Less traditional indications for NT-proBNP assessment

Radek Pudil
Charles University Prague
Department of Cardiology
Faculty Hospital
Hradec Králové, Czech Republic

Current indications for natriuretic peptide assessment:

Assessment of NPs provides information about functional status of myocardium

NPs assessment is very helpful in:

- **diagnostic process**
  - **rapid and accurate diagnosis of myocardial dysfunction, differential diagnosis in dyspnea patients**
- **risk stratification and prognostic tool in pts with:**
  - **acute heart failure, prediction of HF worsening**
  - **acute coronary syndromes**
  - **valvular disordes**
  - **selection pts for heart transplantation**
- **NP guided therapy:**
  - **risk stratification for PAE**
  - **therapy of heart failure**

NPs and COPD:

Use of B-type natriuretic peptide in the risk stratification of acute exacerbations of COPD

- **BNP in 208 consecutive pts with an acute exacerbation of COPD (2-year follow-up)**
- **BNP was significantly elevated during the acute exacerbation compared to recovery *(65 pg/mL vs. 45 pg/mL; p < 0.001)*, particularly in patients treated in ICU *(105 pg/mL; IQR, 66 to 553 pg/mL; vs 60 pg/mL; IQR, 31 to 169 pg/mL; p = 0.007)***
- **BNP > 100 pg/mL predicted the need for ICU care *(HR 1.13; CI: 1.03 -1.24 for an increase in BNP of 100 pg/mL; p = 0.008)***
- **This study showed the potential of BNP levels to predict short-term and long-term mortality rates (areas under the curve were 0.55, SD, 0.71; 95% CI, 0.41 to 0.68, and 0.56, SD, 0.53; 95% CI, 0.45 to 0.66, respectively)**

Stolz D et al. Chest 2008;133(5):1088-94

NPs and pulmonary artery embolism:

NT-proBNP and right ventricle dysfunction:

Significant increase of NT-proBNP was found in almost all pts with clinically significant PAE.

Increase of NT-proBNP above 500 pg/mL in acute phase is associated with increased rate of complications, lower levels are associated with lower rate of complication, shorter time of hospitalization and have better prognosis.

Elevation of NP was described also in pts with precapillary pulmonary hypertension, where can predict mortality.

Summary:

Elevated levels of NP and acute dyspnea can be present not only in pts with LV failure, but also in pts with right ventricular overload in the course of acute PE.

Pruszyk P et al.Eur Resp. J 2003, 22(4): 649-653.

NPs and pulmonary artery hypertension:

NT-proBNP as indicator of severity disease and mortality predictor in patients with PAH

plasma NT–pro-BNP in 61 pts with various forms of chronic precapillary PH, follow-up 25 months

baseline NT–proBNP was an independent predictor of mortality: pts with NT-proBNP above median (168pmol/L) had significantly higher mortality ($p<0.001$)

Andreassen A et al. Am J Cardiol 2006;98:525–529

Serum N-terminal brain natriuretic peptide as a prognostic parameter in patients with pulmonary hypertension

55 pts with severe PH, follow-up 36 months (serial 6MWT, RV catheterization, echocardiography)

NT-proBNP is related to the right heart morphology and dysfunction in PH patients

NT-proBNP level of 1,400 pg/mL was found to be useful in identifying patients with poor long-term prognosis both in the whole studied group and in the IPAH subgroup

Fijalkowska A et al. Chest. 2006;129:1313-1321

NPs and pulmonary artery hypertension:

Role of N-terminal brain natriuretic peptide (NT-proBNP) in scleroderma-associated PAH

109 pts with SSc (- 68 with PAH), evaluation: NT-proBNP, 6MWT, haemodynamics and echocardiography, follow-up 10 months

NT-proBNP in pts with PAH: 1474 pg/mL (SD 2642) (P = 0.0002) vs. 139pg/mL (SD 151)

increase in NTproBNP for every order - four-fold increased mortality

NT-proBNP correlated positively with mean PAP (r = 0.62; P < 0.0001), pulmonary vascular resistance (PVR) (r = 0.81; P < 0.0001), and inversely with SMWD (r = -0.46; P < 0.0001)

NT-proBNP level correlated with NYHA class

SSc pts with NT-proBNP > 395pg/mL have a very high probability of PAH

baseline and serial changes in N-TproBNP are highly predictive of survival

Williams MH. Eur Heart J 2006;27(12):1485-94.

NPs and liver cirrhosis:

NT-proBNP and BNP in patients with cirrhosis: relation to cardiovascular dysfunction and severity of disease

51 pts with liver cirrhosis, haemodynamic evaluation

NT-proBNP and BNP were increased in pts with liver cirrhosis

NT-proBNP and BNP were related to severity of liver disease (Child score, serum albumin, coagulation factors 2, 7, and 10, and hepatic venous pressure gradient) and to markers of cardiac dysfunction (QT interval, heart rate, plasma volume)

Plasma NT-proBNP (pmol/L)	Cirrhosis, Child group			Healthy controls
	A	B	C	
Mean (SD)	10.0* (1.7)	20.7* (4.8)	23.9* (5.7)	2.2 (0.4)
Median (range)	10 (0-22)	17 (20-62)	19 (1-58)	(0-16)

Henriksen JH et al. Gut. 2003 October; 52(10): 1511–1517.

NPs and haemodialysis:

Cardiac biomarkers and survival in haemodialysis patients

cTnT and NT-proBNP in 134 haemodialysis pts (before and after a dialysis session), follow-up 36months

cTnT > 0.03 ng/mL in 39.6% of all pts (hypervolemic pts higher cTnT levels compared to euvolaemic (median 0.054 ng mL, interquartile range: 0.019 – 0.153 vs. 0.005 ng/mL < 0.001 – 0.034; *P* < 0.001)

NT-proBNP increased in all pts (median 4524; IQR: 2000 – 10 250 pg/mL)

in hypervolemic pts, NT-proBNP was significantly higher (11 988 pg/mL, IQR: 5307 – 19 242 vs. 3247 pg/mL, 1619 – 5574, p < 0.001)

ROC: a threshold of cTNT > 0.026 ng/mL and NT-proBNP > 5300 pg/mL as predictors of hypervolaemia

multivariate analysis documented that elevated cTNT and NT-proBNP levels were highly predictive for cardiovascular events.

Eur J Clin Invest 2007; 37 (5): 350–356

NPs and peritoneal dialysis:

NT-proBNP and left ventricular dysfunction in continuous ambulatory peritoneal dialysis patients

30 stable CAPD patients, NT-proBNP, extracellular water (ECW) and left ventricular dysfunction

NT-proBNP 3924 (240 - 74460) pg/mL in all group, no differences in terms of age, gender, presence of DM

NT-proBNP correlated positively with LVMI ($r = 0.628$, $p = 0.003$) and negatively with LV ejection fraction ($r = -0.479$, $p = 0.033$)

no correlation between NT-proBNP and ECW% ($r = 0.227$, $p = 0.25$)

stepwise regression analysis: LV ejection fraction (beta = -0.610, $p = 0.015$) and LVMI (beta = 0.415, $p = 0.007$) were independently associated with the serum NT-proBNP concentration

Lee JA et al. Perit Dial 2006;26(3):360-5

NPs and muscular dystrophies:

NT-proBNP and LV function in patients with muscular dystrophies (MD)

LV dysfunction (LVD) is a clinical manifestation of muscular dystrophy in adults and an important prognostic factor

24 pts with MD (dystrophinopathies - Duchenne, Becker, Stenert myotonic dystrophy, limb-girdle myopathies, facioscapulohumeral myopathies and dysferlinopathy (Miyoshi myopathy)

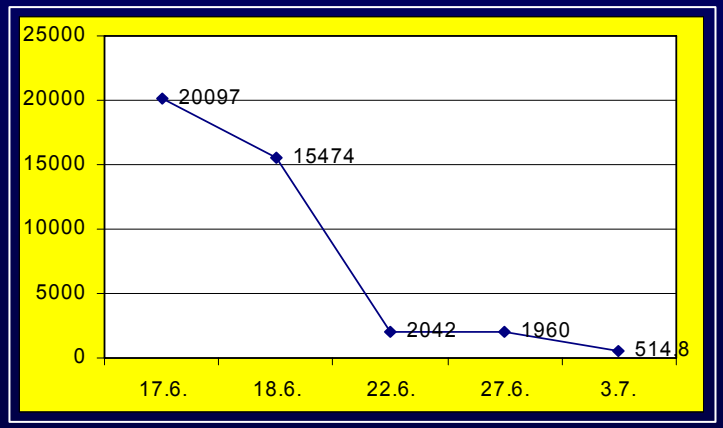
ECG abnormalities were present in 58.3% pts

systolic LVD or left ventricular remodeling in 25% pts

NT-proBNP elevated in 12.5% pts (75% of pts with LVD)

Martins et al.Rev Port Cardiol 2005;24(1):23-35

NT-proBNP in 31 y/o men with Becker dystrophy



Pudil R et al. Acta Medica 2007;50(1):51-6.

NPs and cardiotoxicity detection:

NT-proBNP and left ventricle mass in children treated with anthracyclines

- 19 children pts (an equivalent of doxorubicin dose 240 mg/m^2),
- high prevalence of reduced LVM associated with increased NT-proBNP levels was found
- the average LVM value was 14.4% lower than expected, whereas fourteen patients (73%) had a lower LVM than predicted
- NT-pro BNP in pts with reduced LVM was significantly higher 0.316±0.02 vs 0.17 ± 0.01 pmol/ml, p =0.009
- a cut off NT-proBNP 0.2 pmol/ml was able to differentiate patients with LVM reduction from those with normal or greater than expected LVM

The association of higher NT-proBNP levels with reduced LVM in asymptomatic children after anthracycline administration could be an early indication of subclinical cardiotoxicity.

Germanakis I et al. Int J Cardiol 2006; 108: 212 – 215 .

NPs and cardiotoxicity detection:

NT-proBNP during preparative regimen and hematopoietic cell transplantation in patients with AML

23 patients treated with acute leukemia (20 AML, 3 ALL)

cumulative anthracycline dose: 452.2 ± 87.9 mg/m^2 (median 429.0)

PR: Bu/HD-C	D -7	D -6	D -5	D -4	D -3	D -2	D -1	D 0
Bu 4 mg/kg/day	●	●	●	●				
HD-C 60 mg/kg/day					●	●		
HCT								●

PR: TBI/HD-C	D -7	D -6	D -5	D -4	D -3	D -2	D -1	D 0
TBI 12 Gy (8x 1.5 Gy)			● ●	● ●	● ●	● ●		
HD-C 60 mg/kg/day	●	●						
HCT								●

Horacek JM, Pudil R Exp. Oncol 2007, 29: 43–247

NPs and cardiotoxicity detection:

NT-proBNP during preparative regimen and hematopoietic cell transplantation in patients with AML

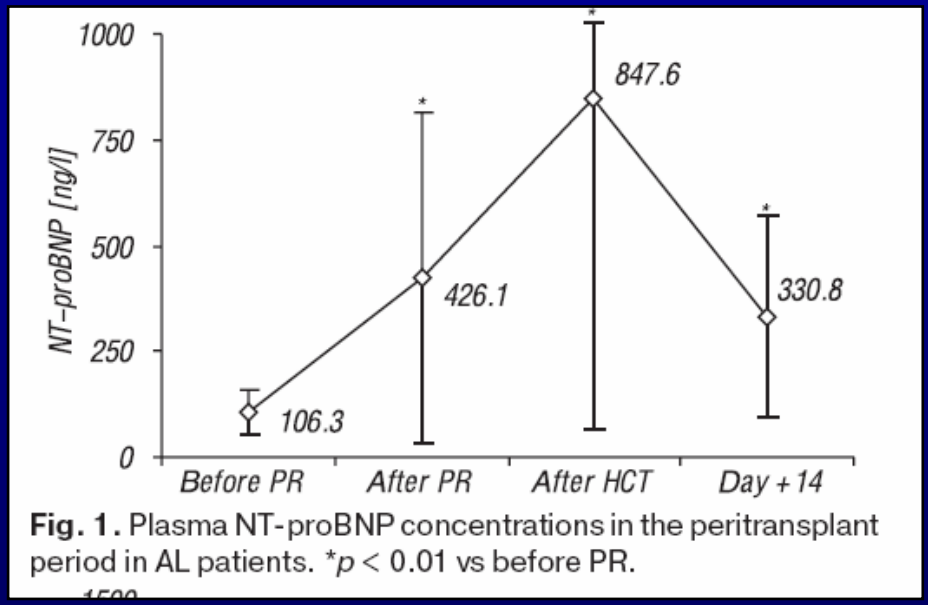


Fig. 1. Plasma NT-proBNP concentrations in the peritransplant period in AL patients. *$p < 0.01$ vs before PR.

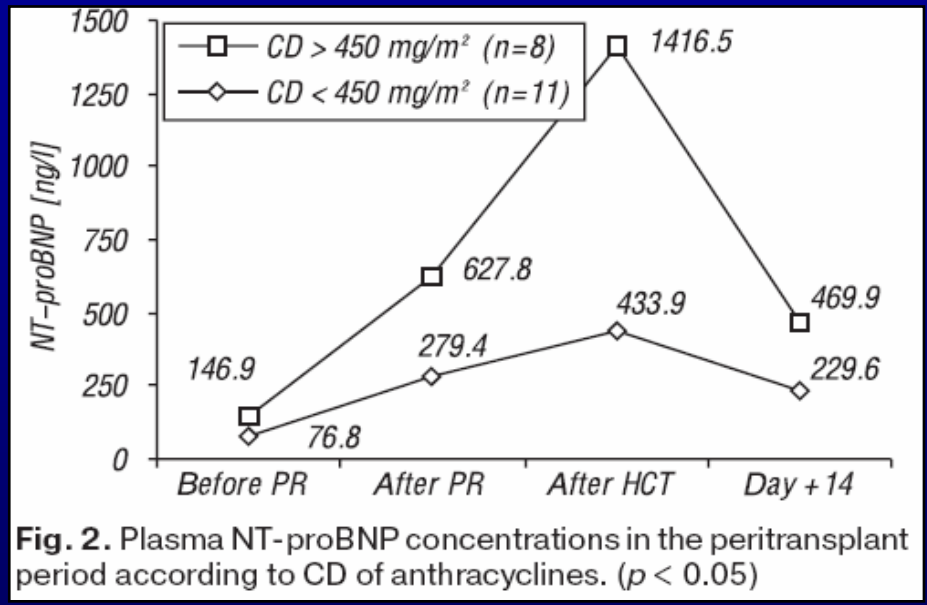


Fig. 2. Plasma NT-proBNP concentrations in the peritransplant period according to CD of anthracyclines. ($p < 0.05$)

Horacek JM, Pudil R Exp. Oncol 2007, 29: 43–247

NPs and cardiotoxicity detection:

NT-proBNP during preparative regimen and hematopoietic cell transplantation in patients with AML

Cardiac biomarkers	1 day before PR	6 h after PR	24 h after PR	1 day after HCT	14 days after HCT
Myoglobin above 76.0 μg/L	0	0	0	0	0
CK-MB mass above 4.80 μg/L	0	0	0	0	0
cTnT above 0.01 μg/L	0	0	0	0	0
cTnI above 0.40 μg/L	0	0	0	0	0
H-FABP above 4.50 μg/L	0	0	0	0	1 (4.8%)
GPBB above 7.30 μg/L	0	5 (23.8%)	5 (23.8%)	4 (19.0%)	2 (9.5%)

PR, preparative regimen; HCT, hematopoietic cell transplantation; CK-MB, creatine kinase MB; H-FABP, heart-type fatty acid binding protein; GPBB, glycogen phosphorylase isoenzyme BB.

***Horacek JM, Tichy M, Pudil R Clin Chem Lab Med 2008*;46(1):148–149**

echoparameters (n=19)	before PR and HCT	after PR and HCT	p
EF [%]	63.4 ± 1.9	61.4 ± 3,5	< 0.05
FS [%]	33.7 ± 2.4	33.7 ± 2.4	NS
systolic LV dysfunction	0	1 (5.3 %)	NS
diastolic LV dysfunction	3 (15.8 %)	6 (31.6 %)	NS
pericardial effusion	4 (21.1 %)	6 (31.6 %)	NS

Horacek JM, Pudil R Exp. Oncol 2007, 29: 43–247

NPs and preeclampsia:

Natriuretic peptides and hemodynamics in preeclampsia

The purpose of this study was to evaluate the relationship between natriuretic peptides (NT-proANP and NT-proBNP) and hemodynamic parameters in preeclampsia.

a cross-sectional study of 19 preeclamptic, 15 chronic hypertensive, and 26 normotensive women in the third trimester of pregnancy

(systolic, diastolic and mean BP, stroke index, heart rate, cardiac index, systemic vascular resistance index)

NT-proANP and NT-proBNP concentrations were significantly higher in preeclamptic women compared to chronic hypertensive and normotensive pregnancies

in preeclampsia NT-proANP correlated significantly with SAP and SVRI

NT-proBNP correlated significantly with SVRI and CI

NT-proANP and NT-proBNP concentrations in preeclampsia reflect high afterload, rather than the function of the heart expressed as SI or CI

Tihtonen KM et al. Am J Obstet Gynecol 2007;196(4):328.

NPs and fetus growth restriction:

Cardiovascular hemodynamics and umbilical artery NT-proBNP in human fetuses with growth restriction

hypothesis: Is fetal NT-proBNP secretion increased in proportion to the severity of fetal cardiovascular compromise in intrauterine growth restriction?

42 growth-restricted fetuses:

fetuses with normal umbilical artery velocimetry (UA)

fetuses with abnormal UA velocimetry and normal ductus venosus (DV) velocimetry

fetuses with abnormal UA and DV velocimetry – the highest NT-proBNP level.

Doppler ultrasonographic examination of cardiovascular hemodynamics within 7 days before delivery

Results:

significant positive correlations were found between UA, DV and LHV PIVs and UA NT-proBNP concentrations

in human fetal growth restriction, increased cardiac afterload and pulsatility in DV blood velocity waveform pattern are associated with elevated UA NT-proBNP concentrations.

Girsen A et al. Ultrasound Obstet Gynecol 2007;29(3):296-303

Clinical significance of NPs assessment in primary non-cardiac patients:

Plasma NP levels are increased not only in heart failure patients, but also in a broad spectrum of diseases, where cardiovascular system is involved into the pathophysiology.

We have data about cardiovascular involvement in renal failure patients (haemodialysis/peritoneal dialysis), COPD patients, pts with pulmonary artery hypertension and PAE, neurological disorders (muscular dystrophies), chemotherapy, preeklampsia, fetal growth restriction etc.

Assessment of NPs can be very useful tool in diagnostic process, risk stratification and prognosis assessment in these groups of patients.


Thank You for Your attention..