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1.1

DIASTOLIC LEFT VENTRICULAR FUNCTION IN RELATION TO CIRCULATING METABOLIC BIOMARKERS IN A GENERAL POPULATION

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Background: The metabolic signature associated with subclinical diastolic left ventricular (LV) dysfunction in the general population is unknown.

Objectives: This population study aimed at identifying a specific profile of circulating metabolites associated with asymptomatic diastolic LV dysfunction.

Methods: In 711 randomly recruited Flemish (50.8% women; mean age, 50.8 years), we assessed echocardiographic indexes of diastolic LV function in relation to 44 circulating metabolites determined by nuclear magnetic resonance spectroscopy. Statistical methods included multivariable-adjusted regression analyses and partial least square discriminant analysis (PLS-DA).

Results: In multivariable analyses with Bonferroni correction, a' was inversely and e'/a' was positively correlated ($p \leq 0.048$) with circulating tyrosine, HDL apolipoproteins, glucose + glutamine, and an unidentified molecule, while a' was also inversely associated with glucose + 2 aminobutyrate and glucose + 2 phosphoglycerate ($p \leq 0.031$). PLS-DA identified three latent factors accounting for 54.4% of the variance. The metabolites associated with better diastolic LV function included, amongst others, glucose + glutamine (variable importance in projection score, 1.201), glucose + 2 aminobutyrate (1.185), and glucose + 2 phosphoglycerate (1.172). The three latent factors, compared with N-terminal prohormone brain natriuretic peptide, increased ($p < 0.0001$) the area under the curve from 0.64 to 0.73.

Conclusions: In the general population, diastolic LV function is associated with a profile of circulating metabolites indicative of energy substrate utilization and protection against oxidative stress. These metabolic markers might lead to the discovery of new targets for prevention and treatment of diastolic LV dysfunction at a subclinical and still reversible stage.

1.2

AGE-DEPENDENT ASSOCIATION OF 24-HOUR PERIPHERAL AND CENTRAL PULSE PRESSURES WITH STROKE VOLUME

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Objective: Pulse pressure (PP) is a complex physiologic trait affected by many variables, including LV contractility (reflected by stroke volume), arterial stiffness, and central-to-brachial amplification. The impact of age on the relationship between stroke volume and central or brachial PP has not been investigated.

Methods: 3765 untreated hypertensive adults (men 56%, age 50 ± 12 years) underwent 24-hour ambulatory BP monitoring (SpaceLabs) and M-mode echocardiography. In a subset of 982 subjects in whom central PP was measured by applying a transfer function to radial pulse wave (SphygmoCor), we also estimated central office (or 24 h) PP by regression equations based on office (or 24 h) PP and MAP, heart rate, age, height and sex ($R^2 = 0.92$ between estimated and measured central PP). The same equations were then applied to the original population to obtain estimated central PP.

Results: Stroke volume had a significant direct association with both brachial and central 24 h PP up to the age of 39 years. The above relationship weakened with age and became mostly non-significant after the age of 40 (all $r < 0.10$). Similar, although weaker, trends were observed for office PP (both brachial and central).

Conclusions: 24-h PP has a strong direct association with LV stroke volume in the young only, and might more exclusively depend on arterial stiffness later in life. Since the above relationship was also observed with estimated central PP, it may not depend on PP amplification. The “young” and “old” pathophysiological patterns of PP may help to explain the increasingly adverse prognostic value of PP observed with advancing age.

1.3

PAST SMOKERS DECELERATE VASCULAR AGING IN THE LONG TERM

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Objectives: Smoking has an unfavorable effect on arterial properties. Vascular aging is an independent predictor of cardiovascular risk. We examined the effect of quitting smoking on the progression of arterial stiffness.

Methods: 142 subjects (mean age 51.9 ± 10.8 years, 94 men) with no established cardiovascular disease were investigated in 2 examinations over a 2-year period. Subjects were categorized in current smokers, non-smokers and ex-smokers. Ex-smokers were further categorized according to the