ELSEVIER

The Journal of Heart and Lung Transplantation

http://www.jhltonline.org

N-terminal pro–B-type natriuretic peptide for monitoring after balloon pulmonary angioplasty for chronic thromboembolic pulmonary hypertension

Steffen D. Kriechbaum, MD,[a,b,1] Christoph B. Wiedenroth, MD,[c,1] Jan Sebastian Wolter, MD,[a,b] Regula Hütz,[a,b] Moritz Haas, MD,[a,b] Andreas Breithecker, MD,[d] Fritz C. Roller, MD,[e] Till Keller, MD,[a,b] Stefan Guth, MD,[c] Andreas Rolf, MD,[a,b,f] Christian W. Hamm, MD,[a,b,f] Eckhard Mayer, MD,[c] and Christoph Liebetrau, MD[a,b,f]

From the [a]Department of Cardiology, Kerckhoff Heart and Thorax Center, Bad Nauheim, Germany; [b]German Center for Cardiovascular Research, Partner Site Rhine-Main, Frankfurt am Main, Germany; [c]Department of Thoracic Surgery, Kerckhoff Heart and Thorax Center, Bad Nauheim, Germany; [d]Department of Radiology, Gesundheitszentrum Wetterau, Bad Nauheim, Germany; [e]Department of Radiology, Justus Liebig University Giessen, Giessen, Germany; and the [f]Medical Clinic I, Division of Cardiology, Justus Liebig University Giessen, Giessen, Germany.

KEYWORDS:
NT-proBNP;
BPA;
CTEPH;
biomarker;
non-invasive monitoring

BACKGROUND: Balloon pulmonary angioplasty (BPA) is an emerging interventional treatment option for chronic thromboembolic pulmonary hypertension (CTEPH). The non-invasive monitoring of CTEPH patients is a clinical challenge. In this study we examined changes in N-terminal pro–B-type natriuretic peptide (NT-proBNP) in patients undergoing BPA for inoperable CTEPH and related them to peri-procedural success.

METHODS: In this study we analyzed a total of 51 consecutive patients who underwent BPA treatment and completed a 6-month follow-up (6-MFU) between March 2014 and March 2017. Serum samples for NT-proBNP measurement were collected before every BPA and at 6-MFU.

RESULTS: The 51 patients underwent 265 interventions involving angioplasty of a total of 410 vessels. The 6-month survival rate was 96.1%. The baseline (BL) mean pulmonary artery pressure (PAP) was 39.5 ± 12.1 mm Hg, pulmonary vascular resistance (PVR) was 515.8 ± 219.2 dynes/s/cm^5 and the median NT-proBNP level was 820 (153 to 1,871.5) ng/liter. At BL, World Health Organization functional class (FC) was ≥III in 96.1% of the patients, whereas, at 6-MFU, 11.8% were in WHO FC ≥III. At 6-MFU, mean PAP (32.6 ± 12.6 mm Hg; $p < 0.001$), PVR (396.9 ± 182.6 dynes/s/cm^5; $p < 0.001$) and NT-proBNP (159.3 [84.4 to 464.3] ng/liter; $p < 0.001$) levels were reduced. The decrease in NT-proBNP levels correlated with the decrease in mean PAP ($r_{rs} = 0.43$, $p = 0.002$) and PVR ($r_{rs} = 0.50$, $p = 0.001$). A reduction in the NT-*pro*BNP level of 46% indicated a decrease in mean PAP of ≥25% (area under the curve [AUC] = 0.71) and a reduction of 61% indicated a decrease in PVR of ≥35% (AUC 0.77).

CONCLUSIONS: Our results demonstrate that NT-proBNP levels decrease after BPA, providing valuable evidence of procedural success. NT-proBNP measurement allows identification of patients who are BPA

[1]These authors have contributed equally to this study.

Reprint requests: Steffen Kriechbaum, MD, Department of Cardiology, Kerckhoff Heart and Thorax Center, Benekestrasse 2-8, 61231 Bad Nauheim, Germany. Telephone: +49 6032 996 2246. Fax: +49 6032 996 2313.

E-mail address: s.kriechbaum@kerckhoff-klinik.de

https://doi.org/10.1016/j.healun.2017.12.006

non-responders and may thus be a valuable adjunct in therapy monitoring.
J Heart Lung Transplant 2018;37:639–646

Chronic thromboembolic pulmonary hypertension (CTEPH) is diagnosed in about 0.1% to 9% of all patients surviving acute pulmonary embolism.[1] The persistence of thrombotic material leads to obstruction of the pulmonary arteries, which compounded by secondary inflammation, cell proliferation and vascular remodeling.[1–3] The result is an elevated pulmonary artery pressure (PAP) and pulmonary vascular resistance (PVR), resulting in long-term impairment of pulmonary hemodynamics and right heart function accompanied by a poor prognosis.[4] The currently established therapy is pulmonary endarterectomy (PEA), a potentially curative approach[1]; however, in up to one third of patients, PEA is not feasible and not indicated, mostly due to the presence of peripheral lesions.[5] For these patients, medical treatment with riociguat is recommended,[1] with balloon pulmonary angioplasty (BPA) considered an emerging interventional treatment option.[6–9]

In the context of CTEPH treatment, natriuretic peptides have predictive value for right ventricular recovery after PEA.[10,11] N-terminal pro-hormone B-type natriuretic peptide (NT-proBNP) has been established as a biomarker in various cardiovascular diseases.[12,13] Its release is related to ventricular wall stress and/or myocardial ischemia/hypoxia, and it is mainly used for diagnosis and predicting the prognosis of patients with acute and chronic heart failure.[12–14]

Elevated NT-proBNP concentrations in CTEPH patients undergoing PEA or BPA have proven to be mostly reversible, except in patients developing chronic right heart failure.[10,11,15] In this context, serial measurement of NT-proBNP in patients undergoing BPA can be used to identify patients at risk. Whereas natriuretic peptides have proven to be reliable markers in the diagnostics and monitoring of patients with systolic heart failure, data for CTEPH patients undergoing BPA are limited.[6,12,15–17] The best time-point to determine NT-proBNP remains unclear: BPA is a staged procedure, and early changes in NT-proBNP after BPA are not well described. The knowledge of NT-proBNP concentrations after BPA could aid the interpretation of postprocedural findings, in particular decreased PAP, improvement of right heart function. This might increase the accuracy of risk stratification in these patients.

The aim of our study was to characterize the time course of NT-proBNP concentrations in patients undergoing BPA as a staged procedure and to determine the value of NT-proBNP as a marker for dynamics of PAP and PVR in the peri-procedural episode and at 6-month follow-up.

Methods

Study population

The present study included 51 consecutive patients who were treated by BPA at the Kerckhoff Heart and Thorax Center and completed a 6-month follow-up (6-MFU) after the final BPA treatment between March 2014 and March 2017. Pre- and post-procedural management data of the patients were recently published.[6,18] In brief, clinical examination, echocardiography, 12-lead electrocardiography (ECG), laboratory tests, 6-minute walk tests, ventilation–perfusion scan, computed tomographic (CT) angiography, right–left heart catheterization and pulmonary angiography were assessed for all patients. The final diagnosis of CTEPH was made according to the current guidelines.[1,19] All patients were presented in an interdisciplinary CTEPH conference to define the therapeutic concept. In this course, it is crucial to assess the technical operability with regard to the localization of the target lesions and the operability in dependence to the patients' comorbidities. BPA was performed as a staged procedure according to standard clinical practice by a dedicated BPA team (interventional radiologist, cardiologist, thoracic surgeon). Between the BPA procedures follow-up examinations were performed that were adjusted to the individual requirements of each patient, always including re-evaluation of clinical status and laboratory findings. Finally, an in-house follow-up examination was performed 6 months after the last BPA procedure.

All patients enrolled in the study gave written informed consent, which included consent for biomarker analyses. The ethics board of the Justus Liebig University of Giessen approved the study (AZ 43/14).

Balloon pulmonary angioplasty

BPA was performed as staged procedure under smooth sedation using femoral or jugular access. A 6F sheath (Vista Brite Tip, Johnson & Johnson, Fremont, CA) was placed in the pulmonary artery, and a 6F guiding catheter (mostly MB1 Launcher, Medtronic, Minneapolis, MN, or JR 4, Dublin, Ireland) was inserted into the pulmonary artery to selectively intubate the obstructed segmental arteries. During the procedure, patients received heparin intravenously at 100 IE/kg to maintain an activated clotting time >250 seconds. The guide-wire (Run-through NS-PTCA, Terumo, Tokyo, Japan) was placed into the sub-segmental arterial branches, passing the obstructing endoluminal material. The sub-segmental branches were then dilated by multiple inflations of semi-compliant balloons (Emerge 2.0/20 mm, 3.0/20 mm and 4.0/20 mm, Boston Scientific, Marlborough, MA). A final fluoroscopy documented the post-procedural morphologic result.

Right heart catheterization

Right heart catheterization (RHC) was performed as a part of the diagnostic work-up.[1] In all BPA patients, RHC was repeated 6 months after the last BPA procedure. RHC was routinely performed via the right internal jugular vein using a 6F sheath and a standard Swan–Ganz catheter. Medication of the patients was not modified before or during RHC; in particular, no vasoactive agents were administered.