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Parathyroid hormone serum concentration in Central European patients with non-ischaemic heart failure as a potential marker of disease severity and poor prognosis

Stężenie parathormonu w surowicy krwi u środkowoeuropejskich pacjentów z nie-niedokrwienną niewydolnością serca jako potencjalny czynnik ciężkości choroby i złego rokowania

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Abstract

Introduction: Parathyroid hormone (PTH) might be considered as a potential marker of disease severity and worse prognosis in heart failure (HF) patients.

The aim of the study was to assess PTH, vitamin D, phosphorus (P), and total calcium (Ca2+) serum concentrations in Central European patients suffering from HF of non-ischaemic origin compared to non-HF volunteers.To evaluate potential correlations among the enumerated parameters, established markers of worse prognosis and declared sun exposure.

Material and methods: Serum intact-PTH, 25-OH vitamin D, P, and total Ca^{2+} concentrations were assessed in a group of HF patients and non-HF volunteers. Patients described their daily profile of sun exposure during the previous eight weeks as "above" or "below" seven hours a week.

Results: The mean PTH concentrations in the non-ischaemic HF group and control group were 79.5 pg/mL and 59.6 pg/mL, respectively ($P = 0.009$). Non-HF volunteers declaring higher sun exposure time had higher serum concentrations of vitamin D compared to those with lower sun exposure time (30.3 *vs.* 23.8 ng/mL, $P < 0.05$), unlike the HF patients (24.1 ng/mL *vs.* 23.2 ng/mL, P = ns). Multiple regression analysis revealed the relationship between age, NT-proBNP (N-terminal pro-brain natriuretic peptide), P, and PTH as a dependent variable.

Conclusions: PTH is significantly elevated in non-ischaemic HF patients compared to non-HF volunteers and correlates with established factors of worse prognosis, including age, estimated glomerular filtration rate (eGFR), aspartate aminotransferase (AST), serum concentrations of creatinine, and NT-proBNP. Declared sun exposure did not affect the serum concentration of vitamin D in the HF group, in contrast to the control group. **(Endokrynol Pol 2017; 68 (3): 299–305)**

Key words: *dilated cardiomyopathy; heart failure; N-terminal Pro-brain natriuretic PePtide; Parathyroid hormone; vitamin D*

Streszczenie

Wstęp: Podwyższone stężenie parathormonu (PTH) jest uważane za potencjalny marker ciężkości choroby i złego rokowania u chorych z niewydolnością serca (NS).

Celem pracy była ocena stężenia PTH, witaminy D, całkowitego wapnia (Ca^{2+}) i fosforu (P) w surowicy krwi środkowoeuropejskich chorych z nie-niedokrwienną NS w porównaniu z grupą bez NS. Określenie potencjalnych zależności wymienionych parametrów z ustalonymi markerami złego rokowania oraz deklarowanym czasem ekspozycji na słońce.

Materiał i metody: W obu grupach oznaczono stężenie aktywnego biologicznie PTH, 25-OH witaminy D, Ca^{2+} i P. Pacjenci deklarowali czas ekspozycji na słońce w ciągu ostatnich ośmiu tygodni jako „powyżej" lub „poniżej" siedmiu godzin w tygodniu.

Wyniki: Średnie stężenie PTH było wyższe w grupie badanej (79,5 *vs.* 59,6 pg/ml, p = 0,009). W grupie bez niewydolności serca u osób deklarujących czas ekspozycji na słońce > 7h/tygodniu obserwowano wyższe stężenie witaminy D (30,3 *vs.* 23,8 ng/ml, $p < 0,05$), zależność ta nie zachodziła u pacjentów z NS (24,1 ng/ml *vs.* 23,2 ng/ml, p = ns). Analiza regresji wieloczynnikowej wykazała zależność między wiekiem, stężeniem N-końcowego fragmentu prohormonu peptydu natriuretycznego (NT-proBNP), P oraz PTH jako zmienną zależną.

Wnioski: Stężenie PTH jest wyższe w grupie pacjentów z nie-niedokrwienną NS w porównaniu z ochotnikami bez NS. Stężenie PTH koreluje z ustalonymi czynnikami złego rokowania jak wiek, estymowany wskaźnik filtracji kłębkowej (eGFR), stężenie kreatyniny, aminotransferazy asparaginianowej oraz NT-proBNP. W przeciwieństwie do grupy kontrolnej, deklarowana ekspozycja na słońce nie wpływa na stężenie witaminy D u pacjentów z NS. **(Endokrynol Pol 2017; 68 (3): 299–305)**

Słowa kluczowe: *kardiomiopatia rozstrzeniowa; niewydolność serca; N-końcowy fragment prohormonu peptydu natriuretycznego; parathormon; witamina D*

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Abbreviations

ALT — alanine transferase
AST — aspartate aminotransferase
CKD — chronic kidney disease
CAD — coronary artery disease
DCM — dilated cardiomyopathy
eGFR — estimated glomerular filtration rate
ESC — European Society of Cardiology
HF — heart failure
MDRD — Modification of Diet in Renal Disease
NT-proBNP — N-terminal pro-brain natriuretic peptide
PTH — parathyroid hormone
P — phosphorus
SD — standard deviation
Ca^{2+} — total calcium

Introduction

It is estimated that 1–2% of the population in developed countries suffers from heart failure (HF), and half of these cases are associated with impaired left ventricle contractility mainly due to coronary artery disease (CAD) or hypertension [1]. Patients with heart failure caused by dilated cardiomyopathy (DCM) of non-ischaemic origin remain an interesting observational group in whom the relationship between the serum concentration of parathyroid hormone (PTH) and other biochemical and clinical parameters was not fully elucidated. PTH is a polypeptide that is produced in the structure of the parathyroid gland in response to the diminution of calcium ions (Ca^{2+}) in the extracellular fluid. Its secretion is based on the principle of a negative feedback loop with the serum concentration of physiologically active Ca^{2+} ions. PTH increases the serum concentration of ionised Ca^{2+} due to an enhancement of its reabsorption in renal tubules and increase in phosphate secretion and osteoclast activation [2]. On the basis of the regulation of alpha-1 hydroxylation of 25-OH vitamin D, it has a crucial effect on the absorption of Ca^{2+} in the intestinal tract [3]. PTH has a significant effect on the cardiovascular system via its widespread receptors in the myocardium, endothelial, and smooth muscle cells. Its biologically active form, known as intact PTH, is secreted by the parathyroid gland and consists of eighty-four amino acids. PTH resolves into two components – active N-terminal PTH and inactive C-terminal PTH, which is excreted via the renal route. The active PTH forms (84-PTH and N-PTH) are mainly metabolised in the liver, resulting in a short half-life of intact PTH, which is relatively independent of renal function, although its serum concentration correlates with the absolute amount of the hormone and its activity [3,4]. The PTH serum concentration is increased in primary hyperparathyroidism, vitamin D deficiency, or chronic kidney disease (CKD). Augmentation of PTH serum concentration in HF patients has a potential negative effect on symptom severity and prognosis.

Material and methods

The aim of this study was to assess the serum concentrations of PTH, total calcium (Ca^{2+}), P, and vitamin D in 65 consecutive patients with non-ischaemic heart failure, who were hospitalised in our centre from March 1, 2012 to September 15, 2014. The control group consisted of sixty-two non-HF volunteers. Exclusion criteria in both groups were: CKD stage four or higher, vitamin D supplementation, diagnosed primary hyperparathyroidism, or malignancy. The blood samples of the HF patients enrolled in the study were collected on admission. The study complies with the Declaration of Helsinki, was approved by the local ethics committee (number of approval KNW/0022/KB1/40/I/12/13), and all patients provided informed consent.

Serum intact-PTH concentration was assessed in both groups using the immunoradiometric assay technique with the DIAsource hPTH-120 min-IRMA Kit (DIAsource Immunoassays S.A., Belgium). The vitamin D serum concentration was assessed using the radioimmunoassay with the DIAsource 25-OH vitamin D total-RIA-CT Kit (DIAsource Immunoassays S.A., Belgium). Serum P and total Ca^{2+} concentrations were assessed using the enzymatic method as described by Spinreact S.A., Spain and the colorimetric Arsenazo III method as described by Biomaxima S.A., Poland. In the HF patients, routine examinations were performed on admission according to the guidelines of the European Society of Cardiology (ESC), which consisted of peripheral blood morphology, creatinine, aspartate (AST), and alanine (ALT) transferases and N-terminal pro-brain natriuretic peptide (NT-proBNP) serum concentrations. The estimated glomerular filtration rate (eGFR) was calculated on the basis of the Modification of Diet in Renal Disease (MDRD) formula. The New York Heart Association (NYHA) functional class assessment and echocardiography examination were performed upon admission to the hospital. Left ventricular systolic function impairment was caused by dilated cardiomyopathy in the majority of cases (60 patients — 92.3% of cases), which were mostly postinflammatory, idiopathic, or, in one female, postpartum in origin. All patients were subjected to invasive coronary angiography to exclude the ischaemic background of HF. Patients were requested to characterise their daily profile of sun exposure during the last eight weeks as "above" or "below" seven hours a week, equivalent to one hour per day. Importantly, the population of Poland, which has approximately forty

Table I. *Group characteristics*
Tabela I. *Charakterystyka grupy*

	HF n = 65 (%)	Non-HF volunteers n = 62 (%)	P
Age	51.6 [42–60]	53.8 [42–64]	ns
Males	53 (80)	45 (70)	ns
Arterial hypertension	32 (49)	33 (53)	ns
Diabetes	17 (26)	13 (21)	ns
Coronary artery disease	0 (0)	27 (43)	$P < 0.0001$
Vitamin D concentration < 30 [ng/mL]	47 (72)	35 (56)	$P = 0.046$
Egfr < 60, ml/min/1.73 m^2	9 (14)	0 (0)	$P = 0.007$
Sun exposure > 7 h/week	12 (20)	41 (70)	$P < 0.0001$
Icd/crt	38 (58)	0 (0)	$P < 0.0001$
Eligible for cardiac transplantation	16 (25)	0 (0)	$P < 0.0001$
Atrial fibrillation	21 (32)	2 (3)	$P < 0.0001$
Left bundle branch block	23 (35)	0 (0)	$P < 0.0001$
Ace-i	65 (100)	29 (46)	$P < 0.0001$
Beta blockers	63 (97)	28 (45)	$P < 0.0001$
Diuretics	57 (88)	13 (21)	$P < 0.0001$
LVEF, %	24.5	55.1	$P < 0.001$
NYHA I	4 (6)	–	
NYHA II	38 (58)	–	
NYHA III	16 (25)	–	
NYHA IV	7 (11)	–	

Data are presented as mean and percentage. ACE-I — angiotensin converting enzyme inhibitors; eGFR — estimated glomerular filtration rate; HF — heart failure; ICD/CRT — implantable cardioverter defibrillator/cardiac resynchronisation therapy; LVEF — left ventricular ejection fraction; NYHA — New York Heart Association

million people, exhibits a temperate climate in Central Europe, and its inhabitants frequently suffer from vitamin D deficiency due to insufficient sun exposure and nutritional supply.

Statistical analysis

The distributions of the examined parameters were analysed using the Shapiro-Wilk test. Values were presented as the mean and standard deviation (SD) or as the median in the 25th and 75th percentiles. Nominal and categorical values were expressed in percentages or proportional rates. Linear variables with normal distribution were compared using Student's t-test. Variables with abnormal distribution were compared using the Kolmogorov-Smirnov, Mann-Whitney U, and Kruskall-Wallis tests. Categorical variables of abnormal distribution were compared using Chi-square test with Yates correction or Fischer's exact test. Quantified Spearman's rho correlation coefficients were used to assess the linear correlations between variables. Multiple regression analysis with PTH as a dependent variable led to a construction of two PTH serum concentration models. The basic model consisted of arbitrarily included parameters while the secondary model was constructed on the base of the backward stepwise method. Differences between the values were medical package (Statsoft Inc.).

Results

The heart failure group (65 participants) and the control group (62 participants) did not differ in age (51.6 *vs.* 53.8, P = ns) and gender (males 80% and 70%, respectively, P = ns). Group characteristics are presented in Table I.

The mean PTH concentration in the non-ischaemic HF group was 79.5 pg/mL, and the range was 3.9–198.8 pg/mL, SD 46.4 pg/mL. In the control group, the mean PTH concentration was 59.6 pg/mL, and the range was 18.3–124.8 pg/mL, SD 23.8 pg/mL. The mean values of serum PTH concentrations were significantly higher in the heart failure group (P = 0.009) (Fig. 1).

The mean PTH values in specific groups of patients divided according to the NYHA functional class were as follows: NYHA I (mean 58.8 pg/mL, range 6.8–77.5 pg/mL),

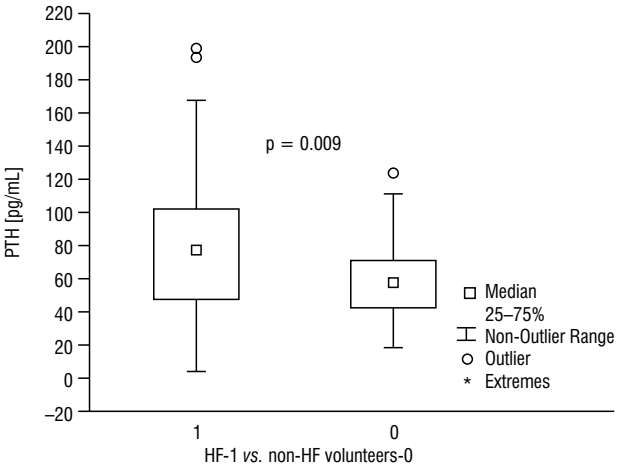

Figure 1. *Parathyroid hormone serum concentration in heart failure patients vs. non-heart failure volunteers*

Rycina 1. *Stężenie parathormonu w surowicy krwi u chorych z niewydolnością serca wobec osób bez niewydolności serca*

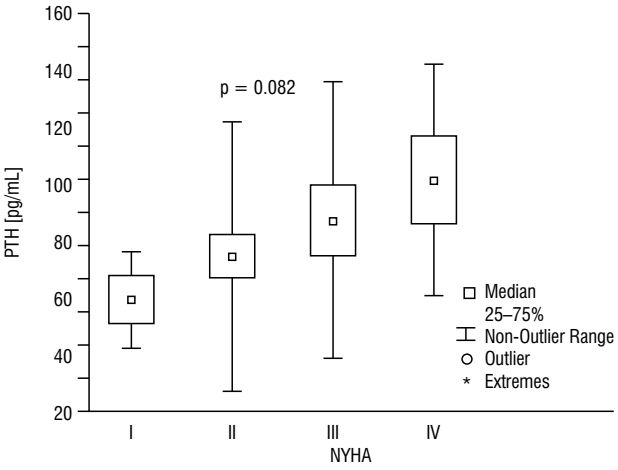

Figure 2. *Parathyroid hormone serum concentration according to New York Heart Association class*

Rycina 2. *Stężenie parathormonu w surowicy krwi zależnie od klasy czynnościowej zgodnie z klasyfikacją Nowojorskiego Towarzystwa Kardiologicznego*

Table II. ***Impact of sun exposure on the examined parameters***
Tabela II. ***Wpływ ekspozycji na słońce na badane parametry***

	HF (n = 65)					non-HF volunteers (n = 62)				
	SE > 7 h/week (n = 12)		SE < 7 h/week (n = 53)		*P*	SE > 7 h/week (n = 41)		SE < 7 h/week (n = 21)		*P*
	Mean	SD	Mean	SD		Mean	SD	Mean	SD	
PTH [pg/mL]	73.0	30.1	80.9	49.5	ns	59.9	26.1	59.0	19.2	ns
Ca^{2+} [mg/dL]	10.0	0.4	9.5	0.6	< 0.025	9.6	0.4	9.6	0.6	ns
P [mmol/L]	1.2	0.2	1.2	0.2	ns	1.3	0.2	1.3	0.2	ns
Vit. D [ng/mL]	24.1	8.3	23.2	13.9	ns	30.3	11.1	23.8	10.8	< 0.05
Age (years)	43.6	10.9	53.4	12.0	< 0.01	56.0	14.2	49.3	17.5	ns

Data are presented as mean and standard deviation. Ca^{2+} — total calcium; HF — heart failure; ns — non-significant; P — phosphorus; PTH — parathyroid hormone; SD — standard deviation; SE (> / <) 7 h/week — sun exposure "above/below" seven hours per week; vit. D — vitamin D

NYHA II (mean 74.4 pg/mL, range 3.9–198.8 pg/mL), NYHA III (mean 87.0 pg/mL, range 8.3–168.3 pg/mL), and NYHA IV (mean 101.2 pg/mL, range 47.3–162.8 pg/mL), which trended towards statistical significance (P = 0.082) (Fig. 2).

The mean Vitamin D concentration was significantly lower in the HF group (23.4 ng/mL *vs.* 28.1 ng/mL, P = 0,006), although in both groups the mean concentration was below optimal range (30 ng/mL). In our group Vitamin D deficiency was not significantly correlated to the disease severity (NYHA class) nor another assessed marker of poor prognosis.

Patients with HF, who declared a sun exposure time greater than seven hours a week, had significantly higher serum Ca^{2+} concentrations (10.0 *vs.* 9.5 ng/mL, P < 0.025) and were significantly younger (43.6 *vs.* 53.4 years, P < 0.01) compared to those who declared the lesser sun exposure values. Differences between other analysed parameters (PTH, P, vitamin D) were statistically insignificant. Non-HF volunteers declaring a sun exposure time greater than seven hours a week had higher serum concentrations of vitamin D than those with lower values (30.3 *vs.* 23.8 ng/mL, P < 0.05), unlike the HF patients (24.1 ng/mL *vs.* 23.2 ng/mL, P = ns). Differences among other values (PTH, P, Ca^{2+}) were statistically insignificant (Table II).

The Spearmann coefficient analysis revealed a statistically significant correlation between the serum concentration of PTH in HF patients and established factors of worse prognosis, such as age (r = 0.26, P = 0.035), creatinine concentration (r = 0.26, P = 0.037), AST (r = 0.32, P = 0.009), NT-proBNP (r = 0.37, P = 0.003), and eGFR (r = –0.36, P = 0.003). Moreover, statistically significant correlations were observed between PTH and Ca^{2+} (r = –0.29, P = 0.02) and PTH and P (r = –0.35, P = 0.004). A correlation between PTH and haemoglobin

(HGB) showed a trend towards statistical significance ($r = –0.21$, P = 0.093). All values are presented in Table III.

The multiple regression analysis with PTH as a dependent variable enabled the construction of a primary model, which consisted of subsequent arbitrarily included parameters: age, LVEF, eGFR and serum blood concentrations of vitamin D, phosphorus, and NT-proBNP. Further calculations according to the backward stepwise method led to the construction of the secondary model, which included age, phosphorus, and NT-proBNP serum blood concentrations. P values were 0.004, 0.012, and 0.022, respectively. All data are presented in Table IV.

Table III. *Spearman correlation coefficients between parathyroid hormone and subsequent values in the heart failure group*

Tabela III. *Współczynniki korelacji Spearmana pomiędzy parathormonem i kolejnymi wartościami u pacjentów w grupie z niewydolnością serca*

	HF (n = 65)		
Parameter	**Mean (interquartile range)**	**Spearman *r***	***P***
Age (years)	51.6 (42–60)	0.26	0.035
Ca^{2+} [mg/dL]	9.6 (9.15–9.95)	–0.29	0.020
P [mmol/L]	1.2 (0.99–1.38)	–0.35	0.004
Vitamin D [ng/mL]	23.4 (13.9–32.6)	–0.18	0.15
eGFR [mL/min/1.73 m^2]	86.4 (68.34–104.22)	–0.36	0.003
Creatinine [mg/dL]	0.7 (0.79–1.15)	0.26	0.037
AST [IU/L]	27.5 (20–31)	0.32	0.009
NT-proBNP, pg/mL	2725.0 (343–2817)	0.37	0.003
Haemoglobin [g/dL]	14.1 (12.9–15.4)	–0.21	0.093
LVEF (%)	25 (16–30)	–0.34	0.7

Data are presented as mean with interquartile range. AST — aspartate transaminase; Ca^{2+} — total calcium; eGFR — estimated glomerular filtration rate; LVEF — left ventricular ejection fraction; NT-proBNP — N-terminal pro-brain natriuretic peptide; P — phosphorus

Table IV. *Multiple regression analysis (backward stepwise method) with parathyroid hormone as a dependent variable in heart failure patients*

Tabela IV. *Analiza regresji wielorakiej metodą krokową wsteczną z parathormonem jako zmienną zależną u chorych z niewydolnością serca*

	Primary model		Secondary model	
Parameter	**B**	***P***	**B**	***P***
Age (years)	1.037	0.044	1.24	0.004
LVEF (%)	0.285	0.642	–	–
Vitamin D [ng/mL]	–0.240	0.571	–	–
P [mmol/L]	–54.186	0.030	–59.56	0.012
eGFR [mL/min/1.73 m^2]	–0.165	0.577	–	–
NT-proBNP [pg/mL]	0.002	0.105	0.003	0.022

eGFR — estimated glomerular filtration rate; LVEF — left ventricular ejection fraction; NT-proBNP — N-terminal pro-brain natriuretic peptide; P — phosphorus

Discussion

According to our best knowledge the issue concerning the dependency between serum PTH concentration in HF patients of non-ischaemic origin and sun exposure in comparison to non-HF volunteers has not been elucidated. The data considering vitamin D and PTH concentration in the Caucasian population of HF patients living in Central Europe remain scarce and unclear. PTH is not routinely evaluated in HF patients, although it may be a potentially important factor in the pathogenesis of HF and is an important clinical factor in anticipating worse prognosis of the disease [6, 7]. It is proposed that maintaining proper PTH serum blood concentration, by normalising serum Ca^{2+} and vitamin D concentrations, effective treatment of CKD, or potentially usage of calcimimetics, may play a positive role in HF patients treatment and decision-making processes [8]. Elevation of serum PTH is induced by several mechanisms, such as activation of the renin-angiotensin-aldosterone system (RAAS), which results in an increase in renal Ca^{2+} ion depletion, a high rate of diuretic intake in this group of patients, progressive renal degeneration due to chronic hypoperfusion resulting in excessive PTH retention, and vitamin D deficiency due to a decrease in physical activity with a subsequent decrease in sun exposure and induction of PTH secretion [9]. Serum PTH concentration is increased by neurohormonal system activation, which primarily plays a compensatory role in the early stage of HF; however, subsequently, it has a growing decompensating impact on the course of the disease [10]. Myocardial cells express PTH-specific receptors, whose stimulation might be responsible for hypertrophy, apoptosis, and fibrosis, which is directly induced by either the activation of protein kinases A and C or arterial hypertension [11]. Numerous biological processes are considered to be crucial in improving or worsening HF [12, 13]. It is widely speculated that elevated PTH contributes to augmentation of catabolic cellular activity and oxidative stress. Pilz et al. proved the impact of increased PTH for cardio-vascular and overall mortality in a large cohort of patients referred to coronary angiography [14]. The hazard ratio (HR) for occurrence of death during a nearly eight-year follow-up period between the third and fourth PTH quartiles was 1.85 for sudden cardiac death and 1.94 for HF cause. Pro-atherosclerotic impact of PTH, although often hypothesised, remains not fully elucidated. Despite the fact that LURIC study investigators failed to assess a clear link between PTH and angiographic

stage of coronary heart disease (CAD), they assumed the association between NT-proBNP, NYHA class, and PTH being an independent predictor of hospitalisation for heart failure [15]. This was consistent also with our study in which we found the relation between PTH and age, NT-proBNP, and phosphorus serum blood concentrations. CAD as a cause of HF was in these cases meticulously excluded by the coronary angiography without significant lesions performed within twelve months prior to the examination. PTH concentration could have been affected by a high intake percentage of diuretics and angiotensin-converting enzyme inhibitors (ACE-I) (88% and 100% of patients, respectively), as well as by the occurrence rate of CKD in the third stage with eGFR < 60 (mL/min/1.73 m^2) in 14% of the patients. It is worth mentioning that in the publication of Schierbeck et al. the percentage of diuretics and ACE-I intake were similar and varied between 76–97% and 57–81%, respectively, in patients divided into quartiles according to PTH serum concentration [16]. Moreover, investigators found a positive correlation of PTH with age, NT-proBNP, and alkaline phosphatase – Pearson correlation coefficients were 0.233, 0.365, and 0.322 (P = 0.004, P < 0.001, and P < 0.001), respectively, and were coherent with our results. Reported negative correlation of PTH with ionised calcium (–0.354, P < 0.001), eGFR (–0.487, P < 0.001), and haemoglobin (–0.208, P = 0.01) support our findings, which are similar although performed in a different group of patients hospitalised due to HF. Correlation between PTH and increased risk ratio of cardiovascular death in elderly males and risk of heart failure occurrence in the population of all patients was demonstrated by Hagstrom et al. [17]. Although there have been several studies denying the role of PTH as a factor correlating with the occurrence of cardiovascular disease [18, 19], in the vast majority of publications PTH is recognised as a predictor of hospitalisation due to HF decompensation and cardiovascular, as well as all-cause mortality [5, 14, 16, 20]. The investigation of Gruson et al. revealed that the serum concentration of bioactive PTH in hospitalised HF patients, as assessed using the third-generation test, was elevated in comparison to healthy volunteers and was correlated with NYHA class and neurohormonal activation, which was also present in our study [21]. Interestingly, this dependency characterised predominantly ischaemic compared to non-ischaemic HF patients. The relationship between PTH concentration and the severity of HF in 150 consecutive patients with HF treated in the outpatient clinic shown by Altay et al. was also consistent with our findings [22]. The study of Sugimoto et al. showed that low-normal serum PTH concentration on admission was related to the increased incidence of in-hospital mortality due to acute decompensated heart failure compared to high PTH values (23.1 *vs.* 11.4, P = 0.013) [23]. Since the deceased patients had significantly higher incidence of diabetes and lower incidence of dyslipidaemia (P = 0.03 and P = 0.045, respectively) they probably represented the group of patients with initially increased risk of not only short- but also long-term mortality. It was reported that impaired secretion of PTH within the physiologic range has a negative impact on contractility of cardiomyocytes [24]. Moreover, the activation of the adrenergic nervous system expressed by the elevation of serum catecholamines results in intracellular calcium overloading and augmentation of oxidative stress. These discrepancies in PTH serum concentrations can be largely explained by the initially different clinical course of acute and chronic heart failure. Polat et al. demonstrated the relationship between 25OHD3 and the echocardiographic findings connected with the negative LV remodelling [25]. We evaluated the possible correlation between PTH and LVEF, which turned out to be statistically insignificant. It might have been caused by the relatively wide interquartile range of LVEF assessments (16–30%) as well as by a frequently observed incoherence between the clinical status and LVEF examination. Serum blood concentrations of vitamin D in HF patients of the Polat et al. study were 24.1 ± 10.4, which was comparable to our findings 23.4 ± 13.0; however, we observed the discrepancy between vitamin D serum blood concentration among the control subjects which were 41.4 ± 20.9 and 28.1 ± 11.3, respectively. At least partially it could be explained by higher solar Direct Normal Irradiation (DNI) in Turkey in comparison to Poland (2000 *vs.* 1000 kWh/m^2) [26]. Interestingly vitamin D serum blood concentrations in patients with HF did not vary significantly according to declared sun exposure (24.1 *vs.* 23.2 ng/mL, P = ns), which suggests a more complex restitution background of vitamin D in the HF setting. In this study, intact-PTH serum concentration (second-generation assessment) in non-ischaemic HF patients correlated with well-established markers of unfavourable prognosis (age, NYHA class, eGFR, NT-proBNP, and creatinine). Moreover, the PTH concentration did not correlate with the vitamin D concentration although the prevalence of its deficit was significantly higher among the HF patients compared to the non-HF volunteers (72% *vs.* 56%, P = 0.046).

Limitations of the study

Certain limitations should be considered when interpreting the findings of our study. Firstly, the analysed data represents a relatively small although highly selected population of consecutive patients with non-ischaemic HF. Secondly, the patients were enrolled and evaluated in one centre by the investigators, which might have generated a potential source of selection bias.

Conclusions

PTH concentration is significantly elevated in a Caucasian population of non-ischaemic HF patients compared to non-HF volunteers. This elevation is correlated with established factors of worse prognosis of HF such as age, eGFR, and serum concentrations of phosphorus and NT-proBNP. Declared sun exposure did not affect the serum concentration of vitamin D in the HF group compared to the control group.

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27. Abbreviations: HF, heart failure; PTH, parathyroid hormone