia.

REDUCED CALORIE WEIGHT LOSS, EXERCISE, VITAMIN D AND LEAN MASS IN POSTMENOPAUSAL WOMEN. A. McTiernan, C. Mason, C. Duggan, L. Xiao, C.Y. Wang *(Seatle, USA)*

Introduction: Loss of muscle mass with aging leads to reduced strength and functionality, with associated adverse health effects (1). Weight loss in elderly obese could contribute to sarcopenia (2). Previous research reported that a combination of weight loss through diet plus exercise improves physical function in elderly adults despite lean mass loss (3). It is not clear to what extent exercise and vitamin D status ameliorates lean mass loss with weight loss interventions in overweight/obese older women. Objectives: We investigated the effects of 12-months' reduced-calorie dietary weight loss and/or aerobic exercise on lean mass in overweight/obese postmenopausal women. We also assessed the effect of baseline serum 25-hydroxyvitamin D (vitamin D) status on change in muscle mass with the interventions. Material and methods: Participants were Seattle, Washington, U.S.A. area postmenopausal women (no menstrual cycles for 1 year), aged 50-75 years, body mass index, BMI ?25.0 kg/m2, and exercising < 100 minutes/week. Exclusion criteria included: use of menopausal hormones in past 3 months; history of serious medical conditions; diabetes; alcohol intake >2 drinks/day; currently smoking; contraindication to study interventions; current participation in structured weight loss program; and use of

weight loss medications. 439 women were randomized to: reduced-calorie weight loss diet (N=118), aerobic exercise (N=117), reduced-calorie weight loss diet plus aerobic exercise (N=116), or control (N=87). The reduced-calorie weight loss diet was a group-based modification of the U.S. Diabetes Prevention Program lifestyle change diet with 10% weight loss goal. The exercise program was 45 min/day, 5 days/week moderate-to-vigorous intensity aerobic exercise (facility + home). DEXA scans were administered at baseline and 12 months for measurement of lean, fat, and bone mass. Serum 25-hydroxyvitamin D was quantified by direct, competitive chemiluminescent immunoassay (DiaSorin LIAISON 25-OH Vitamin D Total assay, Heartland Assays, Inc., Ames, IA). Intra- and inter-assay coefficients of variation were 8.2% and 11.0%, respectively. Mean changes were compared between groups (intent-to-treat) using generalized estimating equations. Pearson correlation coefficients were calculated to assess the relationships between baseline serum vitamin D and body composition variables. We also assessed the association of baseline serum vitamin D status with change in lean mass in the three intervention groups vs. controls using clinical cutpoints for sufficiency (4). Results: 399 (91%) women returned for 12-month measures. Baseline characteristics were mean (s.d.): age 58.0 (5.0) years, weight 83.6 (11.8) kg, BMI 30.9 (4.0) kg/m2, 39.8 (8.1) kg fat mass, 47.2% (4.3) body fat, 40.2 (5.0) kg lean mass, 48.5% (4.2) lean mass, VO2max 22.9 (4.0) kg/ml/min, and exercising 32.8 (44.1) minutes/week. Most (85%) were non-Hispanic white women. Weight decreased by 8.7% ($p<0.001$) in the reduced-calorie weight loss diet group, 2.4% ($p=0.03$) in the aerobic exercise group, and 10.8% ($p<0.001$) in the reduced-calorie weight loss diet plus aerobic exercise group vs. a 0.6% decrease in controls. Baseline vitamin D status was positively associated with percent (%) lean mass (correlation= 0.12, $p<0.01$). Categorizing women by baseline vitamin D levels as < 20 ng/mL (deficient), 20.0-29.9 ng/mL (insufficient), and > 30.0 ng/mL (sufficient) showed strong negative associations of vitamin D category with kilograms weight (p trend=0.0006) and fat mass (p trend=0.0003), and a marginal negative association with kilograms lean mass ((p trend=0.06)). As previously reported (5), compared with a decrease of 0.1% in controls, lean mass changed by -1.9% ($p<0.005$), +0.7% (nonsignificant), and -1.1% (nonsignificant) in reduced-calorie weight loss diet, exercise, and combined reduced-calorie weight loss diet + exercise groups, respectively. Lean mass change in the intervention and control groups did not differ significantly by vitamin D status. As previously reported, (6) change in % body fat also did not differ by baseline vitamin D status. Discussion: The results of this study agree with other studies that have found a reduction in lean mass with dietary weight loss in older adults (3). We found no effect of baseline vitamin D status on change in lean mass with any of the interventions. However, few women had "sufficient" levels of vitamin D (> 30 ng/mL). Although baseline serum vitamin D concentration was positively associated with percent lean mass, this was likely due to the negative association of percent body fat with vitamin D concentration. Conclusion: This study suggests that exercise ameliorates some of the lean mass loss with a reduced calorie weight loss diet, but that vitamin D status does not affect change in lean mass with a reduced calorie weight loss diet, exercise, or both combined. The effect of vitamin D supplementation on lean mass and physical function in older women undergoing a weight loss intervention is currently being tested in a randomized placebo-controlled trial. References: 1) A. J. Cruz-Jentoft et al., Sarcopenia: European consensus on definition and diagnosis: Report of the European Working Group on Sarcopenia in Older People. Age Ageing 39, 412 (Jul, 2010); 2) R. Roubenoff, Sarcopenic obesity: the confluence of two epidemics. Obes Res 12, 887 (Jun, 2004); 3) D. T. Villareal et al., Weight loss, exercise, or both and physical function in obese older adults. N Engl J Med 364, 1218 (Mar 31, 2011); 4) A. C. Ross et al., The 2011 report on dietary reference intakes for calcium and vitamin D from the Institute of Medicine: what clinicians need to know. J Clin Endocrinol Metab 96, 53 (Jan, 2011); 5) K. E. Foster-Schubert et al., Effect of Diet and Exercise, Alone or Combined, on Weight and Body Composition in Overweight-to-Obese Postmenopausal Women. Obesity (Silver Spring), (Apr 14, 2011); 6) C. Mason et al., Effects of Weight Loss on Serum Vitamin D in Post-menopausal Women. . American Journal of Clinical Nutrition, (2011).

SARCOPENIA IN A GROUP OF MEXICAN ELDERS. L.M. Gutiérrez-Robledo, V.E. Arango-Lopera, M. Ulises Pérez-Zepeda *(Mexico City, Mexico)*

Introduction: Sarcopenia has been characterized by progressive loss of skeletal muscle mass, muscle strength, and diminished physical performance. There is not an agreement about how determine it, and there are no standardized measurements of each one of its components. These are some reasons why diverse studies have shown prevalences between 8 and 50%. These lack of consensus translates in sanitary and social costs, due to the incorrect assessment and delayed potential interventions. Objectives: - Determine the prevalence of sarcopenia in Mexican elderly with the EWGSOP criteria. - Determinate the different frequency of sarcopenia in our population in contrast to that reported in the literature. - Evaluate the EWGSOP algorithm to the detection of sarcopenia. - Determinate different prevalences in subgroups by gender, age, BMI and frailty. Material and methods: We conducted a cross sectional study of the basal data of Coyoacan cohort; this cohort is described in detail elsewhere. Subjects included were: >70 years of age, who resided in Mexico city agreeing to participate in the protocol. After signing of informed consent. . The subjecta were assesed at the basal wave. The complete cohort sample consists of 1,124 subjects, but for this study we used a subsample of 345, with no statistical differences in sociodemographic, functionality and quality of life, among other features. The sample size was calculated with the prevalences previously mentioned, with a power of 96 to 99.8%. After the sampling, in a first visit, the subjects were invited to participate in the Protocol, and in a second visit they were measured to obtain anthropometry. The EUGMS criteria were used to define sarcopenia: for muscle mass calf circumference was used, and muscle strength was measured trough hand grip strength and physical performance by means of gait speed. To determine sarcopenia, the algorithm steps were followed: subjects with gait speed greater than 0.8m/s were assessed with hand grip strength; if normal, that was considered with no sarcopenia; if abnormal, along with those subjects with <0.8m/s walking speed, muscle mass was assessed, if abnormal; they were considered sarcopenic. We determined frailty with the SOF criteria: positive answer to three questions, unable to raise from a chair, loss of weight and feeling less energy. If the subject had only one or two criteria was considered pre-frail; and 0 positive answers not frail. We used STATA 11 programme for the analysis of the data. Results: We assessed 345 subjects, with a mean age of 78.5, a proportion of 53.3% of women. The mean for calf circumference was of 33.61cm, for hand grip strength 19.88kPa and for gait speed 0.6m/s. The prevalence of Sarcopenia according EWGMS (42.9%), using calf circumference, but in this study, based on the low sensitivity (44.3%) of the circle, despite the high specificity (91.4%) (Group of Rolland et to the we exclude these subjects, leaving only those who had sarcopenia detected by alteration of grip strength or speed of the motion and the result is that the prevalence of the entity cannot be greater than 57%. Therefore the prevalence of sarcopenia in our population ranges between 42.9 and 57 %. Regarding to gender, we found a greater prevalence in women, the oldest old (>90 year), normal BMI and in prefrail subjects. Discussion: The prevalence of the sarcopenia varies between different populations, ages, gender, diagnosis method and housing website. In this study, using the differential scheme proposed, was found a range of prevalence that corresponds with that reported in other studies. The construction of the definition of sarcopenia has been in permanent change, but every day there is a greater consensus that the real definition should be based on muscle mass, muscle strength and physical performance, but how to measure each of the items is still subject to debate. In addition to the above some researchers determine sarcopenia based, only in the muscle mass, as measured by DEXA, or BIA with the limitation of the fatty infiltration of the muscle, or TAC or RMI, with the limitation of the cost and the difficult access. With reported prevalence rates between 6.3 per cent and 70 per cent. All this could help explain why such marked differences in the prevalence rates have been reported in different studies. This study used the scheme proposed by the European consensus, used also by Landi, 2011 et al, who found a prevalence of 68% in males and 32.5% in women. Being greater in people with a history of CVD, osteoarthritis and with BMI below 21. The prevalence reported in men is similar to ours, the difference is that the population of them, all older than 70 years, was for the institutionalized elderly and probably for that reason we had not a greater prevalence of sarcopenia in elderly people with a history of CVD. However it is not clear the why in our population, the majority of the sarcopenic elders had a BMI normal (adjusted for knee height). The differences by sex and age were similar to other studies, with an increasing prevalence directly proportional to the age. On average, it is estimated that 5-13% of elderly people aged 60-70 years are affected by sarcopenia, and the numbers increase to 11-50% for those aged 80 or above. Regarding frailty we found a greater proportion of non-frail or pre-frail subjects with sarcopenia. Conclusion: The EUGMS criteria could be a useful tool in determining sarcopenia in our population.

IS POSTERIOR NECK MUSCLE CROSS SECTIONAL AREA AS SEEN ON MRI BRAIN SCANS, A GOOD INDICATOR OF GENERAL SARCOPENIA? A.H.M. Kilgour, C. Gray, S. Semple, A. Pattie, D. Subedi, J.M. Wardlaw, J.M. Starr *(Edinburgh, United Kingdom)*

Introduction: Current imaging tests used to study sarcopenia include whole body DEXA and CT or MRI of a large muscle group, usually the quadriceps, inferring that muscle bulk of one group closely relates to total body muscle mass. Thigh muscle CSA in the elderly has been shown to be associated with falls, fractures and the ability to live independently and therefore has been used in studies investigating sarcopenia. Few of the longitudinal aging studies have included any of these measures in their study protocols, whereas several of them include an MRI brain scan. We have previously developed a technique to measure posterior neck muscle cross sectional area (CSA) on MRI brain scans with good inter-rater reliability (0.92-0.99 intra-class correlation coefficient). This has potential as a measure of muscle mass to aid diagnosis of sarcopenia. However, to what extent neck muscle CSA correlates with other muscle groups is unknown. Objectives: To measure the relationship between posterior neck muscle cross sectional area and a commonly used measure of muscle size, mid-thigh cross sectional area. To assess whether posterior neck muscle cross sectional area could be used as a measure of general muscle size. Material and methods: 25 participants from the Lothian Birth Cohort (LBC) 1936 study (who had all undergone a recent MRI brain as part of the LBC study) were recruited to undergo an MRI scan of their mid-thigh. The MRI brain scan included volumetric T1-weighted images acquired at 1.5 Tesla (isotropic 1.3mm voxels). These images were used to measure the CSAs of trapezius, splenius capitis, semispinalis capitis as a combined group; obliquus capitis inferior; and sternocleidomastoid (SCM). All measurements were performed bilaterally in the mid-C2 transverse plane. The mid-thigh MRI scans were obtained on a 3.0 Tesla research machine. The CSAs of the posterior, medial and anterior muscle groups were measured bilaterally at the mid-point between the protuberance of the greater trochanter and the upper border of the patella. All measurements were made using the Analyze image analysis package. Results: Data were analysed for 24 of the participants: one participant had been unable to tolerate the full MRI brain scan. Of these 24 subjects, 11 were female and 13 male. Mean total neck muscle CSA was 22.5cm2 (sd 3.7) for the female subgroup and 38.1cm2 (sd 6.3) for the male subgroup. Mean total thigh muscle CSA was 184.3cm2 (sd 36.5) for the female subgroup and 277.0cm2 (sd 31.3) for the male subgroup. An independent t test showed that both total neck muscle CSA ($p<0.001$) and total thigh muscle CSA ($p<0.001$) were significantly different between the female and male subgroups. The Pearson's correlation coefficient for total neck muscle CSA and total thigh muscle CSA is 0.876. A formula for predicting neck muscle CSA from

thigh muscle CSA was calculated using linear regression: Predicted neck muscle CSA = 1173.404 + (0.095 * total thigh CSA) + (sex (where M=0, F = 1) * -679.089). Discussion: This study shows that there is a strong correlation between neck muscle cross sectional area and thigh muscle cross sectional area, an often used proxy for general muscle mass. The percentage of shared variance between total neck muscle CSA and total thigh muscle CSA was 76.7% and this compares with the first unrotated principal component of the combined, obliquus and SCM neck muscle CSAs which explained 72.2% of variance between them. These findings are consistent with a general muscle size factor that would provide a measure of sarcopenia, when combined with a measure of muscle function. This indicates that posterior neck muscles can be used equally as well as thigh muscles as an index of general muscle bulk. This has important implications as many longitudinal studies involve serial brain scans, many of which will contain this neck muscle data. This will allow sarcopenia to be investigated in these studies without involving any additional scanning. Further studies are needed with larger data sets to investigate this important relationship further, with particular reference to how the relationship changes with age. Conclusion: This study has shown that neck muscle cross-sectional area is strongly correlated with thigh muscle CSA in a group of subjects in their mid-seventies.

ROUTINE DIAGNOSTIC EVALUATION OF ELDERLY PATIENTS: A NOVEL GERIATRIC ASSESSMENT. C.G.M. Meskers, M. Stijntjes, J.H. Pasma, C.K. Jurgens, G.J. Blauw, A.B. Maier *(Leiden, The Netherlands)*

Introduction: Mobility in the elderly patient is a primary disease course modifier and a determinant of dependency and premature death. Underlying determining factors of mobility are diverse, e.g. sarcopenia, decline in cognitive, sensory and cardiorespiratory function. Common geriatric assessment is not well qualified to discriminate between the influence of different ageing systems on mobility and is generally disease bound, i.e. restricted to a specific diagnosis. Understanding mobility determining factors is required for targeted interventions aimed at improving or maintaining mobility. Development of a novel clinical assessment of elderly is necessary for phenotypic identification and redefinition of clusters of patients based on similar mechanisms that cause mobility disorders. Objectives: Main aim is the implementation of a highly standardized, comprehensive and state-of-the-art clinical assessment of mobility disorders within a large geriatric outpatient clinic. The outcome of the clinical assessment is used for redefinition of phenotypes of patients beyond the classical disease definitions and a priori defined phenotypic clusters. The test battery should cover all possible subsystems that modify mobility yet should not exceed one and a half hours in duration. Outcome parameters should be directly available for clinical diagnosis and decision making, next to storage in a database for research purposes. Material and methods: Clinical assessment compromises the measurement of mobility, cognition, the cardiorespiratory and sensory system, i.e. vision, hearing and propriosepsis. Thereby, standard clinical tests are combined with novel technology. Physical performance is analyzed by a gyroscope attached at the lower back during the Short Physical Performance Battery, Timed Up and Go (TUG) test and measurement of gait speed. An instrumented treadmill, i.e. a treadmill with an integrated force plate, is used to assess the influence of fixed gait speeds on the stability and variability during walking. Furthermore, handgrip strength and quadriceps strength (using an instrumented isometric quadriceps chair) are measured. The effect of dual-tasks is examined on preferred overground walking speed as well as during TUG test. Cognitive functioning is assessed by the Mini-Mental State Examination, Visual Association Test and Montreal cognitive assessment. Neurological screening includes the assessment of vision, hearing, coordination, sensibility (two point discrimination) and nystagmus (by using Frenzel's goggles). Patient's anthropometry (standing height, arm span, body mass) is measured, whereby bioimpedance analysis is used to examine body fat mass and skeletal muscle mass. Continuous blood pressure is measured using Finapres in supine position together with the sway during standing using a force plate. Pulmonary function tests, oxygen saturation and electrocardiography will be used to assess cardiopulmonary function. Questionnaires about education, social context, nutrition (short nutritional assessment questionnaire), intoxications, activities of daily living (Katz-ADL) and about mobility and fall history will be filled in by the patient or family. Seven day accelerometry is applied to evaluate the actual level of daily physical activity. Results: Comprehensive diagnostic screening of elderly combined with novel technologies will allow phenotypic identification of subgroups forming clusters of patients based on similar underlying determinants of reduced mobility. This facilitates the development of targeted therapies and interventions that are required for improving and maintaining mobility. Discussion: Current knowledge on feasible and successful interventions for reduced mobility is lacking. Understanding of underlying determinants of mobility is necessary for that. Classical diagnostic evaluation of elderly, however, is limited and qualitatively and quantitatively insufficient. Conclusion: A novel comprehensive diagnostic evaluation of elderly was developed, needed to enable clinical phenotyping and to design successful interventions for reduced mobility and mobility disorders.

IS FUNCTIONAL CAPACITY RELATED TO THE DAILY AMOUNT OF STEPS IN POSTMENOPAUSAL WOMEN? S. Barbat-Artigas, S. Plouffe, S. Dupontgand, M. Aubertin-Leheudre *(Montreal, Canada)*

Introduction: The daily number of steps is usually used as an index of the physical activity level. There is growing evidence that 10 000 steps per day is an amount of physical activity that is associated with indicators of good health (less body fat; better body composition; lower blood pressure; better glucose tolerance). However, to our knowledge, no studies have investigated the relationship between the daily number of steps and the functional capacity. Objectives: The aim of this study was to investigate the relationship between the daily amount of steps and functional capacity. Material and methods: Fifty-seven postmenopausal women aged 50-70 years were recruited. Body composition (Body weight, body mass index (BMI), waist circumference, fat mass (%) and skeletal muscle mass), energetic metabolism (VO2 max, resting energy expenditure (REE), dietary intake (Kcal), physical activity (Total energy expenditure (TEE)) and functional capacity (muscle strength (handgrip and knee extensors), peak muscle power, chair stand, balance and alternate step tests) were measured. Women were divided in three groups (Group 1 (Sedentary; n=19): < 7500 Steps; Group 2 (Moderately active; n=20): 7500 - 10 000 Steps; Group 3 (Active; n=18): >10 000 Steps) according to their daily number of steps (means of steps measured by pedometer (Lifestyle) during 7 consecutive days). Non-parametric tests were used to compare the groups. Results: Body weight (p=0.035) and BMI (p=0.049) significantly decreased while Vo2 max (ml/min/kg; 0.004), daily minutes of activity (<0.001) and TEE (0.004) significantly increased as the number of steps increases. However, we noted no differences for age, skeletal muscle mass, fat mass (%), muscle strength, muscle power and functional capacity between groups. Finally, the proportion of dynapenic, type I and type II sarcopenic women was comparable between the three groups. Discussion: Even if the recommended daily number of steps (10 000) is respected, this seems not to be sufficient to improve the functional capacity compared with individuals considered as sedentary. Furthermore, our results showed that these recommendations do not prevent neither sarcopenia nor dynapenia. It is important to note that any women of the present cohort were involved in structured physical activity. Conclusion: The recommended daily number of steps may not be sufficient to prevent the loss of autonomy which occurs during normal aging. Further studies are needed to explore whether the recommendation in postmenopausal women needs to be: 1) increased (more than 10 000 steps) or; 2) combined with a structured physical activity to improve functional capacities.

GAIT SPEED AND UNDERNUTRITION. G. Abellan van Kan, Y. Rolland, M. Cesari, M. Houles, J. Bauer, B. Vellas *(Toulouse, France)*

Introduction: In theory, undernutrition plays an important role in the development on frailty, but scarce clinical data ara available on the topic. Objectives: Assess if undernutrition (measured by MNA and by blood sampling)is an indepedent associated factor of frailty identified by gait speed. Material and methods: Preliminary data on 124 patients are presented. Gait speed was measured over a 4.5 meter walking course. Usual gait speed was recorded twice and the best measure was retained for analyses. Malnutrtion was assessed by the Mini Nutritional Assessment and by biochemical parameters (PINI: Prognostic Inflammatory and Nutritional Index). Stepwise backward multivariate regression analyses were performed adjusted for main confounders. Results: At risk or malnourished, identified by MNA, [OR 5.54 (1.09-25.3)] and age [OR 1.17 (1.07-1.28)]were the only indepedent associated factors with low gait speed. The PINI failed to be associated after adjustments. Discussion: In this sample, Nutrtional status seems to be asscoaited with frailty identified by low gait speed, although the CI is very large showing heterogeneity of results. New pooled analyses with a German database (a total of 250 participants) will be performed to be presented at the congress. Conclusion: Undernutrition might be a crutial component of frailty. It needs to be proven that nutrtional intervention can reverse the frailty stataus of older adults.

THE CONCEPTUALIZATION AND UTILITY OF FRAILTY FOR OLDER POPULATIONS IN LOW AND MIDDLE INCOME COUNTRIES - FINDINGS FROM THE 10/66 DEMENTIA RESEARCH GROUP PREVALENCE AND INCIDENCE WAVES. A.T. Jotheeswaran, R. Sousa, C.P. Ferri, M. Dewey, D. Acosta, M. Guerra, Y. Huang, J.J. Llibre de Rodriguez, A. Salas, A.L. Sosa, J.D. Williams, M.J. Prince *(London, United Kingdom)*

Introduction: Frailty is a widely studied construct. However, there has been debate and a lack of consensus regarding definitions of the construct and its utility. The two main phenotypes are those of physical frailty, and a broader multidomain phenotype including cognitive, functional, and even social circumstances. Prominent examples of include: a) that recommended originally by Fried, operationalised with five indicators (exhaustion, weight loss, weak grip strength, slow walking speed and low energy expenditure) individuals identified as frail if they met 3 or more of the 5 criteria. In the Cardiovascular Health Study this criterion was associated with disability and morbidity, but independently predicted falls, worsening ADL disability, hospitalization, and death. b) a functional domain model introduced by Strawbridge, based on deficiencies in four domains of functioning (physical, nutritive, cognitive, and sensory), the first model to combine deficits across these domains. This model was assessed in terms of concurrent validity only in a small US sample (the Alameda County Study). c) Frailty indices as a measure of age-dependent deficit accumulation, assessing cumulative burden of for example symptoms, diseases, conditions, and disability (12). Proponents argue that similar rates of deficit accumulation (0.03 per year), and levels of saturation (0.67 of total number of items), regardless of the number and type of deficits included suggest psychometric robustness for an underlying trait of frailty. Such frailty indices tend to be predictive of mortality. Objectives: We aimed to assess the psychometric properties and predictive validity of the common frailty definitions in the context of the 10/66 Dementia Research Group population-based prevalence and incidence waves in Latin America, India and China. Specifically; 1. To study and compare the psychometric properties of the Fried and Strawbridge, addressing the following questions, a) are these unidimensional scales? b) do the scales have hierarchical scaling properties (confirming to IRT principles)? c) is measurement invariance exhibited across different countries and cultures? 2. To compare the predictive validity of the Fried and Strawbridge approaches with respect to the population attributable fractions (PAF) for the incidence of mortality and dependence.

Subsidiary questions to be addressed in these analyses are a) what is the added value of frailty as measured by these approaches over and above disability and morbidity, that is, are there independent associations observed after controlling for major chronic diseases and WHODAS 2.0 disability scores? b) is the whole more than the sum of its parts, that is, does the dichotomised or continuous frailty score provide better prediction of mortality or dependence than its individual elements? Material and methods: In the 10/66 Dementia Research Group's programme of population-based research in low and middle income countries one-phase population-based surveys were carried out (2003-2005, of all older people aged 65 years and over (n=17,945) living in geographically-defined catchment areas comprising 13 sites in nine countries (urban sites in Cuba, Dominican Republic, Venezuela and Puerto Rico, rural sites in Nigeria, and urban and rural sites in Mexico, Peru, China and India). The baseline survey included a clinical interview, an informant interview, and a physical examination generating information regarding dementia diagnosis, mental disorders, physical health, anthropometry, demographics, a chronic diseases risk factor questionnaire, disability, health service utilisation, care arrangements and caregiver strain. Regarding frailty, we collected information on undernutrition (arm circumference), gait speed, cognitive impairment (Community Screening Instrument for Dementia), and self reported exhaustion, weight loss, visual and auditory impairment. We lacked data only on grip strength. Full incidence waves were subsequently completed in Cuba, Dominican Republic, Venezuela, Peru, Mexico and China and a mortality sweep was conducted in India. Between 64% and 73% (by site) were found alive and successfully reinterviewed, between 3 to 5 years after baseline. Principal outcomes include incident dementia, stroke, dependence and mortality. Results: The frailty items did not show hierarchical scaling properties in any of the sites. The overall scale coefficient Hi ranging from 0.11 to 0.28 with coefficients above 0.30 indicating moderate and above 0.60 indicating good scalability. Neither was there evidence to support unidimensionality of component items. Exploratory factor analysis suggested a three factor solution comprising 1. undernutrition and weight loss, 2. underactivity, slow gait and cognitive impairment (+/- exhaustion), 3. visual and auditory impairment. In confirmatory factor analysis, this three factor solution fitted better than the one factor solution in all sites. There was evidence to support the predictive validity of the frailty construct with both the Fried and Strawbridge scales, when dichotomised, predicting the onset of dependence and mortality. While attenuated, these associations, for the most part, were still evident after controlling for morbidity and disability. However, 1. the sum of the population attributable fractions for the individual frailty indicators, collectively provided better prediction than did the scales, particularly when dichotomised 2. frailty indicators were variably associated with the outcomes ? sensory impairment and subjective exhaustion predicted neither mortality nor dependence; undernutrition was a stronger predictor of mortality than dependence; underactivity was a stronger predictor of dependence than mortality. Slow gait and cognitive impairment reliably predicted both outcomes. Discussion: While Fried's definition of frailty as "biologic syndrome of decreased reserve and resistance to stressors, resulting from cumulative declines across multiple physiologic systems" is likely to be applicable to individual organ systems, frailty is best understood as a multidimensional construct. In our analyses at least, we could find no evidence to support the notion of a unitary 'frailty syndrome'. While there is extensive evidence in the literature that deterioration in different systems tends to be correlated, it seems not necessarily, or generally, to be the case that 'it all goes together when it goes'. Nevertheless, the predictive validity of individual frailty indicators, both objectively measured (arm circumference, gait speed, cognitive impairment) and self-reported (weight loss and underactivity) was strongly supported in our analyses. It is clear that several of these indicators provide important information regarding future risk, beyond that already provided by knowledge of diagnoses and disability. The omission of hand grip strength from our battery of assessments was unfortunate. Other research suggests that this, together with gait speed is an important indicator of physical frailty, with strong predictive properties. However, we think it unlikely that inclusion of this one indicator would have materially affected our findings regarding dimensionality. Conclusion: Improvements in prevention and clinical care can be informed from further research into individual indicators of decreased reserve and deteriorating function, and their implications at individual and population level. These should include more sophisticated assessments of physiologic function, capable of being cheaply and easily applied in epidemiological field research.

POSTERS

P1- SARCOPENIA IN THE CHINESE PEOPLE: EPIDEMIOLOGY, MECHANISMS, MANIFESTATIONS AND THERAPEUTIC INTERVENTIONS. J. Wang, Z. Chen *(Beijing, China)*

Introduction: Sarcopenia is often defined as the steady and involuntary loss of skeletal muscle mass and strength leading to various functional declines during aging, causing a variety of adverse functional consequences and substantial health and economic burdens. Objectives: To review the previous data and to provide valuable cues for governmental decision-making and assist in addressing and abating the incidence of sarcopenia in China. Material and methods: The community-dwelling elderly Chinese people aged 70 years and over were reviewed based on previous data published in HongKong and Taiwan. Results: Epidemiological data indicates lower rates (12.3% and 7.6%) of sarcopenia in Chinese men and women aged 70 and over (23.6% and 18.6 in Taiwan elderly men and women) than in white people, with 6% decrease of muscle mass every 10 years after age of 30 years, and a more conspicuous strength decline after age of 80 years (in men) or 75 years (in women) especially in upper and lower limbs. Several lines of evidence show that the underlying mechanisms are characterized by multifactorial degenerative changes in the neuromuscular system, including losses of motor neurons (bodies, dendrites and neuromuscular synapses) and muscle fiber quantity and quality, and other contributing factors such as decreased dietary protein, changed anabolic and sex hormone, and reduced physical activity, etc. Its clinical manifestations mainly include a progressive strength decline and abnormal physical performances, such as frailty, imbalance and falls, etc. Its intervention procedures are mainly divided into three aspects: the physical activities (daily exercises, resistance training and strength training), the nutritional interventions (sufficient daily intakes of proteins, vitamin D and oleic acid, etc.), and the pharmaceutical treatments (testosterone, estrogen and other growth hormones, etc.). Discussion: In the Chinese mainland, the status of sarcopenia has attracted the concerns from research scholars. So far, the nationwide survey for diagnostic criteria, prevalence, underlying mechanism and interventions needs to be performed to fill the vacancy of sarcopenia research. Strength training,nutritional intervention,and physical exercise are the important means and research directions to arrest sarcopenia occurrence. Conclusion: It is confirmed that sarcopenia is an emerging health problem in the Chinese aging population, and the above research data can hopefully provide valuable cues for governmental decision-making and assist in addressing and abating the incidence of sarcopenia in China.

P2- SARCOPENIC OBESITY: CORRELATION WITH FUNCTIONAL LIMITATION AND PSYCHOLOGICAL STATUS IN A METABOLIC-NUTRITIONAL AND PSYCHOLOGICAL REHABILITATION UNIT. S. Tempera, L.M. Ricciardi, A. Guerra, C. Savina, C. Coletti, M. Paolini, L. Scavone, B. Neri, M.R. De Felice, L.M. Donini *(Rome, Italy)*

Introduction: Obesity/low muscle mass combination, appropriately defined as sarcopenic obesity (SO), due to disproportionally poor muscle strength compared to large fat mass, may lead to disability. Objectives: To verify the correlation of SO with the quality of life (SF-36 test) and disability (TSD-OC) and to assess the effectiveness of a metabolic-nutritional and psychological rehabilitation. Material and methods: All patients hospitalized at the Metabolic, Nutritional and Psychological Rehabilitation Unit of the "Villa delle Querce" Institute (Nemi, Rome-Italy) will be observed for a period of one year. Fat Mass and Fat Free Mass are measured with bioelectrical impedance and anthropometry, the muscle strength with handgrip strength test and Short Physical Performance Battery (SPPB) and bodily function with 6 minute walk test (6MWT) and blood chemistry parameters. The depression status (SCL90) and comorbility (SSA-RMN-O and Charlson comorbidity index score) are evaluated as possible interfering factors. Adverse clinical events (ACE) during the rehabilitation period are considered. Results: At the moment 49 patients (30 women, 19 men) were enrolled, mean age 59.8 years (31-78). The incidence of SO is 46.9%. Preliminary data show that SO is a condition that aggravates the recovery phase of functional and psychological status and the quality of life. Finally SO is linked to a higher prevalence of ACEs and seems to require more resources both human and structural.

P3- TIME-COURSE ALTERATION OF GENE EXPRESSION PROFILES UNDERLYING DENERVATED SKELETAL MUSCULAR ATROPHY IN RATS. Y. Satomi, A. Tanokura, K. Horie, E. Ochiai, K. Takagi, K. Yamana, Y. Azuma *(Tokyo, Japan)*

Introduction: As sarcopenia is very linked to disuse muscle atrophy, to investigate on disuse muscle atrophy will be greatly expected to be useful for studies on sarcopenia. Objectives: To examine molecular mechanisms of disuse muscle atrophy, we performed microarray analysis. Material and methods: Sciatic denervation was conducted on male 8-week-old rats, and then soleus samples were isolated and weighted at days 3, 7, and 14 after surgery (n=3/group). The Whole Rat Genome oligo DNA microarray kit Ver3. (4x44K) (Agilent Technologies) was used. The criterion that we chose for identifying differentially expressed genes was that their expression must be altered twofold or more between all sets of the comparison between the denervated individuals and the respective control individuals. Results: The denervation produced significant reductions in weight of soleus as compared with respective controls at days 7 and 14 after surgery. A comparison of expression levels of the genes of the denervation with the control indicated that 1761, 3026, and 5412 were differentially expressed at days 3, 7, and 14 after surgery, respectively. The gene ontology analysis revealed that a number of mitochondria-related genes were down-regulated, some nicotinic acetylcholine receptor-related genes were up-regulated at day 3 after surgery, and some MHC class I-related genes were up-regulated at days 7 and 14 after surgery. Discussion: These results reflected important aspects of the muscle atrophy as the mitochondria-related genes, the nicotinic acetylcholine receptor-related genes, and the MHC class I-related genes are well known in response to denervation, in myasthenia gravis, and in myopathy, respectively. Conclusion: This approach will facilitate future investigation into the molecular mechanisms underlying the development of disuse muscle atrophy and could provide a clue to novel therapeutic interventions for sarcopenia.

P4- GRIP STRENGTH AND INFLAMMATORY BIOMARKERS AS INDICATORS OF PHYSICAL PERFORMANCE IN THE OLDEST OLD: SOME RESULTS OF THE BELFRAIL STUDY (BFC80+). D. Legrand, W. Adriaensen, B. Vaes, C. Matheï, J. Degryse *(Bruxelles, Belgium)*

Introduction: Sarcopenia has been described as an age-related decline in muscle mass in older people. Current definitions of sarcopenia include both a loss of muscle strength and a decline in functional quality in addition to the loss of muscle protein mass. However, it is unclear whether a decline in functional capacity results from the loss of muscle mass and/or the qualitative impairment of the muscle tissue. The age-associated changes in muscle mass explain less than 5% of the variance in the change in strength with ageing. Sarcopenia is associated with many adverse outcomes like increases in morbidity, falls,

institutionalization and onset of disability. It has been suggested that the contribution of muscle mass to certain outcomes may be primarily because of its association with muscle strength. Decreased strength, most often grip strength, has been identified as an important sign of frailty. Grip strength appears to be a robust predictor of functional decline, disability and mortality. Objectives: To study to the relationship between grip strength, muscle mass and physical performance in the oldest of the old and to explore the significance of comorbidity and inflammatory biomarkers in this relationship. Material and methods: The BFC80+ is a prospective, observational, population-based cohort study of subjects aged 80 years and older in three well-circumscribed areas in Belgium (n=567). A cross-sectional analysis was performed using the scores on the Short Physical Performance Battery (SPPB), Grip strength, and the data on comorbidity. Body composition and muscle mass (SMM) were studied using anthropometric methods and bio-electrical impedance. HCRP, IL6 and IL10 concentrations were determined on fasting blood samples. The levels of IL-6 and TNF-? were combined to create an overall measure of pro-inflammatory cytokine status with higher specificity : no pro-inflammatory status, low pro-inflammatory status and high pro-inflammatory status (when both cytokines were elevated). The data from the men and women were treated separately. Different regression models were built using the grip strength scores as an independent outcome variable and age, fat mass, comorbidity, SPPB scores, SMM and inflammatory biomarkers as covariates. Results: The 567 participants (356 women (62.8%) and 211 men (37.2%)) had a mean age of 84.95 (SD 3.86) and 84.34 (SD 3.33) respectively. Between the pro-inflammatory status there are significantly difference for SMM, grip strength and SPPB. At the women there is also a difference for comorbidities. For males and females the grip strength and SPPB is higher in No pro-inflammatory group. At the men the SM is higher in No pro-inflammatory group. The Logistic regression analysis was performed to assess the association of the pro-inflammatory status, physical performance and muscle mass with a low grip strength level. The analyses were adjusted for age, fat mass and total number of chronic diseases. A low grip strength level was positively associated with SPPB (for females (OR = 0.75, 95% CI = 0.62-0.93), for males (OR = 0.75, 95% CI = 0.61- 0.92)). For females a low grip strength was positively associated with SM (OR = 0.70, 95% CI = 0.54- 0.92). Discussion: The present study revealed that a low grip strength level adjusted for age and morbidities is associated at with physical performance level in the oldest. In the oldest the inflammatory biomarkers did not explain the low grip strength level. The association between higher levels of cytokines and loss of muscle mass and strength had observed in others studies but the participants were younger than 80 years old. Conclusion: Our results in the oldest show than the grip strength is a robust indicator of the physical performance level and appears to be poorly related to muscle mass estimations. A low grip strength level is associated at with physical performance level in the oldest but the inflammatory biomarkers did not explain the low grip strength level.

P5- IDENTIFICATION AND CHARACTERIZATION OF COMMUNITY-DWELLING ELDERLY WITH SARCOPENIA: A STUDY PROTOCOL. D.M. Mijnarends, J.M.M. Meijers, R.J.G. Halfens, S. ter Borg, Y.C Luiking, S. Verlaan, J.M.G.A. Schols *(Maastricht, The Netherlands)*

Introduction: Sarcopenia is an age-related decline in muscle mass, strength and physical performance, and is recognised as a geriatric syndrome. Sarcopenia by itself or as a major component of frailty is associated with a risk of adverse outcomes e.g. physical disability, increased risk of falls and fractures, poor quality of life, loss of autonomy and independency, and even death. Depending on the diagnostic criteria, it is estimated that the prevalence of sarcopenia in community-dwelling people above the age of 60 years varies between 10 and 50%. As sarcopenia is relevantly prevalent and because it increases the risk of disabilities and may lead to a higher use of healthcare resources as well as an increased risk of institutionalization, the expected economic burden for the healthcare system is great. Considerable evidence suggests that sarcopenia is a partially reversible cause of disability and can benefit from intervention, particularly at its early stages. Currently, no pharmacological treatment for sarcopenia exists, and thus management focuses on lifestyle interventions related to physical activity, exercise and nutrition. Only recently, consensus was achieved on a theoretical definition of sarcopenia that was supported by several geriatric organizations (Cruz-Jentoft et al, Age Ageing 2010): loss of muscle mass in combination with a loss of muscle function (muscle strength or performance). However, operationalization of this definition in community-dwelling elderly in different settings is not fully clear yet. In order to effectively manage community-dwelling elderly people with sarcopenia, it is important to first identify them by using feasible and valid tools to assess muscle mass, strength and performance. Objectives: 1. Identification of sarcopenic community-dwelling elderly people in different settings by using feasible and valid screening and assessment tools. 2. Acquire insight in the nutritional status, level of physicial activity and other characteristics of community-dwelling elderly with sarcopenia 3. Acquire insight in the impact of sarcopenia on health consequences and health economics. Material and methods: A literature study will be performed to: 1) identify feasible and valid tools to screen and assess sarcopenia in community-dwelling elderly in different settings, using the recently published consensus definition paper (Cruz-Jentoft et al, Age Ageing 2010) as a guide; and 2) identify characteristics and consequences related to sarcopenia, including nutritional status, level of physical activity, frailty and possible and relevant health consequences and health economics (care costs). After selecting the most feasible and valid tools to measure sarcopenia and its characteristics and consequences, key experts will be consulted to obtain their opinion on these pre-selected tools and measures. Further validation and final selection of tools will be done in a pilot study in the target population of this study. Subsequently, the selected tools will be applied in a cross-sectional study in different settings of community dwelling elderly, including: a group receiving no formal care, a group receiving formal home care, a group living in elderly homes and a group of community dwelling elderly visiting fall and geriatric clinics. By comparing sarcopenic with non-sarcopenic elderly in the study population, associations between sarcopenia, subject characteristics, and health and economic consequences will be made. Results: This study will reveal a set of tools to screen and assess sarcopenia in community-dwelling elderly in different settings. Moreover, data from the cross-sectional study will provide information on the prevalence of sarcopenia in community-dwelling elderly in different settings in the Netherlands. Finally, data will be obtained on characteristics of sarcopenic elderly in the community including nutritional status and level of physical activity, as well as health and economic consequences of sarcopenia in this population. Discussion: The concept of sarcopenia is the central topic of this study, as it is expected that prevalence rates are high. Early detection and management of sarcopenia in daily health care practice is considered to be very relevant from different points of view. Related to the elderly, prevention of disabilities, preservation of autonomy and quality of life are of utmost importance. Related to the society, which currently is characterized by a demography of more and more elderly people, diminishing the progressive use of healthcare resources and costs of care are necessary. Conclusion: This study will provide further insight in the relation between sarcopenia, nutritional status, physical activity, health consequences and health economics. Recommendations for future interventions to manage sarcopenia in community-dwelling elderly will be derived from the results of this study.

P6- VITAMIN D AND CALCIUM SUPPLEMENTATION TO PREVENT FALLS AND FRACTURES OF RESIDENTS OF THE ACCOMODATION ESTABLISHMENT FOR DEPENDENT ELDERLY (EHPAD) OF PONTARLIER. PROFESSIONAL PRACTICES ASSESSMENT. A. Bonnet, M. Degois, A. Grillot, E. Ngamba, O. Barrandon, F. Faivre, P. Pfitzenmeyer (Doubs, France)

Introduction: Falls and osteoporotic fractures represent a major public health problem for the elderly, associated with high morbidity and mortality. In this population, vitamin D deficiency is correlated to the occurrence of falls and fractures as well as sarcopenia development. In geriatric institutions, more than 90% of the residents are vitamin D deficient. The scientific literature reports strong arguments in favour of a systematic vitamino-calcic supplementation of institutionalized or housebound elderly people. The optimal supplementation corresponds to a daily administration of 700 to 800 IU vitamin D3, combined with 1000-1200 mg calcium when the daily dietary calcium intake is below the recommended level. Objectives: We propose to evaluate the professional practices concerning vitamin D and calcium supplementation to the Larmont EHPAD (Doubs), in preventing falls and fractures, in order to improve these practices. Material and methods: The chosen method was the clinical audit. We performed a retrospective study at the Larmont EHPAD, reviewing medical documents of the year 2009. One hundred and twenty seven residents present at the institut throughout 2009 were included in our study. Results: Only 13% of the audited residents received a daily supplementation of both vitamin D3 and calcium. Only half of them (6,5%) were given the recommended doses of 800 IU and 1000 mg respectively. Discussion: Besides the ignorance of the recommendations, the infrequent prescription of a daily combined supplementation could be explained firstly by the mediocre compliance of the dosage forms associating vitamin D and calcium, especially in cases of deglutition disturbances or xerostomia. Secondly the preparation and distribution of these treatments by the nurses every day are time-consuming. More generally, our results raise the question about the feasibility of a vitamino-calcic supplementation in the elderly living in institutions in France. Conclusion: The plan of action we propose to ameliorate the current practices includes a flowchart of assistance for the prescription of a vitamino-calcic supplementation, which is expected to improve the preventive measures against falls and fractures at the Larmont EHPAD, as well as the morbidity-mortality rates. The impact of our recommendations will be evaluated in 2012. If this plan is successful, we would like to diffuse the flowchart to all the interested EHPADs of Bourgogne-Franche-Comté and then, at the national level.

P7- MANAGING THE QUALITY OF SLEEP AMONG ELDERLY PATIENTS USING THE PITTSBURGH SLEEP QUALITY INDEX. S. Rajaram, E. Cheah, Z. Dexin, N. Sidek, T.M. Hong, F. Fadillah, H. Hamid *(Singapore)*

Introduction: Sleep is a necessary for life. When normal ageing changes, medical problems, psychiatric problems and psychosocial issues can alter the pattern and quality of sleep as one grows older and thus affect the quality of life. Assessment of sleep patterns enables the nurse to intervene immediately by implementing interventions with the client. The PSQI is composed of 19 self-rated questions and 5 questions rated by a bed partner or roommate (only the self-rated items are used in scoring the scale). The self-administered scale contains 15 multiple-choice items that inquire about frequency of sleep disturbances and subjective sleep quality and 4 write-in items that inquire about typical bedtime, wake-up time, sleep latency, and sleep duration. The 5 bed partner questions are multiple-choice ratings of sleep disturbance. All items are brief and easy for most adolescents and adults to understand. The items have also been adapted so that they can be administered by a clinician or research assistant. Sample self-rated items are provided in Example 30. The PSQI generates seven scores that correspond to the domains listed previously. Each component score ranges from 0 (no difficulty) to 3 (severe difficulty). The component scores are summed to produce a global score (range of 0 21). A PSQI global score >5 is considered to be suggestive of significant sleep disturbance. Cutoff scores are not available for component scales. Objectives: The Pittsburgh Sleep Quality Index (PSQI) (Buysse et al. 1989a) was developed to measure sleep quality during the previous month and to discriminate between good and poor sleepers. 1)Sleep quality is a complex phenomenon that involves several dimensions, each of which is covered by the PSQI. 2)The covered

domains include Subjective Sleep Quality, Sleep Latency, Sleep Duration, Habitual Sleep Efficiency, Sleep Disturbances, Use of Sleep Medications, and Daytime Dysfunction. Material and methods: The Pittsburgh Sleep Quality Index (PSQI) is an effective instrument created by Buysse et.al in 1989. It measured the quality and patterns of sleep in the older adult. It differentiates "poo" from "good" sleep by measuring seven areas: subjective sleep quality, sleep latency, sleep duration, habitual sleep efficiency, and sleep disturbances, use of sleep medication, and daytime dysfunction over a month. The client self relates each of these seven areas of sleep. Scoring of the answers is based on a 0 to 3 scale, 3 reflecting the negative extreme on the Likert scale. A global sum of "5" or greater indicates a "poorâ" sleeper. Results: 7 patients who had sleeping problems were assessed. Data using the PSQI was collected from the 18th of June till the 18th of July 2010. Of these 7 patients, 4 summed up to 5 to 6 as their global PSQI score. 2 were given sleep medication to improve their sleeping patterns and 2 were referred to a psychologist. 3 were found to have subjective sleep problems; 2 were overweight and were asked to start an exercise program. 1 was found to lead a sedentary lifestyle and was encouraged to be active. Discussion: The PSQI was designed to provide a reliable, valid, and standardized measure of sleep quality. Preliminary results with the scale suggest that it is successful on all three counts. Within sleep disorder treatment settings, the test should be useful in providing initial indexes of the severity and nature of sleep disturbances. Within a general psychiatric or medical setting, the PSQI appears to be useful as an initial screen to identify good and poor sleepers. The PSQI is not sufficient to provide accurate clinical diagnoses of sleep disorders. Furthermore, there are no data establishing its sensitivity to change; thus, it is not known whether the scale is useful for monitoring treatment response. Conclusion: The PSQI can be used for both initial assessment and ongoing comparative measurements with older adults across all health settings. The scale can be adapted to enable the client to respond verbally to items on the scale by having the nurse read the statements to the client.

P8- RANDOMISED PHASE III CLINICAL TRIAL OF A COMBINED TREATMENT WITH CARNITINE + CELECOXIB +/- MEGESTROL ACETATE FOR PATIENTS WITH CANCER-RELATED ANOREXIA/CACHEXIA SYNDROME. G. Mantovani, F. Panzone, G. Antoni, R. Serpe, M. Dessi, A. Macciò *(Cagliari, Italy)*

Introduction: Cachexia accompanies the end stage of several chronic diseases, in particular, cancer, and therefore this condition is defined as "cancer-related anorexia/cachexia syndrome" (CACS): it is a multifactorial syndrome characterized by an ongoing loss of skeletal muscle mass (with or without loss of fat mass) that cannot be fully reversed by conventional nutritional support and leads to progressive functional impairment. Objectives: A phase III, randomized study was carried out to compare a two-drug combination carnitine + celecoxib +/- megestrol acetate for the treatment of cancer-related anorexia/cachexia syndrome (CACS): the primary endpoints were increase of lean body mass (LBM), decrease of resting energy expenditure (REE), decrease of fatigue and improvement of total daily physical activity. Secondary endpoints were: improvement of appetite, quality of life (by the EORTC QLQ-C30), increase of physical performance tested by grip strength and six minute walk test, decrease of ECOG PS and Glasgow Prognostic Score (GPS) and decrease of proinflammatory cytokines. Material and methods: Eligible patients were randomly assigned to: arm 1, L-carnitine 4 g/day + Celecoxib 300 mg/day or arm 2, L-carnitine 4 g/day + celecoxib 300 mg/day + megestrol acetate 320 mg/day, all orally. All patients received as basic treatment polyphenols 300 mg/day, lipoic acid 300 mg/day, carbocysteine 2.7 g/day, Vitamin E, A, C. Treatment duration was 4 months. Planned sample size was 120 patients. Results: According to the statistical design an interim analysis was planned for futility after the enrolment of 60 patients. The results did not show a significant difference between treatment arms: therefore, the trial was stopped for futility. Analysis of changes from baseline showed that LBM (by dual-energy X-ray absorptiometry and by L3 computed tomography) increased significantly in both arms. REE and fatigue decreased significantly in both arms. Among secondary endpoints, GPS and ECOG PS score decreased significantly in both arms. Physical performance assessed by 6MWT improved significantly in both arms. Toxicity was quite negligible and comparable between arms. Conclusion: The results of the present study enable us to suggest a simple, feasible, effective and safe, low cost two-drug treatment for CACS including nutraceuticals (i.e., antioxidants): this combination has a favorable cost-benefit profile while achieving optimal patient compliance.

P9- SUPEROXIDE ANION OVERPRODUCTION BY NADPH OXIDASE AS A NEW BIOMARKER OF SARCOPENIA IN OLDERS ADULTS. G. Baptist, A. Terminet, F. Greslou, A.M. Dupuy, J.P. Cristol, C. Jeandel *(Montpellier, France)*

Introduction: Physical performance measured by gait speed is being recognized as a major instrument for screening sarcopenia in older people, because it predicts loss of autonomy, hospitalization, survival, and could be associated to frailty. A threshold of 0.8 m/s has been proposed for clinical practice. Oxidative stress, mediated in part by superoxide anion produced by NADPH oxidase, could be involved in the pathophysiogenesis of sarcopenia. Objectives: In this study, our objective was to evaluate superoxide anion production, and its interactions with sarcopenia identified by a gait speed under 0.8m/s. Material and methods: Between october 2003 and may 2009, 310 old subjects from the area of Montpellier (Southern France) were included in this study on the basis of a consecutive consultation in an ambulatory unit in the department of Gerontology. Inclusion criterias were: age over 60 years old, ability to walk without aid or with cane, and consent to participate to study. Exclusion criterias were: concomitant treatment with iron or vitamins, active infectious disease, cancer and auto-immune diseases, and active hepatitis. Usual gait speed was determined using an 8 meters long electronic carpet (GAITRite®), and consisted of the average of three trials, and was considered as "slow gait speed" if under 0,8m/s. High-sensitive CRP, creatinine, HDL, LDL, total cholesterol, transthyretin (TTR), albumin, and alpha-1-acid glycoprotein (AAG), fibrinogen, and homocystein were evaluated using routine methods. Renal function was evaluated by 175MDRD. Superoxide anion production in whole blood was determined using lucigenine in presence or absence of PMA as previously described [11]. Percentage of activation of NADPH oxidase (PMA-induced superoxide production x 100 / PMA-free superoxide production) was used as an index of PMA-induced overproduction of anion superoxide. Results: Among the 310 participants, 30 subjects had missing data for the measurement of oxidative stress, Hcy, CRP or total cholesterol. So, 280 subjects, 191 women (68.2%) and 89 men (31.8%), were included in the statistical analysis. They were 79.89 +/- 6.14 years old, with a body mass index (BMI) of 25.84 +/- 15.23 kg/m2. Their mean score of comorbidities CIRS-G was 6.49 +/- 2.88. The average walking speed was 0.723 m / s (+/ - 0.258). 179 elderly patients (63.9%) walked under 0.8m/s. Compared to olders who walked faster than 0.8m/s, they were older ($p < 0.001$), have more comorbidities (CIRS-G, $p=0.025$), mainly cardiac, neurological and renal diseases. Sex ratio, body mass index (BMI), and prevalence of diabetes were not different. PMA-induced oxidative burst, as well as the mean percentage of activation, were higher in slow walkers ($p = 0.036$ and $p=0.019$, respectively). In addition, high response to PMA, defined as the third tertile of PMA-induced/basal production, appears significantly associated with slow gait speed ($p=0.004$). Low-grade chronic inflammation is associated with slow gait speed as evidenced by high fibrinogen ($p=0.006$) and high leukocyte count ($p=0.016$). By contrast, high levels of CRP (> 2.8mg/L) or AAG (>0.92g/L) did not reach significance. Chronic kidney disease (GFR<60ml/min/1.73m2) and hyperhomocysteinemia (>18.3 µM) were significantly associated with slow gait speed ($p=0.032$ and $p=0.031$ respectively). By contrast, nutritional parameters (albumin, TTR, cholesterol) were not associated with slow gait speed. After selection, we found 3 factors independently associated with sarcopenia (ie gait speed under 0.8m/s), in order of decreasing odds ratios (table 3): age above 83 years old (OR=2.83, $p=0.002$), fibrinogen above 3.5 g / L (OR = 2.15, $p=0.007$), and overproduction of anion superoxide exceeding 207% (OR = 1.91, $p=0.028$). Discussion: Multivariate analysis clearly shows that microinflammation, identified by a fibrinogen threshold of 3,5g/L, and superoxide anion overproduction are significantly associated with slow walking speed ($p=0.007$ and $p=0,028$ respectively. The fibrinogen threshold of 3.5 g/L, which is in the "normal range" (2-4g/L), highlights the impact of low-grade chronic inflammation in decreased gait speed in older adults. This result confirms and extends the previously observed association of fibrinogen levels with functional decline, frailty or mortality. Moreover, our results support a greater interest of a single determination of fibrinogen compared to a single determination of CRP to evaluate the chronic low-grade state of inflammation in olders with slow gait speed. The weakness of CRP association ($p=0.121$), which has been recognized as a reliable marker of low-grade inflammation, could be related to the variability of CRP due to its short half-life. Our results are coherent with the meta-analysis reported by Danesh et al, showing a stronger association between fibrinogen and cardiovascular risk compared to CRP.Adjusted on CRP values, fibrinogen has also been independently associated with non-cardiovascular mortality, including cancer. As a result, these statements objective that fibrinogen should be a privileged biomarker in studying decreased physical function in olders adults. To our knowledge, this study shows for the first time the link between an overproduction of superoxide anion, mainly due to NADPH oxidase activation, and sarcopenia identified by slow gait speed in older people. A percentage of activation of NADPH oxidase greater than 207%, corresponding to the third tertile in our population, almost doubles the risk of walking slower than 0.8m/s (OR=1.91, $p=0.028$). Epidemiological studies have demonstrated that aging is strongly associated with an increase in superoxide anion production mainly originated from NADPH oxidase complex. However, no relationship between NADPH oxidase activation and sarcopenia has previously emerged from these studies. The potential link between sarcopenia and oxidative stress was only supported in humans by indirect markers of oxidative stress, whereas free radicals overproduction was associated to sarcopenia in animal models. These datas strongly support a link between overproduction of free radicals by NADPH oxidase and sarcopenia in humans. Our study recognizes some limitations. First, we didn't evaluate superoxide anion overproduction in components of sarcopenia, such as muscle strengh and muscle mass. More studies are needed to confirm this link. Secondly, our finding of an increased superoxide anion production did not take into account a potential decrease in antioxidant defense mechanism described in elderly which could further enhance oxidative stress. Conclusion: Sarcopenia in older adults, defined by gait speed under 0.8m/s, is associated with superoxide anion overproduction by NADPH oxidase.

P10- MODIFICATION OF PROTEINS INVOLVED IN KEY CELLULAR PATHWAYS AND DECREASED PROTEASOME ACTIVITY CHARACTERIZE SENESCENT HUMAN MUSCLE PROGENITOR CELLS. M. Baraibar, J. Hyzewicz, A. Rogowska-Wresinska, R. Ladouce, P. Roepstorff, G. Butler-Browne, B. Friguet *(Paris, France)*

Introduction: Age-related decline in skeletal muscle mass and function has been attributed at least in part to a reduction in the regenerative potential of resident stem cells, also known as satellite cells or myoblasts. In response to injury, satellite cells proliferate as myoblasts and then differentiate and fuse to form newly regenerated muscle fibers. Human myoblast replication and differentiation is compromised with age, contributing to the loss of muscle mass and force after the fourth decade of life. However, the molecular events related to myoblast dysfunction during ageing remains elusive. Objectives: To investigate the molecular mechanisms underlying myoblasts impairment during ageing, focusing in the changes occurring in the proteome, both at the expression level and the identification of proteins preferentially modified directly by oxidation or indirectly by reaction with

secondary products of oxidative stress. Material and methods: A parallel proteomic analysis aimed at identifying differentially expressed proteins as well as those targeted by carbonylation has been performed. The senescence-induced changes of the proteome at the expression level were studied using the two dimensional in gel electrophoresis (2D-DIGE) technology. We next pursued the identification of the modified proteins using a bidimensional gel electrophoresis based proteomic approach coupled with immunodetection of HNE-, AGE-modified and carbonylated proteins. Selected proteins spots were then identified by mass spectrometry. Results: Evidence is provided for the accumulation of oxidized proteins, as well as proteins modified by glycation-glycoxidation and conjugated with lipid peroxidation products during replicative senescence of human myoblasts. Proteins involved in crucial cellular pathways such as energetic metabolism, protein synthesis and degradation, cell morphology and cellular assembly were identified as heavily modified in senescent cells. In addition, the chymotrypsin-, trpsin- and caspase-like peptidase activities of the proteasome, the main intracellular proteolytic system implicated in the removal of abnormal and oxidized proteins, were also found decreased in aged myoblasts. Discussion: Taking together, our results indicate that proteins involved in several cellular pathways are affected during senescence and the impairment of these pathways may be implicated in human myoblasts dysfunction during ageing. Conclusion: Our results indicate that the imbalance between the generation of oxidatively modified proteins and their elimination; as well as the impairment of key cellular pathways due to accumulation of damaged proteins can contribute to myoblast dysfunction during skeletal muscle ageing.

P11- ASSESSMENT OF SARCOPENIA AND VISCERAL FAT ACCUMULATION - A CASE DESCRIPTION. A.K.P. Kayano, M. Najas, J. Toniolo Neto (Sao Paulo, Brazil)

Introduction: In the daily clinical practice we frequently find patients with sarcopenia associated with obesity. According to the European Working Group on Sarcopenia in Older People (EWGSOP), sarcopenia is clinically defined as a syndrome characterized by progressive and generalized loss of muscle mass and strength with an increased risk of adverse outcomes such as functional loss, worsening of quality of life and death. In elderly, the loss of muscle mass and strength is frequently independent from the body mass index. In the Geriatrics office, in addition to comprehensive geriatric assessment, we frequently need tools to better characterize the metabolic and muscle mass profiles in elderly patients. The newly available technologies in Brazil helps this characterization through the measurement of the body composition and can be used in the clinical practice associated with serum markers such as C-reactive protein and functional tests such as gait speed. Objectives: Demonstrate a comprehensive geriatric assessment using methods recently incorporated into the private clinical practice in Brazil such as: dual X-ray absorptiometry (DEXA), abdominal computed tomography for evaluation of visceral fat, inflammatory markers and assessment of the gait speed. Material and methods: Case study of patient EMK, 65 years old, followed by three years in a Brazilian private office. Due to family history of cardiovascular disease, this patient came to the service for further evaluation. Results: Patient functionally independent for basic and instrumental activities of daily life. Patient presents dyslipidemia and benign prostatic hyperplasia. The current medication is Atorvastatin 10mg per day. The patient does not perform programmed physical activity. The patient's weight was 86 kg, height 175,5cm, body mass index 27,9kg/m2. The patient presented C-reactive protein of 0,18mg/dL, fasting glucose of 110, LDL of 73mg/dL and HDL of 60mg/dL. This patient has presented a DEXA showing 30,135 (36%) grams (g) of fat, 51,917g (62%) of lean mass. The abdominal CT scan shows 55% of visceral fat and 45% of subcutaneous fat. Visceral fat/ subcutaneous fat rate is 122.5%. The described patient presents high levels of C-reactive protein, proportional increase in visceral fat and elevation in the total body fat. His gait speed was 1,5m/s. There is a proportional reduction in the lean body mass of this patient, with appendicular lean mass divided by height squared of 7,95kg/m2. Therefore, this patient presents visceral fat accumulation and reduction in the body mass index of skeletal muscle. With these results, dietary changes were proposed, aiming the reduction of saturated fats, increased intake of soluble and insoluble fibers and weight control. The performance of aerobic physical activity was encouraged. Discussion: The assessment of the body composition with DEXA is one of the methods that can be used in the clinical practice for individual characterization of the reduction in the muscle mass (one of the sarcopenia components). However, for populational screening of visceral fat accumulation, anthropometric measures should be used, and for sarcopenia screening in the elderly, according to the algorithm EWGSOP, the gait speed should be evaluated initially, followed by the prehension strength and muscle mass. Evidences show that the fat distribution and not only the total amount of body fat are important as a cardiovascular risk. Thus, the use of abdominal computed tomography to quantify visceral fat associated with DEXA has an important role. Abdominal fat in the elderly is associated with increased risk of congestive heart failure, and through the release of adipocytokines and glucotoxic and lipotoxic agents, it can lead to metabolic, cardiac and vascular dysfunction. The metabolic effects and the systemic changes related to atherosclerosis caused by the accumulation of visceral fat are probably exacerbated in patients with sarcopenia or presarcopenia, as demonstrated in a study of Odamaki et al, 2010 in patients with advanced renal disease in dyalitic therapy. The use of multiple combined tools can assist the screening of metabolic syndrome and sarcopenia in an individual level in the private practice. Early diagnosis can alter the initial prescription of the non-pharmacological treatment. Conclusion: The use of these tools in the daily clinical practice can assist in making decisions regarding the prevention and control of the visceral fat which may be associated with increased inflammatory factors and consequently, the greatest reduction in the muscle mass. Patients undergoing this evaluation show good compliance to non-pharmacological measures such as physical activity, reduction of saturated fats, increased consumption of soluble and insoluble fibers and weight control.

P12- MUSCLE PROTEOME AND TRANSCRIPTOME DURING AGING OF LOU/C/JALL RATS. D. Delalande, I. Piec, M. Gueugneau, C. Coudy-Gandhillon, J. Alliot, A. Listrat, R. Taylor, D. Bechet *(Aubière, France)*

Introduction: Aging affects most tissues and many physiologic functions. The age-dependent loss of skeletal muscle mass, strength, and function (named sarcopenia) obviously results in impaired locomotion, but is also associated with increased susceptibility to illness, as muscle is the major body reservoir of amino acids. In humans, it is now acknowledged that muscle weakness associated with sarcopenia is a risk factor for falls and frailty (Yu et al, 2007), and that loss of skeletal muscle mass is predictive of all cause mortality in the elderly (Szulc et al., 2010). Multiple phenomena are involved in the development of sarcopenia. Intrinsic factors include altered hormonal levels, high levels of inflammatory cytokines, neuronal remodelling, or deficiencies in muscle regeneration. Extrinsic factors such as a poor nutritional status or physical activity also play major roles in the etiology of sarcopenia. From a histological perspective, muscle aging is characterised by a decrease in myofibre size and number, altered capillary density and a preferential loss of fast twitch muscle myofibres. At a cellular level, muscle aging is accompanied by perturbations in protein turnover (Combaret et al., 2009) and a decrease in the number of muscle satellite cells available for maintenance of the skeletal muscle (Renault et al., 2002). At the molecular level, important modifications in contractile, cytoskeletal and in essential regulatory components were previously reported (Piec et al., 2005), but the precise mechanisms of sarcopenia remain to be identified. Objectives: Muscle aging contributes significantly to both loss of autonomy and increased morbidity, but the mechanisms involved are complex and likely result from the alteration of a variety of interrelated functions. In order to better understand the molecular mechanisms underlying muscle aging, we combined transcriptomics, two-dimensional gel electrophoresis, Western blot proteomics, and histology to identify new markers of sarcopenia. Material and methods: Our study was performed with 7 month (young-adult), 18 month (mature-adult) and 30 month (old) LOU/c/jall rats. LOU/c/jall rats have been established as a model for research into aging based on physiological and behavioural data. The most interesting characteristic of this strain of rat for aging studies is the absence of severe pathologies, such as obesity, diabetes, nephropathy, or tumor development. Histology: Immunohistochemistry was performed on serial cross-sections (10 µm) of gastrocnemius muscle and using classical procedures to characterize extracellular matrix (ECM, Sirius red), myofibre oxidative metabolism (Cox), apoptosis (TUNEL). Images were captured with an Olympus DP-72 camera coupled to an Olympus BX-51 microscope, and processed through a homemade program developed under Visilog 6.7. Proteomics: Two-dimensional gel electrophoresis (2D-PAGE) were realized in triplicate for each rat gastrocnemius. Isoelectrophoretic separations were conducted with a Protean IEF Cell system and for different pH gradients (4-7 and 6-11). Separation by protein mass was carried out using Protean Plus Dodeca Cell. Coomassie G-250 stained gels were IR scanned (Odyssey) and analysed with SameSpot software. Spots of interest were identified by MALDI-ToF MS or nanoLC-MS/MS (LTQ Velos). Transcriptomics: For each age group, three independent muscle RNA isolations were realized. Biotinylated fragmented cRNAs were hybridised to Affymetrix rat genome 230-2.0 arrays. Rat Genome arrays contain 31042 probe sets to analyse the expression levels of over 30248 transcripts and variants from over 28757 well-characterized rat genes. Chips were scanned using a GeneChip® Scanner-3000. After RMA (Robust Multiarray Average) normalization, we identified the genes differentially expressed with age by performing VarMixt tests (Delmar et al., 2005), and adjusted for multiple testing using 5% FDR (False Discovery Rate) and the Benjamini and Hochberg method. Gene ontology (GO) analyses were carried out using the web interface driven DAVID tool and using 5% FDR. Results: Histology of muscle aging: At the structural level, old gastrocnemius muscles exhibited pronounced reduction in cross-sectional area, with glycolitic muscle fibres being the most affected. Old muscles also presented smaller myonuclear domain, and an increased proportion of apoptotic nuclei. Histology showed in old muscle profound modifications in extracellular matrix (ECM), as evidenced by increases in ECM area and density of fibroblasts, all indicative of chronic inflammation. Aging was also associated with centralization of myonuclei, and fibre type grouping, suggesting myofibre regeneration and neuromuscular remodelling, respectively. Transcriptomics of muscle aging: To better understand the molecular mechanisms underlying sarcopenia, gene expression analysis was performed for gastrocnemius from young adult, mature and old rats. We expected that young adult and mature adult muscles present similar profiles of RNA expression, but differ from old muscle. Indeed using VarMix and 5% FDR, amongst 16091 probe sets none was differently expressed between 7-month and 18-month rat muscles. In contrast we identified 1304 probe sets and 971 genes that were statistically differentially expressed at 5% FDR between old rats and the other (young or mature) adult rats. Significant changes in GO terminology were observed at 5% FDR, indicating that 6 majors functions are markedly altered with age at the transcriptional level in skeletal muscle. These functions (apoptosis, muscle regulation, immune response, proteolysis, angiogenesis, axogenesis) were in agreement with our immunohistochemical observations. Proteomics of muscle aging: Because mRNA levels do not predict changes in protein levels and post-translational modifications, we also realized high resolution differential proteomic analyses in young, middle-age and old muscles. 2D-PAGE and subsequent mass spectrometry analyses identified 64 (for pH 4-7 gels) and 12 (for pH 6-11 gels) differentially expressed sarcopenia markers out of > 1500 matched spots on the 2 types of gels. Furthermore, as 2D-PAGE does not enable the identification of regulatory proteins which are expressed at low levels, we also carried out Western-blots. Amongst 744 antibodies of the BD Biosciences platform, 339 were detected, which led to the further identification of 42

regulatory proteins that are differentially expressed between adult and old rats. Discussion: Our data revealed important modifications in expression of contractile components and of myofibrillar regulatory proteins, which may account for dysfunctions in contractile properties of the old muscle. Modifications in contractile proteins were compensated for by increases in cytoskeletal proteins and in ECM components which may be important for the altered mechanical properties of the old muscle. Other features, such as decline of glycolytic, shuttle enzymes, Krebs and respiratory chain enzymes, all support reduced energy metabolism that may partly account for muscle weakness in the elderly. Some of the highlighted changes related to the differential expression of proteins implicated in detoxification of reactive oxygen species and overexpression of molecular chaperones. Conclusion: Our studies support that chronic inflammation, neuronal remodelling, perturbed energy metabolism, altered antioxidant and contractile systems, and upregulation of cytoskeletal structures are typical features of the aging muscle. By comparing three ages, which include young and mature adults versus old animals, we have identified a group of proteins which characterize muscle aging and may account for some of these features. Several biomarkers were previously unrecognized as differentially expressed in old muscles, and may represent novel starting points for elucidating some mechanisms of sarcopenia.

P13- EFFECTS OF A RESISTANCE PROGRAM, WITH ELASTIC STRAPS, ON THE STRENGTH AND MUSCLE MASS OF INDEPENDENT ELDERLY. A.R.C. Ruzzarin *(Caxias do Sul, Brazil)*

Introduction: The modern world is ageing. In 2025, it is estimated that 25% of the world's population will be constituted of elderly. The loss of muscle mass for the elderly, called sarcopenia, is one of the main causes of the disability, loss of autonomy and in the quality of life decrease of these individuals. Studies show that resistance exercises are one of the keys to combat Sarcopenia. The materials used for the practice of resistance are mostly weight training machines or free weights. These materials are viewed with certain prejudice and as difficult to access by the elderly. Objectives: Our objective was to evaluate elastic straps as a material for resistance exercise, and to compare the results with the traditional materials used, evaluating its efficiency in the combat on elderly sarcopenia. Material and methods: The study sample was composed of 42 seniors, sedentary to power exercises and other factors of exclusion. There was a 16-week training with the same protocol load, repetitions and intervals, 21 patients trained with elastic straps and 21 patients trained with weights and ankle weights. The project included an initial evaluation that consisted of anthropometric measurements (carried out with tape measure, WCS stadiometer, Wood model; a Plena scale, Sport model) skinfolds (Cescorf aplicômetro), body bioimpedance (Malthron device) sitting and standing up tests and arm strength tests 10. Adaptive period of four (04) weeks which was used to adapt the elderly to the proposed material, automate their performance using the material, and prepare their muscle-tendon-ligament and bones. During this time the proper actions and executions of movements were put into action. They are: Elastic straps were cut to be 1 meter long. In the center of them, it was placed a mark with a black ballpoint pen, marking the center of the strap. This center should be located in the center between the two legs of the elderly, when in the lower limbs, and the legs should be separated by a distance of 1 palm. The group that used elastic belts was encouraged throughout the work to leave the elastic strap extended, making use of hyperextension only during the execution of the movement. The sessions were held twice a week, lasting around 60 minutes each, with 48 to 72h intervals between them. During the study period were controlled variables of food and sleep through questionnaires. In all sessions, it was checked the initial and final blood pressure of each senior. All subjects were advised to avoid the Valsalva maneuver and perform the exercises until the last repetition, and the load used should be based on the score of 8.5 or 9, according to Borg scale. After the period of the protocol a final evaluation was performed with the same components and criteria of the initial evaluation. Results: No statistically significant difference ($p > 0.05$) was found when comparing the two groups at the beginning of the study, pointing to the homogeneity of the same for the variables of interest investigated and the socio-demographic characteristics. The ANOVA showed no group x test interaction ($p > 0.05$). Significant differences were observed in the initial stage compared to the final phase ($P < 0.05$) on the variable of body fat percentage (%), percentage of muscles (%), weight of body muscle mass (kg), mass body fat (kg), percentage of body water (%), body water (L), sitting and standing test and arm strength test. The results of this study show that after the trial, both groups reduced the percentage of body fat and weight. Group 1 (elastic straps) early study showed 34.15% gordural body. After thetraining period the corresponding figure was 27.65% ie a reduction of 19.03.group 2 (thera band) of the initial test showed 33.01% body fat. At the end of the study, this index decreased to 30.11, a reduction of 8.78%.. Group 1 and Group 2 had at baseline 65.9% and 67.03 of muscle mass. At the end of the study groups had 71.8%, group 1, ie, an increase of 8.94% and69.72% group 2, an increase of 4.01%. In the body water variable we had increments of 4.24 in group 1 and 3.74 in group 2. Discussion: These results are confirmed by current literature Rogers et al, 2002 and Melov et al, 2007 where the muscle stimulation performed with materials that stimulate muscle contraction, predominantly white fibers, as the main factor of motion, leading to a gain of strength and muscular endurance, thus improving the quality of life of the elderly, preserving their strength or slowing the losses related to white muscle fibers, or quick contraction. Cortes and collaborators, in a study of strength maintenance and independence that lasted 12 weeks, on elderly women, with a resistance protocol of low to moderate loads using conventional equipment for weight training, 2 times a week, had gains of 13.10 % and 14.40% for upper limbs and 25.90% to 43.50% for lower limbs. In the study by Rogers et. al (2002), with older african-american women, of 62-94 years, lasting for 4 weeks and 3 weekly sessions in a training consisting of exercises for the lower limbs (elastic bands) and upper limbs (dumbbells and elastic bands) concluded that the group trained with elastic straps for the lower limbs, increased by 20% their percentage of strength and the one trained with the combination of straps and dumbbells for the upper limbs increased by 24%, in relation to control. Both studies had similar results to ours, but in our study we obtained a more significant gain, in average values, which can be attributed to a greater number of total sessions, as other studies had a duration of 12 and 4 weeks. In our study, the group using elastic straps did not used any other material, its gain being attributed exclusively elastic straps, while in the study by Rogers et al. there was and increment done by dumbbells for the upper limbs and in the study by Côrtes the gains are attributed to traditional equipment. Candeloro et al, (2007) conducted a study with elderly women between 65 and 70 years in a hydrotherapy training lasting 16 weeks with two weekly sessions of about 60 minutes each , with protocols of low intensity, and found significant improvements in flexibility and strength. However the improvements on the strength have been concluded by the author as "partial". These findings are consistent with the current literature that states that significant effects of strength gains must be accompanied by a protocol of medium or strong intensity. Exercises with low loads have similar results as in other studies that use protocols with cardiovascular characteristics, these are not very suitable for strength gains, especially in elderly independents. Conclusion: The use of elastic straps in resistance training is valid and effective as stimulatory material for maintenance, strength and muscle mass gain in elderly patients. When the elastic straps were compared with the traditional materials, they proved to be just as effective when used in similar protocols by non-athlete elderly.

P14- EPIDEMIOLOGICAL STUDY REGARDING THE FRAILTY IN AN ELDERLY SAMPLE WITH CARDIOVASCULAR AND DISMETABOLIC PATHOLOGY. D.E. Roditis, E. Lupeanu *(Bucharest, Romania)*

Introduction: Recently, there were reported growing weights of "frail and vulnerable adults" in the older population. It was estimated that in the community, 10 - 25% of those over 65 years are frail and 46% of those over 85 years are frail. Some studies highlighted the need to consider the utility of frailty measures for the geriatrician in clinical practice and the public health planner, as well as for the research gerontologist. Fried's definition of the concept considers the presence of three or more of five clinical factors: unintentional weight loss (10 pounds or more in a year), general feeling of exhaustion, weakness (as measured by grip strength), slow walking speed and low levels of physical activity. Sarcopaenia or the "melting of flesh" is the major cause of frailty in the opinion of some gerontologists. It consists in the loss of muscle mass and diminishment of muscle function that occur with aging. This lack in muscular mass has as consequences different metabolic disorders and finally, even the loss of person's independence. Objectives: Our work pointed out - the assessment of frailty weight in a sample of inpatient older persons and - the links that exist between some elements of Fried's phenotype: muscular weakness (as consequences of sarcopaenia) and low levels of physical activity. Material and methods: 96 inpatients (average age = 68.5 years) suffering from cardiovascular and dismetabolic pathology were assessed clinically and also through socio-medical evaluation, by a questionnaire which pointed out physical functionality using ADL, IADL, "Timed Up and Go Test", Handgrip Test and Nottingham Scale. Results: In our work, the diagnosis of frailty was based on Fried's phenotype criteria. So, Fried's performance score indicated this syndrome in 35.4% cases of the entire sample. Separately, on genders, the weights were 35% for men and 35.4% for women. After age groups, Fried scores were 35.2% for "50-74 years" and 50% in "75 years and over" group. Some significant data: 1) Unintentional weight loss was greater in men group (22.2%) comparative to women's situation (a percent of 13.3%) and also more important in older group, "75-90 years" (20%) comparative to the group "50-74 years" (13.3%). This difference of weight loss was consensual to the existence of a rate of sarcopaenia, bigger in men and in older age group; 2) Hand's grip strength of women was three times lower than those of men; 3) Subjective exhaustion was higher among women (40.8%) comparative to men (25%) and was higher among the older persons (42.7% in "65 years and over" group and 60% in "75 years and over" group); 4) IADL functioning showed only 39.8% complete independent persons in the entire sample. Discussion: In the following, the links between the elements of Fried phenotype are discussed. Low levels of physical activity appeared as a result of muscular weakness. The assessment of the patients using Nottingham revealed an affection of mobility. In a decreasing order, the motor deficit was showed in different situations: (a) for the affection of legs musculature, by two activities: ? the difficulty in prolonged orthostatic posture (53.5%) and the difficulty in stairs climbing/descending (47.9%); (b) for the affection of trunk and abdominal musculature, the motor deficit was suggested by difficulty in trunk bending (42.3%) and ? difficulty in reaching things put on high shelves (22.5%).The last activity and also the difficulty in (self)dressing (which appeared in 22.5% cases) suggested a weakness of hands and arms musculature. Finally, the item: "I walk only inside home" appeared in a very low percent (5.3%) and suggested a general tiredness, possible an advanced frailty for those patients. Statistical analysis, through some correlation indexes, pointed out the links between physic activities (named before), and the weakness of the legs or hands musculature. So, the weakness of legs musculature was tested by "Up and Go Test". It correlated on the first place with the "difficulty in prolonged orthostatic posture" ($r = .456$ / $p = .000$). The hands and arms weakness evaluated by "Handgrip Test" significantly correlated firstly with the item "heaviness in reaching things put on high shelves" ($r = .352$ / $p = .012$). Conclusion: In our sample consisting of patients suffering of cardiovascular and dismetabolic conditions, Fried's score performance was very high, especially in the age group "75 years and over". There were 50% frail persons in that group. We considered "unintentional weight loss" as an expression of sarcopaenia. Also, we considered its consequences, the other Fried's elements: hands weakness, legs weakness and the general sensation of exhaustion. As a result of these effects of muscular weakness, the subjects appeared with low levels of physical activity. They were evaluated through

ADL, IADL functionality and Nottingham Scale. The impaired physical functionality significantly correlated with general musculature weakness. In summary, frailty is a vital issue in the treatment of the elderly.

P15- REDUCED LOWER EXTREMITY MUSCLE MASS IS AN IINDEPENDENT RISK FACTOR FOR INCIDENCE OF FALLS. Y. Tabara, M. Igase, E. Uetani, T. Kido, N. Ochi, K. Kohara, T. Miki *(Toon, Japan)*

Introduction: Sarcopenia of the lower extremities may become an important risk factor for falls and fracture. Objectives: We conducted a longitudinal epidemiological study to clarify the associations between lower muscle mass and incidence of falls. Material and methods: The study subjects comprised 449 middle-aged to elderly persons (69 years old) who attended the medical check-up program at Ehime University Hospital. Femoral muscle cross-sectional area (CSA) was measured from a CT image at a point one-third from the femoral neck. Incidence of falls was investigated by a structured questionnaire and followed by investigating the personal medication records. Results: Mean CSA was 131±17 cm2 (male) and 94±13 cm2 (female). CSA was strongly collated with body weight (male: r=0.698, p<0.001, female: r=0.687, p<0.001). During the 1.9 years follow-up period, incidence of falls was observed in the 19.4% of subjects. Female subjects who experienced falls were significantly older (72±6, 69±5 years old, p<0.001) and had a lower muscle mass (91±15, 95±12 cm2, p=0.030). Multivariate analysis identified lower muscle mass (HR 0.97 (0.94-0.99), p=0.038) but not fat area (p=0.368) was an independent risk factor for falls after adjustment of age, height, and body weight. Conclusion: Reduced lower muscle mass was independent risk factor for the incident of falls.

P16- SARCOPENIA AND FRAILTY IN BRAZILIAN ELDERLY FROM THE SABE SURVEY: HEALTH, WELLNESS AND AGING. L.A. Gobbo, L. Pires Corona, T. da Silva Alexandre, Y. Aparecida de Oliveira Duarte, M. Lucia Lebrao, M. de Fatima Nunes Marucci *(Sao Paulo, Brazil)*

Introduction: Sarcopenia is a geriatric syndrome characterized as a progressive decline in skeletal muscle mass (SMM) and it is also accompanied by the loss of muscle strength and physical performance, leading to frailty, which can cause lack of independence and autonomy, promoting a higher risk of morbidity and mortality. Several definitions used to identify sarcopenia have been suggested. Analysis of total and/or appendicular SMM of the elderly compared to an adult population or to specifically defined cutoffs points is more often applied. Muscle strength, usually measured by handgrip strength, is also an alternative method. However, recently, the European Working Group on Sarcopenia in Older People (EWGSOP) proposed a definition for this syndrome which considers not only SMM, but also muscle strength and physical performance, measured by gait speed. Objectives: The purpose of this study was to analyze the association between frailty and sarcopenia, according to the EWGSOP definition, in Brazilians elderly of the SABE Survey (Health, Wellness and Aging). Material and methods: The study population consisted of elderly (? 60y), both sexes, participants of the SABE Survey, a longitudinal, epidemiological and household survey held in the city of São Paulo, Brazil, started in 2000, reaching 2,143 aged individuals. In 2006, the cohort survivors were reassessed (n = 1,115), and a new cohort was started, with men and women aged 60 to 65 years old (n = 298). In our study, it was used data from the survivors of the first cohort in 2006 and from the new cohort, totalizing 1,413 elderly. The variables of this study were sarcopenia (independent variable) and frailty (dependent variable). Sarcopenia was identified in the sample according to the EWGSOP definition, which consist in the analysis of the gait speed, muscle strength and SMM. The gait speed was measured as the velocity, in m/s, in a 3 meter course. Muscle strength was identified by handgrip strength, and it was used the values above and under the 20th percentile, according to gender and body mass index, to identify normal or low muscle strength, respectively. The SMM was predicted by the Lee et al. (2000) equation, which considers the measurement of body weight and height, besides information about age, gender and race. After the prediction of SMM, it was calculated the muscle mass index (MMI, in kg/m2), by the ratio of SMM, in kg, and height, in meters, to the square. To identify those with normal or low MMI, it was used cutoffs values proposed by Janssen et al. (2004): low ? 8.50 kg/m2 < normal, for men, and low ? 5.75 kg/m2 < normal, for women. According to the EWGSOP definition, sarcopenia was identified in those who presented: 1) gait speed equal or inferior to 0.8 m/s and low MMI, or 2) gait speed higher than 0.8 m/s, but low handgrip strength and MMI. Frailty was identified in the elderly according to the criteria proposed by Fried et al. (2001), which consist in the analysis of five components: 1) exhaustion, measured by 2 self-report questions from the CES-D, 2) unintentionally weight loss ? 3 kg (self-reported) in the last year, 3) low physical activity, measured by the short version of the International Physical Activity Questionnaire (IPAQ), 4) slowness (the lowest quintile of walking speed test), stratified by gender and height, and 5) low grip strength, stratified by gender and body mass index. It was classified in the frailty group those who were identified at least three of the five components. The sample was stratified by sex and age groups (60-74 years and ? 75 years). Chi-square test with Rao-Scott correction for sample-design (survey) and logistic regression was used to verify the association between sarcopenia and frailty, adjusted by gender, age groups and body mass index (BMI). Statistics was performed using analysis for complex samples, in the statistical software Stata 11. Results: Of the entire sample, 1,228 was eligible to participate in this study. Considering the sample as representative of the city of São Paulo, the proportion of sarcopenic elderly was 8.58% for the total sample (men = 9.46%; women = 7.99%) while frailty was 14.19% (men = 11.94%; women = 15.68%). In the chi-square analysis, it was verified association between frailty and sarcopenia, frailty and age groups and sarcopenia and age groups (p<0.001). Gender was not associated to sarcopenia (p=0.30) and it was only marginally associated to frailty (p=0.06). Since the measurement of muscle strength and gait speed were used by both sarcopenia and frailty identification, a variation inflation factor test (VIF) was performed. The VIF test presented no colinearity among the variables. Unadjusted logistic regression presented a positive association between frailty and sarcopenia (OR 2.97; IC 95% 1.80 ? 4.91). When the logistic regression was performed adjusted by gender, age groups and BMI, it was also verified a positive association, with an OR of 2.38 (IC 95% 1.30 4.37). Discussion: The proportions of sarcopenia in the sample is inside the range presented by other studies in different countries. To our knowledge, this is the first study to analyze the association between frailty and sarcopenia, according to the new definition proposed by the EWGSOP. The results presented by the logistic regression indicates a higher risk of sarcopenic elderly to be frail, independently of gender, age groups and BMI. A definition for sarcopenia that includes not only SMM, but also strength and physical performance variables, can be a more feasible option, when compared to only a single variable, such as SMM, since this geriatric syndrome is beyond morphological components; it also involves functional system, which can be determinant to the development of frailty in the elderly. Conclusion: According to the new definition proposed by the EWGSOP, sarcopenia was positively and significantly associated to frailty, independently of gender, age groups and body mass index.

P17- UNDERSTANDING AND CONTROL OF NORMAL AGEING CAN HELP US BETTER WITHSTAND NATURAL SARCOPENIA NOT CONNECTED WITH DISUSE AND/OR DISEASE. A. Khalyavkin *(Moscow, Russia)*

Introduction: Non-pathological sarcopenia is a very important but only one of the many facets of normal senescence. For this reason general anti-ageing remedy must be useful for sarcopenia cure, too. However, both the causes of and processes involved in ageing remain unclear. A heterochronic parabiosis reveals that senescence is an actively regulable process. Together with this finding the biological age problem has elucidated variability in the rate of age-related changes connected with senescence. But until now principles which would make possible an evaluation of theoretically attainable minimal rate of senescence realizable in conditions, which induce organisms to function optimally have not yet been elaborated. At the same time a preliminary analysis of the facts taken as a whole shows that they are compatible with the hypothesis that living conditions exist which are conducive to a significant deceleration (theoretically to a rate of zero) of the human ageing process. Objectives: The main objective of our research is to reveal the high plasticity of ageing process as well as possibility of it deceleration and even reversibility. Material methods: We used the critical analysis of the array of published experimental findings and our particular interpretation of these findings in order to unite at the one conception many separate and various data obtained from the molecular level up to the level of population. Results: The detection and processing of environmental cues just as the adequate response to these signals are crucial for the survival of the individual. It is thus not surprising that a large number of different tissues and organs belonging to physiological systems are adjusted to the most probable range of natural environmental pressure characterizing selected ecological niche. This is because organism reacts as a whole on a set of external influences by means of certain changes in numerous control and regulatory systems at the physiological levels as well as via some changes in signal transduction pathways at the cellular level. Part of such changes may, in principle, modify the ageing pattern according to concrete circumstances. For this reason study of natural ageing process by means of observation or investigation of animals in captivity as well as human beings in highly comfortable conditions would be both artificial and potentially misleading. Recent findings emphasize the importance of signaling in the regulation of life history traits. This opens an opportunity to modulate organisms' ageing and life span without changing environmental conditions towards more adequate ones in laboratory experiments. Such modulation may be important in the cases when it is difficult or impossible to create experimental conditions adequate to minimal (possibly near zero) ageing rate. In fact, modified products of properly mutated genes involved in regulatory control circuits can (in some cases) erroneously transform inadequate external cues of artificial experimental conditions to the regular reaction of an organism on the quite natural environment. The latter may favour the life span extension by means of ageing deceleration and/or an increase in stress resistance. Discussion: The influences of all external factors induce organisms to function in one physiological regimen or another, because the effectiveness of self-maintenance depends not only on the structural and functional peculiarities of an organism but also indirectly on the external conditions in which it exists. Exactly as an enzyme activity has a bell-shaped dependence on temperature, pH etc. Therefore, one can assume that the control system even of a potentially non-senescent organism is able to sustain a physiological regimen of complete self-maintenance not in any circumstances but only within a certain range of changes in the total external conditions known as "environmental pressure". Outside the zone of optimal environmental pressure self-maintenance will be incomplete. The reserve capacity of organism will start to diminish, and it will begin to age. Exactly as really ageless creatures, such as amoebae, hydras etc. start to age in sub-threshold environment. It is possible that the same simple cause may lie at the base of human senescence. The more so because it is supported by the features of the somatic stem-like cells and by the correlation between parameters of mortality statistics for different countries, the populations of which live in varying climatic, social and economic conditions. This Strehler-Mildvan correlation is similar to the mortality pattern for populations of potentially non-senescent organisms, which age in conditions preventing, to varying extents, the complete self-maintenance of the organisms. Conclusion: In conclusion, ageing is susceptible to environmental influence and genetic modification. This opens up the distinct possibility that ageing could be significantly retarded by appropriate genetic and environmental intervention. Our interpretation of the Strehler-Mildvan correlation suggest, that the human body experience

senescence in conditions preventing the total self-maintenance of organisms due to inadequate control system regimen. In this connection it is possible to find living conditions, physiological regimens and some pertinent means which will reduce or even eradicate and reverse both natural ageing and sarcopenia.

P18- NUTRITIONAL STATUS AND WOUND HEALING IN ELDERLY HOMEBOUND PATIENTS. I. Persidsky *(Long Beach, USA)*

Introduction: Without appropriate nutrition there is very little chance of healing chronic wounds in older adults. By itself, malnutrition threatens skin integrity, especially if patients are bed or chair bound. On the other hand, unlike other factors contributing to chronic wounds, malnutrition is fairly simple to correct. Objectives: Assessment and monitoring of nutritional status could be easily done with several simple laboratory tests, which is particularly important in patient whose anthropometric measures are unobtainable. Materail and methods: Retrospective analysis of albumin and prealbumin levels in 23 elderly (83.3±7.7), homebound patients (7 men and 16 women) with either pressure point of pelvis, trunk, and heels (n=16), or stasis of lower extremities (n=7)ulcers was done. All wound treatments were standardized. Results: Patients with pressure ulcers had lower levels of albumin (average 2.99±0.56 g/dl) and prealbumin (average 16.4±5.1 mg/dl) than individuals with stasis (3.86±0.67 g/dl and 21.3±4.2 mg/dl respectively) ulcers regardless of the stage of the wound. In patients with pressure ulcers when standard management was done, there was no significant wound healing, if albumin (2.9±0.54 g/dl) and prealbumin remained low (15.6±0.5 mg/dl). Increase of prealbumin from 14.4±2.0 to 18.5±1.9 mg/dl was closely associated with wound improvement. Although albumin levels correlate with healing as much, in patients, whose wounds improved significantly or healed levels were higher (3.46±0.15 g/dl) than in those who did not respond to treatments (2.6±0.34). All stasis lesions improved without any significant changes in either albumin (3.86±0.67 to 3.96±0.54 g/dl) and or prealbumin (21.3±4.2 to 22.5±4.7 mg/dl). Discussion: Above results not only confirm an importance of nutrition in healing of pressure ulcers, but also . Lack of relationship between nutrition and resolution of stasis ulcers could be explained by both different mechanism of these lesions development and absence of malnutrition in these patients to begin with. Of course an important question remains how to improve nutritional status. In above series appetite stimulants and hyperalimentation with high protein formula (orally or through gastrostomy tube) were used. Inability to offset malnourishment results in failed wound healing. Conclusion: 1. Malnourishment is associated with development of pressure, but not stasis ulcers; 2. Albumin and prealbumin are good markers of malnutrition in the elderly in relation to pressure ulcers development. 3. Prealbumin, but not albumin levels are excellent indicators of progress in wound healing and nutrition improvement

P19- THE ASSOCIATION BETWEEN FUNCTIONAL TESTS AND ENERGY EXPENDITURE OF WEEKLY PHYSICAL ACTIVITY IN ELDERLY: A COMMUNITY BASED RESEARCH IN TAICHUNG. T.M. Lee, N.H. Meng, C.K. Chang, C.C. Lin, W.Y. Lin, T.L. Yu *(Taichung, Taiwan)*

Introduction: Previous studies reported physical inactivity is a risk factor of cardiovascular disease, obesity, DM, and osteoporosis. Some researches showed people with regular physical activity have healthier profiles. Objectives: We hypothesized that muscle strength and function are highly associated with weekly physical activity energy expenditure. Therefore, the aim of the study is to examine the association between functional test and weekly physical activity energy expenditure in a Taiwanese metropolitan elderly population. Material and methods: This is a community-based cross-sectional study in elders aged 65 years old and older registered at 8 Lis of North district in Taichung City, Taiwan in 2009. A total of 942 elders with completed demographic data and weekly physical activity energy expenditure from structured questionnaires were included. All participants received anthropometric data and functional movement eveluation. Elders were divided into 4 groups according to quartiles of sex-specific physical activity energy expenditure. Chi-square test, one-way ANOVA, logistic regression and linear regression were applied for data analysis. Results: Elders with lowest quartile of physical activity energy expenditure were inactivity. The results showed that elders with inactivity are significant associated with older in age, single or widow, lower education level, stroke history, smoking, higher BMI, longer resting time. Inactivity was associated with lower muscle strengh and endurance of lower extremities, poor balance, and slow walking speed. After adjusting for anthropometric data and demographic data, linear regression shows the effect of inactivity on leg press, six minutes walking test(p for trend <0.05), squating in 20 seconds, timed up and go are still significant. Discussion: Structured physical activity questionnaires are a common tool to measure physical activity energy expenditure. After considering all related factors, our results show a linear increasing relation between six minutes walking test and physical activity, suggesting that inactivity associated with poor muscle strength and function. Conclusion: Structured physical activity questionnaires are a common tool to measure physical activity energy expenditure. To explore its relationship with functional tests in elders helps us evaluate how physical activities effect the results of functional tests.

P20- FATIGUE, FATIGABILITY AND PHYSICAL FRAILTY. M. Viorel Zamfir, F. Matei, I. Mihai Covlescu *(Bucharest, Romania)*

Introduction: Fatigue is one of the domains of physical frailty. In Fried phenotype, fatigue is measured using two questions from Center for Epidemiological Studies Depression Rating Scale (CES-D).Fatigue is a complex construct covering general subjective, physical, social, psychological and cognitive dimensions.Using the two questions from CES-D is a general assessment which does not cover all these dimensions of fatigue. Moreover, fatigue in daily activities as the physical fatigue, has been found as an independent predictor for disability. On the other side, exhaustion has not been found to be an independent predictor of for new-onset disabilities. One also must take into consideration the phenomenon of self-pacing; not being fatigued but having low activity level is a false negative situation. Sarcopenia is a core component of physical frailty so one might think taking into account muscle power in fatigue assessment. Fatigability, defined as fatigue per level of activity, might be a better approach to assess fatigue domain from physical frailty. Because Fried criteria for fatigue do not capture all this variations in multiple dimensions, a more in depth assessment should be used instead. Objectives: 1. To assess fatigue profile in older patients with physical frailty; 2. To establish the importance of fatigability and of self-pacing phenomenon in fatigue appearance; 3. To establish the dimensions of fatigue assessed by fatigue criteria used in Fried phenotype. Material and methods: This is a cross-sectional study on consecutive patients hospitalized in April 2011 at National Institute of Gerontology and Geriatrics "Ana Aslan", Bucharest.Inclusion criteria were age greater than 70 years. Exclusion criteria were diagnosis of dementia, mild cognitive impairment, Parkinson disease; or neoplasm diagnosed in the prior 10 years. Patients enrolled in the study were asked to complete Multidimensional Fatigue Inventory (MFI-20), Avlund Mobility Scale, Medical Outcomes Survey Short-Form-36 (MOS SF-36) and Hospital Anxiety and Depression Scale. Except specific items from MOS SF-36, the questionnaires were referring to the week prior to the hospitalization. MFI scoring was according to author instructions (Smets et al 1995). For Avlund Mobility Scale dimensions, it was considered the next scoring: - Mob-T score: 0 or 1~ normal, >=2 ~ fatigued (1*) - Upper Limb score: 0~ normal, >=1~ fatigued - Lower Limb score: 0~ normal, >=1~ fatigued. 1* Threshold of 1 was set because one question refers to fatigue when walking in poor weather, which reflects an important physical activity; Frailty was assessed using Fried criteria: - weight loss more than 5 kilos in the past year; - 2 specific questions from CES-D to assess fatigue: walking speed at normal pace on 5m distance, using the threshold of 1m/s; - grip strength assessed with a hydraulic hand dynamometer, two measurements for each hand, taking into consideration the maximal value for the dominant hand; (2*) - activities in the week prior to the hospitalization were assessed using Physical Activity Scale for the Elderly (PASE) questionnaire; 2*Threshold values from the CHS study (Fried et al 2001) were used. We also recorded: -demographic and lifestyle parameters; -social factors: marriage status, number of children, familial relationships (good/not), frequency of family visits (often/rarely), living alone/with somebody; -co-morbidities, sleep problems (present/not) -MMSE. Barthel Index, Lawton-Brody IADL; -basic laboratory values; -medication received prior to and during hospital admission. Written consent was taken from the patients and the study had the approval of local ethics committee. Results: We present here the preliminary results of the study. There were 48 patients, mean age = 76.7 years, 17 males and 31 females. According to Fried phenotype, there were 12 frail patients, 24 pre-frail and 12 were fit. The Spearman statistical test was used to asses a correlation score between Avlund Mobility scale scores and Fried fatigue score. Also the correlation between: Mob-T scale (Mob-T), Lower Limb scale (LL), Upper Limb scale (UL) was assessed in pair with the Fried fatigue score. Each of the two fatigue-related questions from CES-D (scored 0-3 as in CES-D instructions) and the Fried fatigue component score (0/1) were compared. The choice for this statistical test over other statistical tests available for making comparisons in distributions of two sets of data, it was done because it was desired not to have strong assumptions like a normal distribution of fatigue among patients, or statistical independence of data, that might influence the results. The Spearman test enables us to give a measurement coefficient of how correlated are the two paired tests and it is suited for the problem that is analyzed in this study. It was found that a moderate to large negative correlation exists between Avlund scores and CES-D fatigue questions (either individual questions or Fried fatigue component score). Spearman rho (Rs) scores are presented in brackets. Rs takes values between [-1,1] and the meaning is as it follows: Rs= -1, total inverse correlation, Rs=0 independence Rs=1, total correlation: -CESD-Q1: Mob-T (-0,9), LL (-0,77), UL (-0,79); -CESD-Q2: Mob-T (-0,38), LL (-0,91), UL (-0,90); -Fried fatigue score: LL score (-0,45), UL score (-0,4); (no correlation was found for MobT: 0,02). The correlation between MFI scores with Fried fatigue score, revealed a moderate-large correlation for the General Fatigue dimension (MFI-GF) and CES-D fatigue questions (either individual questions or Fried fatigue component score) - MFI-GF : CESD-Q1 (0,53); CESD-Q2 (0,48); Fried fatigue score (0,56). Also it was observed that a moderate positive correlation exists between Physical and Motivation subscales and CESD - individual questions (but not with Fried fatigue component score): - CESD-Q1: MFI-Physical (0,45), MFI-Motivation (0,33) ; - CESD-Q2: MFI-Physical (0,59), MFI-Motivation (0,43). Discussion: We found an interesting negative correlation between fatigue as assessed by Fried fatigue criteria and Avlund Mobility Scale. In prior studies, both were found to be independent predictors of disability in older people. The fact that they seem not to be present in the same patients make us think that there are two different groups: one who fatigue at low-level activities, positive for Fried fatigue criteria; and another who pace themselves, having fatigue in a certain activities of daily lving (such as dressing, washing themselves, taking shoes on or combing), but restricting the average and also maximal level of physical activities, so that they do not reach the threshold to feel an effort in every activity they do. Fried fatigue criteria might not be enough to cover all patients with fatigue at risk for poor physical outcomes. There is a need to assess different dimensions of fatigue in order to establish the risk for functional impairment. In addition to Fried fatigue criteria, we propose the use of Avlund Mobility scale, a simple instrument to measure fatigability. Conclusion: Although this is a small cross-sectional study, it proves the importance of self-pacing phenomenon in older fatigued patients. It also proves that Fried fatigue criteria might not be enough to include all patients with fatigue and Avlund Mobility Scale should be added to fatigue assessment. Keywords: fatigue, fatiguaeability, frailty, Avlund Mobility Scale.

P21- MALNUTRITION IN NURSING HOME RESIDENTS AND ITS ASSOCIATION WITH SARCOPENIA. B. Saka, F. Tufan, G. Bahat Ark, S. Ak, S. Engin, E. Kark, H.L. Azkaya, N. Yael, M. Akif Karan *(Istanbul, Turkey)*

Introduction: Turkey is one of the fastest aging countries. In 1985 4.2% of the population (2.2 million) were old aged (65 years) while the last population studies show that this rate has increased to 7.3% (5.3 million) (1). With aging, prevalence of the chronic diseases and cancer is increased, cognitive functions declined and undernutrition is seen in an increased proportion of the population (35-40%). All these factors associated with aging render these individuals susceptible to malnutrition. Malnutrition is even more frequent in nursing homes and hospitals. Recent data show that undernutrition is associated with worse health outcomes in the elderly compared to younger individuals (2). We investigated the nutritional status of the elderly residents (?60 years old) of Istanbul Metropolitan Municipality, Istanbul Darulaceze Nursing Home. Objectioves: We sought the association of malnutrition with chronic diseases and sarcopenia. Material and methods: In October 2010 we screened 349 residents with mini nutritional assessment (MNA) in a cross-sectional study. Medical histories including geriatric problems like dementia and depression and results of the geriatric assessment tool were recorded. Weights and heights of the residents were determined. Presence of sarcopenia was assessed with the use of handgrip strength and pinch strength with a standardized handheld dynamometer. Association of nutritional status with clinical findings and sarcopenia were investigated. Results: 177 of the residents were males and 172 of them were females (51 and 49% respectively). Mean age was 75±9 (males: 72±8, females: 78±9). 167 were younger than 75 years, 129 were between 75-84 years and 53 were ?85 years old. 185 (53%) of the individuals were in normal nutritional status, 117 (%33.5) were in risk of malnutrition and 47 (%13.5) had malnutrition. Malnutrition rate was 6% in residents below 75 years old while it was 22.6% above 85 years old. There was significant difference between body mass indices of residents with normal nutritional status and residents with malnutrition risk or malnutrition (28.9±5.7 vs. 23.4±4.5 kg/m2, p<0.0001). Similarly pinch strength and handgrip strength were significantly lower in residents with malnutrition risk or malnutrition compared to residents with normal nutritional status (pinch strength 5.82±2.05 vs. 6.98±2.36, handgrip strength 17.98±8.09 vs. 22.75±8.96, p<0.0001 for both comparisons). Pinch and handgrip strength suggested presence of sarcopenia in 274 (78.5%) residents. Malnutrition was present in 51% of the residents with sarcopenia (x2: 17.011, p<0.0001). 135 (38.7%) of the residents had dementia, 55 (15.7%) had depression, 27 (7.8%) had Parkinson's disease, 13 (3.6%) had history of cerebrovascular accident, and 6 (1.8%) had cancer. Malnutrition risk or malnutrition was present in 85 (63%) of 135 residents with dementia (x2: 21.225, p<0.0001). Logistic regression analysis showed only sarcopenia was independently associated with malnutrition (B=-1.068, Wald=7.886, p=0.005). Discussion: Being underweight is associated with higher mortality as being overweight. In white adults, all-cause mortality is generally lowest with a BMI of 20.0 to 24.9. Malnutrition and sarcopenia are the most probable factors to be responsible of worse outcomes in underweight older adults. thus, investigation of factors associated with both conditions as well as their interrelation is important. Our study which was carried out in one of the largest nursing homes in our country showed high rates of malnutrition and malnutrition risk. It also provided important information about factors associated with malnutrition. Of note the most strongly associated factor with malnutrition was sarcopenia in this study. Conclusion: When poor health outcomes associated with malnutrition and sarcopenia are considered, screening of the nursing home residents for the presence of these two geriatric problems may yield important health benefits. A more detailed and multicenter screening of malnutrition and sarcopenia is needed. Furthermore, interventional studie which aim to fight these two important health problems are urgently needed.

P22- THE ROLE OF MUSCLE PERFORMANCE AND SENSORY FUNCTION IN BALANCE DEFICITS: THE BALROOM PROJECT. J.H. Pasma, A.B. Maier, C.G.M. Meskers, H. van der Kooij *(Den Haag, The Netherlands)*

Introduction: Low muscle mass, sarcopenia, is related to detrimental outcome at old age, such as physical disability and mortality. Loss of muscle mass results from a reduced number of muscle fibers and atrophy of remaining fibers. This leads to impaired mechanical muscle performance, i.e. decrease in muscle strength, power and work. In every day tasks, muscle performance is also determined by the nervous system (innervating nerves and the central nervous system) and sensory systems. Balance deficits may primarily be caused by impaired muscle performance. It is also influenced by, or in combination with, sensory dysfunction of proprioception, vestibular organ and vision or deficits in sensory integration and processing. In general, older adults show a higher postural sway during double and single static leg stance. Furthermore, they have a longer response time as result of induced postural perturbations and changes in the visual surrounding compared to younger adults. Simultaneous cognitive tasks can further impact balance. Up till now, balance, muscle performance and sensory function are assessed as separate entities in older adults. It is however difficult to disentangle integration and processing of these systems simultaneously. All systems are within a feedback loop. The postural sway is controlled by the muscle performance using feedback of body position and movement received from the sensory systems. Cause and effect are intermingled and current clinical measurements cannot identify the underlying mechanisms responsible for balance. There is a clear clinical need for a methodology that can distinguish between the impact of sarcopenia and other systems in balance deficits. Within the present project (STW- NeuroSIPE 10737), we aim to develop a new perturbation equipment, the Balance test Room (BALROOM), that quantifies balance deficits and discriminates between the dysfunction of contributing systems in a fast and easy way. Objectives: Development of a new perturbation equipment which can make early and differential diagnosis in older adults presenting with balance deficits due to various causes in less than 15 minutes. The equipment will be implemented and evaluated in daily clinical care for older adults. Material and methods: To identify the contribution of each system involved in balance control, a control engineering approach will be used. This includes a model of the contributing systems in balance, external and sensory perturbations applied on the body and closed loop system identification techniques (CLSIT). When one of the sensory systems is perturbed, the central nervous system may rely more on the information from other sensory systems maintaining balance. Using a joint input-output approach several properties of the muscles and other systems can be determined. Specific changes in system properties due to sarcopenia can thus be identified. Results: Obtained system parameters can be related to balance deficits to identify weak links in balance. They will be assessed in a cohort of older adults with mobility disorders, referred to a geriatric outpatient clinic and during pharmacological intervention. Discussion: The equipment to be developed, in combination with advanced data processing techniques, will fulfill the clinical need to identify the weakest links in balance deficits. This is required to target therapy. The used technique is optimal for disentangle the integration and processing of all systems. Impaired muscle performance as a result of sarcopenia may be the primary cause for balance deficits in older adults, but may also be compensated by the nervous and the sensory systems. The distinction between sarcopenia and compensating mechanisms is a key to understand mobility disorders at old age. Conclusion: A combination of dedicated hardware and advanced control engineering techniques will disentangle muscle performance and sensory function, integration and processing within balance deficits. BALROOM will fulfill a clear clinical need to target therapy and will be integrated in daily clinical care.

P23- MUSCLE CHARACTERISTICS AND REGENERATIVE POTENTIAL IN PATIENTS WITH CHRONIC SYSTEMIC INFLAMMATION. K.G.M. Beenakker, B.J. Duijnisveld, V. Mouly, G. Butler-Browne, A.B. Maier *(Leiden, The Netherlands)*

Introduction: The age-related loss of skeletal muscle mass (sarcopenia) is a major contributor to disability and mortality. Between the age of 20 to 80 years the average reduction in muscle cross-sectional area amounts to 40%. The size and number of muscle fibers are under control of satellite cells, the muscle's progenitor cells that lie inactivated between the basal lamina and the sarcolemma. A decline in satellite cell number and the regenerative potential of the satellite cells, as well as muscle fiber type II atrophy has been reported to occur during aging. Morphologically, muscle fibers and satellite cells of elderly subjects show an accumulation of lipofuscin granules, a marker for oxidative damage. Despite the clinical importance, the pathophysiological mechanisms behind the development of sarcopenia are not yet well known. A possible cause of the development of sarcopenia is systemic, low-grade chronic inflammation. Increased systemic pro-inflammatory cytokine levels have been observed during ageing and recently associated with poor muscle strength. In patients suffering from rheumatoid arthritis (RA) the levels of inflammatory markers are severely high, already at middle age, despite of anti-inflammatory treatment. In these patients muscle strength is significantly lower compared to the general population. Objectives: In the present study we aim to determine the impact of chronic systemic inflammation on age-related histological muscle characteristics, the proportion of fiber type II atrophy, the level of lipofuscin and the number as well as the in vitro regenerative potential of satellite cells. As a model for chronic inflammation, we examine muscle biopsies from patients with RA who have a significantly higher pro-inflammatory profile when compared to patients with osteoarthritis (OA). Material and methods: The study population included patients suffering from RA (n=10) and OA as controls (n=27) undergoing elective knee replacement surgery. Two muscle biopsies were taken from the distal part of the medial vastus muscle during elective knee replacement operation. An ATPase method was used to determine the proportion of type II muscle fibers. The level of auto-fluorescence was determined to quantify the amount of lipofuscin. A multi-labeling method was used to determine the number of Pax7 and NCAM positive satellite cells per fiber. Regenerative potential was determined by measuring myogenic purity, viability, growth speed, maximum proliferative capacity, differentiation, mean telomere length and senescence / apoptosis associated protein expression of satellite cells in vitro. Results: The mean age for the RA patients was 63.6 years and for the OA patients 66.0 years, with an equal distribution of females in both groups. Markers of inflammation were significantly higher in RA patients compared to OA patients. Between both patient groups, no significant differences were found in the percentage of type II fibers area, the level of lipofuscin and the number of satellite cells. In vitro, satellite cells of the RA and OA patients had the same myogenic purity, viability, growth speed, maximum proliferative capacity, differentiation and expression of proteins associated with senescence / apoptosis. However, mean telomere length was shorter in RA patients compared to OA patients. Discussion: No differences were found in age-related muscle characteristics and in the regenerative potential of satellite cells in RA and OA patients. These results were not expected, because muscle wasting is characteristic for chronic inflammatory diseases like RA. Evidence arises that the microenvironment of satellite cells and systemic factors play a significant role in determining cellular function. Heterochronic parabiosis experiments in mice showed that rejuvenation of the systemic environment causes satellite cells to activate and proliferate, which underlines the influence of circulating factors on muscle regeneration.The strength of this study is the long disease duration and high levels of inflammation in RA patients compared to OA patients. Results could have been influenced by other factors than chronic systemic inflammation like inactivity levels and medication use. Conclusion: In conclusion, we provide new evidence that chronic systemic inflammation does not affect age-related muscle characteristics, nor the in vitro regenerative potential of human satellite cells. This result underscores the in vivo influence of inflammatory factors on muscle regeneration. Identification of mechanisms influencing

muscle regeneration by modulation of its microenvironment may improve strategies to regenerate human muscle and to slow down the development of sarcopenia.

P24- METABOLIC SYNDROME ALTERS THE PROPORTION AND MORPHOLOGY OF SKELETAL MYOFIBRES IN ELDERLY MEN. M. Gueugneau, C. Coudy-Gandhillon, B. Meunier, C. Barboiron, A. Listrat, L. Feasson, J.C. Barthelemy, B. Picard, D. Bechet *(Saint Gènes Champanelle, France)*

Introduction: One of the most noticeable effects of the increasing age is the atrophy of the skeletal muscle. Age-related reduction in muscle mass, strength and resistance is referred to as sarcopenia (Janssen et al, 2000; Faulkner et al, 2007). In order to understand the cellular mechanisms associated with sarcopenia, many studies have investigated the distribution and morphology of muscle fibres according to their contractile and/or metabolic type. Several authors have shown that the proportion and cross-section area of type I fibres remain similar or increase with aging, whereas an atrophy of type II fibres is widely acknowledged (Andersen, 2003; D. Antona et al, 2003; Lee et al, 2006; Narici and Maffulli, 2010). In addition, the elderly muscle usually exhibits fibre-type grouping and alterations in fibre shape. Many fibres appear 'flattened', 'crushed' or 'banana-shaped', and this flattening of muscle fibres is more pronounced among type II fibres than type I fibres (Andersen, 2003; Lee et al, 2006; Lexell and Downham, 1991). It is also well recognized that with increasing age, the alterations in muscle mass and function favor the apparition of metabolic syndrome which is a multiplex risk factor for cardiovascular disease (Jurca et al, 2005). Given that old subjects exhibit decrease in muscle strength and mass, they present an increased risk to develop metabolic syndrome, which can lead to cardiovascular diseases and thereby to increased mortality. Despite critical clinical outcomes, the effect of the metabolic syndrome on muscle characteristics of old individuals have not been investigated. Objectives: The purpose of the present work was to describe age-dependent and metabolic syndrome-associated changes in the proportion and morphological characteristics of myofibers in a human skeletal muscle. Material and methods: The study was performed with biopsy samples of the vastus lateralis muscle from 15 young (YO, 25 years), 13 elderly (EL, 75 years) and 11 elderly with metabolic syndrome (EL-MetS, 75 years). Serial transverse sections (10 µm) were performed using a cryostat at -20°C. Sections were stained with monoclonal antibody (mAb) A4, which labels type I and type I-IIA fibres, and mAb N2, which labels type II and hybrids fibres, and they were revealed with Dylight-conjugated secondary antibodies. An average of 380 fibres was analyzed for each individual. The cross-sectional area, perimeter, proportion and shape of all myofibres were measured for each individual via a homemade visual basic program developed under Visilog 6.7 software. Standard statistical methods were used to calculate means ± SE. For comparisons between YO, EL and EL-MetS, a Student's t test was used. The 0.05% confidence level was chosen for statistical significance. Results: Fiber type proportions: Aging was found to strongly alter the proportion of fibre types in the human vastus lateralis muscle. The proportion of type I fibres significantly increased (+31%) in elderly (EL) when compared to young (YO). In contrast, the proportion of the type II fibres, especially type IIA (-14%), significantly decreased in EL when compared to YO. Metabolic syndrome apparently reverted the effect of aging on fibre type proportions, as no difference was any more observed when fiber proportions of elderly with metabolic syndrome (EL-MetS) were compared to those of YO or EL muscles. Fiber cross-section area: Changes in fibres cross-section areas (CSA) were also investigated during aging and as a result of metabolic syndrome. In human vastus lateralis, aging alone significantly increased CSA of type I fibres (+16%). In contrast there was in EL a significant decrease in CSA of type II fibres, especially type IIA (-15%), when compared to YO. Metabolic syndrome did not modify CSA of type I fibers in old muscles. However, the metabolic syndrome tended to revert the effect of aging on type II fibres, as no difference was any more observed between type II CSA of EL-MetS muscles and those of YO or EL muscles. Fiber shape: To highlight alterations in muscle fibre shape, a shape factor (SP = area/4 perimeter2) index was calculated. As a result of aging alone, deformation (SP) of muscle cells was found to significantly increase only for type IIA fibers, which also atrophy in the old muscle. Interestingly, metabolic syndrome in elderly strictly altered the shape of the most abundant fibers, as SP of type I, IIA and IIX significantly increased in EL-MetS when compared to YO. In addition, the metabolic syndrome-dependent deformation was more important for type IIX fibres than for type I and type IIA fibres. Discussion: In the elderly, age-related changes in vastus lateralis mainly affect type I and IIA fibres. In agreement with previous reports of D. Antona (2006) and Lee (2006), we demonstrate that the proportion and area of type I fibres significantly increase during aging, whereas conversely, the proportion and area of type IIA fibres decrease. As similarly reported by Lexell (1991) in vastus lateralis, the young subjects therefore present a higher proportion of type IIA fibres , whereas elderly men exhibit a higher proportion of type I fibres. In the present study, we further highlight that metabolic syndrome in elderly men sharply alters the composition and morphology of skeletal muscle fibres. Indeed, we show that type I and type IIA fibres present similar proportions (40%) in vastus lateralis of EL-MetS. Furthermore we provide evidence for increased deformation of most fibres in seniors affected by metabolic syndrome. With regard to the deformation of fibres, and more particularly of glycolytic fibres, we hypothesize that the observed alterations may be related to a poor innervation of muscle fibres because nerves are very sensitive to high level of glucose, which is generally the case in EL-MetS. In type I fibres and as suggested by Clark (2011), increased fiber size could diminish oxygen and substrate supply for the metabolic processes in the central area of cell. To assess these hypotheses, studies on the metabolic activity are currently performed. Moreover, transcriptomic and proteomic investigations are carried out to better understand the mechanisms leading to these modifications in human skeletal muscle. Conclusion: Results of age-related changes in vastus lateralis that are presented in this study are consistent with the data from the literature. Importantly, the present work underlines that metabolic syndrome in elderly men promotes alterations in skeletal muscle myofiber morphology. This observation has not previously been demonstrated and may be important to better understand the cellular mechanisms associated with this pathology.

P25- DEGENERATIVE PROCESSES AT THE NEUROMUSCULAR JUNCTION INVOLVING THE C-TERMINAL AGRIN FRAGMENT AS A CAUSE FOR SARCOPENIA. M. Drey, J.M. Bauer, C.C. Sieber, P. Dahinden, R.G. Fariello, J.W. Vrijbloed *(Nuremberg, Germany)*

Introduction: Sarcopenia has been considered as a great burden for the affected individual and for aging societies as well. Among different etiologic factors under discussion, the degeneration of the neuromuscular junction (NMJ) may play a major role. The equilibrium between the pro-synaptic agent agrin and its counterpart neurotrypsin is essential for a structurally intact and well functioning NMJ. Agrin is inactivated by cleavage from neurotrypsin, a synaptic protease, which frees a soluble 22 kDa C-terminal Agrin Fragment (CAF) that can be detected in human serum. Experiments with transgenic mice overexpressing neurotrypsin in spinal motoneurons show a correlation between skeletal muscle atrophy and deterioration of synaptic connections. Objectives: The present study tested the hypothesis whether CAF serum concentration represents a reliable marker for sarcopenia in humans caused by degeneration of the NMJ. Material and methods: In 68 (47 female) prefrail community-dwelling older adults CAF serum concentration was measured by Western plot technique. Appendicular lean mass (aLM) was measured by Dual energy X-ray Absorptiometry (DXA) and divided by squared body height. Results: In males a high correlation (r = -0.563) between CAF serum concentration and aLM was found, whereas in females this was not the case (r = -0.044). When cut-offs for aLM (female: 5.75kg/m^2, male: 8.5kg/m^2) and CAF (4ng/ml for both sexes derived from healthy age matched controls) were applied, 57% of sarcopenic males suffered from sarcopenia caused by NMJ-degeneration, whereas just 9% of the females did. Discussion: The strong association between aLM and CAF in males points to an enhanced NMJ's deletion through an unbalanced neurotrypsin/agrin system in more than half of the patients. The missing correlation in female suggests a broader etiology of sarcopenia and a lower percentage of patients in whom NMJ-degeneration plays a role. Conclusion: This pilot evaluation of CAF as a marker for sarcopenia caused by NMJ-degeneration is promising pointing in the direction of a neurogenic cause of sarcopenia in a substantial subpopulation of patients. Future investigations characterizing patients with muscle biopsy and EMG investigations are necessary to further elucidate the role of CAF.

P26- ROLE OF MUSCLE MASS AND FORCE-VELOCITY CHARACTERISTICS OF THE KNEE EXTENSORS IN PHYSICAL FRAILTY. E. Van Roie, S.M. Verschueren, S. Boonen, A. Bogaerts, E. Kennis, W. Coudyzer, C. Delecluse *(Leuven, Belgium)*

Introduction: As life expectancy continues to rise worldwide, age-related loss of function and mobility have become a major public health issue, threatening the independency and quality of life of older adults. The phenomenon of sarcopenia, first introduced by Dr. I.H. Rosenberg as the age-related decrease in skeletal muscle mass, is found to be a strong predictor of this physical frailty. Early detection of persons at risk is thus crucial in developing effective strategies aimed at avoiding a dramatic increase of the incidence of sarcopenia and physical frailty in the graying society. Identification of sarcopenia is actually based on measurements of muscle mass. However, maintenance or even gain in muscle mass at age does not necessarily prevent degeneration in muscle strength and power. Recent findings illustrate that muscle power and the ability to develop a high velocity during muscle contraction appear to be stronger predictors of everyday function of older adults, compared to muscle mass that seems less decisive for activities of daily living. It is clear that measurements solely based on muscle mass may not be sensitive enough to detect early deficits in muscle function. Determining the force-velocity characteristics of skeletal muscle in elderly by means of standardized tests on an isokinetic/isotonic dynamometer may therefore be expected to be more effective in identifying the risk of physical frailty. However, there is a paucity of research regarding the relationship between these force-velocity characteristics, muscle mass and the onset of physical frailty in older adults. Objectives: The first objective of this study was to determine the contribution of muscle mass versus force-velocity characteristics of the knee extensors to functional performance in elderly women. The second objective was to identify the knee extensor strength and velocity levels associated with a reduced functional performance. Material and methods: Subjects were 123 institutionalized women (aged 79.67 ± 5.25 years). Muscle mass of the upper leg was determined by computed tomography. Force-velocity characteristics of the knee extensors were evaluated with isometric, isokinetic, and ballistic tests on a Biodex System 3 dynamometer. Isometric strength at a knee joint angle of 90° (ISO), dynamic strength at a speed of 60°/s (DYN), maximal speed of movement (SoM unloaded) and speed of movement with standardized resistance of 20% (S20), 40% (S40), and 60% (S60) of the isometric maximum, were recorded. Functional performance related to daily activities was assessed with the modified Physical Performance Test (mPPT). This test battery consists of nine functional items: (i) lifting a book from waist height to a shelf at shoulder level, (ii) putting on and taking off a coat, (iii) picking up a penny from the floor, (iv) turning 360°, (v) walking 15 m, (vi) ascending one flight of stairs, (vii) climbing four flights of stairs, (viii) the chair rise test and (ix) the Romberg test for balance. The score of each item ranged from 0 (the inability to complete the task) to 4 (the highest level of performance), with a summary performance score (mPPT-score) of maximum 36 points. Subjects were divided in three frailty categories: 'not frail' (32-36, n=34), 'mildly frail' (25-31, n=70) and 'moderately frail' (17-24, n=19). Pearson correlation coefficients were used to determine whether muscle

mass, muscle strength, and speed of movement were significantly associated with functional performance. In addition, all muscle variables were entered in a multiple forward stepwise regression model to determine the contribution of each variable to functional performance. Finally, to define functionally relevant threshold values, receiver operator characteristic (ROC) curves were obtained for each muscle characteristic that significantly contributed to the model. As it is imperative that persons at risk for functional difficulties can be detected at an early stage, our categories of 'not frail' and 'mildly frail' (i.e. starting to have functional limitations) were applied in the ROC curves to define 'good' and 'poor' functionality, respectively. From these ROC curves, diagnostic threshold values were identified as those yielding the most favorable compromise between specificity and sensitivity. Results: The mPPT-score showed moderate to high correlations with muscle mass, muscle strength and velocity measurements. With regard to speed of movement during ballistic tests, these correlations became stronger when external loadings decreased and thus when speed of movement increased. Importantly, maximal speed of movement showed the highest correlation with functional performance (r=.68, P<.05). In a forward stepwise regression model, only maximal speed of movement (SoM) and isometric strength (ISO) remained independently associated with mPPT (R^2=.49), with SoM accounting for the majority of the variance. As SoM and ISO were found to be significant contributors to functional performance, the ROC method was used to select the diagnostic threshold value of these muscle parameters for the identification of persons at risk for functional limitations. The threshold value that optimally differentiates between women with mild (mPPT-score of 25 to 31) or without (mPPT-score â32) physical frailty, was 350°/s for SoM and 1.46Nm/kg for ISO. Sensitivity and specificity ranged from 74% to 77% and from 71% to 77%, respectively. Discussion: In accordance with previous research, muscle mass of the upper leg, muscle strength and speed of movement measurements of the knee extensors were significantly correlated with functional performance in elderly women. Muscle mass, however, was not an independent determinant of functional performance when included in the same regression model as muscle strength, suggesting that muscle mass primarily contributes to functional performance through its association with muscle strength. Importantly, maximal speed of movement of the knee extensors was identified as a key component in everyday function, suggesting that it might be a particularly useful parameter to screen for physical frailty. Based on this parameter, a discriminating threshold value of 350°/s could be determined as a sign of being at risk for physical frailty. Aside from maximal speed of movement, isometric muscle strength also contributed to functionality. A sufficient 'potential of the musculature to generate force' (strength) is a prerequisite for speed production and must also be considered as an essential factor in functional performance. An isometric or dynamic (60°/s) knee extensor strength measurement can be an alternative when velocity measurements are not achievable in particular settings. However, this method may not be able to detect persons at risk who still have sufficient strength but already show deficits in speed of movement. Conclusion: These findings highlight the importance of maximal speed of movement in the onset of functional difficulties in elderly women. This parameter may be a useful component to gain a better insight in the process of physical frailty. The results also suggest that exercise interventions in the elderly should not focus solely on general strength training, but also on functional training at higher velocities specifically targeting muscle power.

P27- THE CASSIHOP (THE CLINICAL ASSESSMENT OF SARCOPENIA IN HOSPITALIZED PATIENT) PILOTE STUDY : DESIGN AND METHODOLOGY. C. Dupuy, G. Abellan van Kan, S. Gillette, B. Vellas, Y.Rolland *(Toulouse, France)*

Background: Sarcopenia is an important field of research in geriatrics as it is considered to be responsible for functional limitations and disability. Lack of strength or functional limitations such as slow walking speed are strong predictors of adverse health outcomes (falls, fractures, comorbidities, hospitalizations) (1-2) and death (3-5). Recently, a group of European experts has determined and suggested different defining stages of sarcopénie (The 'presarcopenia' stage : low muscle mass without impact on muscle strength or physical performance ; The 'sarcopenia' stage : low muscle mass, plus low muscle strength or low physical performance ; The 'Severe sarcopenia' : low muscle mass, low muscle strength and low physical performance) (6). Epidemiological studies realized last year, suggest that after 50 years of age, muscle mass is reported to decline at an annual rate of approximately 1 to 2% in the healthy population. However, we believe that « acute » muscle mass loss can occur consequently to certain events, particularly during hospitalisations, leading to quicker functional decline. This decline will probably be enhanced if the hospitalisation occurs in a frail and sarcopenic population. Hypothesis: Our hypothesis is that for these sarcopenic subjects, muscular-mass loss is more predictive of performance decline than the quantity of muscular mass itself. Currently, we are unable to evaluate the level of muscular loss associated with functional status decline as no follow-up data of sarcopenic patients is available. Primary objective : To identify if a clinically relevant muscle loss (change of AMM - Appendicular Muscle Mass) in older adults with sarcopenia who have suffered a recent hospitalisation is a risk factor of functional decline. Study design : Cassihop pilote study is a monocenter prospective follow-up (Pilot Phase). The pilot study will be run within the Internal Medicine and Clinical Gerontology Department of the CHU of Toulouse (Pr Bruno Vellas). Study timeline : 15 month. Inclusion criteria : - men or women aged 65 years and older, hospitalized, who fall [to find oneself involuntarily on the floor or in a lower position then to begin with] repeatedly [≥ 2 falls during a period of 12 months]. - patient with low gaitspeed evaluated by a walking test on 4 meters (<1m/s) or low muscle strength, - patient with sarcopania measured by DEXA (ratio AMM/heigt2 ≤ 7,23 kg/m2 on men and 5,67 kg/m2 on women),This criteria is recommended by an international consensus as the cut-off to define sarcopenia (7), - patient, who after being informed about the study, agreed to participate. Measures and procedures during the follow-up visits : Follow-up visits will be done at 1 month and 12 months after the inclusion visit. Data collected during these two visits will be identical to those gathered during the pre-selection evaluation (MMSE, gait speed and grip strength and DEXA) and the inclusion visit (SPPB, ADL, IADL, MNA, GDS 4 items, CAM,). Events which occurred between each visit will also be collected (treatment modifications, non drug-related managed, intercurrent diseases, hospitalisations...). In the case of new hospitalisation occurring during the follow-up (between the 1st month and the 12 months visit) within the Internal Medicine and Clinical Gerontology Department, a gait speed test and grip strength test, a SPPB and a DEXA will need to be done, if the health status of the patient allows it. Number of subjects : The 60 subjects included during the pilot phase in order to confirm our hypothesis concerning the prevalence of a muscular mass-loss. References : (1) Abellan van Kan G, Rolland Y, Andrieu S, et al. 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P28- DIETARY INTAKE OF VITAMIN D AND MUSCLE MASS IN OLDER WOMEN. RESULTS FROM A LARGE CROSS-SECTIONAL POPULATION-BASED EPIDOS-TOULOUSE STUDY. C. Dupuy, G. Abellan van Kan, S. Gillette, B. Vellas, Y. Rolland *(Toulouse, France)*

Objective. The benefits of vitamin D intakes to prevent muscle mass decline remain unknown. The importance of the vitamin D in the bone metabolism has been established for a long time but currently there is a renewed of interest for this vitamin because of its possible role during the ageing process in a certain number of clinical events such as falls, fractures, strength, balance, and cognitive disorders, the occurrence of certain cancers and certain inflammatory diseases (1-7). During the past decade, the vitamin D was the subject of larger number of studies which suggested an association between a low rate of 1,25-hydroxy-vitamine D and a decrease of muscle strength, of poor capacity of balance and improved the risk of fall and fractures (8-9). Nevertheless, we ignore this day if this advantageous effect is secondary to an increase of the muscle mass or to an other physiological functions. Fundamental data show a potential effect of the vitamin D on the protein synthesis of the muscular fiber (10-11). Knowledge in this domain advanced and they know now that the vitamin D is involved in numerous pathophysiological mechanisms. It is a hormone having present membranaires intracellular receptor on numerous cells including the muscular cells (12). Our objective was to determine whether the weekly dietary intakes of vitamin D could be associated with muscle mass among older adults. Methods. 968 community-dwelling women (mean age 80.34±3.88years) free of vitamin D drug supplements from the EPIDOS study, were divided into 2 groups according to the baseline weekly vitamin D dietary intakes (either inadequate <35μg/week or recommended ≥35μg/week). Weekly vitamin D dietary intakes were estimated from a self-administered food frequency questionnaire. Muscle Mass was assessed using the DXA (Dual-energy X-ray absorbsiometry). DXA estimated whole body composition measurements. Muscle mass was based on appendicular skeletal muscle mass (ASM). ASM corresponds to sum of two upper and lower limb muscular masses in kilogram. Age, sun exposure at midday, number of chronic diseases, education level, living arrangements, physical activity, gait speed, handgrip, body mass index and whole body composition were considered as potential confounders. Results. Compared to women with recommended weekly vitamin D dietary intakes (n=831; mean age 80,26±3,89years), the women with inadequate intakes (n=137; mean age 80,81±3,81years) had approximately the same mean muscle mass (p=0,2013). There was not a linear association between weekly vitamin D dietary intakes and ASM (β=0,002; p=0,368). Conclusions. The weekly dietary intakes of vitamin D were not associated with muscle mass in older women. References : (1) Annweiler C, Beauchet O. (2009) Relationship between bone, fracture, and exercise: the key role of vitamin D. Archives of internal medicine 169(17):1638; author reply, (2) Annweiler C, Beauchet O, Berrut G, Fantino B, et al. (2009) Is there an association between serum 25-hydroxyvitamin D concentration and muscle strength among older women? Results from baseline assessment of the EPIDOS study. The journal of nutrition, health & aging 13(2):90, (3) Annweiler C, Bridenbaugh S, Schott AM, Berrut G, et al. (2009) Vitamin D and muscle function: new prospects? BioFactors (Oxford, England) 35(1):3-4., (4) Annweiler C, Schott AM, Montero-Odasso M, Berrut G, et al. Cross-sectional association between serum vitamin D concentration and walking speed measured at usual and fast pace among older women: The EPIDOS study. J Bone Miner Res. (5) Annweiler C, Schott AM, Rolland Y, Blain H, Herrmann FR, Beauchet O. Dietary intake of vitamin D and cognition in older women: a large population-based study.Neurology. 2010 Nov 16;75(20):1810-6.)]. (6) Braddy KK, Imam SN, Palla KR, et al. Vitamin D deficiency/insufficiency practice patterns in a veterans health administration long-term care population: a retrospective analysis. J Am Med Dir Assoc 2009;10:653. (7) Holick MF.

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P29- SARCOPENIA AND NUTRITIONAL STATUS, ANTHROPOMETRIC MEASUREMENTS AND BODY COMPOSITION IN A GROUP OF MEXICAN ELDERLY WOMEN. M.C. Velazquez-Alva, M.E. Irigoyen-Camacho, V.E. Pedraza *(Mexico city, Mexico)*

Introduction: Sarcopenia is defined as the loss of skeletal muscle mass associated with the aging process and is important to consider the relationship of this condition with the nutritional status and the body composition in different elderly groups. Aspects such as anorexia, decreased caloric intake and the exercise are associated with the decline of skeletal muscle mass. Objectives: Identify the nutritional status and body composition with the prevalence of sarcopenia in a group of Mexican elderly women. Material and methods: A cross-sectional study design was used in this study. The women selected were patients of the geriatric service of a central hospital in Mexico City. This hospital is part of the public healthcare systems. The nutritional status was identified using the Mini Nutritional Assessment (MNA) classification, according three categories were constructed: undernutrition, risk of undernutrition and without undernutrition (normal nutrition). Body composition was assessed by Bioimpedance analysis (BIA). We used a tetrapolar foot-to-foot bioelectrical impedance equipment (Model TBF-300, Tanita Corporation of America, Inc, Arlington Heights, IL; Tanita-BIA). Grip strength was measured, in the dominant hand, using a hand dynamometer (Takei Ltd.,Tokyo, Japan). A series of three grip strength measurements were taken and the highest two were averaged to provide one measure in each person. The appendicle skeletal muscle mass (ASM) was estimated applying the Baumgartner equation: ASM (kg) = 0.2487(weight) + 0.0483(height) - 0.1584(hip circumference) + 0.0732(grip strength) + 2.5843(sex) + 5.8828. The skeletal muscle mass index (SMI) was obtained as follow: ASM/height2 (kg/m2). A SMI < 5.67 kg/m2 was used as cut-off point to identify sarcopenia. Results: 130 female patients were included in the study; their mean age was 78.0 ± 6.9 years-old. According to the MNA results 73% of the women were at risk of undernutrition, 15% showed undernutrition, and only 12% were classified in the normal category. Significant differences in the mean values of the main anthropometric measurements were detected ($p<0.05$). Also body composition compartments and grip strength were different among the three nutritional categories of the MNA score ($p <0.05$). The prevalence of sarcopenia, based on the SM Index, was 47.0% (n = 61). Sarcopenia indicators were statistically significant different between the average values of anthropometric measurements (except for stature) and the body composition measurements ($p <0.0001$). SMI was of 4.9±0.1, 5.6±01 and 5.8±0.1 in the patients with undernutrition, risk of undernutrition and normal nutrition, respectively ($p <0.001$). ASM was 10.6 ± 0.4, 12.4±0.2 and 13.7±0.4 ($p<0.001$) in the patients with undernutrition, risk of undernutrition and normal nutrition, respectively. Discussion: The results of this study indicated that the nutritional status of the patients is poor considering the high frequency of undernutrtion and risk of undernutrition detected in the elderly women studied. It was observed that the results of the MNA showed differences in the body composition compartments. The European consensus on definition and diagnosis of sarcopenia in older people mentioned that among the variables which must be taken into account to the estimation of sarcopenia are: muscle mass, muscular strength (grip strength) and physical performance (walking speed.) In our study, the parameter used to define sarcopenia was the application of Baumgartner formula that includes in the equation the grip strength. Appling this equation to our data it was possible to identify associations between sarcopenia and nutritional status, anthropometric measurements and body composition. We found a higher frequency of sarcopenia among patients with undernutrition and at risk of undernutrition, than among those well-nourished elderly women. Conclusion: Undernutrition and the risk of undernutrition were conditions highly prevalent in the study group. The patients with undernutrition and sarcopenia presented the lowest values in the anthropometric measurements, body composition and grip strength. It is necessary to carry out more studies in order to contribute to the understanding of sarcopenia and its association with the nutritional status and the body composition, in order to develop adequate nutritional support programs.

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