



CPPEI 2016

1st Congress of
Cardiovascular Prevention
in Pre-Elderly and
Elderly Individuals

Bratislava June 30 – July 2, 2016

The Immune Phenotypes of Circulating Microparticles with in Chronic Heart Failure Patients with Metabolic Syndrome

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Background:

The role of pattern of circulating endothelial cell-, platelet-, and monocyte-derived microparticles in metabolic syndrome (MetS) patients with chronic heart failure (CHF) is not still understood.

The aim of the study was to investigate a pattern of circulating MPs in MetS patients with CHF in relation to neurohumoral and inflammatory activation.

Methods:

The study retrospectively evolved 101 patients with MetS (54 subjects with CHF and 47 patients without CHF) without documented coronary artery stenosis 50% at least of one artery and 35 healthy volunteers. Biomarkers were measured at baseline of the study. Circulating MPs were phenotyped by flow cytometry technique.

Results:

The results of the study have shown that circulating numerous of platelet-derived and monocyte-derived MPs in subjects with MetS (with or without CHF) insufficiently distinguished from level obtained in healthy volunteers. We found elevated level of CD31+/annexin V+ MPs in association with lower level of CD62E+ MPs. All these led to decreased CD62E+ to CD31+/annexin V+ ratio among patients with MetS in comparison with healthy volunteers, as well as in MetS patients with CHF compared with those who did not demonstrated CHF. Therefore, we found that biomarkers of biomechanical stress (NT-proBNP) and inflammation (hs-CRP, osteoprotegerin) remain statistically significant predictors for decreased CD62E+ to CD31+/annexin V+ ratio in MetS patients with CHF.

In conclusion, decreased CD62E+ to CD31+/annexin V+ ratio reflected impaired immune phenotype of MPs may be discuss surrogate marker of CHF development in MetS population.

Cardiovascular Preventive Management in Pre-Elderly and Elderly Patients with Type 2 Diabetes Mellitus in Primary Care

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The aim of this study was to assess the adherence to guidelines on cardiovascular (CV) prevention and target attainment for pre-elderly and elderly patients with type 2 diabetes mellitus (DM) in general practice.

Methods:

79 family physicians registered all elderly patients with diagnosis of DM during regular office visits. All physicians performed detailed physical examinations and completed the special designed questionnaire. Blood samples were taken for lipid profile and glucose level. We used data from paper medical record about cardiovascular risk factors and their treatment.

Results:

We studied 765 patients (363 males and 402 females). DM patients remain undertreated with statins (49% treated), even so those with a cardiovascular history (68% treated). Although more patients received antihypertensive treatment (86%) compared to hypolipidemic medication (56%), the proportion of patients attaining targets for total cholesterol (TC) (30%), HDL-cholesterol (HDL-C) (61%), and LDL-cholesterol (LDL-C) (39%) exceeded far those attaining blood pressure control (18%). The primary endpoint of reaching the goal for LDL-cholesterol (100mg/dL) was attained by 37% of patients, of which only 9% reached the more stringent target of LDL-C

Conclusions:

The majority of DM pre-elderly and elderly patients are treated for hypercholesterolemia and hypertension, although, there is still under treatment, especially in patients with cardiovascular disease. Therefore, wider implementation of process and outcome indicators, which proved to be related, and continuous evaluation of their result, is needed.

Prevalence of Cardiovascular Risk Factors in Elderly from an Agricultural Area of Morocco

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Background:

Although a number of risk factors for cardiovascular morbidity and mortality have been identified in young and middle-aged adults, their prevalence and importance are less known in the elderly. In Morocco, elderly people have a risk profile different from that of younger subjects, but representative data on risk factors for cardiovascular disease in the elderly are difficult to find in the literature.

Objective:

To investigate the prevalence of Cardiovascular risk factors among elderly in the city of El Jadida, Morocco.

Methods:

Data were collected from a randomized sample of 537 elderly individuals aged ≥ 60 years, who visited the public health centers. Socioeconomic and demographic data, as well as data on lifestyle, weight, height, waist circumference, blood pressure and medications used were collected. The studied cardiovascular risk factors were: arterial hypertension, diabetes mellitus, total obesity, central obesity, dyslipidemias, smoking and alcohol consumption. The Chi-square test was used for the analyses of the associations, with significance being set at 5%.

Results:

The data show that 66,1% of the sample have hypertension; 24,2% general obesity; 25,3% central obesity; 14,9% diabetes mellitus; 23,4% dyslipidemia; 6,7% smoke and 10% consume alcohol. The population studied showed elevated total cholesterol, total triglycerides and low HDL-C levels among 4%, 12,3% and 16,2% respectively. Obesity and central obesity were more prevalent in women while hypertension was in men's.

As for the simultaneity, 11,4% of the elderly did not present any cardiovascular risk factor. The simultaneity of two or more cardiovascular risk factors occurred in 54,3% of the elderly and was more frequent among women.

Conclusion:

Cardiovascular risks occur simultaneously in more than half of the elderly sample with hypertension, central obesity and total obesity as the most prevalent. The study raised the need to promoting health and prevention strategies this age category.

Drug-Induced Torsade De Pointes In The Very Old: Is It Inevitable?

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Introduction:

Drug-induced torsade de pointes (TdP) is a life-threatening arrhythmia which may be preventable.

Methods:

A systematic review was conducted for all case reports on drug-induced TdP in very old (≥ 80 years) patients in order to study how preventable was it in retrospect. Overall, 56 case reports on drug-induced TdP in patients aged 80-97 years were reviewed. Modifiable risk factors for drug-induced TdP (i.e., hypokalemia, severe hypomagnesemia, digitalis toxicity, etc.) as well as non-modifiable risk factors (i.e., acute coronary syndrome, female sex, congestive heart failure, etc.) were recorded in each case report. Preventable drug-induced TdP was defined as TdP appearance following a reckless administration of a QT interval prolonging agent (i.e., despite known QT interval prolongation or history of TdP, together with other QT interval prolonging agents, in higher than recommended doses, etc.).

Results:

Overall, 44 (78.6%) patients were females and 19 (33.9%) patients had congestive heart failure. Drug-induced TdP was preventable in almost half (n=24; 42.9%) of the case reports. The most (n=11; 19.6%) prevalent reckless administration of a QT interval prolonging agent was together with other QT interval prolonging agents, and the most (n=9; 16.1%) prevalent modifiable risk factor for drug-induced TdP was hypokalemia – although most of the times it was diagnosed only following the arrhythmia.

Conclusions:

Although non-modifiable risk factors for drug-induced TdP are prevalent in very old patients with drug-induced TdP, almost half of the times it is preventable. Physicians should anticipate and avoid hypokalemia, and also avoid a reckless administration of two or more QT interval prolonging agents at once in this population.

Associations between Sociodemographic Characteristics, CHD and Mortality among Muscovites Aged 55 Years and Older

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Aim:

To investigate the association between sociodemographic characteristics of elderly Muscovites and all-cause and CVD mortality according to CHD.

Methods:

The representative sample of 1,876 subjects (47.9% males and 52.1% females) aged 55 and older were examined in the baseline survey of the Stress, Aging and Health in Russia (SAHR) study. The SAHR is a prospective population-based cohort study that is being conducted in Moscow. The following sociodemographic characteristics were included into analysis: age; sex; education (low, medium, high); marital status (never, married, divorced, widowed); poverty scale (relatively rich, prosperous, poor). Poverty scale was constructed on the basis the questionnaire. CHD was defined as `definite` and `possible` based on Rose questionnaire and ECG by Minnesota Code. During a median of follow-up period of 5.36 years, 332 deaths were identified. Hazard proportional risk model (Cox) was applied for hazard risks (HR) evaluation with 95%CI. Education was used as a strata.

Results:

After adjusting for age, sex the married participants compared with unmarried had decreased risk of all-cause deaths (HR = 0.47; 95% CI: 0.29-0.80; p=0,005). Marital status wasn't associated with CVD mortality. Risk of all-cause and CVD mortality for poor group was significantly higher compared with prosperous group (HR = 0.7; 95% CI: 0.53-0.94; p=0,02; HR = 0.64; 95% CI: 0.45-0.93; p=0,02, respectively). After addition the CHD to the risk model the same associations between mortality and marital (HR = 0.50; 95% CI: 0.30-0.85; p=0,01) or poverty (HR = 0.72; 95% CI: 0.54-0.96; p=0,03, HR = 0.67; 95% CI: 0.46-0.97; p=0,03, respectively) status were found.

Conclusions:

Sociodemographic characteristics as age, sex, education, marital and poverty status had independent impact into mortality regardless to CHD.

Green Tea Polyphenols Facilitate Cholesterol-Induced Liver Damage in Mice

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Background and aims:

Green tea polyphenol extracts (GTE) are used as cholesterol-reducing agents in hyperlipidemic subjects; however, they have been reported as one of the most hepatotoxic nutraceuticals. We investigated the effect of GTE in a model of cholesterol-induced steatohepatitis in mice.

Methods:

Male C57BL mice 8 weeks old were fed for 6 weeks with one of four diets: Normal diet (ND); ND +1% w/w polyphenols (ND+GTE); High cholesterol diet, ND + 1% cholesterol+ 0.5% cholate w/w (HCD); HCD + 1% polyphenols w/w (HCD+GTE). Hepatic steatosis, oxidative and inflammatory markers were measured at the end of the experiment, as well as pathways of bile acid synthesis.

Results:

Feeding with HCD resulted in hepatic steatosis. Increase in blood and liver cholesterol, reduction in blood triglycerides (TG) and increased in liver TG. GTE increased synergistically hepatic steatosis only in animals subjected to HCD but not in ND treated mice. GTE elevated blood levels of SGOT, SGPT, and bile acids in HCD treated animals. Inflammatory and oxidative markers in the livers were also enhanced, including liver mRNA expression of TNF-alpha, IL-6, SAA1, SAA2, iNOS and levels of 4-hydroxynonenal protein adducts. GTE treatment-induced modulation in bile acid synthesis of the cholesterol removal pathways from the classical regulated cyp7a pathway to the alternative acidic pathway.

Conclusions:

Hepatotoxicity induced by green tea polyphenols is facilitated by HCD-fed mice, which is associated with oxidative stress, inflammation and alteration in bile acids synthesis pathway.

Can A Short Period of Cardiac Rehabilitation in Post ACS Patients Be Effective For A Long Term Prognosis?

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Background:

The benefit of cardiac rehabilitation on ischemic patients is well known, especially in the short term post the rehabilitation program, and less in the long term of outcomes.

Aim of study:

To compare the outcomes of post ACS patients with versus without performing a cardiac rehabilitation program following the hospitalization, within 4-6 years of follow-up.

Methods:

156 Patients who underwent ACS between years 2006-2008, were followed. 80 had performed a cardiac rehabilitation program of 3-6 months following the acute event (Group A), while the rest of patients (Group B; n=76) had not. All patients were followed for 4-6 years post the ACS for outcomes including cardiac and non-cardiac hospitalizations, PTCA, CABG, CHF development, cardiac arrhythmias, renal failure and death.

Results:

The follow-up results were as follows (Group A vs. Group B, respectively): Age – 60y+/-10.5 vs. 64+/-11, P=ns; Number of cardiac hospitalizations – 61 vs. 129; Number of non-cardiac hospitalizations – 36 vs. 119; PTCA intervention – 10 vs. 14; CABG – 2 vs. 3; CHF development – 5 vs. 6; Cardiac arrhythmias – 2 vs. 8; Renal failure – 3 vs. 4; and Death – 1 vs. 9

Conclusions:

The results clearly indicate that post ACS patients who performed a rehabilitation program following the event demonstrated a better outcome, cardiac and non-cardiac, than those without rehabilitation, within a long term follow-up period of 4-6 years. A possible explanation might be that patients who participate in rehabilitation programs are more aware of healthy lifestyle in general, which might reduce such outcomes even in the long term of follow-up.

Peripheral Brain-Derived Neurotrophic Factor is related to Cardiovascular Risk Factors in Active and Inactive Older Adults

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Regular exercise plays an important preventive and therapeutic role in heart and vascular diseases, and beneficially affects brain function. In blood, the effects of exercise appear to be very complex and could include protection of vascular endothelial cells via neurotrophic factors and decreased oxidative stress. The purpose of this study was to identify the age-related changes in peripheral brain-derived neurotrophic factor (BDNF) and its relationship to oxidative damage and conventional cardiovascular disease (CVD) biomarkers in active and inactive men.

Seventeen older males (61-80 years) and 17 young males (20-24 years) participated in this study. According to the 6-min Åstrand-Ryhming bike test, the subjects were classified into active and inactive groups.

The young and older active men had a significantly better lipoprotein lipid profile, antioxidant status as well as reduced oxidative damage and inflammatory state. The active young and older men had significantly higher plasma BDNF levels compared to their inactive peers. BDNF was correlated with VO₂max ($r = 0.765$, $p < 0.001$). In addition, we observed a significant inverse correlation of BDNF with atherogenic index (TC/HDL), hsCRP and oxLDL.

The findings demonstrate that an active lifestyle reflected in higher VO₂max was associated with a higher level of circulating BDNF which in turn were related to conventional CVD risk factors and oxidative damage markers in young and older men.

Effects of Long-Term Testosterone Undecanoate Injection (TU) Therapy On Lipid Pattern In Hypogonadal Men: Real-Life Data From A Registry Study

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Objective:

Registry to assess long-term effectiveness and safety of TU in a urological setting compared to an untreated hypogonadal control group.

Material and Methods:

Observational, prospective, cumulative registry of 656 men (age: 60.72±7.15 years) with testosterone (T) levels ≤12.1 nmol/L and hypogonadal symptoms. 360 men (T-group) received TU 1000 mg/12 weeks following an initial 6-week interval. 296 men opted against TTh and served as controls (CTRL). Measurements were taken twice a year. Changes over time between groups were compared by using a mixed effects model for repeated measures with a random effect for intercept and fixed effects for time, group and their interaction. Changes were adjusted for age, weight, waist circumference (WC), fasting glucose, blood pressure and lipids to account for baseline differences between the two groups.

Results:

(All values in mmol/L.) Total cholesterol (TC) decreased from 7.20±1.05 to 4.78±0.19 (T-group) and increased from 6.30±1.19 to 6.78±1.13 (CTRL). Model-adjusted estimated between-group difference at 8 years: -2.56 (p

HDL increased from 1.41±0.46 to 1.94±0.48 (T- group) and increased from 1.26±0.53 to 1.57±0.69 (CTRL), between-group difference: 0.50 (p

LDL decreased from 4.20±1.05 to 2.68±0.82 (T-group) and increased from 3.46±1.48 to 3.99±1.46 (CTRL), between-group difference: -1.83 (p

Triglycerides decreased from 3.09±0.56 to 2.12±0.08 (T-group) and increased from 2.92±0.55 to 3.11±0.60 (CTRL), between-group difference: -1.13 (p

TC:HDL ratio decreased from 5.63±1.93 to 2.63±0.67 (T-group) (p0.0001) and decreased from 6.17±3.45 to 5.61±3.52 (CTRL;NS), between-group difference: -4.08 (p0.0001).

Non-HDL cholesterol decreased from 223.73±32.89 to 109.76±19.54 mg/dL (T-group) and increased from 194.58±51.30 to 201.32±55.09 mg/dL (CTRL), between-group differences: -119.71 mg/dL (p

No patient dropped out.

Conclusions:

Long-term TTh with TU in hypogonadal men resulted in improvements in lipid profile. There was a worsening except for HDL in untreated controls.

Effects of Long-Term Testosterone Undecanoate Injection (TU) Therapy on Blood Pressure, Pulse Pressure and Heart Rate in Hypogonadal Men: Real-Life Data from a Registry Study

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Objective:

Registry to assess long-term effectiveness and safety of TU in a urological setting compared to an untreated hypogonadal control group.

Material and Methods:

Observational, prospective, cumulative registry of 656 men (age: 60.72±7.15 years) with testosterone (T) levels ≤12.1 nmol/L and hypogonadal symptoms. 360 men (T-group) received TU 1000 mg/12 weeks following an initial 6-week interval. 296 men opted against TTh and served as controls (CTRL). Median follow-up in both groups was 7 years. Measurements were taken twice a year,

8-year data were analysed. Changes over time between groups were compared by using a mixed effects model for repeated measures with a random effect for intercept and fixed effects for time, group and their interaction. Changes were adjusted for age, weight, waist circumference, fasting glucose, blood pressure (BP) and lipids to account for baseline differences between the two groups.

Results:

Systolic BP (mmHg) decreased from 151.28±16.97 to 129.98±6.59 (p0.0001) in the T-group and increased from 139.46±15.00 to 140.34±13.29 (p0.001) in CTRL, model-adjusted estimated difference between groups at 8 years: -24.34 (p0.0001).

Diastolic BP (mmHg) decreased from 90.59±11.57 to 74.36±4.57 (p0.0001) in the T-group and increased from 79.55±9.19 to 81.09±8.42 (p0.01) in CTRL, difference between groups: -16.04 (p0.0001).

Pulse pressure decreased from 60.69±7.69 to 55.62±4.88 (p0.0001) in the T-group and remained stable from 59.91±10.16 to 59.25±6.91 (NS) in CTRL, difference between groups: -8.10 (p0.0001).

Heart rate (bpm) decreased from 77.53±3.67 to 72.44±2.09 (p0.0001) in the T-group and increased from 76.16±4.97 to 77.64±4.04 (p0.01) in CTRL, difference between groups: -5.98 (p0.0001).

Conclusions:

Long-term TTh with TU in an unselected cohort of hypogonadal men resulted in improvements in the blood pressure, pulse pressure and heart rate, whereas there was a worsening except for pulse pressure in untreated controls. Long-term TU was well tolerated and excellent adherence suggested a high level of patient satisfaction.

Analysis of Blood Level of 25-Hydroxivitamin D₃ in Predialysis Patients and Correlation with Parathormone, Calcium and Phosphorus Level in the Blood

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Background:

Vitamin D₃ is essential for many physiological actions like bone metabolism, calcium metabolism, phagocytosis and so on. Appropriate vitamin D₃ turnover is essential for many physiological functions. Aim of study is to analyze vitamin D₃ level in the blood in predialysis patients and evaluate efficacy of early supplementation therapy with vitamin D₃ in these patients.

Methods:

Vitamin D₃ level in form of 25-hydroxivitamin D₃ was measured using combination of enzyme immunoassay competition method with final fluorescent detection (ELFA). Level of 30 ng/ml of vitamin D₃ was used as satisfied. Patients with stage III-V of renal failure were evaluated. Parathormone was measured by immunoassay technique. Concentration of calcium and phosphorus (as phosphate ion) were measured using standard colorimetric methods.

Results And Discussion:

Group of 118 predialysis patients was analyzed. Among them only 17 (14,41 %) have no vitamin D₃ deficiency. Moderate deficiency, level between 20-30 ng/ml have 28 (23,73 %) patients. Level between 10-20 ng/ml have 58 patients 49,15 %) In 15 (12,71%) patients vitamin D₃ deficiency was very severe, less than 10 ng/ml. Parathormone was within normal range (9,5-75 pg/ml) in all predialysis patients.

Supplementation of vitamin D₃ is recommended for dialysis patients as well as for those with stage 3 and 4 of CKD, if basal level of 25(OH)D₃ is less than 30 ng/ml. These guidelines recommend vitamin D₃ supplementation any time if parathormone is above normal range, nevertheless of level of vitamin D₃ in the blood.

Kidneys are the primary sites for hydroxylation of vitamin D₃. The process is slow down if global kidney function become worse.

Conclusion:

Vitamin D₃ deficiency was registrated in many of predialysis patients, and because of overall importance of vitamin D₃ supplementation therapy is recommended as soon as possible.

Prevalence and Treatment of Hypertension in Elderly Kidney Transplant Recipients

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Background:

Hypertension is a major problem among the population of kidney transplant recipients (KTRs). It is estimated that it affects more than 60% of those patients. The antihypertensive treatment requires a multidrug therapy and individual approach to the patient in order to achieve proper control of blood pressure.

The aim:

The aim of the cross-sectional, observational study was to evaluate the prevalence and antihypertensive treatment in the group of elderly KTRs in comparison to younger patients.

Materials/Methods:

We analyzed a group of 861 KTRs with hypertension (526M, 335F) (mean age of 52,6 years, range 19 to 85 years) transplanted in years 1986-2014 were under control in 2014. The group consisted of 63% of patients under 60 years old and 39% of older than 60 years old. The analysis of the antihypertensive treatment was based on their medical documents.

Results:

The prevalence of hypertension and need of the antihypertensive treatment was noticed in 93,7% of younger patients (average number of medications 2,23) and in 97,2% of the older KTRs (average number of medications 2,75). The most commonly used drugs in the first group were: β blockers, selective calcium antagonists, ACE/ARB, α blockers and diuretics: 83, 54, 40, 32, 30%, respectively; while in the older group the percentage of mentioned medication was as follow: 83, 54, 48, 48, 51%. The most common antihypertensive therapy in the younger group was a two-drug therapy (27%), while in the older: triple-drug treatment (32%). In both groups the most frequently drug combination was a set of β blocker and calcium antagonist: 35,4% and 37% respectively.

Conclusions:

1. Hypertension is a common comorbidity occurring in KTR
2. The elderly patients use more medications to achieve proper control of blood pressure.
3. Diuretics and α blockers are more frequently used in the group of older KTRs.

Assessment of Cardiovascular Risk During Peritransplant Period In Renal Transplant Recipients.

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Background:

Cardiovascular (CV) diseases are the leading cause of death among patients with chronic kidney disease, including patients on dialysis and after kidney transplantation (KTx). The aim of study was the retrospective assessment of CV risk in renal transplant recipients during the peritransplant period.

Material And Methods:

Evaluation of CV risk was made using the Revised Cardiac Risk Index (RCRI). 110 KTx recipients (64m/46f) mean aged 47,5 years old (range 18-80) participated in the study. 45% of participants were >50 years of mean age 68 years. In the study group the mean time of dialysis before KTx was 28,5 months, but in the older subgroups was 31,5 months. In 82% of recipients the RCRI index was 2 points. The remaining patients 18% had RCRI ≥ 3 points. RCRI index was 2 points in 80% of patients in the older subgroup and in 20% of them RCRI was ≥ 3 . Before KTx, CV disease in the study group and in older subgroup was diagnosed in 15.4% and 26%, respectively and 11 CV events occurred in 8.1% patients. 7 of all CV incidents occurred in 6 patients >50 years of age.

Results:

In the perioperative period, there were no CV events. The study group was observed for 5 years after KTx and during this time, 14 CV incidents occurred (7 in older group). Most of CV incidents occurred during the first 25 months after KTx. Significant correlations were found between RCRI and both age and time spent on dialysis ($P < 0.001$).

Conclusions:

- Elder patients with long lasting dialysis vintage are at higher risk of CV disease after Ktx.
- In studied group RCRI was not an indicator of the CV in perieperative period.
- Patient with very high RCRI had a risk of CV disease in two year period after Ktx.

Atorvastatin And Pravastatin Differentially Regulate Akt/Mtor Activation In Cardiac Myocytes And Differentially Alter Mortality In Mice With Inherited Cardiomyopathy

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Cholesterol-lowering statin drugs are used as first-line treatment for prevention and treatment of cardiovascular disease. Besides LDL-C lowering statins also harbor pleiotropic effects that were shown to improve endothelial function, inhibit inflammation, and reduce fibrosis. Cardiac specific-inactivation of the Vinculin (Vcl) gene by MLC2v-Cre (cVclKO) causes myocardial fibrosis, ventricular arrhythmias and heart failure. Human Vcl mutations were identified in patients with dilated cardiomyopathy. We hypothesized that statin treatment may benefit cardiac function in cVclKO mice.

Wild-type and littermate cVclKO mice underwent either atorvastatin, pravastatin or vehicle treatment. After two months, atorvastatin and pravastatin reduced direct non-fasting LDL-C (mg/dl) [Mean±SEM, vehicle 14.38±0.92, atorvastatin 9.25±0.77, and pravastatin 11.78±0.64, n=8-9 each, p<0.02 (atorvastatin or pravastatin compared to vehicle)]. Echocardiography was performed in two-week intervals for seven months and showed that atorvastatin, pravastatin, or vehicle did not effect declining fractional shortening and wall thicknesses in cVclKO mice. Kaplan Meyer survival analysis revealed increased mortality in atorvastatin treated cVclKO compared to vehicle and pravastatin treated cVclKO mice (n=20-24 each, p<0.001). In healthy wild-type mice atorvastatin, but not pravastatin induced, 1) swollen/misaligned mitochondria 2) accumulation of protein aggregates, and 3) repression of mitochondrial and endoplasmic reticulum-related genes. In ventricular myocytes atorvastatin, but not pravastatin (both at 1-10mM) induced ER-stress, down-regulated Akt (Ser473)/mTOR (p70S6 Kinase, S6RP) survival signaling, reduced ERK 1/2 (T202/Y204) and RhoA activation. Atorvastatin also reduced protein expression of caveolin-1, dystrophin, EGFR and insulin receptor b in cardiac myocytes.

Taken together, LDL-C lowering by atorvastatin (lipophilic), but not pravastatin (hydrophilic), inhibited pro-survival signaling in cardiac myocytes and altered mitochondrial ultrastructure in healthy mice. In cVclKO mice pravastatin at the given dosage increased cVclKO survival, whereas atorvastatin increased sudden death. Our data suggest adverse effects of potent LDL-lowering in arrhythmia-prone cVclKO mice with non-ischemic heart failure. These findings may have translational relevance in certain patient populations.

Liraglutide Improves Metabolic Parameters and Carotid Intima-Media Thickness in Elderly Women in Menopause with Type-2 Diabetes: An 18-Month Prospective Study

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Background:

Liraglutide, a glucagon-like peptide 1 analogue, exerts several beneficial non-glycemic effects in patients with type-2 diabetes (T2DM). However, its effects on cardiovascular risk markers are still largely unknown. We investigated such effects of liraglutide in pre-elderly and elderly diabetic women with different stage of menopause.

Materials and Methods:

We performed an 18-month prospective, real-life study. Sixty women with T2DM were enrolled and divided in three groups: 1) 20 pre-elderly women mostly in perimenopause 53±7 years; 2) 24 elderly women in menopause 65±2 years, and, 3) 16 elderly women in postmenopause 74±3 years. All of them were naïve to incretin-based therapies and treated with metformin only (1500-3000 mg/day). Liraglutide (1.2 mg/day) was added to metformin for the entire study. Fasting plasma samples for metabolic parameters were collected and carotid-intima media thickness (cIMT) was assessed by B-mode real-time ultrasound.

Results:

After 18 months of the treatment, fasting glycemia and HbA1c reduced significantly in all 3 groups. Waist circumference decreased significantly in the pre-elderly group (from 109±19 to 103±18 cm, p=0.004), both waist circumference (101±10 to 97±8 cm, p<0.0001) and body weight (BW, 73±12 to 70±13 kg, p=0.008) in the elderly women in menopause, while in the oldest, postmenopausal women all 3 measured anthropometric parameters reduced significantly (Table). Total- and LDL-cholesterol reduced only in the pre-elderly (5.22±1.77 to 4.39±1.02 mmol/l, p=0.0206 and 3.15±1.52 to 2.31±0.84 mmol/l, p=0.0099, respectively), while triglycerides only in the third group (Table). cIMT improved significantly in the pre-elderly (0.99±0.18 to 0.77±0.14 mm, p<0.0001), but also in postmenopausal elderly women (Table) where the changes in cIMT were correlated with changes in triglycerides (r=0.638; p=0.008).

Conclusion:

Liraglutide improves cardio-metabolic risk factors in pre-elderly and elderly diabetic women. The effect seems to be more pronounced in elderly women with later stage of menopause. Future, larger studies are needed to confirm these findings.

Keywords: Liraglutide; cardiovascular risk; pre-elderly women, elderly women

Table.

	<i>Baseline</i>	<i>After 18 months</i>	<i>p=</i>
<i>Weight (kg)</i>	75±12	69±13	0.0019
<i>BMI (kg/m²)</i>	31±5	29±6	0.0089
<i>Waist circumference (cm)</i>	104±13	98±15	0.0041
<i>Fasting glicemia (mmol/L)</i>	8.22±2.89	6.84±2.71	0.0201
<i>HbA1c (%)</i>	8.41±0.50	6.44±0.78	<0.0001
<i>Total cholesterol (mmol/L)</i>	4.31±0.80	4.52±0.74	0.3280
<i>Triglycerides (mmol/L)</i>	1.86±0.83	1.56±0.64	0.0141
<i>HDL-cholesterol (mmol/L)</i>	1.32±0.26	1.41±0.33	0.4421
<i>LDL-cholesterol (mmol/L)</i>	2.30±0.60	2.14±0.87	0.5375
<i>Carotid IMT (mm)</i>	0.98±0.16	0.80±0.14	0.0015

Effect of Bergamot on Cardio-Metabolic Parameters in Pre-Elderly and Elderly Subjects with Hypercholesterolemia: A 6-Months Prospective Study

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Background:

The scientific interest in alternative therapeutic approaches for dyslipidemia is increasing. Recent studies demonstrated the lipid lowering activity of *Citrus bergamia* juice, known as bergamot, mostly attributed to the high amount of flavonoids. We evaluated the effect of this natural supplement on lipids, atherogenic lipoproteins and carotid intima-media thickness (cIMT) in pre-elderly and elderly patients with moderate hypercholesterolemia.

Materials and Methods:

Fifty pre-elderly (men 32 and women 18, mean age 48±10 years) and 30 elderly subjects (men 10 and women 20, mean age 68±5 years) with moderate hypercholesterolemia (plasma low density lipoprotein [LDL]-cholesterol concentrations between 160 and 190 mg/dl [between 4.1 and 4.9 mmol/l]) were included. A Bergamot-derived extract (Bergavit[®], Italy) was administered at a fixed dose daily (150 mg of flavonoids), for 6 months. Subfractions of LDL were measured by gel electrophoresis. With this methodology the LDL subclasses are distributed as 7 bands (LDL-1 and LDL-2 large, less atherogenic, and LDL-3 through LDL-7, small, dense and atherogenic). Subclinical atherosclerosis was assessed by cIMT using B-mode ultrasound.

Results:

After 6 months, in both, pre-elderly and elderly patients, Bergavit[®] reduced total- and LDL-cholesterol, while a reduction in triglycerides achieved statistical significance only in the elderly, and HDL-cholesterol increased only in pre-elderly subjects (Table 1 and 2). A significant increase in LDL-1 was seen in both groups, accompanied by decreased small, dense LDL-3. Additionally, LDL-4 particles decreased significantly only in the pre-elderly group. cIMT decreased in both groups. However, body weight (from 85±22 to 79±15 kg, p=0.0489) and body-mass-index (from 30±7 to 28±5 p=0.0466) decreased significantly only in the pre-elderly.

Conclusion:

After 6 months of supplementation bergamot significantly improved the lipid and lipoprotein profiles in both pre-elderly and elderly subjects with moderate hypercholesterolemia. Such benefits need to be confirmed by larger studies of longer duration.

Keywords: Bergamot, cardiovascular risk, carotid IMT, LDL lipoproteins.

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Table 1. Effect of bergamot in the pre-elderly subjects

	<i>Baseline</i>	<i>After 6 months</i>	<i>p=</i>
Total cholesterol (mmol/l)	6.6±0.4	5.9±1.0	<0.0001
HDL-cholesterol (mmol/l)	1.2±0.2	1.4±0.4	0.0015
Triglycerides (mmol/l)	1.8±0.6	1.6±1.0	0.1238
LDL-cholesterol (mmol/l)	4.6±0.2	3.8±1.0	<0.0001
Carotid IMT (mm)	1.1±0.3	0.9±0.1	0.0010
LDL-1 (%)	40.9±0.3	48.8±0.3	<0.0001
LDL-2 (%)	40.4±0.2	39.9±0.2	0.8026
LDL-3 (%)	14.7±0.2	9.6±0.2	0.0010
LDL-4 (%)	3.6±0.1	1.6±0.1	0.0031
LDL-5 (%)	0.4±0.0	0.1±0.0	0.0666
LDL-6 (%)	-	-	-
LDL-7 (%)	-	-	-

Table 2. Effect of bergamot in the elderly subjects

	<i>Baseline</i>	<i>After 6 months</i>	<i>p=</i>
Total cholesterol (mmol/l)	6.7±0.4	5.5±1.0	<0.0001
HDL-cholesterol (mmol/l)	1.3±0.3	1.3±0.4	0.2036
Triglycerides (mmol/l)	1.8±0.7	1.4±0.5	0.0020
LDL-cholesterol (mmol/l)	4.5±0.2	3.5±0.8	<0.0001
Carotid IMT (mm)	1.3±0.7	0.9±0.2	<0.0001
LDL-1 (%)	41.8±0.4	51.2±0.4	<0.0001
LDL-2 (%)	41.4±0.3	39.3±0.4	0.3463
LDL-3 (%)	14.2±0.3	8.0±0.3	<0.0001
LDL-4 (%)	2.5±0.1	1.4±0.2	0.3523
LDL-5 (%)	0.1±0.0	0.1±0.0	0.8956
LDL-6 (%)	-	-	-
LDL-7 (%)	-	-	-

A Natural Supplement Containing Curcuma Longa, Guggul and Silymarin Improves Metabolic Parameters in Pre-Elderly and Elderly Patients with the Metabolic Syndrome

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Background:

Several plant extracts have shown beneficial effects on metabolic syndrome (MetS) components. The effects of a natural supplement Kepar® (Rikrea, Italy), containing curcuma longa, silymarin, guggul, chlorogenic acid and inulin, on metabolic and oxidative stress parameters were assessed in pre-elderly and elderly patients with MetS.

Materials and Methods:

We recruited a total of 78 patients: 29 pre-elderly (20 men and 9 women, mean age 53±7 years) and 49 elderly patients (25 men and 24 women, mean age 68±5 years) with MetS (diagnosed by the American Heart Association/National Heart, Lung, and Blood Institute AHA/NHLBI criteria). All of them received Kepar® for 4 months, at a fixed dose of 2 pills/day, as add-on therapy to on-going treatments which were maintained at fixed doses. Two pills of Kepar® contain 160 mg of curcuma longa, 102 mg of silymarin, 24 mg of guggul lipids, 14 mg of chlorogenic acid and 2.5 mg of inulin.

Results:

In both, pre-elderly and elderly subjects we found significant reductions in body weight (from 86±14 to 83±13 kg, p=0.001 and from 78±12 to 77±12 kg, p=0.011), body mass index (from 30±5 to 29±5 kg/m², p=0.003 and from 30±5 to 29±5 kg/m², p=0.020) and waist circumference (from 105±13 to 102±12 cm, p=0.009 and from 104±10 to 103±9 cm, p=0.020). Fasting glucose decreased significantly only in the elderly (from 7.8±4.2 to 6.6±1.5 mmol/L, p=0.030), while total cholesterol only in the pre-elderly (from 4.9±1.3 to 4.5±1.1 mmol/L, p=0.029). No significant changes were found in the other assessed parameters, including oxidative stress parameters, in any group.

Conclusion:

It seems that Kepar® exerts several beneficial effects in patients with MetS after only few months, regardless of age. These findings are encouraging but they remain to be confirmed by larger studies with a longer follow-up period.

Keywords: natural supplement, oxidative stress, metabolic syndrome, cholesterol, curcuma longa, silymarin, guggul, chlorogenic acid, inulin.

Exenatide Once Weekly Reduces Carotid Intima-Media Thickness and Improves Endothelial Dysfunction in Pre-Elderly Patients with Type-2 Diabetes

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Background and Aims:

Exenatide once-weekly (LAR) exerts favorable effects on glycemic control, lipid metabolism, blood pressure and other cardiovascular (CV) risk factors in subjects with type 2 diabetic (T2DM). However, the effect of exenatide LAR on carotid atherosclerosis and endothelial dysfunction in pre-elderly T2DM patients is still unknown.

Materials and Methods:

Eleven patients (age: 59±9 years), with T2DM naïve to incretin-based therapies were treated with exenatide LAR at a fixed dose of 2 mg, as add on to metformin (from 1500 up to 3000 mg/day) for 8 months. Exclusion criteria included the presence of a previous major CV event. Carotid intima-media thickness (cIMT) was assessed by color doppler ultrasound, while endothelial dysfunction by flow mediated dilation (FMD) of the brachial artery. Statistical analysis was performed using Wilcoxon test and Spearman correlation analysis.

Results:

After 8 months of therapy, exenatide LAR significantly improved anthropometric parameters, A1c, LDL- and HDL-cholesterol as well as cITM and endothelial dysfunction (Table). No significant correlations were found between changes in cIMT or FMD and changes in all the other evaluated parameters.

Conclusion:

This is the first study assessing the effects of exenatide LAR on cIMT and FMD in pre-elderly T2DM patients. We found that exenatide LAR has beneficial effect on subclinical carotid atherosclerosis and endothelial dysfunction, and this effect seems to be independent of glycemic control. The present study is on-going, with a total cohort of 60 patients included (NCT02380521).

	Baseline	After 8 months	<i>p</i> =
Weight (kg)	98±19	92±21	0.0049
BMI (kg/m ²)	33±6	32±6	0.0058
Waist circumference (cm)	110±13	106±14	0.0126
Fasting glycaemia (mmol/l)	8.9±2.4	8.0±3.0	0.0910
HbA1c (%)	8.0±0.3	6.5±0.7	0.0033
Total cholesterol (mmol/l)	4.6±0.8	4.5±0.9	0.0292
Triglycerides (mmol/l)	1.3±0.4	1.3±0.7	0.5334
HDL-cholesterol (mmol/l)	1.22±0.2	1.29±0.3	0.0258
LDL-cholesterol (mmol/l)	2.8±0.7	2.5±0.8	0.0128
Flow mediated dilation (%)	7.5±1.0	8.9±0.9	0.0033
Carotid IMT (mm)	1.0±0.13	0.86±0.11	0.0044