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Inflammation and microvascular dysfunction in elderly patients with ST elevation acute myocardial infarction treated with primary PCI

A. Demarchi¹, A. Somaschini¹, S. Cornara¹, M. Ferlini², A. Ravera¹, A. Mandurino-Mirizzi¹, R. Camporotondo³, M. Ferrario Ormezzano², L. Oltrona Visconti², G.M. De Ferrari¹. ¹ Coronary Care Unit – Fondazione IRCCS Policlinico San Matteo and University of Pavia, Department of Molecular Medicine, Pavia, Italy; ²Division of Cardiology, Fondazione IRCCS Policlinico San Matteo, Pavia, Italy; ³Coronary Care Unit, Fondazione IRCCS Policlinico San Matteo, Pavia, Italy

Background: An acute myocardial infarction generates a strong inflammatory response which may be harmful as it is associated with ischemia/reperfusion damage and no-reflow phenomenon. Very little is known about the inflammatory response in elderly patients with ST Elevation Acute Myocardial Infarction (STEMI) and about the role that inflammation has on the microvascular damage in this population that is usually underrepresented in cardiovascular trials.

Purpose: We evaluated the inflammatory response and its relationship with microvascular damage in patients older than 75 years with STEMI treated with primary percutaneous coronary intervention (pPCI).

Methods: We enrolled 40 patients (pts) with STEMI undergoing pPCI. We determined high sensitivity C-Reactive Protein (hsCRP) on serum samples collected before and 6–12–24–36h after PCI and we considered the peak value for each patient. Effective tissue reperfusion and microvascular damage have been determined by assessing Myocardial Blush grade (MBG) and Corrected TIMI Frame Count (CTFC). Variables were log-normalized for most statistical tests.

Results: Twenty-two percent of our patients had an age above 75 years. There were no differences between the two groups in the incidence of diabetes, anterior MI, use of glycoprotein IIb/IIIa inhibitors or pain-to-balloon time. None of our patients had a history of chronic inflammatory diseases. Patients with age above 75 years showed higher hsCRP peak: 1.62 mg/dl (IQR=0.6-5.9) vs 0.67 mg/dl (0.4–1.4), p=0.03. Also, there was a significant association between age above 75 and no reflow phenomenon expressed as a MBG value of 0–1 (50% vs 13.8%, respectively in elderly and younger patients, p=0.04). There was a positive linear correlation between age and a slow coronary flow due to microvascular dysfunction expressed as a high CTFC value (R=0.4; p=0.03). The multivariable regression model showed that age was a predictor of CTFC value (beta=0.36; p=0.032).

Conclusion: Elderly had a higher inflammatory response during the first hours of an acute MI compared to younger patients; microvascular damage and no-reflow phenomenon were also more frequent in the elderly subgroup.

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The uric acid paradox for cognitive dysfunction in the elderly patients with heart failure: nutritional status as a significant moderator?

A. Tsuchiya, M. Nagai, K. Dote, M. Wakabayashi, K. Nakamura, M. Katou, S. Sasaki, N. Oda, E. Kagawa, Y. Nakano, A. Yamane, T. Higashihara. *Hiroshima City Asa Hospital, Department of Cardiorogy, Hiroshima, Japan*

Background: Cognitive decline, malnutrition and heart failure (HF) frequently coexist in the elderly. Although several studies reported an association between serum uric acid (sUA) and cognitive function in general population, the relationship was contradictory. We hypothesized that sUA might be associated with cognitive dysfunction in the elderly with HF. In addition, we investigated whether nutritional status moderates the relationship or not.

Purpose: To investigate the relationships among cognitive function, sUA and serum albumin in the elderly patients with HF.

Methods: Cognitive function was evaluated using mini-mental state examination (MMSE) in 152 elderly inpatients in stable phase of HF (82.8±6.2 years old, female 51%). Measurement of sUA and serum albumin at admission as well as echocardiography were performed.

Results: According to the quartile of MMSE score (<19, \geq 19 to 24 <, \geq 24), significant associations of MMSE score were observed with sUA (8.3 vs 7.3 vs 6.2mg/dl, p<0.01) and serum albumin (3.4 vs 3.6 vs 3.6g/dl, p<0.05) among three groups. In the logistic regression analysis adjusted for the confounders including age, gender, left ventricular ejection fraction, brain natriuretic peptide level, systolic blood pressure, diuretics use and use of antihypertensive medications, sUA (β =1.28, 95% CI: 1.07 to 1.53, p<0.01) as well as serum albumin (β =0.24, 95% CI: 0.09 to 0.65, p<0.01) were significantly associated with cognitive dysfunction (defined as MMSE score <19). The interaction term of sUA by serum albumin (ρ <0.05). Only in the group with higher half of serum albumin, sUA had significant relationship with cognitive dysfunction (β =1.52, 95% CI: 1.06 to 2.18, p<0.05).

Conclusions: Higher sUA was shown as a significant indicator of cognitive dysfunction specifically in the elderly HF patients with higher serum albumin. These results highlight the importance of stratifying by nutritional status for a clinical intervention on the relationship between sUA and cognitive dysfunction in the elderly with HF.

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Cognitive impairment: a mediator for the relationship of visit-to-visit blood pressure variability and long sleep duration with cardiovascular death in the elderly

M. Nagai, K. Dote, M. Kato, S. Sasaki, N. Oda, E. Kagawa, Y. Nakano, A. Yamane, T. Higashihara, S. Miyauchi, A. Tsuchiya. *Hiroshima City Asa Hospital, Cardiology, Hiroshima, Japan*

Background: Visit-to-visit blood pressure (BP) variability, short or long sleep duration and cognitive impairment were shown to be associated with cardiovascular disease, although there were no studies that reported those comprehensive relationships for the cardiovascular disease. Here, we investigated the impact of visit-to-visit BP variability, sleep duration and cognitive impairment on the cardiovascular disease.

Purpose: To investigate the relationships among visit-to-visit BP variability, sleep duration, cognitive impairment and cardiovascular disease in the elderly at high-risk of cardiovascular disease. In addition, the issue whether cognitive impairment moderates the relationships of visit-to-visit BP variability and sleep duration with cardiovascular disease was analyzed.

Methods: Among the total population of 1723 peoples in the Soryo Town, BP measurements, assessment of sleep duration and cognitive function were performed in 201 subjects (mean age 79.9 yrs at baseline, 75% females) with one or more cardiovascular risk factors. Based on 12 visits ($1 \times /month$ for 1 year), we calculated visit-to-visit BP variability expressed as the standard deviation (SD) and delta (maximum-minimum) BP. The cognitive function was evaluated using a mini-mental state examination (MMSE), whereas self-reported sleep duration questionnaire was used to classify the patients according to sleep duration.

Results: In the Cox-regression analysis adjusted for age, gender, body mass index, diabetes mellitus, low-density lipoprotein and fasting blood glucose, delta systolic BP (SBP) (HR: 7.4, 95% CI: 1.3–44, p<0.05) and long sleep duration (>9h per night) (HR: 1.03, 95% CI: 1.003–1.064, p<0.05) were significant predictors of cardiovascular death during the mean 6.1-year follow-up. Consistent with cognitive impairment (MMSE score less than 25) as a mediator of the relationships of delta SBP and long sleep duration, the inclusion of cognitive impairment in that multivariate Cox model appreciably attenuated those association (p=0.07 and p=0.3, respectively).

Conclusions: Exaggerated visit-to-visit SBP variability and long sleep duration were significant predictors of cardiovascular death in high-risk elderly patients at cardiovascular disease. Cognitive impairment was suggested to serve as a mediator for the relationship of visit-to-visit SBP variability and long sleep duration with cardiovascular outcome.

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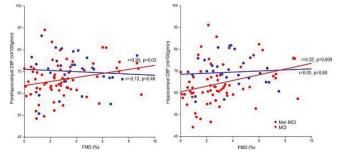
Hippocampal cerebral blood flow depends on systemic endothelial function in individuals with mild cognitive impairment: the Train the Brain-Mind the vessel study

R.M. Bruno¹, L. Pratali², R. Sicari², F. Stea², N. Berardi³, G. Tognoni⁴,
U. Bonuccelli¹, L. Ghiadoni¹, S. Taddei¹, D. Scelfo⁵, L. Biagi⁵, M. Tosetti⁵,
L. Maffei³, E. Picano² on behalf of The Train the Brain Consortium. ¹University of Pisa, Pisa, Italy; ²Institute of Clinical Physiology of CNR, Pisa, Italy; ³Institute of Neuroscience of CNR, Pisa, Italy; ⁴Azienda Ospedaliero - Universitaria Pisana, Pisa, Italy; ⁵IRCCS Stella Maris, Pisa, Italy

Background: Dementia has been recently viewed as a predominantly vascular disorder. Indeed, reduced brain NO availability causes increased β -amyloid deposition by several mechanisms, including hypoperfusion.

Purpose: To investigate whether a relationship exists between cerebral blood flow in the hippocampal and parahippocampal regions (crucial areas for memory and processing of non-verbal / spatial information) and systemic endothelial function in individuals with mild cognitive impairment (MCI), a subclinical condition predisposing to dementia.

Methods: Cerebral blood flow in the hippocampus and parahippocampus (CBFhipp and CBF-parahipp) were evaluated by magnetic resonance imaging (arterial spin labeling, GE HDxt 1.5 T Signa Neuro-optimized System). Systemic endothelial function was evaluated by flow-mediated dilation (FMD) in the brachial artery. **Results:** Complete data about CBF and FMD at enrollment were available for 66 individuals with MCI and 32 without (non-MCI). The two groups were matched for age (75±5 vs 74±5 years respectively, p=0.22), sex (men 45,5% vs 50%, p=0.18) and mean BP (96±10 vs 97±9 mmHg, p=0.41). FMD was



significantly lower in MCI than in non-MCI (2.93±2.18 vs 3.74±2.03%, p=0.02); CBF-hipp (64.3±9.43 vs 69.5±7.03 ml/100 gr/min), p=0.002) and CBF-parahipp (66.3±8.02 vs 70.0±8.12 ml/100 gr/min, p=0.002) were significantly lower in MCI as well. Among MCI, FMD was significantly correlated with CBF-parahipp (r=0.26, p=0.03) and CBF-hipp (r=0.32, p=0.009). In a multiple regression model, including age, sex, mean BP, BMI, brachial artery diameter as confounders, FMD remained an independent determinant of CBF-parahipp (beta=0.93, r2=0.063, p=0.04). A similar finding was obtained with CBF-hipp (beta=1.31, r2=0.089, p=0.01). Nor CBF-parahipp (r=-0.13, p=0.48) neither CBF-hipp (r=0.05, p=0.80) were correlated with FMD in non-MCI group.

Conclusions: An independent association between hippocampal and parahippocampal CBF and systemic endothelial function is present in individuals with MCI.

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Financial crisis and health of older Mediterranean adults: the multinational MEDIS Study (2005-2015)

A. Foskolou¹, S. Tyrovolas², G. Soulis¹, A. Mariolis³, A. Matalas¹, C. Lionis⁴, E. Polychronopoulos¹, L. Sidossis¹, D.B. Panagiotakos¹ on behalf of MEDIS. ¹Harokopio University, Athens, Greece; ²University of Barcelona, Parc Sanitari Sant Joan de Déu, Fundació Sant Joan de Déu, CIBERSAM, Barcelona, Spain; ³General Hospital of Sparta, Health Center of Areopolis, Areopolis, Greece; ⁴University of Crete, Clinic of Social and Family Medicine, School of Medicine, Heraklion, Greece

Background/Introduction: Over the last decade, a lot of Mediterranean people live below the poverty line, due to the deteriorated global economic situation. There is evidence that many behaviors have changed during the past few years, leading people to worse health and mental condition.

Purpose: The aim of the present work is to investigate how the existing financial crisis has affected the behaviors and the health status of older people living in the Mediterranean islands.

Methods: During 2005–2015, 2749 older people (65+) from 20 Mediterranean islands (Malta Republic, Turkish Gökçeada, Italian Sardinia and Sicily, Republic of Cyprus and 15 Greek islands) voluntarily enrolled. Older adults were stratified into two main groups, i.e., those enrolled before 2009 and those during or after 2009. The selection of 2009 was made because many Mediterranean countries were mainly affected by the world economic crisis that year and on. Clinical, lifestyle, socio-demographic characteristics were evaluated and a lifestyle index was also used (range 0: good lifestyle – 6: poor lifestyle) as the cumulative score of the presence or absence of smoking, physical activity, MedDietScore and Geriatric Depression Scale.

Results: Older Mediterranean people enrolled in the study from 2009 and on, showed social isolation, increased smoking and were more prone to depressive symptoms (p's<0.02). Adjusting for age, sex, region, history of hypertension, diabetes, hypercholesterolemia, work status and cohabitation, those enrolled after 2009 were associated with a worse lifestyle index (Beta = 0.30, p<0.001). The post-2009 enrolled participants had a 50% increase towards the unhealthier behaviors using the developed health index as compared to those enrolled before 2009 (i.e., 0.30 standard deviations, 0.30 x 1.0 = 3 out of 6 units higher values). **Conclusions:** The impact of the global financial crisis seems to be particularly

acute for older adults of lower socio-economic status, not only in financial terms but also because changes contribute to a worse health prognosis, following the adoption of unhealthy habits.

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Correlation between vascular age and surrogate markers of atherosclerosis and vascular aging

R. Di Stefano¹, F. Shams², L. Ghiadoni³, E. Imbalzano⁴, M. Nuti¹, S. Taddei³, R. De Nicola². ¹Cardiac, Thoracic and Vascular Department - University of Pisa, Pisa, Italy; ²IMT Institute for Advanced Studies, SYSMA - System modelling and analysis, Lucca, Italy; ³University of Pisa, Department of Clinical and Experimental Medicine, Pisa, Italy; ⁴University of Messina, Department of Clinical and Experimental Medicine, Messina, Italy

Background: The evaluation of Vascular Age, according to the definition given using the cardiovascular risk score tables, is a method of estimating individual cardiovascular risk, which may represent a new therapeutic target for physicians. However, the association of Vascular Age with surrogate markers of atherosclerosis and vascular aging, able to identify vascular alterations at the sub-clinical, asymptomatic stages, has not been determined yet.

Purpose: To explore the relationship of Vascular Age with common carotid artery intima-media thickness (CCIMT), arterial stiffness, and vascular aging in 222 individuals at different cardiovascular risk.

Methods: A software for Vascular Age calculation was developed as a part of an App specifically directed to physicians. Vascular Age was defined as the age of a person with the same predicted risk but with all other risk factors in normal range. The risk factors considered were age, gender, smoking, total cholesterol and systolic blood pressure. We used the SCORE project scales for European countries with low cardiovascular risk, considering 10-year fatal cardiovascular disease risk

as the probability of cardiovascular death. In 222 individuals (116 M, 106 F, age 56±9 years, 14% smokers), data on CCIMT, obtained using echotracking systems, and on arterial stiffness, measured through pulse wave velocity (PWV), were obtained and correlated to Vascular Age and to classical risk factors through Kendall rank correlation test followed by Bonferroni correction or by t test when appropriate.

Results: Cardiovascular risk (by SCORE) resulted 2.7±3.5%. Vascular Age resulted significantly higher (62±11 years) than actual age, with an average increase of 6±5 years. The increase was greater in males than in females (M: 7±5 years; F: 4±4 years, p<0.0005). CCIMT (mean value: 0.7±0.1 mm) was significantly associated with sex and systolic blood pressure; PWV (mean value: 8.4 ± 1.7 m/s) was significantly associated with smoking and systolic blood pressure. Both CCIMT and PWV showed a significant correlation with Vascular Age (CCIMT: tau=0.18, p<0.0005). CCIMT we also significantly correlated (tau=0.14, p<0.05).

Conclusions: The correlation between Vascular Age and measures of vascular damage such as CCIMT and PWV (used for screening, prevention and improvement of subject stratification beyond classical risk factors) supports the clinical usefulness of Vascular Age. Therefore, a model based not only on the calculation of the traditional risk, but also on Vascular Age could lead to an improvement in the treatment of cardiovascular risk factors, motivating patients to change their lifestyle and follow therapeutic indications.

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Successful ageing - continental vs insular Mediterranean areas and Western vs Eastern Greek Mediterranean islands - of older adults: the multinational MEDIS study

A. Foskolou¹, S. Tyrovolas², A. Mariolis³, C. Lionis⁴, A. Matalas¹, E. Polychronopoulos¹, L. Sidossis¹, D.B. Panagiotakos¹ on behalf of MEDIS. ¹Harokopio University, Athens, Greece; ²University of Barcelona, Parc Sanitari Sant Joan de Déu, Fundació Sant Joan de Déu, CIBERSAM, Barcelona, Spain; ³General Hospital of Sparta, Health Center of Areopolis, Areopolis, Greece; ⁴University of Crete, Clinic of Social and Family Medicine, School of Medicine, Heraklion, Greece

Background/Introduction: The longevity factors, as well as successful ageing ones, are not clear. However, it is said that the life course may be determined by environmental and genetic factors, as well as attitudes.

Purpose: To evaluate the role of continental and insular area of living on successful ageing among older Mediterranean adults, as well as to compare Western Mediterranean islanders with Eastern Greek ones on terms of lifestyle, health status and successful ageing.

Methods: During 2005–2015, 2693 older people (65+ years of age) from 20 Mediterranean areas (Malta Republic, Italian Sardinia and Sicily, Republic of Cyprus, 15 Greek islands and the continental area of Mani) voluntarily enrolled. Mani and Mediterranean islands have common cultural characteristics. On the second part of the analysis, this was stratified into two main groups, i.e. people from the Eastern Greek islands and those from Western Mediterranean. Clinical, lifestyle characteristics were evaluated, as well as the level of successful ageing (range 0–10) and the cardiometabolic risk score as the sum of risk factors, i.e., hypertension, diabetes, hypercholesterolemia and obesity (range 0–4). To evaluate the level of adherence to the Mediterranean diet, the MedDietScore (range 0–55) was used.

Results: Continental older adults had lower cardiometabolic risk score as compared to those living in insular areas $(1.3\pm0.9 \text{ vs} 1.7\pm1.1 \text{ risk}$ factors/participant, p<0.001). Contrasting older islanders and older adults living in continental region, the former was found to have higher level of successful aging by 11% compared to the latter (1.55\pm0.88 vs 1.40\pm0.63, p<0.001). Eastern Greek Mediterranean islanders had less depression symptoms (p<0.001), more friends (p=0.001) and adapted to a greater extent to the Mediterranean diet (34.2\pm4.0 vs 31.7\pm5.4, p<0.001), but they were less active (p<0.001) than olders from West Mediterranean islands. The cardiovascular disease risk score of the overall sample was 1.9\pm1.1; Eastern Greek islanders had higher score compared to their counterparts of Western Mediterranean islands (2.0±1.1 vs 1.5±1.1 risk factors / participant, p<0.001). As about the successful aging score of the overall sample, this was 2.6±1.4; Western islanders had higher score compared to older adults from Eastern Greek islands (3.4±1.2 vs 2.1±1.2, p<0.001).

Conclusions: Older Mediterranean insular residents had worse health status but higher level of successful ageing than those living in the continental Mediterranean area. Overall cardiovascular disease risk seems to be low in Western Mediterranean islanders, while at the same time successful ageing score seems to be higher; these particularities may be attributed to various environmental, cultural and lifestyle particularities.

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New frailty assessment based on routine nurse anamnesis before discharge is a strong predictor of all-cause mortality in patients with myocardial infarction

P.M. Haller, S. Weis, B. Jaeger, K. Huber. Wilhelminen Hospital, Vienna, Austria

Introduction: Age and frailty are well-established risk factors in patients with acute myocardial infarction (AMI). Many frailty assessments are based on ques-