Original Article

N-terminal Prohormone B-type Natriuretic Peptide and Cardiovascular Function in Africans and Caucasians: The SAfrEIC Study

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Background: **This study compared NT-proBNP levels and the association with cardiovascular markers between Africans and Caucasians from South Africa.**

Methods: **This cross-sectional study involved 201 Africans and 255 Caucasians from the North West province, South Africa. Serum NT-proBNP concentrations, blood pressure, pulse wave velocity and arterial compliance were measured.**

Results: **NT-proBNP levels were significantly higher ($P < 0.001$) in Africans than Caucasians, also after adjusting for gender, body mass index (BMI) and pulse wave velocity ($P = 0.008$). This significant difference became borderline significant after adjusting for systolic blood pressure (SBP) ($P = 0.060$), and non-significant after adjusting for arterial compliance ($P = 0.35$). In single regression, a significant positive correlation of NT-proBNP with SBP ($r = 0.26$; $P < 0.001$) and pulse pressure (PP) ($r = 0.28$; $P < 0.001$) were shown for Africans only. After multiple adjustments, the associations of NT-proBNP with SBP and PP remained significant in Africans (SBP: $\beta = 0.187$, $P < 0.01$; PP: $\beta = 0.234$, $P < 0.001$), with no significant associations in Caucasians.**

Conclusions: **NT-proBNP levels were higher in Africans than Caucasians, independently of BMI and gender. This difference was partly driven by higher SBP and lower arterial compliance in Africans. NT-proBNP was persistently associated with SBP and PP in Africans, but not in Caucasians. These associations may suggest early vascular changes contributing to cardiac alterations in Africans.**

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Keywords. NT-proBNP; Blood pressure; Ethnicity; Cardiovascular function; Compliance

Introduction

The N-terminal prohormone B-type natriuretic peptide (NT-proBNP) has been underlined in the assessment and diagnosis of congestive heart failure [1]. Since NT-proBNP has a much longer half-life than BNP, it is used as a reliable biochemical predictor and marker of cardiovascular risk [2]. Patients with cardiac hypertrophy and resulting systolic and diastolic dysfunction are subjected to increasing myocardial stress load, causing a rise in plasma levels of NT-proBNP [3]. Normally, NT-proBNP is up-regulated in the atria as a response to this cardiac overload [4,5], but is also extensively secreted by the ventricular cardiomyocytes as a result of elevated cardiac wall stress [5,6]. NT-proBNP functions as a ventricular cardiac hormone and partakes in the control of myocardial structure and function [7]. It is also involved in the lowering of sodium reabsorption in the kidneys, resulting in decreased blood volume and subsequent arterial pressure [8,9], therefore counteracting left ventricular wall tension and increasing plasma volume [10,11]. In a study of coronary atherosclerosis, plasma NT-proBNP levels were significantly lower in African Americans compared to Caucasians [10,12], but less is known in the bi-ethnic populations of South Africa.

In general, black South Africans are subjected to rapid epidemiologic and socioeconomic transition as opposed to the gradual westernisation of African Americans; and this transition increases the incidence of cardiovascular related morbidity and mortality [13,14]. In a large study on hospitalised black South Africans, it became evident that most patients were presented with advanced cardiac disease, predominantly heart failure [14]. This was more prominent in patients from urban settings [15], however despite the high prevalence of cardiovascular disease amongst these black South Africans, the cause is still inconclusive. It is

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evident that health inequalities exist between Africans and Caucasians and could largely be due to socioeconomic transition [16]. Although some information is available on the associations between NT-proBNP and measures of cardiovascular function in American and European Caucasians, there exists an inherent lack of information with regard to the South African population [14,17].

The aims of this comparative study were to compare NT-proBNP levels between Africans and Caucasians and also to explore the associations of NT-proBNP with markers of cardiovascular function in this target population.

Methods

Study Population and Procedures

The South African study regarding the role of Sex, Age and Ethnicity on Insulin sensitivity and Cardiovascular function (SAfrEIC) was a cross-sectional study that in total involved 756 Africans and Caucasians (aged 20–70 years) from the North West Province of South Africa. Pregnant or lactating women were initially excluded from the study. In the present study, persons who were diagnosed positive with the human immunodeficiency virus (Africans: $n = 114$; Caucasians: $n = 1$) were excluded, as well as eight participants who were diabetics (type 1 or 2), 91 participants that used antihypertensive or anti inflammatory medication and participants older than 55 years ($n = 86$). After excluding the relevant cases, a total of 456 participants (201 Africans and 255 Caucasians) were included.

Ten to 20 participants visited the Metabolic Unit facility daily at the Potchefstroom campus of the North West University from March until July in 2007. All the procedures were comprehensively explained to the participants and they all gave written informed consent to participate in the study. A participant sheet that guided them through the different research stations where various measurements were done was given to each person. Basic health and demographic questionnaires were completed during the morning. In the event where abnormalities were identified in a participant (i.e. hypertension or diabetes), the participant was advised to visit their local clinic, hospital or physician. An informative description regarding the results of the health assessment was given to each participant at the end of the study. This study was approved by the Ethics Review Board of the North West University and the study protocol conformed to the ethical guidelines of the Declaration of Helsinki (2008) for investigation of human participants.

Cardiovascular Measurements

The OMRON HEM-757 (Omron, Kyoto, Japan) apparatus was used to determine systolic and diastolic blood pressure with the cuff on the left upper arm in the sitting position. Two blood pressure measurements were done, the first after an initial 10 min resting period and the second reading after a 5 min waiting period. Participants with a systolic blood pressure (SBP) $\geq$140 mmHg and/or diastolic blood pressure (DBP) $\geq$90 mmHg were considered hypertensive [18]. Pulse pressure was subsequently calculated by subtracting the DBP from SBP. Heart rate, cardiac output, stroke volume, arterial compliance and total peripheral resistance were determined with the Finometer apparatus (FMS, Finapres Measurement Systems, Amsterdam, The Netherlands). The carotid dorsalis-pedis pulse wave velocity (PWV) was measured with the Complior SP Acquisition system (Artech-Medical, Pantin, France).

Anthropometric Measurements

Applying standard procedures, body height was measured to the nearest 0.1 cm by using the Invicta Stadiometer (IP 1465, London, UK) and body weight was measured to the nearest 0.1 kg (Precision Health Scale, A & D Company, Japan). Subsequently, the body mass index (BMI) was calculated for each participant as weight (kilograms) divided by height (metres) squared. The waist circumference was measured at the maximal girth with a Holtain non-stretchable, flexible metal measuring tape [19].

Biochemical Measurements

All participants were requested to fast for a period of 8 h. Fasting lipids (total cholesterol, high-density lipoprotein cholesterol, and triglycerides), serum glucose, γ-glutamyl transferase, creatinine and high-sensitivity C-reactive protein were determined with the Konelab autoanalyzer (Thermo Fisher Scientific Oy, Vantaa, Finland). The Cockcroft–Gault formula [20] was used to determine estimated creatinine clearance ($mL\,min^{-1}$) = (140–age) × mass (kg) × constant/serum creatinine ($\mu mol\,L^{-1}$), where the constant is 1.23 for men and 1.04 for women. Serum cotinine was determined with the IMMULITE 2000 nicotine metabolite assay (Siemens Medical Solutions Diagnostics Ltd., Los Angeles, CA). Insulin was determined with the ST AIA-PACK IRI kit (TOSOH AIA, Inc., Toyama, Japan; catalogue no. 025260) using a two-site immune-enzymometric assay. HOMA-IR (homeostasis model assessment) was calculated by using the following formula: fasting serum insulin ($\mu U/mL$) × fasting plasma glucose ($mmol\,L^{-1}$)/22.5. Serum NT-proBNP was determined using the Elecsys proBNP sandwich immunoassay on an Elecsys 2010 (Roche Diagnostics, Mannheim, Germany). Human immunodeficiency virus status was determined directly after blood sampling with rapid tests according to the protocol of the National Department of Health of South Africa. Serum was used for testing with the First Response Test and was repeated with the Pareeshak test to confirm results. All tests were done at the same laboratory in South Africa, except NT-proBNP analyses which were done for all participants in Denmark.

Statistical Analyses

Statistica software v10.0 (StatSoft, Inc., Tulsa, OK, USA) was used for database management and statistical analyses. Normal distribution of the variables was tested prior to any further statistical analyses. Variables that did not fulfil