International Journal of Cardiology 212 (2016) 318–323

Contents lists available at ScienceDirect

International Journal of Cardiology

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

B-type natriuretic peptide levels in patients with pericardial effusion undergoing pericardiocentesis☆

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ARTICLE INFO

Article history:
Received 5 January 2016
Received in revised form 29 February 2016
Accepted 19 March 2016
Available online 22 March 2016

Keywords:
B-type natriuretic peptide
Pericardial effusion
Pericardiocentesis

ABSTRACT

Objectives: Pericardial effusion is characterized by progressive accumulation of fluid within the pericardial space, resulting in increased intra-pericardial pressure and compression of the heart. As B-type natriuretic peptide (BNP) is secreted by the ventricles in response to increased myocardial stretch, we hypothesized that pericardial effusion, as well as its resolution, might influence BNP plasma levels.

Methods: We prospectively measured, in 146 consecutive patients with pericardial effusion, BNP plasma levels at baseline, soon after, and 24 h after pericardiocentesis. A scoring system based on 7 clinical and echocardiographic parameters was developed, and patients were classified according to the number of variables as having low (0–2), intermediate (3–4), or high (5–7) severity score.

Results: Out of the 146 patients, 42 (29%) had normal values (<100 pg/ml), whereas 104 (71%) had high BNP values at baseline. In the whole population, baseline BNP levels significantly decreased as the severity score increased ($r = -0.21$; $P = 0.01$). 24 h after pericardiocentesis, a significant increase in BNP was observed in patients with intermediate ($P = 0.004$) score and with high ($P < 0.001$) severity score; no increase occurred in low score patients ($P = 0.56$). The higher was the severity score, the steeper was the increase in BNP through the three time-points considered ($P = 0.04$).

Conclusions: The results of the present study show that BNP plasma levels are suppressed in the presence of severe pericardial effusion, and that they rise after pericardiocentesis. Future studies should investigate the role of BNP in assisting clinicians in the decision-making process of pericardial fluid drainage.

1. Introduction

Pericardial effusion is a condition characterized by the slow or rapid accumulation of fluid within the pericardial space resulting in impaired diastolic filling and cardiac output caused by increased intra-pericardial pressure [1–4]. Several systemic, cardiac, and pericardial diseases may cause pericardial effusion [1–3]; moreover, all interventional procedures, such as percutaneous coronary intervention, transcatheter aortic valve implantation, pacemaker/implantable cardioverter defibrillator implantation, and arrhythmias ablation, are emerging causes of pericardial effusion and cardiac tamponade [5–7]. Early recognition of echocardiographic and clinical signs of cardiac tamponade is of critical relevance since pericardial effusion can be life-threatening if not resolved by elective or urgent percutaneous or surgical drainage of the pericardium.

In patients with cardiogenic shock, immediate pericardiocentesis is mandatory and life-saving. Conversely, in patients without shock, where symptoms and signs may be misleading due to their low sensitivity and specificity, a score system may help to assist clinicians to guide indication for pericardial drainage [8]. The proposed scoring systems applied for the triage of pericardial effusion are based on effusion size and on echocardiographic and clinical assessment of hemodynamics [8–11]. To date, however, no cardiac biomarker has been widely investigated, in addition to the established clinical and echocardiographic parameters, in terms of an adjunctive tool to discriminate cases of pericardial effusion with uncertain indication to mechanical drainage.

B-type natriuretic peptide (BNP) is a neurohormone secreted by the ventricles in response to increased wall tension or other myocardial stresses [12,13]. The presence of pericardial effusion, as well as its resolution, might influence BNP plasma levels. On the one hand, BNP production could be suppressed by the constraining effect of the fluid that burdens around the heart, despite the increased intra-cardiac pressure. On the other hand, it should possibly increase in response to fluid drainage and recovery in ventricular distensibility. To our knowledge, the BNP behavior in patients with pericardial effusion has been investigated

☆ All authors take responsibility for all aspects of the reliability and freedom from bias of the data presented and their discussed interpretation.

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http://dx.doi.org/10.1016/j.ijcard.2016.03.075
0167-5273/

only in two small series, producing controversial results [14,15]; therefore, its potential value to help clinical decision remains thus far undefined.

In this observational study, we prospectively measured BNP plasma levels in a consecutive, unselected cohort of patients undergoing pericardiocentesis, and we evaluated its potential capacity to reflect pericardial effusion severity.

2. Methods

2.1. Study population

This prospective, observational study was conducted at Centro Cardiologico Monzino, between January 9th, 2004 and February 23th, 2015. We enrolled all consecutive patients undergoing drainage of pericardial effusion by pericardiocentesis, for both diagnostic and/or therapeutic purposes. Patients requiring emergency pericardiocentesis for cardiac arrest, as well as those requiring mechanical ventilation or other pharmacological and/or mechanical circulatory support, and those experiencing any major peri-procedural complication were excluded from the study

The study protocol conforms to the ethical guidelines of the 1975 Declaration of Helsinki, the study was approved by the Ethics Committee of our Institute, and informed consent was obtained from all patients.

2.2. Study protocol

In all patients, BNP was measured before, soon after (within 1 h) pericardiocentesis, and at 24 h, by an automated immunochemiluminescent assay for BNP (Alere TRIAGE® BNP Test for Beckman Coulter® Immunoassay System). A decision limit of <100 pg/mL was used to identify normal values [16]. The total coefficients of variation for BNP determination were no greater than 6.6%

An echocardiographic evaluation was performed in all patients before pericardiocentesis and the following variables were collected [17]: left ventricular ejection fraction (LVEF), end-diastolic pericardial effusion size, right atrial collapse (invagination of the right atrial wall occurring in late diastole and early systole), right ventricular collapse (invagination of the right ventricular free wall occurring in early diastole), inferior cava vein plethora (>2 cm) with lack of inspiratory collapse (<50%), and abnormal inspiratory decrease of mitral valve flow (>40%) at Doppler analysis.

Based on echocardiographic and clinical evaluation, a simple bedside scoring system, adopted in the daily clinical practice in our Institute, and including 7 variables, was used. A value of 1 was assigned when a factor was present, and 0 when it was absent. For each patient, the score was calculated as the sum of the number of variables (range 0–7) recorded before pericardiocentesis initiation. The following clinical and echocardiographic variables were included in the score: 1) systolic arterial blood pressure ≤ 100 mm Hg; 2) heart rate ≥ 100 beats/min; 3) at least one clinical sign or symptom among oliguria (<0.5 ml/kg/h in the preceding 6 h), Stage 1 acute kidney injury in the previous 72 h, defined according to the Acute Kidney Injury Network classification [18], pulsus paradoxus >10 mm Hg, or dyspnea at rest; 4) right atrial collapse; 5) right ventricular collapse; 6) absence of cava vein collapse during inspiration; 7) severe circumferential pericardial effusion (>2 cm in diastole). The score was calculated by two independent physicians (C.R. and M.R). Inter-observer agreement was very good (Cohen's Kappa > 0.9 for all parameters). According to the resulting score, patients were classified as with low (0–2), intermediate (3–4), or high (5–7) severity score.

2.3. Pericardiocentesis

Expert operators performed pericardiocentesis by a percutaneous puncture under echocardiographic and/or fluoroscopic guidance, according to the more suitable approach (sub-xiphoid or thoracic intercostal). A pig-tail catheter was then inserted for drainage of the effusion. In patients treated with oral anticoagulants, warfarin was temporary withdrawn, and pericardiocentesis was performed when an INR < 1.5 value was achieved, if feasible.

2.4. Statistical analysis

Continuous variables are presented as mean ± SD, and they were compared using the *t*-test for independent samples. Variables not normally distributed are presented as median and interquartile ranges (IQR), and they were compared with the Wilcoxon Rank-Sum test. Categorical variables were compared using the chi-square test or the Fisher's exact test, as appropriate. Because BNP values showed a non-normal distribution, they were transformed into the natural logarithm.

Pearson correlation was used to detect possible correlations between BNP and clinical factors at different measurement times. Trends of variation of BNP from baseline to the two time-points after pericardiocentesis (slope) were assessed by linear regression analysis and were correlated with the severity score groups (low vs. intermediate vs. high) by Pearson correlation. General linear model analysis was used to assess whether the severity score independently predicted trends of BNP variation from baseline to 24 h after pericardiocentesis.

All tests were two-sided, and a P value < 0.05 was required for statistical significance. All calculations were computed with the SAS software package (V. 9.4, SAS Institute Inc., Cary, NC).

3. Results

A total of 146 patients (mean age 65 ± 14 years, 81 men) undergoing pericardiocentesis were enrolled in this study (Table 1).

The median baseline BNP level in the whole population was 195 (IQR 90–319) pg/ml. It was not different in patients who developed pericardial effusion acutely (<7 days) and chronically (>7 days, or unknown; 257 [IQR 129–577] pg/ml vs. 188 [IQR 86–318] pg/ml, respectively; P = 0.11). Out of the 146 patients, 42 (29%) had normal (<100 pg/ml) BNP levels at baseline, whereas 104 (71%) had high BNP values. The baseline characteristics of patients with normal and high BNP levels are shown in Table 2. Patients with high BNP levels were older, had lower LVEF and higher serum creatinine concentration (sCr); moreover, they were more likely to have atrial fibrillation.

In the study population, baseline BNP levels significantly decreased as the severity score increased (Fig. 1). Moreover, progressively lower baseline BNP levels were found going from score 0 to score 7 (P = 0.05 for trend). An inverse relationship between baseline BNP and the severity score (low vs. intermediate vs. high) was found (r = −0.21; P = 0.01). After adjustment for age, LVEF, sCr, and atrial fibrillation, the severity score still inversely correlated with baseline BNP (r = −0.20; P = 0.01).

The percentage of patients showing an increase in BNP levels soon after pericardiocentesis and at the 24-h evaluation is shown in Fig. 2.

Table 3 shows univariate correlates of BNP increase from baseline to the two time-points considered after pericardiocentesis, in terms of both absolute changes and overall trend (slope). In particular, at 24 h, significant correlations between BNP increase and severity score, absence of cava vein collapse, and trans-mitral flow variation were found. Moreover, when the BNP increase slope among the three points was considered, significant direct correlations with the severity score and with the total removed fluid volume were found.

Baseline and post-pericardiocentesis BNP values in patients grouped according to the severity score are shown in Fig. 3. A significant increase in BNP was observed in patients with an intermediate score and, to a greater extent, in those with a high severity score. Conversely, no change occurred in low severity score patients. The higher was the severity score the steeper was the increase in BNP levels through the three time-points considered, with a significant difference in BNP trends among the three groups (Fig. 4). Notably, the severity score independently predicted BNP