controls (6.3 [2] vs. 3.9 [1.9] ng/mg Cholesterol; p = 0.004). 24S-HC and 27-HC levels were respectively five and 20-fold higher in the arterial tissue of PAD individuals than in those of the controls (p = 0.016 and p = 0.001). Plasma C-reactive protein correlated with plasma 24S-HC (r = 0.51; p = 0.010), 25-HC (r = 0.75; p < 0.001), 27-HC (r = 0.48; p = 0.015), and with tissue 24S-HC (r = 0.40; p = 0.041) and 27-HC (r = 0.46; p = 0.023). Conclusion: The accumulation in the arterial intima of oxysterols originated enzymatically, and not by the action of free radicals, is associated with the severity of atherosclerotic disease and of the systemic inflammatory activity in individuals with severe PAD.

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A40768

HDL size is more accurate than HDL cholesterol to predict carotid subclinical atherosclerosis in individuals classified as low cardiovascular risk

Riobaldo M.R. Cintra, Eliana S. Parra, Natalia B. Panzoldo, Vanessa H.S. Zago, Daniel Z. Scherrer, Jamal Baracat, Edna Nakandakare, Eder C.R. Quintao, Wilson Nadruz Jr., Eliana C. Faria, Andrei C. Sposito

Universidade Estadual de Campinas, Campinas, SP, Brazil
University of Sao Paulo, SP, Brazil

Background: Misclassification of patients as low cardiovascular risk (LCR) remains a major concern and challenges the efficacy of traditional risk markers. Due to its strong association with cholesterol acceptor capacity, high-density lipoprotein (HDL) size has been appointed as a potential risk marker. Hence, we investigate whether HDL size improves the predictive value of HDL-cholesterol in the identification of carotid atherosclerotic burden in individuals stratified to be at LCR. Methods: 284 individuals (40–75 years) classified as LCR by the current US guidelines were selected in a three-step procedure from primary care centers of the cities of Campinas and Americana, SP, Brazil. Apolipoprotein B-containing lipoproteins were precipitated by polyethylene glycol and HDL size was measured by dynamic light scattering (DLS) technique. Participants were classified in tertiles of HDL size (<7.57; 7.57–8.22; >8.22 nm). Carotid intima–media thickness (cIMT) <0.90 mm (80th percentile) was determined by high resolution ultrasonography and multivariate ordinal regression models were used to assess the association between cIMT across HDL size and levels of lipid parameters. Results: HDL-cholesterol was not associated with cIMT. In contrast, HDL size >8.22 nm was independently associated with low cIMT in either unadjusted and adjusted models for age, gender and Homeostasis Model Assessment 2 index for insulin sensitivity, ethnicity and body mass index (odds ratio 0.23; 95% confidence interval 0.07–0.74, p = 0.013). Conclusion: The mean HDL size estimated with DLS constitutes a better predictor for subclinical carotid atherosclerosis than the conventional measurements of plasma HDL-cholesterol in individuals classified as LCR.

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A40770

Green synthesis of gold nanoparticles with aminolevulinic acid of: A novel theranostic agent for atherosclerosis

Karina O. Goncalves, Monica N. Silva, Leticia B. Sicchieri, Lilia C. Courrol

Unifesp, Diadema, SP, Brazil

Introduction: In this study, ALA gold nanoparticles (ALA:AuNPs) functionalized with polyethylene glycol (PEG) were synthetized and administered to rabbits to evaluate its use in clinical practice as theranostic agent for atherosclerosis. This was done by measuring the porphyrin fluorescence extracted for the rabbit's blood and feces. An increase in the blood and feces porphyrin emission after ALA:AuNPs administration suggests that ALA was incorporated by the gold nanoparticles, its structure was preserved, and a rapid conversion into endogenous porphyrins occurred, overloading the synthetic pathway that lead to the PPIX accumulation. Results: The results show that the functionalized gold nanoparticles reached atheromatous plaques and its ALA was converted to PPIX. The selective accumulation of PPIX in plaques provides a contrast between control animals and those with atherosclerosis. Conclusions: An increase in the blood and feces porphyrin emission after ALA:AuNPs administration suggests that ALA was incorporated by the gold nanoparticles, its structure was preserved, and a rapid conversion into endogenous porphyrins occurred, overloading the synthetic pathway that lead to the PPIX accumulation. The high accumulation of PPIX in tissues is thought to be the result of uncontrolled cell proliferation that accompanied the growth of atheromatous plaques. This finding indicated that ALA:AuNPs can aid in the early diagnosis and therapy of atherosclerosis with high sensitivity.

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A40842

High-density lipoprotein (HDL) phospholipid content and cholesterol efflux capacity are reduced in patients with low HDL-cholesterol and subclinical atherosclerosis

Jose Carlos Lima Jr., Natalia B. Panzoldo, Eliane S. Parra, Vanessa H.S. Zago, Isabela C. Vieira, Felipe Vendrame, Valeria N. Figueiredo, Edna Nakandakare, Eder C.R. Quintao, Eliana C. Faria, Andrei C. Sposito

Universidade Estadual de Campinas, Campinas, SP, Brazil
University of Sao Paulo, SP, Brazil

Introduction: Low HDL-cholesterol (hypoalphalipoproteinemia) is considered an independent risk factor for atherosclerosis. This inverse relationship has been attributed to different protective properties, such as cholesterol efflux, inhibition of platelet aggregation, and their antioxidant and anti-inflammatory activities. Thus, we explored the association between functions of HDL in patients free of cardiovascular disease and hypoalphalipoproteinemia or atherosclerotic burden. Methods: Study participants were classified according to their plasma HDL-cholesterol levels: below the 10th percentile, a group with low HDL-C (LH; ≤32 mg/dL; n = 33), between percentiles 40 and 60, intermediate group (IH; 40–67 mg/d; n = 33) or above the 90th percentile, a group with high levels of HDL-C (HH; ≥78 mg/d; n = 35). The chemical composition of HDL, particle size, cholesterol efflux capacity, antioxidant activity, susceptibility to oxidation, anti-inflammatory activity and ability to inhibit platelet aggregation were measured in 101 patients. Intima–media thickness of the carotid arteries (CIMT) was determined by high-resolution ultrasonography. Results: The LH group was associated with increased CIMT (0.72 ± 0.3 vs. 0.61 ± 0.20 in IH and 0.65 ± 0.15 in HH; p ≤ 0,001), increased HDL-triglyceride (4 ± 2% vs. 4 ± 2% in IH and 3 ± 1% in HH, p ≤ 0.001), reduced HDL-phospholipid (12 ± 4% vs 14 ± 5% in IH and 13 ± 3% HH, p = 0.035), reduced size of HDL particle (7.33 ± 0.33 nm vs. 7.72 ± 0.45 nm in IH, and 8.49 ± 0.42 nm in HH, p ≤ 0.001), and reduced cholesterol efflux capacity (9 ± 3% vs. 12 ± 3% in IH and 11 ± 4% in HH, p ≤ 0.001). CIMT > 1 mm was associated with reduced HDL size (7.55 ± 0.49 nm vs. 7.89 ± 0.64 nm, p ≤ 0.001), antioxidant activity (37 (23)% vs 49 (42)%, p = 0.018), and reduced cholesterol efflux

capacity (31 ± 14% vs. 40 ± 14%, p = 0.02).We found a statistically no significant difference for the other functional features or HDL properties between the groups. Conclusions: Small HDL particles, low HDL phospholipid content and decreased cholesterol efflux capacity were related to magnitude of subclinical atherosclerosis and hypoalphalipoproteinemia in a primary care population.

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A40880

Peri/epicellular protein disulfide isomerase reshapes vascular architecture to counteracts constrictive remodeling

Haniel A. Araujo, Leonardo Y. Tanaka, Gustavo K. Hironaka, Thais L. Araujo, Celso K. Takimura, Andres I.T. Morales, Annelise S. Casagrande, Paulo S. Gutierrez, Pedro A. Lemos Neto, Francisco R.M. Laurindo

Instituto do Coracao, Sao Paulo, SP, Brazil

Whole-vessel remodeling critically determines lumen caliber in vascular (patho)physiology and is reportedly redox-dependent. We hypothesized that cell-surface pool of the endoplasmic reticulum (ER) redox chaperone Protein Disulfide Isomerase-A1 (peri/epicellular = pecPDI), known to support thrombosis, also regulates disease-associated vascular architecture. In human coronary atheromas, PDI expression inversely correlated with constrictive remodeling and plaque stability. In rabbit iliac artery overdistension model, there was unusually high PDI upregulation (~25-fold vs. basal 14 days post-injury), involving both intracellular and pecPDI. Silencing PDI by siRNA in vitro induced ER stress markers upregulation and apoptosis (assessed by TUNEL assay). PDI knockdown also upregulated proliferation marker PCNA and decreased differentiation marker calponin-C. In contrast, pecPDI neutralization with anti-PDI antibodies (PDIAb) did not enhance ER stress or apoptosis. In vivo pecPDI neutralization with PDIAb-containing perivascular gel from days 12–14 post-injury promoted ca. 25% decrease in maximally dilated arteriographic vascular caliber and corresponding whole-vessel circumference loss at optical coherence tomography, without changing neointima, suggesting constrictive remodeling. This was accompanied by decreased oxidant generation and nitrogen oxide production. Constrictive remodeling was corroborated by marked changes in collagen organization, switching from circumferential to radial fiber orientation and to more rigid fiber type. Cytoskeleton architecture was also disrupted, with loss of stress fiber coherent organization and switch from thin to medium-thickness actin fibers, all leading to impaired viscoelastic ductility. Total and PDI-associated expressions of beta1-integrin, as well as cell-surface reduced beta1-integrin levels, were diminished after PDIAb treatment, implicating beta1-integrin as a likely pecPDI target during vessel repair. Integrin signaling is a master regulator of mechanobiology connecting the extracellular matrix environment to focal adhesion and actin-cytoskeleton. Indeed, FAK phosphorylation, a downstream beta1-integrin effector, was decreased by PDIAb. Thus, PDI is highly upregulated after injury and reshapes matrix and cytoskeleton architecture to support an anticonstrictive remodeling effect. Such findings suggest an important role for PDI in lumen maintenance during vascular remodeling by regulation of mechano-adaptive mechanisms.

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A40897

Biochemical and histopathological parameters analyzed in rabbits fed a diet enriched with fat/sucrose/cholesterol and treated with vitamin D

Juliana G. Carvalho, Patricia N. Sakae, Mauricio M. Pastrelo, Thiago S. Gomes, Francisco A.H. Fonseca, Silvia S.M. Ihara

Universidade Federal de Sao Paulo, Sao Paulo, SP, Brazil

Introduction: Low levels of Vitamin D increase risk of cardiovascular diseases. This study aims to assess the effects of vitamin D in an experimental model of rabbits fed a diet enriched with fat/sucrose/cholesterol (FSC). Methods: The rabbits were fed a chow enriched with fat 10%/sucrose 40%/cholesterol 0.5% for three months and thereafter, the chow were substituted for FSC with cholesterol 0.1% or standard chow for more 3 months. The following groups were formed: I — FSC 0.5/0.1%; GII — FSC 0.5/0.1% + Vit D 1000 IU/day; GIII — FSC 0.5%/ standard chow (SC) and GIV — FSC 0.5%/ standard chow + 1000 IU of Vit D/day. In periods of 0, 3 and 6 months the following parameters were evaluated: weight, lipid profile and serum glucose. After 6 months the animals were euthanized and the aortas were removed for atheroma plaques analysis. Statistical analysis was performed by Kruskal–Wallis non-parametric tests followed by Dunn's test. Results: After 6 months, the following values were observed, respectively, in groups I, II, III and IV: total cholesterol (mg/dL):420 ± 128; 363 ± 119; 149 ± 136; 162 ± 132. Triglycerides(mg/dL): 172 ± 58; 202 ± 79; 74 ± 24; 63 ± 13. Glucose (mg/dL):97 ± 5; 92 ± 13; 100 ± 18; 106 ± 11. Plaques in aorta(%): 83 ± 24,62; 84,64 ± 23,22; 15,38 ± 5,95; 24,11 ± 8,81. Intima/media ratio in arch aorta: 2.98 ± 2.16; 2.57 ± 1.06; 2.74 ± 1.22; 1.35 ± 0.39*. Thoracic aorta: 2.13 ± 1.15; 1.80 ± 1.05; 1.54 ± 0.52; 1.48 ± 0.42. Abdominal aorta: 1.73 ± 0.55; 2.06 ± 1.23; 1.59 ± 0.41; 1.15 ± 0.47. The histopathological aspects of aortas in groups III and IV were more fibrous than in groups I and II, independently of vitamin D treatment, however, lower intima/media rate was observed in the group IV that had received the standard diet and vitamin D. Conclusion: The normalization of the diet improved the lipid profile and atherosclerotic plaques in aorta, with beneficial effect of vitamin D.

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A40924

Comparison of coenzyme Q10 and herbal *Withania somnifera* supplements on fatigue parameters and biochemical profile in dyslipidemic patients with statin in chronic use

Renata A. Silva, Cristiane Kovacs, Carlos D. Magnoni, Natalia C.F.R. Marques

Instituto Dante Pazzanese de Cardiologia, Sao Paulo, SP, Brazil
VP Consultoria Nutricional Divisao de Ensino e Pesquisa, Sao Paulo, SP, Brazil

Introduction: The statin class of drugs is the first choice in dyslipidemic patients, to reduction of plasma cholesterol levels, especially LDL (low density lipoprotein) for the prevention of cardiovascular disease (CVD). However, fatigue is a side effect in some patients, possibly by inhibiting melovanato conversion to coenzyme Q10 (CoQ10), a cofactor in the electron transport chain for the energy formation, in the same cascade of cholesterol formation. CoQ10 supplementation helps reduce the effects caused by continuous use of statins. In traditional Chinese Medicine, the *Withania somnifera* (or Ashwagandha), is considered an adaptogen herbal and indicated for fatigue and hipocholesterolemic use. Methods: In this