B-type natriuretic peptide level in adult patients after successful repair of coarctation of the aorta

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Abstract

Introduction: The aim of the study was to evaluate BNP in adults after successful surgery of CoAo.
Material and methods: Seventy-four patients after surgery of CoAo entered the study group aged 31.2±9.8 and operated at age 10.4±6.8. The control group consisted of 30 healthy volunteers (18 males) aged 32.2±6.6. 2D and Doppler echocardiography was performed. Patients were divided into two groups: with or without DAo restenosis. All patients underwent an exercise treadmill test. Patients were enrolled in the study if they were found to have untreated HT or if a two-week cessation of hypotensive therapy was possible. In all cases BNP level was measured.
Results: 32 patients showed normal BP while 10 had exercise-induced HT. The remaining patients had chronic HT. The maximal systolic gradient in DAo was comparable in all groups. In 33 patients residual DAo stenosis was noted (DAo+) 36.6±9.8 mm Hg, and in another 41 it was not (DAo–) 15.9±5.1. The maximal transvalvular aortic pressure gradient was 11.7±6.2 mm Hg. BNP in the study group was higher than among controls, though it was higher in the DAo+ subgroup than in the DAo– subgroup. BNP level also correlated with patients' age at the time of operation (R=0.275, P=0.02), and with transaortic gradient (R=0.233, P=0.04).
Conclusions: BNP in adults after CoAo repair is significantly elevated, which may be due to the pressure load of LV.

Key words: BNP, heart failure, GUCH, coarctation of the aorta.

Introduction

Surgical correction of coarctation of the aorta (CoAo) has been carried out successfully for more than fifty years [1-4]. Long-term follow-up has proven that the effects of surgery are better if performed at a younger age [2, 3, 5], though this procedure in infants may result in a higher frequency of residual descendent aorta stenosis [6-11]. In the majority of adults, after CoAo correction, systemic hypertension (HT) is observed and earlier presentation of coronary artery disease (CAD) is also noted, which may lead to heart failure – one of the causes of premature death in this group of patients [2, 3]. Although the majority of patients claim that their exercise capacity is satisfactory, this assessment is subjective and does not fully reflect their clinical status [2, 3, 11]. Serum B-type natriuretic peptide (BNP) level is an accepted diagnostic and prognostic tool in heart failure studies [12-16]. The importance of BNP has been proved in both acute and chronic heart failure, even at the sub-clinical stage [12, 15, 17, 18]. An increase in BNP levels in heart

failure is a well recognized sudden death risk factor [19]. The value of BNP levels has also been documented in some congenital heart diseases [13, 20-25], HT [25, 26] and patients with left ventricle outflow tract obstruction [27-30]. To our knowledge, there have been no previous reports analyzing BNP levels in patients after successful surgery of CoAo.

The aim of the study was to evaluate serum levels of BNP in adults after successful surgery of CoAo, and to find possible correlations between BNP and arterial hypertension, increased left ventricle afterload (described as increased transaortic gradient), residual descending aorta stenosis or patients' age at the time of operation.

Material and methods

Patients were enrolled in the study from among 107 patients after surgical correction of CoAo. Patients qualified for inclusion in the study group if they did not present with evident CAD or diseases of the respiratory system and were psycho-physically capable of performing an exercise test. Seventy-four patients entered the final study group (45 males) aged 19-61 (average 31.2±9.8) operated at age 0.5-34 (average 10.4±6.8). The control group consisted of 30 healthy volunteers (18 males) aged 26-46 (average 32.2±6.6). The majority (65 patients, 88%) had been operated by the same surgeon using the Dacron patch implantation method while 3 (4%) were operated by the subclavian flap method and 6 (8%) by the end-to-end method. In one patient an aortic valve prosthesis (St. Jude 24) had been previously implanted. Eight patients were re-operated owing to descending aorta stenosis, one had undergone a transdermal invasive procedure for the treatment of re-coarctation, and one had an aortic stent graft implanted owing to descending aortic aneurysm. All patients were in the first NYHA functional class and showed sinus rhythm. Serum creatinine levels did not exceed 140 µm/l, and aminotransferase levels were twice below normal range.

Echocardiograms were produced using a General Electrics Vivid 7 echocardiograph, with 2.5 MHz electronic probes in 2D, M and Doppler acquisition modes. The morphology of the heart, left ventricular systolic function using Simpson's formula (normal value was an inclusion criterion) and the degree of valvular insufficiency were assessed (severe aortic insufficiency was an exclusion criterion). Maximum transaortic gradient was estimated (AoGrmax). Residual descending aorta stenosis was assessed in suprasternal view and restenosis was defined as a gradient of at least 25 mm Hg [2]. Based on this measure patients were divided into two groups: those without restenosis in the descending aorta (DAo–) and those with restenosis (DAo+). All studies were conducted by the same echocardiographer, who was blinded with regard to other results.

In order to separate patients with exercise-induced arterial hypertension, all patients underwent a symptom-limited treadmill exercise test using a modified Bruce protocol. Each patient's baseline blood pressure (BP) was measured in the right arm using a mercury manometer. The measurement was repeated immediately after completion of exercise. Exercise-induced hypertension was diagnosed if peak-exercise systolic blood pressure exceeded 200 mm Hg [9] in patients with normal baseline blood pressure. Hypertension was defined according to the ESH/ESC 2003 criteria – BP ≥140/90 [31]. In the study were enrolled those individuals with untreated hypertension or those for whom a two-week cessation of hypotensive therapy was possible.

Serum BNP level was measured using an immunoradiometric method – Shionoria BNP (Schering CIS Bio International).

Data are presented as mean ± standard deviation (x ± SD). The statistical analysis was performed using Student's t-test for independent variables if the data distribution was normal. The Mann-Whitney test was used for dependent variables. Relationships were evaluated using Spearman rank correlation coefficients. Results were considered to be of statistical significance when p level was <0.05.

Software used: STATISTICA for Windows (license no. 6097048609D519).

Results

Thirty-two patients had normal blood pressure (HT-), 10 showed exercise-induced hypertension (HTex), and the remaining 32 suffered from chronic hypertension (HT+). The maximal systolic gradient in DAo was comparable in all groups: HT– patients 25.5±14.0 mm Hg, HTex 30.6±15 mm Hg, HT+ 24.6±13.4 mm Hg. In 33 patients residual descending aortic stenosis was noted (DAo+) 25.0 to 60.2 mm Hg (mean 36.6±9.8 mm Hg), while in the remaining 41 it was not (DAo–) 5.5 to 24.0 mm Hg (mean 15.9±5.1 mm Hg). The maximal transvalvular aortic pressure gradient was from 4.1 to 28.5 mm Hg (mean 11.7±6.2 mm Hg). The serum BNP level in the study group was higher than among controls: 31.05±33.68 vs.10.61±6.3 pg/ml (p=0.0001). In the DAo+ subgroup BNP was higher than in the DAo– subgroup: 41.2±43.8 vs. 23.7±20.8 pg/ml (P=0.02). Differences in BNP levels were also observed in relation to hypertension, though this was not found to be statistically significant: HT+ (35.59±11.02 pg/ml), HT– (28.62±7.78 pg/ml), HTex (25.20±5.07 pg/ml). It was also noted that BNP level positively correlated with patients' age at the time of surgery (R=0.275, P=0.02) (Figure 1), and with transaortic gradients (R=0.233, P=0.04) (Figure 2). However, the level of BNP did not correlate with descending aorta gradients or blood pressure values.

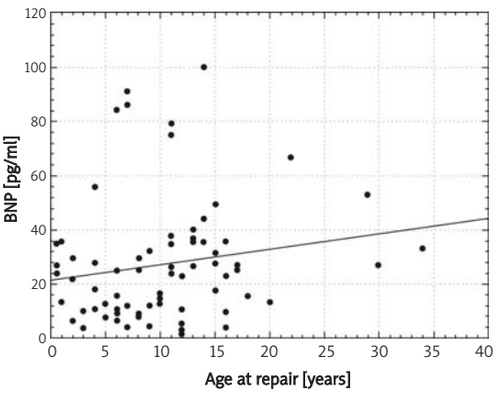

Figure 1. BNP level correlation with patients' age at the time of surgery

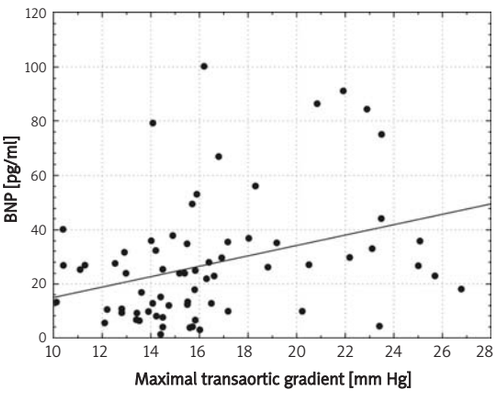

Figure 2. BNP level correlation with maximal transaortic gradient

Discussion

The serum level of BNP in adults after repair of coarctation of the aorta was essentially elevated. Based on the published data it is known that BNP level is raised in patients with hypertension or left ventricle outflow tract (LVOT) obstruction [27-30, 30, 32]. Both abnormalities are often observed in patients after repair of CoAo. Despite continuous progress in paediatric cardio-surgery, it has been shown that hypertension prevalence in this group of patients has not decreased and, according to different authors, reaches 15 to 75% [4-10, 12, 22]. Moreover, in 10 to 56% of patients with normal blood pressure at rest, exertion hypertension is observed [1-3, 7, 9-13]. In this study only a trend in BNP level increase in patients with rest/exertion hypertension was observed, though this finding was not statistically significant. This might be owing to the small number of patients and high range of BNP values in individuals. The range of BNP values may reach up to more than twelve times the maximal normal values specified in the laboratory, which makes an analysis of the clinical significance of BNP very difficult [14-16]. BNP levels did not correlate with blood pressure values, which is consistent with some reports [26] but in opposition to other authors [32]. BNP level was, however, significantly higher in patients with residual pressure gradient in the descending aorta. Furthermore, as in the study of Westerlind and coworkers [33], BNP levels in our population after the repair of CoAo correlated with LVOT gradients. A similar relationship in patients with aortic valve stenosis has been reported by other investigators [27, 29, 30]. Gerber and coworkers [27] reported that, in asymptomatic patients with aortic valve stenosis, an elevated BNP level was observed and that a high baseline value of BNP was an independent risk factor of heart failure progression in short-term follow-up. Increased LVOT pressure gradient causes left ventricular hypertrophy, diastolic dysfunction and finally overt heart failure. One may suppose, along with other investigators, that increase in left ventricle wall tension is a stimulus for BNP production [19, 27, 28, 30]. Investigating the population of patients with different congenital heart defects, Law and coworkers [18] showed that a raised BNP level in this heterogeneous population is related to systemic ventricle wall tension, though this is not dependent on anatomy. In adults after repair of CoAo it is important to consider that aortic branches proximal to the stenosis are stiffened. An early operation of the coarctation will sustain good compliance of the coronary arteries, though diminished reactivity persists [10]. Abnormalities in the coronary arteries are present in 25 to 37% of the population [1, 2, 4, 9]. It is known that elevated BNP level accompanies CAD [16, 34] and thus we cannot exclude CAD as a trigger for the raised BNP in our patients. Moreover, BNP level correlated with age at the time of surgery, which may point to the extent of myocardial damage prior to surgery. This also supports the need for early surgical repair of CoAo [2-4, 9]. Elevated BNP level may also be observed in adults with other congenital heart diseases [20-25]. Mir and coworkers [35] and Bolger et al. [13] noted that raised BNP level in these patients depends on the degree of heart failure and on the anomaly of heart anatomy. None of our patients, analyzed after CoAo repair, manifested overt heart failure. In such situations elevated BNP levels have been considered by some authors to be a marker of occult heart failure [14, 19]. Our results indicate that this group of patients should be closely monitored and offered effective hypertension treatment, and that early invasive treatment should be considered if descending aorta stenosis is present.

In conclusion:

1) the serum BNP level in adults after CoAo repair is significantly elevated;

2) the rise in BNP levels seems to be due to the pressure load of the left ventricle, though myocardial damage prior to surgery cannot be excluded;
3) hypertension does not influence the BNP level in this group of patients.

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