Nutrition, Metabolism & Cardiovascular Diseases (2018) xx, 1–7

Available online at www.sciencedirect.com

Nutrition, Metabolism & Cardiovascular Diseases

journal homepage: www.elsevier.com/locate/nmcd

N-terminal pro B-Type natriuretic peptide is inversely correlated with low density lipoprotein cholesterol in the very elderly

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Received 27 November 2017; received in revised form 13 February 2018; accepted 19 February 2018
Handling Editor: Laura Calabresi
Available online ■ ■ ■

KEYWORDS
Natriuretic peptides;
Lipid metabolism;
LDL-cholesterol;
Very elderly;
Cardiovascular disease

Abstract *Background and aims:* Laboratory studies on human adipose tissue and differentiated adipocytes indicate that natriuretic peptides (NPs) affect lipid metabolism and plasma cholesterol. Few previous clinical studies in non-elderly populations found associations between NPs in the physiological range and cholesterol. Aim: evaluate the association between NT-proBNP and lipid profile in very elderly hospitalized patients characterized by a wide range of NT-proBNP levels.
Methods and results: Cross-sectional study on 288 very elderly patients hospitalized for medical conditions, in which increased NT-proBNP levels are very common. NT-proBNP, total cholesterol (TC), HDL cholesterol (HDLc) and triglycerides were collected just few days before discharge. Patients taking lipid-lowering drugs and patients with an admission diagnosis of acute heart failure were excluded. Calculated LDL-cholesterol (LDLc) was used for the analyses. Mean age: 87.7 ± 6.2 years; female prevalence (57.3%). Median NT-proBNP: 2949 (1005–7335) pg/ml; mean TC: 145.1 ± 40.3 mg/dl; mean HDLc: 38.4 ± 18.6 mg/dl; median triglycerides: 100 (75–129) mg/dl; mean LDLc: 84.0 ± 29.5 mg/dl. We found negative correlations between NT-proBNP and both TC and LDLc (Rho = −0.157; p = 0.008 and Rho = −0.166; p = 0.005, respectively), while no correlations emerged between NT-proBNP and HDLc (Rho = −0.065; p = 0.275) or triglycerides (Rho = −0.009; p = 0.874). These associations were confirmed considering NT-proBNP tertiles. The inverse association between NT-proBNP and LDLc was maintained even after adjusting for confounding factors.
Conclusion: Our real-life clinical study supports the hypothesis that NPs play a role on cholesterol metabolism, given the association found between LDLc and NT-proBNP even in very elderly patients where NT-proBNP values are often in the pathological range.

Acronyms: ADL, activities of daily living; ANP, atrial natriuretic peptide; BMI, body mass index; BNP, B-type natriuretic peptide; BP, blood pressure; BSC-D, duration of the period between hospital admission and blood sample collection; CAD, coronary artery disease; COPD, chronic obstructive pulmonary disease; CRP, C-reactive protein; CV, cardiovascular; CVD, cardiovascular disease; DM2, type 2 diabetes mellitus; eGFR, estimated glomerular filtration rate; GIC, geriatric index of comorbidity; HDLc, high-density lipoprotein cholesterol; HF, heart failure; Hgb, hemoglobin; LDLc, low-density lipoprotein cholesterol; LDLR, low-density lipoprotein receptor; MetS, metabolic syndrome; NPRA, natriuretic peptides receptor A; NPRC, natriuretic peptides receptor C; NPs, natriuretic peptides; NT-proBNP, N-terminal pro B-type natriuretic peptide; PAD, peripheral arterial disease; SD, standard deviation; TC, total cholesterol; TIA, transient ischemic attack.

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https://doi.org/10.1016/j.numecd.2018.02.013
0939-4753/

Please cite this article in press as: Spannella F, et al., N-terminal pro B-Type natriuretic peptide is inversely correlated with low density lipoprotein cholesterol in the very elderly, Nutrition, Metabolism & Cardiovascular Diseases (2018), https://doi.org/10.1016/j.numecd.2018.02.013

Introduction

Cardiac natriuretic peptides (NPs) play a relevant role not only in blood pressure (BP) regulation, blood volume and sodium balances, but also in glucose and lipid metabolisms in both adipose and muscle tissues [1]. Scientific evidence suggests that higher NPs levels are associated with less obesity and metabolic syndrome (MetS) and a decreased risk of incident type 2 diabetes (DM2) [2]. Cardiac NPs system includes atrial NP (ANP) and B-type NP (BNP). ANP is likely to have a more physiological action, by influencing and controlling normal cardio–renal activities, while BNP is released mainly in response to muscular wall stretch, resulting from increased intravascular volume and/or cardiac transmural pressure, in conditions of cardiac stress, such as heart failure (HF) [3]. In common clinical practice, BNP and N-terminal proBNP (NT-proBNP) tests are recommended by guidelines for diagnosis, prognosis and guided therapy of HF, and also for risk stratification in patients with acute coronary syndromes [4]. Elderly patients have often raised NT-proBNP levels, due to the high prevalence of heart diseases [5]. Previous studies have evaluated the associations between plasma NPs levels, lipid profile and prevalence of dyslipidemia. However, most of these studies did not involve elderly subjects [6,7]. To date, there is still conflicting evidence on the relationship between lipid profile and pathological levels of NPs. In a large cardiovascular (CV) disease-free cohort, the relationship was lost for higher NT-proBNP values [8]. Hypothesizing that NPs might affect lipid metabolism not only at physiological range, but also at pathological levels, we investigated the associations between plasma NT-proBNP levels and lipid profile in a “real life” clinical setting, by analyzing very elderly patients hospitalized for medical conditions.

Methods

Study population

Cross-sectional study on 288 very elderly consecutively admitted to an Internal Medicine and Geriatrics Department, from January 2015 to December 2016. We considered the following exclusion criteria: current therapy with lipid-lowering drugs or other drugs that could affect lipid profile (for example corticosteroids), clinical conditions that could affect lipid profile such as dysthyroidism, end-stage renal or liver diseases, advanced cancer and cachexia and an admission diagnosis of acute HF confirmed by a cardiologist (after clinical examination and echocardiography in the emergency room).

Clinical evaluations

Blood samples were collected after clinical stabilization of the acute illness, just few days before discharge. We considered the following lab parameters: NT-proBNP, hemoglobin (Hgb), white blood cells count, creatinine, estimated Glomerular Filtration Rate (eGFR), glycemia, albumin, total cholesterol (TC), calculated low-density lipoprotein cholesterol (LDLc), high-density lipoprotein cholesterol (HDLc), triglycerides, non-HDL cholesterol (non-HDLc, defined by the formula: TC − HDLc). Admission C-reactive protein (CRP) levels were also considered for the analyses. Creatinine was determined in serum or plasma using a creatinine Jaffé of second generation in a Cobas c501 Roche analyzer and the eGFR was estimated using the CKD-EPI equation [9]. After blood sampling, NT-proBNP was measured using Elecsys proBNPII electrochemiluminescence immunoassay in a Cobas e601 immunoassay Roche analyzer. This assay contains two monoclonal antibodies that recognize epitopes located in the N-terminal part (1–76) of proBNP (1–108).

The Mini-Cog, which combines two simple cognitive tasks (3-item word memory and clock drawing) with an empirical algorithm for scoring, was performed to evaluate cognitive impairment, using a cut point of <4 [10]. To evaluate patients' functional status, the 7-point MDS Activities of Daily Living (ADL) Hierarchy scale was used [11]. The ADL Hierarchy scale groups activities of daily living according to the stage of the disablement process in which they occur. The ADL Hierarchy Scale ranges from 0 (no dependence) to 6 (total dependence). ADL disability was categorized as follows: no impairment (ADL Hierarchy Scale score <2), assistance required (ADL Hierarchy Scale score 2–4), and dependence (ADL Hierarchy Scale score ≥ 5). The Geriatric Index of Comorbidity (GIC) was used to determine the burden of comorbidities [12] and it was categorized as low comorbidity (GIC classes 1 or 2) and high comorbidity (GIC classes 3 or 4). Polypharmacy was defined as the use of 5 or more drugs before hospital admission.

Clinical investigations have been conducted according to the principles expressed in the Declaration of Helsinki. All patients gave written informed consent. This observational study was approved by the local institutional ethics committee.

Statistical analysis

Data were analyzed with the Statistical Package for Social Science version 13 (SPSS Inc. Chicago, Illinois, USA). A value of $p < 0.05$ was defined as statistically significant. All continuous variables were expressed as mean $\pm$ SD or as median and interquartile range for markedly skewed variables. NT-proBNP was analyzed as a continuous and as a discrete variable. NT-proBNP tertiles: 1° Tertile: $\leq$1391 pg/ml; 2° Tertile: 1392–5301 pg/ml; 3° Tertile: $\geq$5302 pg/ml. NT-proBNP and CRP were natural logarithmically transformed to normalize their distributions. Categorical variables were expressed as absolute number and percentage. Pearson and Spearman correlations were used to analyze the relationship between continuous variables. The unpaired t test, analysis of variance (ANOVA) and Kruskal–Wallis test were used to compare quantitative variables. Variables with significant associations identified on univariate analyses were tested in multiple linear regression to create adjusted models; covariables were

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