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Research Article

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Prealbumin, C Reactive Protein to Prealbumin Ratio and Their Association with Nt-Probnp In Patients with And Without Major Cardiovascular Disease or Chronic Renal Failure

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Abstract

We aimed to investigate the association between prealbumin (PAB) and C reactive protein to prealbumin (CRP/PAB) ratio, as markers of inflammation and/or malnutrition and NT-proBNP in patients with or without major cardiovascular disease (MCVD) or chronic renal failure (CRF).

Methods

Overall, 303 individuals, with available data for NT-proBNP levels and echocardiographic examination, were included in the study.

Results

Mean age was 75.63 ± 9.79 years and 56.4 % were categorized as Non MCVD - non CRF. NT-proBNP concentrations ranged from 16 to 35572 pg/mL .

In the non MCVD - non CRF group a higher NT-proBNP level was noted in the individuals having at least 3 factors of undernutrition than in the others (141.00 [84.75 – 346.00] pg/mL vs 91.00 [49.00 – 197.00] pg/mL respectively; P = 0.012), Log NT-proBNP was positively correlated with age and negatively correlated with albumin and PAB levels in both groups. In individuals without MCVD and CRF unlike the others, log NT-proBNP was not significantly correlated with CRP levels, CRP/PAB ratio, creatinine levels, creatinine clearance or left ventricular ejection fraction (LVEF).

With the multivariate linear regression in the whole study population significant effects on log NT-proBNP were noted, for age (P< 0.001), MCVD (P < 0.001), PAB (P < 0.001) and creatinine levels (P < 0.001). The effect of body mass index (BMI) was nearly significant (P = 0.051). Gender, log CRP, CRP/PAB ratio, hypertension and diabetes did not contribute significantly to the model.

Conclusion: *Prealbumin, a marker of both inflammation and malnutrition is strongly associated with NT-proBNP independently of MCVD and creatinine levels. In patients without MCVD and CRF, NT-proBNP levels could help to assess for the risk of inflammation-malnutrition especially in the older.*

Keywords: pre-albumin, C reactive protein to prealbumin ratio, N-terminal pro-B-type natriuretic peptide, renal failure, cardiovascular disease, inflammation, malnutrition.

Introduction

N-terminal pro-brain natriuretic peptide (NT-pro BNP) is a non-bioactive polypeptide secreted by cardiomyocytes in response to changes in pressure inside the heart that are related to heart failure and other cardiac problems [1, 2]. Thus, NT-proBNP, commonly measured in cardiac diseases, is mainly known as a cardiac biomarker with high diagnostic and prognostic values [2-4]. But, NTproBNP is cleared by the kidney and, in patients with chronic kidney disease, levels of NT-proBNP are usually increased as a consequence of increasing secretion and decreasing renal clearance [5].

Various parameters, such as age, gender, body mass index (BMI), hemoglobin level, creatinine level, hypertension, diabetes, left ventricular ejection fraction (LVEF) have been reported to influence the levels of NT-proBNP [3, 6-8].

The association between nutritional status, inflammation and NT-proBNP has been less studied and was mainly described in patients with heart failure or end stage renal disease undergoing dialysis [7,9]. The mechanisms of these associations in these diseases are still unclear and several factors may be involved.

Serum prealbumin (PAB), an indicator for the early detection of protein energy malnutrition is also considered as a marker of inflammation and, the C reactive protein to prealbumin ratio (CRP/PAB ratio) has been suggested as a comprehensive marker of inflammation and malnutrition [10-12].

The measurement of NT-proBNP is not commonly performed in individuals in apparently good health or in individuals without cardiac and renal disease. Thus, studies on these associations in individuals without these diseases are scarce. It would be of clinical interest to examine whether the combination of inflammatory and nutritional markers could be associated with a cardiac biomarker.

Objectives

This study aimed to investigate the association between prealbumin and C reactive protein to prealbumin ratio, as markers of inflammation and/or malnutrition and NT-proBNP in patients with or without major cardiovascular disease or chronic renal insufficiency.

METHODS

Patient Population

Data of patients admitted to the medical unit in a health establishment in Guadeloupe, aged 55 years and over, between 2019 and 2022 were considered for this study. Patients without measurement of NT-proBNP and without a cardiological evaluation including an echocardiographic examination were excluded.

The protocol of this study was approved by the institutional ethic committee (CE -2022-01)

Data Collection

For each patient, we collected the following data: age, personal cardiovascular medical history, treatment at entry, the presence of acute or chronic inflammatory pathologies, use of antihypertensive or antidiabetic treatments and biological data at entry.

Height and weight were measured with participants standing without shoes and lightly clothed.
Body mass index (BMI) was calculated as weight/height2 (kg/m2).

The measurements were made by trained nurses and physicians. Blood pressure was measured according to a standardized protocol with automatic sphygmomanometers.

Laboratory Measures

Blood samples were obtained from participants after overnight fasting. Laboratory values were measured by automated and standardized methods and referred to single measures. Serum albumin, serum prealbumin (PAB), highly sensitive C-reactive protein (CRP) and serum creatinine (SCr) concentrations were determined. Creatinine clearance was estimated by the CKD method -EPI. Plasma cholesterol and triglycerides were measured by enzymatic methods (Boehringer Mannheim).

CRP levels were measured using an immunoturbidimetric method (Roche Diagnostic). NT-proBNP was assessed using a Siemens (DPC) Immulite 2000 chemiluminescence immunoassay based on N-terminal polyclonal sheep antibody.

Echocardiograhy

Standard transthoracic echocardiographic examination was performed by a cardiologist, who was blinded to the clinical data of the study subjects. All echocardiographic measurements were done according to the guidelines of the American Society of Echocardiography [13]. Left ventricular ejection fraction (LVEF) was calculated using the Simpson biplane method from 2 chambers and 4 chambers' apical views.

Definition of Clinical Parameters

Hypertension. systolic blood pressure > 140 or a diastolic blood pressure > 90 mmHg or history of hypertension and current use of antihypertensive medication.

Inflammation was defined as a serum concentration of CRP >5 mg/L

Nutritional Status

For the purpose of this study, patients having at least 3 of the 5 following criteria were considered at risk of undernutrition.
- weight loss ≥ 5% in 1 month or ≥ 10% in 6 months or ≥ 10% compared to the usual weight before the onset of the disease;
- BMI <21 kg/m2
- reduction in food intake ≥ 50% for more than 1 week, or any reduction in intake for more than 2 weeks compared to the usual quantified food consumption,

- low albumin level: albumin level < 35 g/L.
- low prealbumin level: prealbumin level < 0.20 g/L.

Heart failure: Documented history of cardiac insufficiency or LVEF < 50 %.

Coronary artery disease: (CAD) diagnosed by physician, angina pectoris, myocardial infarction, coronary artery bypass.

Major cardiac vascular disease (MCVD): CAD or heart failure

Chronic Renal failure (CRF): serum creatinine levels > 1 mg/dL (88.4017µmolL or 10 µg/mL)

High values of NT-proBNP according to the Cleveland Clinic's Reference Range as levels ≥ 125 pg/mL for patients aged 0-74 years and ≥ 450 pg/mL for patients aged 75-99 years *https://my.clevelandclinic.org/health/diagnostics/22629-b-type-natriuretic-peptide*

Statistical Analysis

Characteristics of the study participants are reported as means (SDs) or geometric means (IQR) for continuous variables and numbers (percentages) for categorical variables. NT-proBNP and CRP levels were log-transformed to normalize their distribution. The study population was stratified by tertiles of NT proBNP concentrations.The chi-squared test was used to test percentage differences between groups. To test mean differences, we used analysis of variance (ANOVA) for comparison between groups. We also performed the analyses while considering i) patients without cardiovascular disease and without renal failure (non MCVD - non CRF), ii) those with major cardiovascular disease or with renal failure (MCVD or CRF) and iii) the overall study population.

The Pearson correlation test was used to study the relationships between NT-proBNP and other continuous variables.

A multivariate linear regression was performed to assess the associations of log NT-proBNP levels as dependent variable with age, sex, BMI, prealbumin, CRP, creatinine levels and other variables of interest. The effects of the covariates were assessed by the values of the regression coefficients β.

The IBM SPSS Statistics software version 21 was used for data analyses. All tests were two-sided and a P value < 0.05 was considered significant.

Results

Overall, data of 303 hospitalized individuals, with available data for NT-proBNP levels and echocardiographic examination, were considered for study.

Mean age of the study population was 75.63 ± 9.79 years (range 55 to 96 years), 53.8% were women and 56.4 % were categorized as non MCVD - non CRF. NT-proBNP concentrations ranged from 16 to 35572 pg/mL in the overall study population. The medians (interquartile range) were 101.00 [53.00 – 224.00] pg/mL in the non MCVD - non CRF group, 260.00 [102.00 – 1073.00] pg/mL in the MCVD - CRF group and 146.00 [65.00 – 403.00] pg/mL in the overall study population

In the non MCVD - non CRF group a higher NT-proBNP level was noted in the individuals having at least 3 factors of undernutrition than in the others (141.00 [84.75 – 346.00] pg/mL vs 91.00 [49.00 – 197.00] pg/mL respectively; P = 0.012), data not shown.

According to the Cleveland Clinic's Reference range, an elevated level of NT-proBNP, was noted in 41.6 % of patients aged 55-74 years (NT-proBNP ≥ 125 pg/mL) and in 31.4 % of patients aged 75-98 years (NT-proBNP ≥ 450 pg/mL). But there was no significant difference in age between individuals with normal and elevated levels of NT-proBNP (75,43 ± 9,37 vs 75,99 ± 10,55 respectively; P = 0.634).

Among the whole study group, we noted the following comorbidities: 92.1% for hypertension and 45.2%, 23.9%, 38.1%, 6.6%, 15.2% and 11.6%, for diabetes, obesity, renal failure, coronary artery disease (CAD), sepsis-inflammatory disease and heart failure (HF), respectively.

Table 1 and figure 1 present the baseline characteristics of the study population, i) stratified by tertiles of NT proBNP concentrations resulting in three groups: T1 (NT proBNP < 86 pg/mL; N = 101), T2 (NT proBNP ≥ 86 and < 260 pg/mL; N = 101) and T3 (NT proBNP ≥ 260 pg/mL; N = 101) and ii) according to presence/absence of MCVD or CRF.

Taking into account these tertiles, the three groups did not differ in terms of means BMI, CRP, CRP/PAB ratio, total cholesterol or prevalence of gender, BMI < 21 Kg/m2, PAB < 0.10 g/L, hypertension and diabetes mellitus.

Higher mean age, creatinine levels, or higher frequencies of PAB < 0.20 g/L, CAD, heart failure, LVEF < 50 % were noted in T3 (top NT proBNP levels) whereas individuals in this group had lower means albumin, PAB, creatinine clearance, LVEF or frequency of obesity.

Taking into account, the presence/absence of MCVD or CRF, those without MCVD and CRF were younger, had lower NT-proBNP and creatinine levels, higher creatinine clearance and LVEF. They also were more likely to have PAB < 0.20 g/L and less likely have diabetes.

Table 1: Baseline characteristics of the study population according to tertiles of NT-proBNP concentrations and to the presence or not of Major Cardiovascular disease or Chronic Renal Failure

		Tertiles of NT-proBNP levels (pg/mL)				MCVD or CRF		
Variables	**Whole study population N =303**	**< 86 Group 1 N = 101**	**≥ 86 and < 260 Group 2 N = 101**	**≥ 260 pg/mL Group 3 N = 101**	***P***	**No N =171**	**Yes N= 132**	***P***
Sex (men) (%)	46.2	42.6	48.5	47.5	0.663	60.6	35.1	<0.001
Age (years)	75.63 ± 9.79	71.63 ± 8.48	76.06 ± 10.15	79.19 ± 9.24	<0.001	74.02 ± 9.96	77.71 ± 9.19	0.001
BMI (Kg/m2)	26.84 ± 9.61	27.42 ± 5.89	27.46 ± 13.92	25.62 ± 7.02	0.320	25.94 ± 6.87	27.99 ± 12.19	0.073
Obesity (%)	23.9	31.6	25.0	14.7	0.022	24.1	23.6	0.931
BMI < 21 Kg/m2 (%)	19	13.3	21.9	22.1	0.202	23.0	14.1	0.055
Hypertension (%)	92.1	91.3	91.7	93.3	0.865	72.4	83.5	0.022
Diabetes (%)	45.2	45.5	43.6	46.5	0.911	36.8	56.1	0.001
Heart failure (%)	11.6	2.0	3.0	29.7	<0.001	--	26.3	--
CAD (%)	6.6	3	4	12.9	0.008	--	15.0	--
MCVD (%)	15.2	4.0	6.9	34.7	<0.001	--	35.3	--
Sepsis-Inflammation (%)	15.5	14.9	15.8	15.8	0.975	15.9	15.0	0.840
At least 3 factors Of undernutrition	15.3	10.2	17.7	27.4	0.009	16.1	21.1	0.291
Hemoglobin g/dL	12.32 ± 1.83	13.19 ± 1.71	12.16 ± 1.71	11.63 ± 1.74	<0.001	12.47 ± 1.80	12.13 ± 1.86	0.115
CRP (mg/L)	2.70 [0.60 – 9.80]	2.90 [0.60 – 7.10]	2.00 [0.70 -7.90]	3.30 [0.60 – 21.85]	0.284	2.75 [0.60 – 9.55]	2.60 [0.65 – 9.90]	0.601
CRP >= 5 mg/L (%)	38.1	37.4	35.4	41.6	0.651	39.2	36.8	0.682
Albumin (g/L)	37.42 ± 6.62	38.37 ± 4.86	38.10 ± 8.54	35,81 ± 6,64	0.010	38.04 ± 7,43	36.62 ± 5.30	0.065
Albumin < 35 g/L (%)	29	20.8	27.7	38.6	0.019	25.9	33.1	0.175
PAB (g/L)	0.21 ± 0.08	0.24 ± 0.07	0.22 ± 0.11	0.19 ± 0.07	<0.001	0.20 ± 0.07	0.23 ± 0.10	0.031
PAB < 0.10 g/L (%)	9.2	5.0	8.9	13.9	0.091	8.8	9.8	0.777
PAB < 0.20 g/L (%)	35.0	19.8	38.6	46.5	<0.001	40.6	27.8	0.021
CRP/PAB ratio	0.15 ± 0.56	0.06 ± 0.22	0.20 ± 0.76	0.19 ± 0.56	0.165	0.10 ± 0.39	0.20 ± 0.72	0.138
CRP/PAB ratio >= 0.050	25.4	19,2	22,2	34,7	0.029	26.5	24.1	0.629
T cholesterol (mmol/L)	4.43 ± 1.53	4.51 ± 1.14	4.44 ± 1.04	4.64 ± 2.15	0.739	0.10 ± 0.39	0.20 ± 0.72	0.862

Creat (µmol/L)	92.60 ± 46.70	82.92 ±	82.80 ± 26.37	112.11 ± 64.80	<0.001	68.53 ± 12.53	123.80 ± 55.57	<0.001
Creat clear (ml/mn)	68.74 ± 25.35	74.94 ± 19.43	72.4 ± 21.29	58.84 ± 30.95	<0.001	82.51 ± 18.85	50.91 ± 21.27	<0.001
Creat >= 10 µg/mL (%)	38.1	25.0	33.7	55.4	<0.001	--	86.5	--
NT-proBNP (pg/mL)	146 [65 – 403]	44 [34 – 65]	146 [114 - 196]	767 [399 - 2162]	<0.001	101 [53 - 224]	260 [102 - 1073]	<0.001
LVEF %	62.50 ± 9.05	64.26 ± 5.46	64.49 ± 6.23	58.76 ± 12.54	<0.001	64.18 ± 6.31	60.30 ± 11.35	<0.001
LVEF < 50 % (%)	5.3	0.0	0.0	15.8	<0.001	--	12	--

Data are mean ± standard deviation and geometric means (interquartile range)

MCVD: Major Cardiovascular disease; CRF: Chronic renal failure. BMI: body mass index; NT proBNP: N terminal fragment of the prohormone brain natriuretic peptide; PAB : prealbumin; CRP: C reactive protein; CRP/PAB ratio: C reactive protein to prealbumin ratio; Creat; creatinine; Creat clear : creatinine clearance; LVEF: Left ventricular ejection fraction.

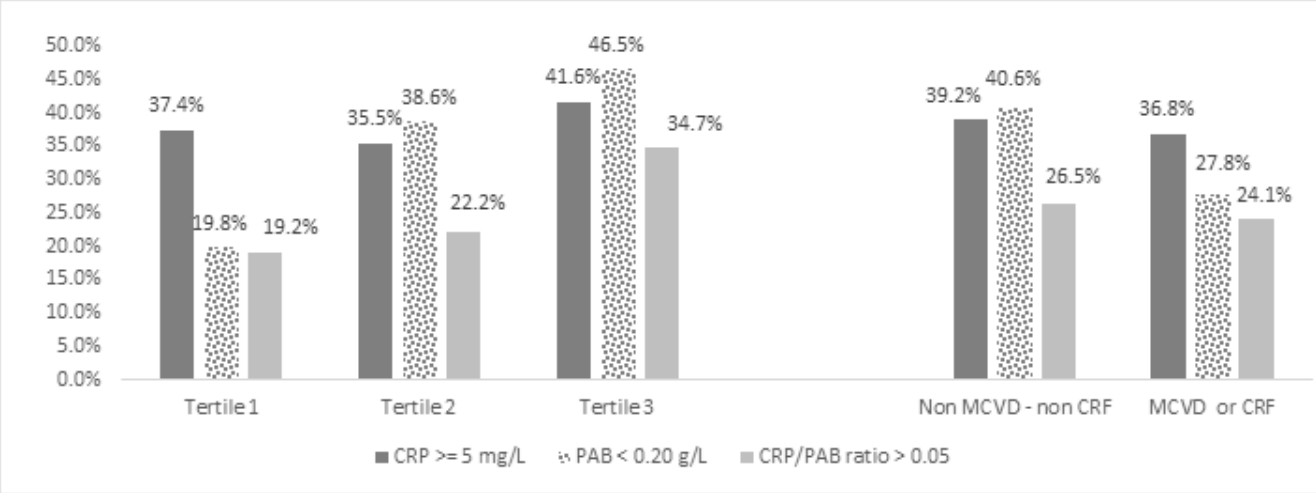

Figure 1: CRP, Prealbumine, CRP to prealbumine ratio according to A) tertiles of NT-proBNP concentrations in the whole study population and B) Presence/Absence of Major cardiovascular disease and Chronic Renal Failure

Tertile 1 : < 86 pg/mL , tertile 2 : ≥ 86 and < 260 pg/mL , tertile 3 : ≥ 260 pg/mL

A - CRP >= 5 mg/L : P = 0.651, PAB < 0.20 g/L : P < 0.001, CRP/PAB ratio > 0.050 : P = 0.029

B - CRP >= 5 mg/L : P = 0.682, PAB < 0.20 g/L : P= 0.021, CRP/PAB ratio > 0.050 : P = 0.629

Table 2. Log NT-proBNP was positively correlated with age and negatively correlated albumin and PAB levels in all groups. In individuals without MCVD and CRF negative correlations were found between log NT-proBNP with BMI (r = –0.188; P = 0.016). In these individuals, unlike those with MCVD or CRF, log NT-proBNP was not significantly correlated with CRP levels, CRP/PAB ratio, creatinine levels, creatinine clearance or LVEF.

Table 2: Correlations between Log NT-proBNP et continuous variables

	non MCVD - non CRF N = 171		MCVD or CRF N = 132		Whole study population N = 303	
	r	P			*r*	*P*
Age (y)	0.336	*<0.001*	0.272	*0.002*	0.335	*<0.001*
BMI (Kg/m²)	-0.188	*0.016*	-0.141	*0.115*	-0.101	*0.086*
CRP (mg/L)	0.074	*0.167*	0.273	*0.002*	0.182	*0.002*
Albumin (g/L)	-0.181	*0.018*	-0.239	*0.006*	-0.217	*<0.001*
Prealbumin (g/L)	-0.352	*<0.001*	-0.373	*<0.001*	-0.294	*<0.001*
CRP/ PAB ratio	0.080	*0.302*	0.174	*0.046*	0.165	*0.004*
Creatinine level (µmolL)	-0.133	*0.083*	0.278	*0.001*	0.360	*<0.001*
Creatinine clearance (ml/ mn)	-0.040	*0.601*	-0.281	*0.001*	-0.351	*<0.001*
LVEF %	-0.069	*0.367*	-0.458	*<0.001*	-0.381	*<0.001*

MCVD: Major Cardiovascular disease; CRF: Chronic renal failure. BMI: body mass index; NT proBNP: N terminal fragment of the prohormone brain natriuretic peptide;: C reactive protein; CRP/PAB ratio: C reactive protein to prealbumin ratio; LVEF: Left ventricular ejection fraction.

Table 3 presents the results of the multivariate linear regression exploring the effect of gender, age, BMI, hemoglobin level, MCVD, hypertension, diabetes, CRP levels, PAB levels, CRP/PAB ratio, and creatinine levels as independent variables on log NT-proBNP in the whole study population.

Significant effects were noted, for age (P < 0.001), MCVD (P < 0.001), PAB (P < 0.001) and creatinine levels (P < 0.001). The effect of BMI was nearly significant (P = 0.051). Gender, log CRP, CRP/PAB ratio, hypertension and diabetes did not contribute significantly to the model. This model accounted for 48.9% (adjusted r2= 0.489) of the variability in log NT-proBNP.

Table 3: Multivariate linear regression for NT-proBNP concentrations (Log NT-proBNP) in the overall study population

Variables		Beta	*P*
Age (y)		0.217	***<0.001***
Sexe		0.006	***0.901***
BMI (Kg/m²)		-0.087	***0.052***
MCVD		0.428	***<0.001***
Prealbumin (g/L)		-0.204	***<0.001***
Hemoglobin_g/100ml		-0.210	***<0.001***
CRP/ PAB ratio		-0.099	***0.070***
CRP Log		0.046	***0.384***
Diabetes		-0.016	***0.729***
Hypertension		0.066	***0.158***
Creatinine _µmolL		0.226	***<0.001***

MCVD: Major Cardiovascular disease; CRF: Chronic renal failure. BMI: body mass index; NT-proBNP: N-terminal fragment of the prohormone brain natriuretic peptide; CRP: C reactive protein; CRP/PAB ratio: C reactive protein to prealbumin ratio.

Discussion

Although NT-pro BNP is a common indicator for the diagnosis of acute and chronic heart failure and the evaluation of its severity, other factors such as age, BMI, hemoglobin levels, renal function, are known to be closely associated with the levels of the prohormone. The associations, with inflammation and undernutrition have been less described. Interestingly, we assessed in this study, the cross-sectional relationship between NT-proBNP and biomarkers of malnutrition-inflammation in presence and absence of major cardiovascular disease or chronic renal failure in patients hospitalized for various conditions. Prealbumin level was independently and steadily associated with elevated NT-proBNP concentrations and this association cannot not be explained solely by the presence of cardiovascular disease and renal chronic complications.

As in other studies NT-proBNP levels increased with age and, although gender was not associated with NT-proBNP levels in our study population, higher levels has been more reported in women than in men [14, 15].

We noted a lower prevalence of obesity in the top tertile of NT-proBNP and an inverse relationship between BMI and circulating levels of NT-proBNP. This negative relationship has been demonstrated in various studies, in subjects with and without heart failure or renal insufficiency [16-19]. We found no significant difference in prevalence of diabetes according to tertiles of NT-proBNP levels in our study population but, insulin resistance has been associated with lower natriuretic peptide levels and higher NT-proBNP with lower diabetes risk [6,20].

NT-proBNP was negatively correlated with LVEF and creatinine clearance. Prevalence of MCVD et CRF were higher in the top tertile of NT-proBNP. NT-proBNP is part of the natriuretic peptides family and these peptides are involved in the pathogenic mechanisms leading to major cardiovascular diseases, such as heart failure (HF), coronary artery disease and hypertension [2]. Renal dysfunction affects BNP and NT-proBNP since cardiac and renal dysfunction are frequently combined [21]. Additionally, NT-proBNP is cleared by the kidney thus, its level is directly influenced by kidney function and elevated levels are also observed in patients with renal dysfunction without clinical evidence of cardiovascular disease [22].

In the present study, the relationships between NT-proBNP and inflammation-malnutrition were evaluated using PAB and CRP/PAB ratio. C-reactive protein, a positive acute phase reactant, has been recognized as a useful marker of inflammation [11, 23]. Prealbumin whose concentrations are closely related to early changes in nutritional status is considered as a useful marker to assess protein energy malnutrition in hospitalized patients [10]. But PAB is also a negative acute-phase protein. Negative acute phase reactants are downregulated, and their concentrations decrease during inflammation [11]. Thus, the CRP/PAB ratio has also been suggested as a marker of both inflammation and malnutrition. [12].

Prealbumin, was negatively correlated with NT-proBNP in the individuals with and without MCVD and CRF. But, associations between malnutrition, inflammation and NT-proBNP were mainly assessed in patients with CRF and particularly in that undergoing hemodialysis and in patients with major cardiovascular disease [5,7,12,24, 25, 26].

We found greater prevalence of MCVD and CRF in the third tertile (NT proBNP $\geq$ 260 pg/mL) but also greater prevalence of decreased PAB (PAB < 0.20 g/l) and high CRP/PAB ratio (ratio $\geq$ 0.050, the 75th percentile threshold). CRP values and CRP/PAB ratio were positively correlated with NT-proBNP levels in the MCVD - CRF group.

Previous studies showed that inflammation increased levels of NT-proBNP in heart failure [26, 27]. In severe heart failure, there is a deterioration of liver function [27]. The consumption of PAB increases and its liver synthesis decreases resulting in reduced PAB levels [27]. Consecutively, proinflammatory cytokine markers such as CRP increase progressively [28].

Malnutrition can complicate many chronic diseases including heart failure and CRF [29-31]. In individuals with CRF, there is a progressive decline in nutritional parameters highlighting a protein energy wasting (PEW) which has been associated with elevated level of NT-proBNP [7,30-32].

All individuals in our study have had a cardiological evaluation including an echocardiographic examination excluding a potential role of heart failure or CAD in the study group without MCVD and CRF. Surprisingly, there was no significant difference in prevalence of inflammatory disease or sepsis, parameters of undernutrition ($\geq$ 3 factors), CRP $\geq$ 5 mg/L, CRP/PAB ratio > 0.050, between the two groups. Prevalence of decreased PAB (< 0.20 g/L) was higher in individuals without MCVD or CRF than in the others. In addition, in the multivariate linear regression performed in the whole study population, PAB was negatively associated with log NT-proBNP independently of MCVD and CRF whereas the association with CRP and CRP/PAB ratio were not significant.

As explained before, in our study group without MCVD and CRF, NT-proBNP levels were significantly higher in those having at least 3 factors of undernutrition than in the others. These results are consistent with those of a previous study in asymptomatic Asian participants which were prospectively recruited in a cardiovascular health screening program (mean age 49.6 ± 11.4 years) [33]. In these participants, NT-proBNP levels were substantially increased in the malnourished (versus well-nourished) groups, in lean and obese participants [33].

Elevated levels of NT-proBNP were also reported in patients with sepsis or inflammatory diseases in the absence of cardiac disease [34-36].

Globally, several mechanisms could be involved in the relationship between malnutrition, inflammation and NT-proBNP. Among them, age may play a particular role given its relationship to both NT-proBNP and malnutrition inflammation. Mean age of our study population was 75 years. It is known that muscle wasting, cachexia, malnutrition and chronic inflammation tend to occur concomitantly with aging. Proinflammatory cytokines such as TNF-α and IL-1β are increased in cachexia and could increase production of brain natriuretic peptide from cardiomyocytes [26,37]. In fact, inflammatory cytokines induce brain natriuretic peptide production in vitro [37].

In sepsis, the primary mechanism for the elevation of NT-proBNP remains unclear. The effects of hemodynamic variations and of proinflammatory cytokines have also been suggested [26,38-40]. In patients with chronic inflammation (e.g rheumatoid arthritis),

without clinical heart failure, increased NT-proBNP concentrations may indicate subclinical cardiovascular disease but also a chronic inflammatory state [36].

Limitations of the Study

This study has some limitations including its observational design and its small sample size. In addition, we did not use a nutritional screening tool to assess the malnutrition risk and measurements of biomarkers were limited to one time-point. Other asymptomatic cardiac or progressive kidney diseases may also be present in the non-MCVD non-CRF group and medications which may impact natriuretic peptide levels, were not taken into account.

But, the main strength of this study is that the association between NT-proBNP concentrations and decreased PAB levels was assessed independently of major cardiovascular disease and of serum creatinine levels limiting thus the potential effect of progressive kidney disease.

Conclusion

Our results argue for a strong relationship between NT-proBNP and malnutrition-inflammation syndrome independently of major cardiovascular disease and renal failure. Prealbumin, marker of both inflammation and malnutrition is more strongly associated with NT-proBNP than CRP or CRP/PAB ratio in our study population. In patients without cardiovascular disease and without renal failure, NT-proBNP levels could help to assess for the risk of inflammation-malnutrition especially in the older population.

Nonetheless, further researches are needed to assess the potential role of NT proBNP as a predictor of malnutrition risk and to establish the prognostic value of NT-proBNP in malnourished subjects in terms of mortality and morbidity.

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Competing Interests

The authors declare that they have no competing interests.

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