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The relation between serum level of brain natriuretic peptide and amount of left to right shunt in patients with congenital heart disease

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Abstract
Background: In responses to atrial and/or ventricular stretches, natriuretic peptides including atrial natriuretic peptide (ANP), brain natriuretic peptide (BNP), and pro-BNP are produced. In congenital heart diseases with a left-to-right shunts, including atrial septal defect (ASD), ventricular septal defect (VSD), and patent ductus arteriosus (PDA), the levels of BNP in the blood may be utilized as a marker for evaluating the amount of the shunt (Qp/Qs) and the extent of the hemodynamic abnormalities.
Methods: This work was performed on 60 individuals ranging in age from 6 months to 18 years old, all infants and children had isolated VSD, ASD or PDA with left to right shunt (diagnosed by Echocardiography) Participants were split in to three groups: ASD: (n= 24). VSD (n= 25). PDA (n= 11).
Results: A significant correlation was existed among the Qp/Qs ratio and level of pro BNP in serum (P value = 0.001), the pro-BNP serum level ≥ 125 pg/ml is related to significant Qp/Qs ratio (more than 1.5).
Conclusion: Pro Pro-BNP may be utilized as a screening tool to determine the requirement for further intervention for individuals having ASD, VSD, and PDA based on their hemodynamic burden.

Keywords: Congenital heart disease, brain natriuretic peptide, left to right shunt, serum level

Introduction

Among of the cardiac peptides that rises with ventricular dysfunction is B-type natriuretic peptide. This hormone originates in the ventricle, secreted as pre-pro brain natriuretic peptide (BNP), and then is enzymatically broken down into pro-BNP as consequence of myocardial strain. Natriuretic peptide levels in the serum are accurate indicators of heart failure, and several studies have shown their values in prognosis [1, 2].

B-type NP is a sensitive and predictive indicator of cardiac function and is mostly secreted in cases of ventricular hemodynamic stress and congestive cardiac failure. Congestive heart failure may be diagnosed using BNP as a beneficial indicator. In instances of left to right shunts, which include ventricular septal defects (VSD), atrial septal defects (ASD), and patent ductus arteriosus (PDA), the blood levels of pro-BNP is elevated [3, 4].

Approximately thirty percent of all instances of congenital heart disease (CHD) contain a left to right shunt, involving ASD, VSD, and PDA. Depending on the size, severity, and other factors of the shunt, these lesions may be corrected medically or surgically [5].

It appears that through assessing the blood level of B-type natriuretic peptide, the extent of the shunts can be identified and morbidities like recurrent pulmonary infections, failure to thrive, congestive heart failure, and Eisenmenger syndrome may be avoided. This is because echocardiographic outcomes are not always adequate to determine the severity of hemodynamic abnormalities [6].

This study aimed to determine whether the levels of BNP in serum may be employed as an indicator to determine the amount of the shunts (Qp/Qs) and the extent of the hemodynamic disturbance in congenital cardiac diseases with left-to-right shunts, which includes ASD, VSD, and PDA.

Patients and Methods

This work was performed on 60 patients ranging in age from 6 months to 18 years old, all infants and children had isolated VSD, ASD or PDA with left-to-right shunt (diagnosed by Echocardiography). Following permission from the Ethics Committee of Tanta University Hospitals, Egypt, the research was conducted from December 2020 to March 2022. The patients' family provided written permission that was based on full disclosure.

Criteria for exclusion included severe sickness (including dehydration, sepsis, and respiratory conditions), heart failure brought on by myocarditis, cardiomyopathy, and coronary artery abnormality like anomalous left coronary artery from the pulmonary artery (ALCAPA) or aortic arch coarctation, complex congenital heart diseases include ASD, VSD or PDA (as tetralogy of fallout's, double outlet right ventricle), residual shunt after closure of ASD, VSD or PDA.

Patients were divided into three groups: ASD: n= 24. VSD n= 25. PDA n= 11.

Each participant was subjected to: Clinical examination, general taking of history that include proper history was taken to detect symptoms suggestive of significant shunt via ASD, VSD and PDA such as dyspnea, easy fatigue and chest infection in the form of cough, expectoration noticed by the patient or the mother.

The echocardiographic examination was performed with the patient lying on a standard hospital bed. Oral chloral hydrate was used to sedate the children blew 5 years in a dosage of 50-100 mg/Kg body weight (total dose not to exceed 1.5 gm).

Apical four chamber view: Used for assessment of presence of VSD, evaluation of its type (apical, mid muscular & outlet muscular VSD & shunt across

Apical five chamber view: Used for assessment of left ventricular outflow tract velocity (LVOT VTI) by Doppler evaluation, evaluation of size & shunt across perimembranous VSD.

Parasternal long view: Used for assessment of Left Ventricular Outflow Tract diameter.

Parasternal short view: Used for assessment of right ventricular outflow tract velocity & diameter by Doppler assessment & evaluation of presence of patent ductus arteriosus PDA (assessment of size & shunt across PDA)

Subcostal view: For assessment of type, size of ASD.

Assessment of amount of left-to-right shunts by calculation of QP/Qs ratio non-invasively by 2D echocardiography.

When deciding whether to do surgery on a kid who has an ASD, VSD, or PDA, for example, the Qp / Qs ratio is highly helpful. A shunt that produces a Qp: Qs ratio of > 1.8:1 is probably to need intervention, but another of < 1.5:1 may be considered as insignificant. Utilizing velocity time integral (VTI) measurements obtained via Doppler-echocardiography at the pulmonary (RVOT VTI) and aortic (LVOT VTI) valves, one may calculate left ventricular outflow tract (LVOT) and the right ventricular outflow tract (RVOT) areas,

Calculation of QP/QS ratio according to this equation1: Qp = RVOT VTI x π x (RVOT area2 / Qs=LVOT VTI x π x (LVOT area2/2) Qp/Qs Ratio = Qp/Qs

A BNP test is done by drawing 3 cc blood from a vein in patient arm using a small needle from each patient, following separation, the blood specimens were obtained. The temperature of the plasma was set at -80 C. Utilising florescence immunoassay triage kits, the pro-BNP level was determined. The results from the test are usually ready in 15 to 20 minutes and contrasted with the number of left-to-right shunts (Qp/Qs ratio).

Statistical analysis

SPSS v22 (IBM Inc., Chicago, IL, USA) was utilized for the statistical analysis. Mean and standard deviation (SD) were utilized to display quantitative information. Frequency and percentages (%) were used to illustrate qualitative parameters. The ANOVA test was utilized to contrast between more than two means. Chi-square test: used for comparison between two groups regarding qualitative data. A two tailed P value < 0.05 was considered significant.

Results

No substantial variation was existed among three groups (ASD, VSD, PDA) as regard age, body weight and sex. Table 1.

Table 1: Age, body weight and sex distribution in study population

		ASD	VSD	PDA	F. test	P. value
Age (months)		57.63±62.71	65.34±66.26	32.45±37.81	1.131	0.330
Weight (kg)		16.43±11.08	18.21±10.96	11.58±6.77	1.556	0.220
Sex	Male	9 (37.5%)	12 (48%)	6 (54.5%)	X^2=1.041	0.594
	Female	15 (62.5%)	13 (52%)	5 (45.5%)		

Data are presented as mean ± SD or frequency (%)

No substantial variation was existed among three groups (ASD, VSD, PDA) regarding the size of the defect and the grade of the shunt. Table 2.

Table 2: Size of defect in study population

Size of shunt in mm		ASD	VSD	PDA	F. test	P. value
		5.62±3.33	4.34±1.61	3.71±1.90	2.173	0.171
Grade of the shunt	Small	14 (58.3%)	11 (44%)	5 (45.5%)	X^2=8.306	0.081
	Moderate	6 (25%)	6 (24%)	4 (36.4%)		
	Large	4 (16.7%)	8 (32%)	2 (18.1%).		

Data are presented as mean ± SD or frequency (%)

No substantial variation was existed among the three groups (ASD, VSD, PDA) regarding the QP/QS ratio. Table 3.

Table 3: QP/QS ratio in study population

QP/QS ratio		ASD	VSD	PDA	F. test	P. value
		1.47±0.49	1.42±0.70	1.76±1.03	0.981	0.381
QP/QS ratio	Mild	12 (50%)	15 (60%)	6 (54.5%)	X^2=5.235	0.264
	Moderate	9 (37.5%)	5 (20%)	1 (9.1%)		
	Large	3 (12.5%)	5 (20%)	4 (36.4%)		

Data are presented as mean ± SD or frequency (%)

No substantial variation was existed among the three groups (ASD, VSD, PDA) regarding the QP/QS ratio. Table 4.

Table 4: Pro BNP value in study population

		ASD	VSD	PDA	F. test	P. value
Pro BNP value in pg/ml		100.42±43.05	100.48±55.0	132.0±69.05	1.565	0.218
Pro BNP value in pg/ml	Low	20 (83.3%)	19 (76%)	7 (63.6%)	X^2=5.235	0.264
	High	4 (16.7%)	6 (24%)	4 (36.4%)		

Data are presented as mean ± SD or frequency (%)

A substantial correlation was existed among the Qp/Qs ratio and serum pro BNP level. Table 5, Figure 1.

Table 5: Relation between QP/QS ratio & pro BNP level

QP/QS ratio	Pro BNP value in pg/ml		Total	Chi- square	P-value
	Low	High			
Mild	33 (71.7%)	0	33 (55.0%)	X^2=50.311	0.001*
Moderate	13 (28.3%)	2 (14.3%)	15 (25.0%)		
Severe	0	12 (85.7%)	12 (20.0%)		

Data are presented as frequency (%)

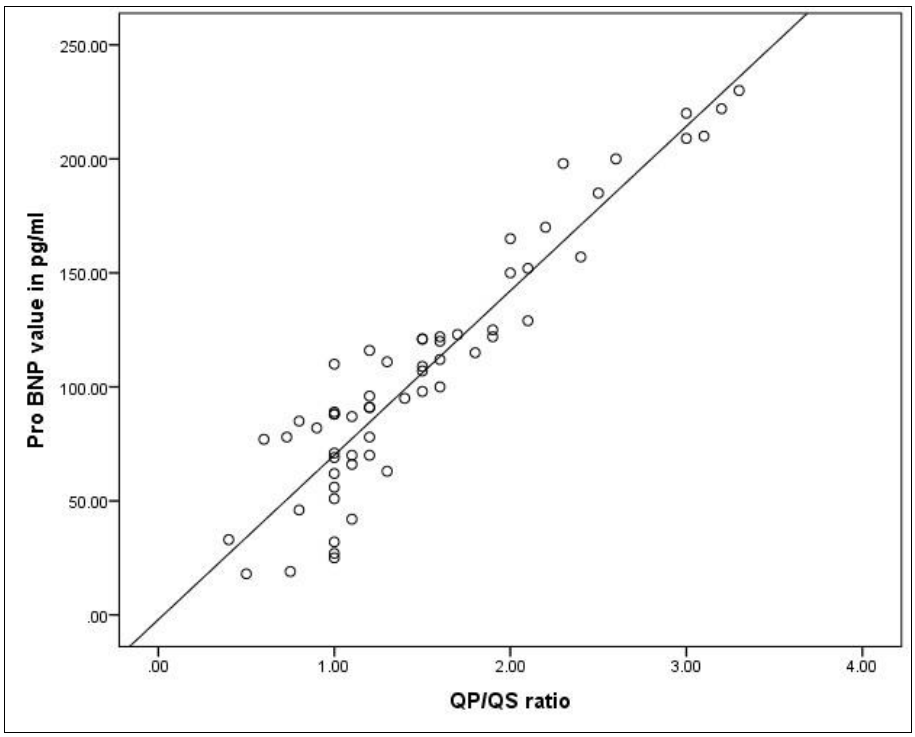


Fig 1: Relation between QP/QS ratio & pro BNP level

Example of cases

Case 1: Male patient aged 2.0 years & 7 months diagnosed with apical muscular VSD=3.4 mm with left to right shunt across RVOT velocity time integral calculated by Doppler study across RVOT from parasternal short view =23.92 cm, LVOT VTI velocity time integral calculated by Doppler study across LVOT from apical five chamber view =21.27 cm. RVOT diameter calculated from parasternal short view=1.16 cm. LVOT diameter estimated from parasternal long view=1.6 cm. QP/QS ratio = 1.0. In this case the pro BNP level =33 pg /ml (less than 125 pg/ml). Figure 2.

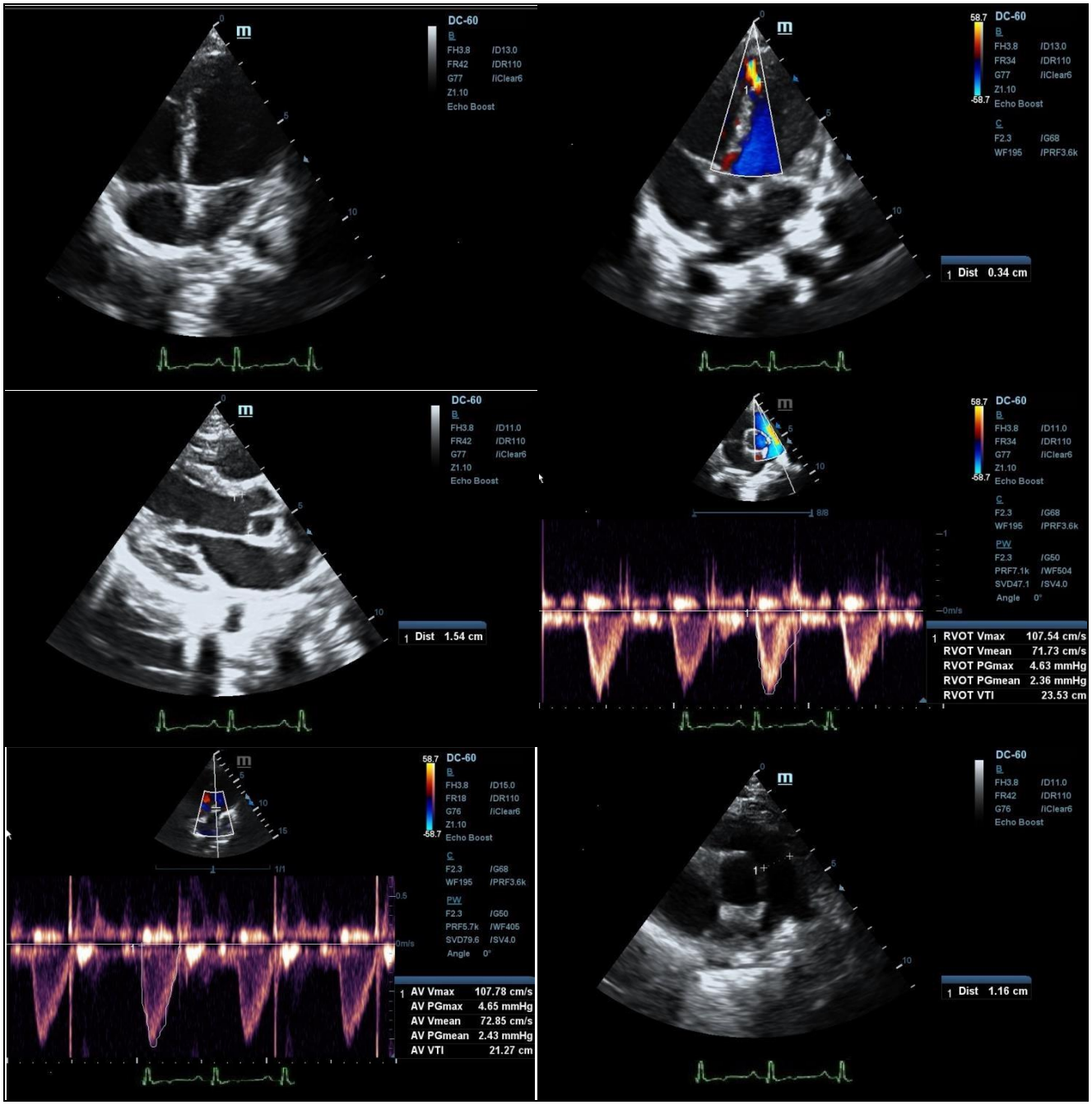


Fig 2: Apical muscular VSD

Case 2: Female patient aged11 month diagnosed with Patent dustus arteriosus measuring 4.4 mm form it is pulmonary end & 3.9 mm from its aortic end with left to right shunt across.

RVOT velocity time integral calculated by Doppler study across RVOT from parasternal short view =23.53 cm. LVOT VTI velocity time integral calculated by Doppler study across LVOT from apical five chamber view =21.01 cm.

RVOT diameter calculated from parasternal short view=1.14 cm.

LVOT diameter calculated from parasternal long view=1.04 cm.

QP/QS ratio =1.3. In this case the pro BNP level = 110 pg/ml (less than 125 pg /ml). Figure 3.

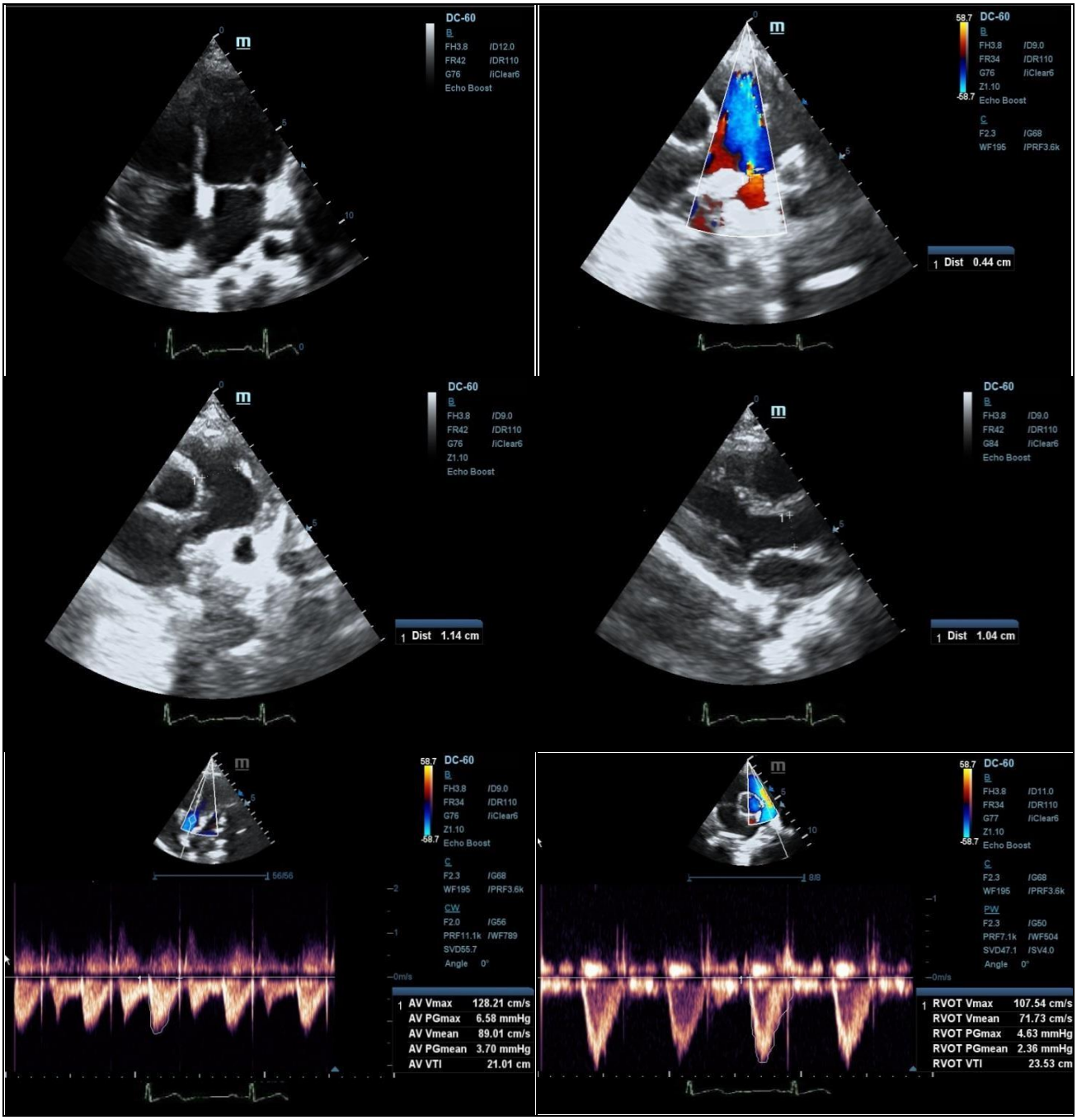


Fig 3: Patent ductus arteriosus

Case 3: Female patient aged 4 years presented for the first time with large atrial septal defect ASD measuring 16 mm with left-to-right shunt across the RVOT velocity time integral calculated by Doppler study across RVOT from parasternal short view =24.11cm. LVOT VTI velocity time integral calculated by Doppler study across LVOT from apical five chamber view =19.36 cm. RVOT diameter calculated from parasternal short view =2.32 cm. LVOT diameter calculated from parasternal long view =1.59 cm. QP/QS ratio =2.65. In this case the pro BNP level =200 pg/ml (more than 125 pg/ml). Figure 4.

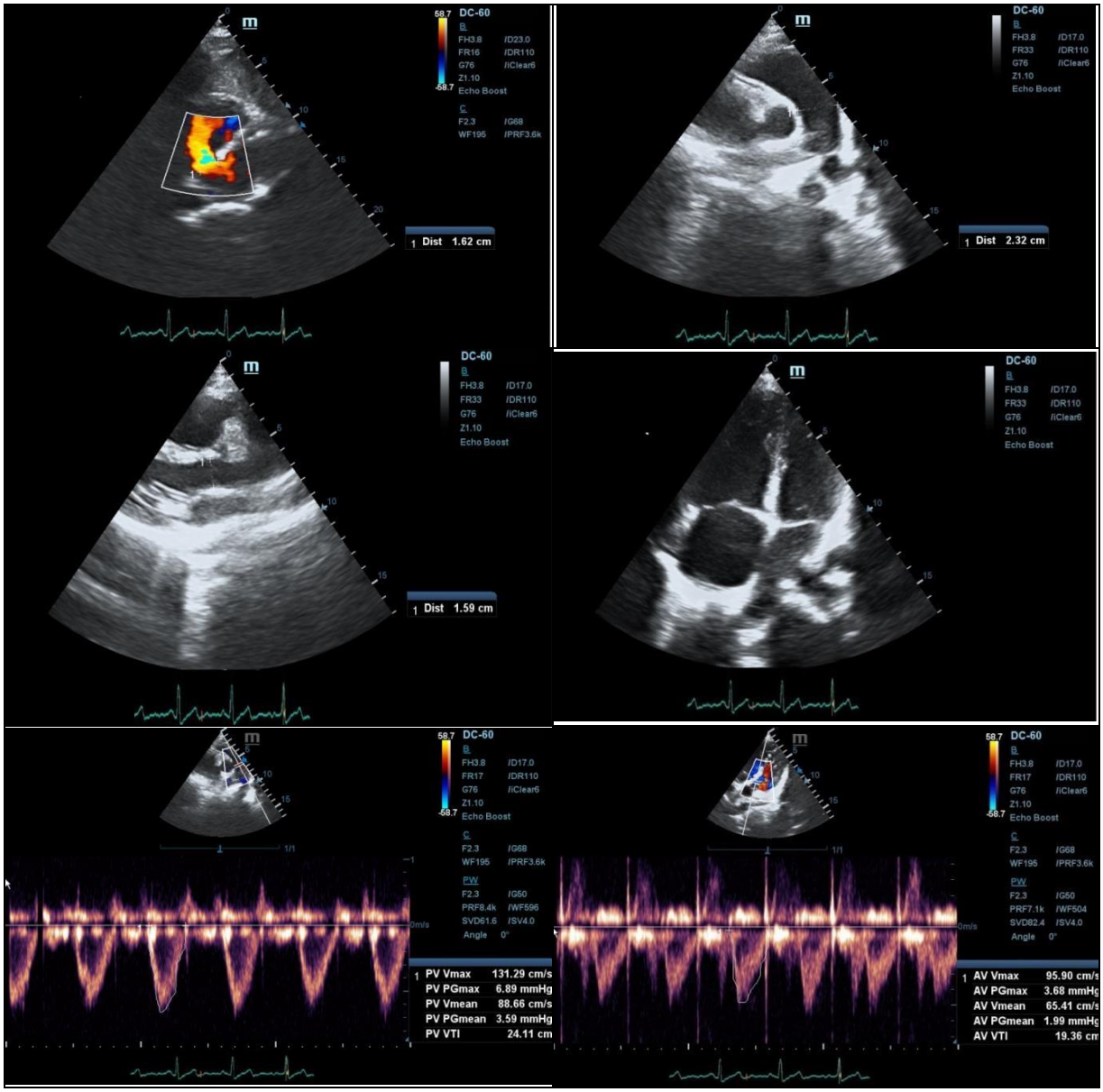
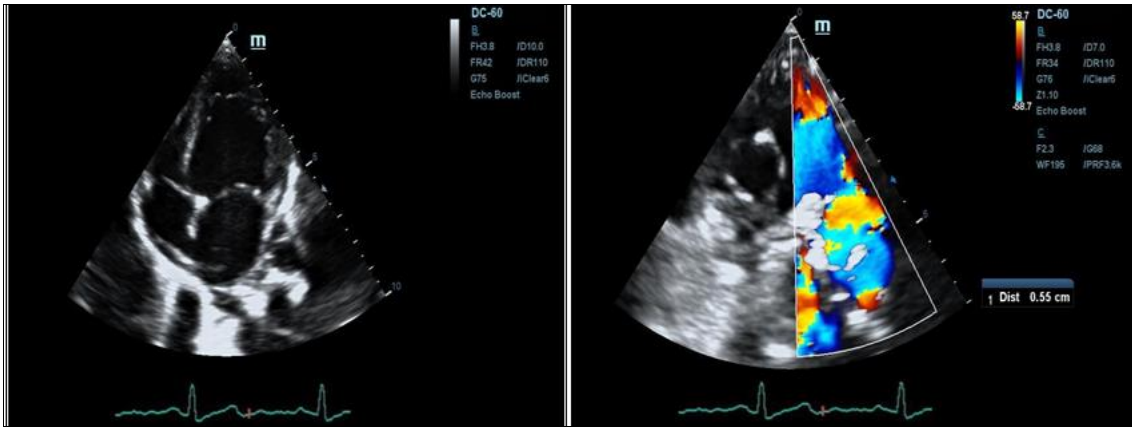


Fig 4: Atrial septal defect

Case 4: Female patient aged11 month diagnosed with Patent dustus arteriosus measuring.
5.5 mm form it is pulmonary end & 5.3 mm from its aortic end with left to right shunt across.
Right ventricular out flow tract velocity time integral estimated by Doppler study across RVOT from parasternal short view =22.98cm. LVOT VTI velocity time integral estimated by Doppler study across LVOT from apical five chamber view =13.87 cm.
RVOT diameter estimated from parasternal short view =1.14 cm.
LVOT diameter estimated from parasternal long view =0.83 cm.
QP/QS ratio =3.1. In this case the pro BNP level =210pg/ml (more than 125 pg/ml). Figure 5.



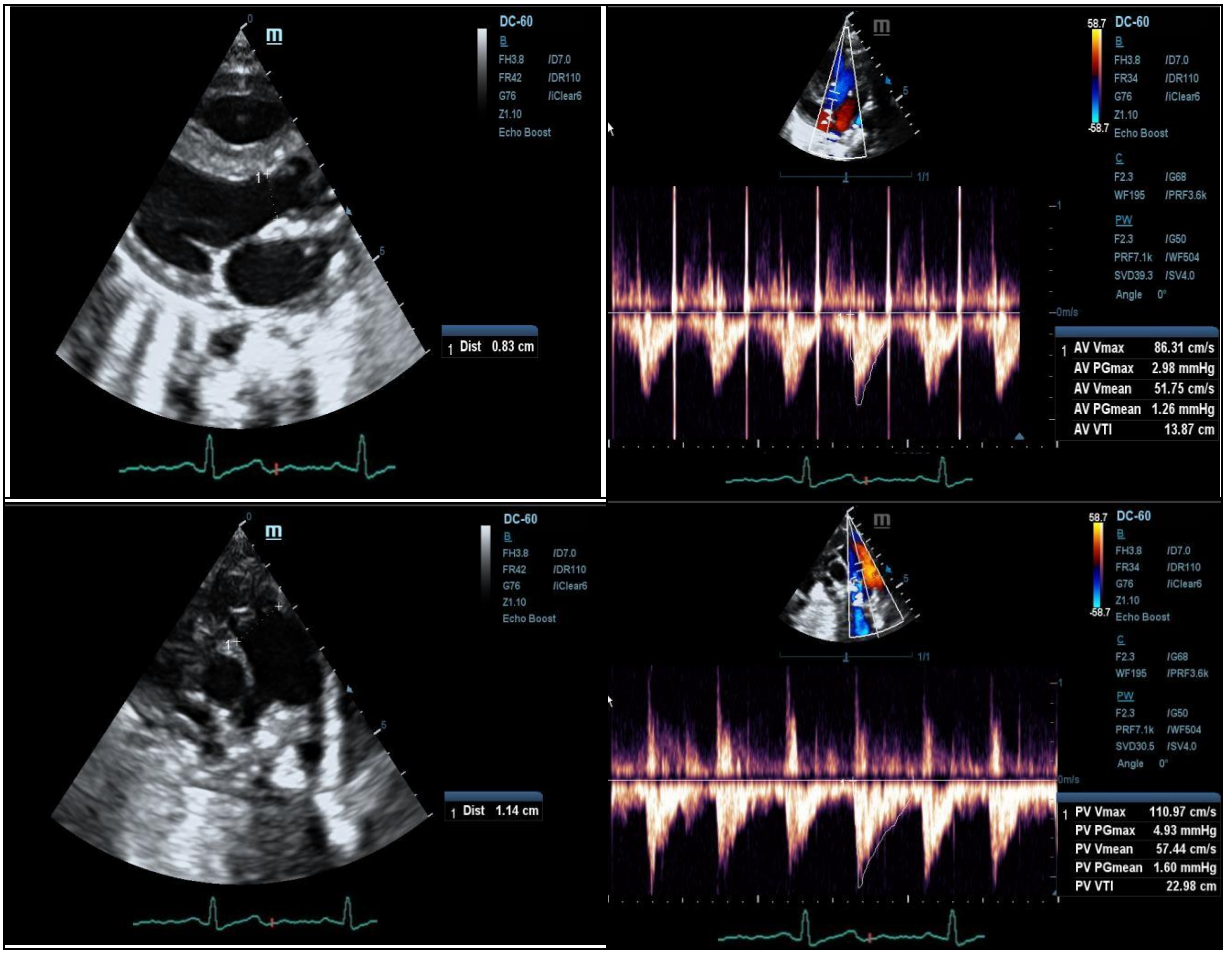


Fig 5: Patent Ductus Arteriosus

Discussion

In instances of severe left-to-right shunts, like in atrial septal defect and ventricular septal defects (ASD, VSD), and patent ductus arteriosus (PDA), the serum pro-BNP levels are elevated [4, 5].

In our investigation, the left-to-right shunts in individuals with VSD, ASD, and PDA was significantly correlated with the blood level of pro-BNP. The BNP levels and the Qp/Qs ratios were shown to be significantly correlated in the research by Ozhan *et al.* [6]. Serum BNP levels may thus be utilised as a screening tool for the assessment of VSD and ASD in light of the findings of this investigation. In the research conducted by M. Kavga *et al.* [7], there were no statistically significant variations in BNP among the ASD group and group B. The study included 76 kids (38 boys/38 girls, mean age 22.4 months) with CHD (Group A: 23 with ventricular septal defects [VSD], 31 with atrial septal defects [ASD], 8 with ASD and VSD, and 14 with patent ductus arteriosus [PDA]), and 34 children who were in good health. BNP levels were substantially greater in PDA patients. BNP and Qp/Qs showed a positive correlation. In the investigation by Ozyurt *et al.*, [8] a significant correlation among the patients' mean N-terminal pro-BNP levels and Qp/Qs⩾1.5 in both defect types and the control group was discovered. N-terminal pro-BNP levels of ⩾113.5 pg/ml was related with good sensitivity and specificity for identifying the substantial shunt for ventricular septal defect. Additionally, 57.9 pg/ml was the cutoff limit for diagnosing the substantial shunt for atrial septal defect.

Law *et al.*'s research [9] assessed 33 individuals with left ventricular (LV) failure. 11 of them had cardiac failure, and 22 of them underwent angiography. The Cavo pulmonary shunt, aortopulmonary shunt, and control groups all had statistically significant mean blood BNP values. Additionally, this research found a strong correlation between serum BNP levels and mean left end diastolic pressure (8 mm Hg), mean pulmonary arterial pressure (14.5 mmHg), and mean right atrial pressure (6.5 mm Hg).

A significant association between pro-BNP levels and the underlying cause of left to right shunt was discovered by statistical analysis.

According to Jansle *et al.*'s research [10], a BNP level greater than 15 pg/mL was more beneficial for patients who required therapies.

According to C.G. Cowley *et al.*'s study, [11] the degree of left ventricular outflow blockage was associated with the BNP values for this group, which varied from <5.0 to 1060.0 pg/ml. According to the findings of the research by Noori *et al.*, [12] 68.19% of cyanotic sufferers were boys, compared to 51.28% and 60% for cyanotic individuals and controls, respectively. Additionally, the severity of the illness was substantially correlated with the mean values of HB, RV, and O_2 saturation (O_2 Sat). BNP had correlation with PA (p<0.05 and r=021) and PA had correlation with pulmonary-to-systemic blood flow ratio (Qp/Qs) ratio (P<0.05 and r=0.45), resistance (Rp/Rs) ratio (p<0.05 and r=0.59), RV (p<0.001 and r=0.28) and O2Sat (p<0.05 and r=0.36) respectively. According to the study's findings, BNP levels in children with CHD were higher than those in healthy children, and pulmonary hypertension and BNP levels were shown to be positively correlated.

Conclusion

Pro-BNP may be utilized as a screening tool to determine the requirement for further intervention for individuals having ASD, VSD, and PDA based on their hemodynamic burden.

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Conflict of Interest: Nil.

References

1. Hutchinson KR, Guggilam A, Cismowski MJ, Galantowicz ML, West TA, Stewart JA Jr., *et al*. Temporal pattern of left ventricular structural and functional remodeling following reversal of volume overload heart failure. J Appl. Physiol. 2011;111:1778-1788.
2. Gilboa SM, Salemi JL, Nembhard WN, Fixler DE, Correa A. Mortality resulting from congenital heart disease among children and adults in the United States, 1999 to 2006. Circ. 2010;122:2254-2263.
3. Pierpont ME, Basson CT, Benson DW Jr., Gelb BD, Giglia TM, Goldmuntz E, *et al*. Genetic basis for congenital heart defects: current knowledge: a scientific statement from the American Heart Association Congenital Cardiac Defects Committee, Council on Cardiovascular Disease in the Young: endorsed by the American Academy of Pediatrics. Circ. 2007;115:3015-3038.
4. Kliegman RM, Behrman RE, Jenson HB, Stanton BM. Nelson textbook of pediatrics e-book: Elsevier Health Sciences; c2007.
5. Choi BM, Lee KH, Eun BL, Yoo KH, Hong YS, Son CS, *et al*. Utility of rapid B-type natriuretic peptide assay for diagnosis of symptomatic patent ductus arteriosus in preterm infants. Pediatrics. 2005;115:255-261.
6. Ozhan H, Albayrak S, Uzun H, Ordu S, Kaya A, Yazici M, *et al*. Correlation of plasma B-type natriuretic peptide with shunt severity in patients with atrial or ventricular septal defect. Pediatr Cardiol. 2007;28:272-275.
7. Kavga M, Varlamis G, Giannopoulos A, Papadopoulou-Legbelou K, Varlamis S, Bompotis G, *et al*. Correlation of plasma B-type natriuretic peptide with shunt volume in children with congenital heart disease involving left-to-right shunt. Hellenic J Cardiol. 2013;54:192-198.
8. Ozyurt A, Baykan A, Argun M, Pamukcu O, Uzum K, Narin F, *et al*. Does N-terminal pro-brain natriuretic peptide correlate with measured shunt fraction in children with septal defects? Cardiol. Young. 2016;26:469-76.
9. Law YM, Ettedgui J, Beerman L, Maisel A, Tofovic S. Comparison of plasma B-type natriuretic peptide levels in single ventricle patients with systemic ventricle heart failure versus isolated cavopulmonary failure. Am J Cardiol. 2006;98:520-524.
10. Jan SL, Fu YC, Hwang B, Lin SJ. B-type natriuretic peptide in children with atrial or ventricular septal defect: A cardiac catheterization study. Biomarkers. 2012;17:166-171.
11. Cowley C, Bradley J, Shaddy R. B-type natriuretic peptide levels in congenital heart disease. Pediatr. Cardiol. 2004;25:336-340.
12. Noori NM, Teimouri A, Shahramian I, Akhavan Sales S. Evaluation of brain natriuretic peptide plasma levels in children with congenital heart diseases. Int. J Pediatr. 2016;4:3615-3626.

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