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Decoding right heart function after congenital heart defects repair: NT proBNP in time perspective

Abstract

Objective: To evaluate the relationship between serum NT-proBNP levels and transthoracic echocardiographic (TTE) parameters of right ventricular (RV) function in patients who underwent surgical correction of congenital heart defects (CHD), comparing early (≤10 years post-surgery) and late (>10 years post-surgery) follow-up groups.

Methods: This cross-sectional study included 98 patients divided into two groups based on the time elapsed since surgical correction of CHD. NT-proBNP serum concentrations were measured, and TTE was used to assess RV size and function, including TAPSE, FS-RVOT, RV FAC, TAI index, and tissue Doppler parameters (S', E'/A'). Statistical analyses included correlation coefficients and linear regression models.

Results: In the early postoperative group, NT-proBNP showed significant negative correlations with TAPSE (p=0.0001), FS-RVOT (p=0.003), RV FAC (p=0.008), TAI index (p=0.023), and S' (p=0.002). A positive correlation was noted with mPAP (p=0.032). Linear regression demonstrated TAPSE = 17.04 - 0.001*NT-proBNP (R^2=0.259, p<0.0001). In the late group, NT-proBNP correlated only with TAI index (p=0.005) and showed no significant correlation with other TTE parameters.

Conclusion: NT-proBNP is a useful marker of RV dysfunction within the first decade after CHD surgery but loses predictive power beyond 10 years postoperatively, except for TAI index. Long-term follow-up should incorporate both biomarkers and advanced imaging to detect subclinical RV dysfunction.

Keywords: right ventricle, congenital heart defect, NTproBNP, echocardiography, follow up

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Introduction

Congenital heart defects (CHDs) often require surgical correction early in life. Despite successful initial correction, many patients face long-term complications related to right ventricular (RV) performance. NT-proBNP is a neurohormonal marker of myocardial stress. Several studies highlight its value in predicting adverse outcomes post-CHD surgery, especially in the context of volume and pressure overload on the RV.[1-4] This study aims to compare NT-proBNP serum levels and TTE-derived parameters of RV function in two distinct postoperative timeframes.

Materials and methods

This cross-sectional study involved 98 patients following CHD correction, divided into Group I (≤10 years postoperative) and Group II (>10 years postoperative). Inclusion criteria were previous correction of CHD (e.g., tetralogy of Fallot, ASD). Exclusion criteria included residual shunts, significant left heart disease, and renal dysfunction. NT-proBNP was measured using electrochemiluminescence immunoassay. TTE assessments included TAPSE, FS-RVOT, RV FAC, TAI index, tissue Doppler S' and E'/A' ratios, and mPAP estimation. Correlation analyses (Spearman's rho) and linear regression were performed.

Results

Group I (n=61) exhibited significant negative correlations between NT-proBNP and TAPSE (r=-0.468, p=0.0001), FS-RVOT (r=-0.379, p=0.003), RV FAC (r=-0.387, p=0.008), TAI index (r=-0.291, p=0.023), and S' (r=-0.382, p=0.002) (Tables 1–4). A positive correlation was seen with mPAP (r=0.280, p=0.032). Group II (n=37) showed significant correlation only between NT-proBNP and TAI index (r=-0.448, p=0.005), with no significant correlations to other parameters (Figures 1 & 2).

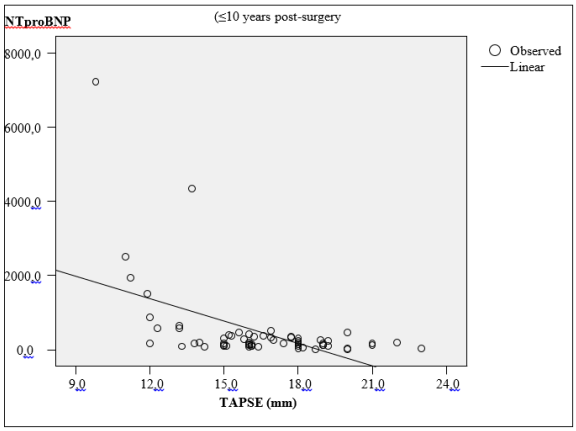

Figure 1 Correlation between NTproBNP and TAPSE values (≤10 years post-surgery).

TAPSE= NTproBNP x 17,04 - 0,001.

Table 1 Correlation between NT-proBNP type natriuretic peptide with right heart chamber dimensions and age in patients after surgical correction of congenital heart anomaly, up to 10 years after surgery

	rho Spearman's	LEI index	RV/LV ratio	Age
NTproBNP	Correlation coefficient	,372(**)	,360(**)	-,294(*)
	p	,004	,006	,021
	N	59	57	61

Table 2 Correlations of NT-proBNP type natriuretic peptide with parameters that monitor right ventricular volume load, in patients after surgical correction of congenital heart anomaly, up to 10 years after surgery

	Spearman's rho	mPAP	PAAT(ms)	PVR	TAPSE(mm)	FS-RVOT(%)	RVOT-SE(mm)	RV-FAC(%)	S/D	TAI index	IVA
NTproBNP	Correlation coefficient	,280	-,245	,182	-,468	-,379	-,387	-,337	,070	-,291	-,206
	p	,032	,062	,168	,0001	,003	,002	,008	,596	,023	,114
	N	59	59	59	61	59	59	61	59	61	60

Table 3 Linear regression equation

Equation	Model summary					Parameter estimation	
	R Square	F	df1	df2	Sig.	Constant	b1
Linear	,259	20,577	1	59	,0001	17,044	-,001

Table 4 Correlations of NTproBNP type natriuretic peptide with parameters that monitor right ventricular volume load in patients after surgical correction of congenital heart disease, >10 years post-surgery

	Spearman's rho	mPAP	PAAT(ms)	PVR	TAPSE(mm)	FS-RVOT(%)	RVOT-SE(mm)	RV-FAC(%)	S/D	TAI index	IVA
NTproBNP	Correlation coefficient	,144	-,161	-,055	-,278	-,077	-,177	-,218	-,004	**-,448(**)**	-,172
	p	,396	,341	,743	,091	,650	,295	,189	,982	**,005**	,310
	N	37	37	38	38	37	37	38	37	37	37

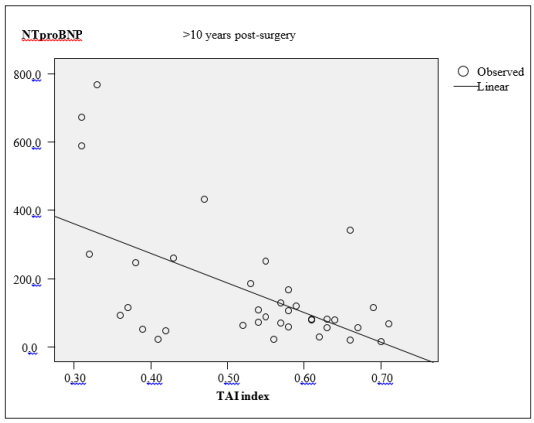

Figure 2 The correlation between NTproBNP and TAI index values is shown in a scatter diagram (r2=0.331).

Discussion

Our findings align with studies by Valente et al.,[1] and Geva et al,[2] confirming the progressive loss of sensitivity of NT-proBNP in detecting RV dysfunction beyond the first decade after surgery. This may reflect compensatory mechanisms or myocardial remodeling. In early follow-up, NT-proBNP correlates well with TTE indices such as TAPSE and RV FAC, in agreement with ESC guidelines on adult congenital heart disease follow-up. Notably, TAI index remains associated with NT-proBNP even in the late period, suggesting its sensitivity to subclinical dysfunction. Similar trends were observed in studies evaluating late postoperative follow-up after tetralogy of Fallot repair.[3-5]

While the right ventricle (RV) is also affected in heart failure, its response to dysfunction may differ from the left ventricle. In some cases of right heart failure, particularly when the left ventricle is still relatively well-functioning, the right ventricle may not stretch or stress its muscle fibers to the same degree as the left ventricle. This can lead to lower NT-proBNP levels despite the presence of RV dysfunction.[6,7]

In clinically compensated patients, even with some degree of RV dysfunction, the body's compensatory mechanisms might keep NT-proBNP levels within a normal range. These mechanisms may include increased heart rate and contractility, or dilation of the right ventricle to maintain cardiac output. These adaptations can reduce the overall stretch of the heart muscle, and thus, the release of NT-proBNP may not be as significant as in cases of decompensated heart failure.[8]

The lack of correlation between NTproBNP levels and indices of right ventricular systolic function, even those less dependent on preload, such as the tricuspid S' wave, may be explained. In left ventricular dysfunction, levels of this peptide generally correlate with functional class, whereas in clinically compensated patients, proBNP levels may be close to normal values. It is therefore not surprising that in our study there was no correlation between proBNP and right ventricular systolic function, since most patients showed no or few symptoms.[9,10]

In a meta-analysis by Gong et al., using data from 32 published studies involving 7,571 individuals with congenital heart defects, evidence was provided for the prognostic value of NTproBNP in patients undergoing cardiac surgery. Compared with those with low NTproBNP levels, patients with high serum NTproBNP concentrations had a significantly increased risk of mortality and cardiovascular events, while the risk of other postoperative outcomes was comparable between the two groups. These results suggest that regular postoperative follow-up of patients with congenital heart

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defects after cardiac surgery may be necessary to assess their long-term cardiovascular risk, which may be helpful for early identification and timely intervention for cardiovascular events and, therefore, reducing the incidence of cardiovascular-related mortality.[11]

The main challenge in treating these patients is progressive right ventricular dilatation and dysfunction caused by pulmonary regurgitation and/or residual obstruction, leading to heart failure, arrhythmias, or sudden death. Severe pulmonary regurgitation will be present in 40-80% of patients 5-10 years after correction; while at 35 years of postoperative follow-up, 40% of patients will undergo pulmonary valve replacement.[12]

Pulmonary valve replacement is associated with improved right ventricular volume, improved left ventricular function, reduced tricuspid regurgitation, and improved functional status.[13]

A national multicenter retrospective study in the United Kingdom, which included 707 patients older than 15 years after surgical repair of tetralogy of Fallot, concluded that patients older than 35 years had significantly worse mortality after pulmonary valve replacement compared with younger patients and higher mortality compared with the general population. This suggests that there are still cases in which the timing of initial pulmonary valve replacement is not optimal, which warrants a reassessment of the criteria for intervention. The 10-year mortality rate after pulmonary valve replacement was 4.2%, and the second rate was 6.8%. An age of 35 years at pulmonary valve replacement was identified as the optimal cutoff for late mortality. Patients older than 35 years had a 5.6-fold risk of death after 10 years compared with those younger than 35 years (10.4% vs. 1.3%, P<0.001), more concurrent tricuspid valve repair/replacement (15.1% vs. 5.7%, P<0.001), and surgical treatment of arrhythmias (18.4% vs. 5.9%, P<0.001). In those younger than 50 years, there was an 8.7-fold risk of late death compared with the general population, higher for those with pulmonary valve replacement after 35 years than for those younger than 35 years of age (hazard ratio 9.9 vs. 7.4).[14]

Heart failure (HF) is a growing concern because survival of patients with even the most complex congenital heart disease lesions has markedly improved. HF has become the leading cause of mortality in the adult congenital heart disease population, and addressing the substrate for HF in the pediatric population has become imperative.[15]

The main conclusion of the study by Palm et al. is that Zlog-proBNP overcomes the strong age dependency of NT-proBNP and is a powerful prognostic marker for age-independent exclusion and prediction of MACE in children with CHD. iIt is expected that zlog-proBNP to play a pivotal role in the future management of children with heart diseases.[16]

The study by Cantinotti et al. emphasizes that BNP/NT-proBNP measurements are useful in conjunction with other clinical assessments to evaluate heart failure in children with congenital heart disease. In essence, the study suggests that while BNP and NT-proBNP are valuable tools, they should be interpreted with caution and within the context of a comprehensive clinical evaluation for children with heart failure due to congenital heart disease.[17]

Additional studies demonstrated that BNP and NT-proBNP are useful in prediction of MACE in adults with heart failure, while the lone prospective trial of these hormones in children showed only minimal discrimination caused by again limitations in sample size and heterogeneity of diagnoses and age groups.[18,19]

NT-proBNP levels can only be partly explained by echocardiographic parameters because the observed relationships were significant but not strong. To evaluate the exact correlation impact of ventricular function on NT-proBNP levels, investigation for each cardiac diagnosis is needed, including other possible influences such as arrhythmias, valvular disease, and surgical history.[20]

Finally and crucially, the optimal timing for resolving residual lesions in congenital heart defects through surgery or percutaneous interventions is discussed, along with advanced heart failure management strategies and medical therapy aimed at preventing further right ventricular dilation and/or systolic deterioration or promoting reverse remodeling.[21]

Conclusion

NT-proBNP is a sensitive marker of right ventricular dysfunction within the first decade after CHD surgery. Its utility diminishes beyond ten years, with TAI index remaining an exception. Long-term surveillance of these patients should integrate both NT-proBNP and advanced imaging modalities, particularly for detecting subclinical RV impairment.

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None.

Conflicts of interest

The authors declare that there are no conflicts of interest.

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