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Evaluation of Left Ventricular Diastolic and Systolic Functions in Children with Bronchiolitis Followed up at High-Flow Nasal Cannula Oxygen Therapy

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Abstract

Background: We aimed to investigate left ventricular (LV) functions in children undergoing high-flow nasal cannula (HFNC) treatment for bronchiolitis and associations between LV functions and vital signs, hemogram and C-reactive protein (CRP) levels.

Methods: In this prospective study, we enrolled a cohort of 32 patients with bronchiolitis and 36 healthy children between January 2022 and January 2023. Upon admission, we conducted both conventional and tissue Doppler echocardiography assessments to examine the LV systolic and diastolic functions. Vital signs, venous blood gas, hemogram and CRP values were recorded and explored their potential correlations with LV functions.

Results: While there was no difference in mitral E, A, E/A between the bronchiolitis and control groups, a statistically significant difference was found in mitral E'($p = 0.000$), A'($p = 0.000$) and E'/A'($p = 0.001$). There was no significant difference in the two groups in terms of LV systolic functions. There was a negative correlation with respiratory rate and E/A, Deceleration time (DT), LV Cardiac output (CO) and LV Stroke volume (SV). SpO2 was positively correlated with LV end-systolic volume, LV end-diastolic volume, LV SV and LV CO. Serum platelet level was negatively correlated with E/A, DT, LV SV and LV CO.

Conclusion: While systolic functions were normal in patients with bronchiolitis, diastolic functions were impaired and this may be due to viral exposure. Notably, as the severity of bronchiolitis increased, a corresponding deterioration in LV functions was observed. Platelet level was inversely proportional to the severity of LV systolic and diastolic functions.

Keywords: Bronchiolitis, children, high-flow nasal cannula theraphy, left ventricular functions

Introduction

Bronchiolitis is responsible for the majority of lower respiratory tract infections in children under 2 years of age and accounts for 18% of hospital admissions.[1] An average of 200,000 children worldwide die from bronchiolitis and positioning it as the second most prevalent cause of mortality under 1 year of age.[1] The agent responsible for 75-80% of cases is Respiratory Syncytial Virus (RSV).[2]

The use of high-flow nasal cannula oxygen therapy (HFNC) is increasing in acute hypoxemic respiratory failure such as moderate and severe bronchiolitis.[3] It reduces respiratory effort in respiratory failure, improves oxygenation and provides patient comfort, positioning it as a valuable alternative to noninvasive mechanical ventilation and conventional oxygen therapy.[4]

HFNC reduces resistance and anatomical dead space in the upper airways, provides constant airway pressure and reduces respiratory effort.[5] Adjustable and humidified oxygen flow protects from mucosal injury.[6]

Prior researches have explored the impact of bronchiolitis on cardiac function, with a predominant focus on the right ventricle (RV).[7,8] However, the number of studies specifically addressing the left ventricle (LV) remains limited.[9]

We hypothesized that the left ventricle (LV) might exhibit discernible effects, particularly in cases of moderate and severe bronchiolitis, thus warranting a comprehensive investigation. Our objective was to assess LV systolic and diastolic functions in pediatric patients with bronchiolitis undergoing HFNC therapy in the Pediatric Emergency Department. Additionally, we aimed to explore potential correlations between the blood gas, hemogram and C-reactive protein (CRP) values that taken routinely, vital signs and LV functions.

We thought that the LV might also be affected, especially in moderate and severe bronchiolitis and should be investigated further. We aimed to investigate LV diastolic and systolic functions in children with bronchiolitis followed up at HFNC theraphy in Pediatric Emergency Department and examine the correlation between the blood gas and hemogram values and vital signs obtained from these patients and LV functions.

Method

This study included children admitted to Ondokuz Mayıs University Medical Faculty Pediatric Emergency Department with respiratory distress from January 2022 to January 2023, diagnosed with bronchiolitis, and treated with HFNC. Exclusion criteria encompassed syndromic patients, individuals with congenital or acquired heart conditions, and children with chronic lung disorders. The informed written consent was obtained from each patient and secured approval from the ethics committee (OMU KAEK 2023/183).

The study group comprised 32 patients, while the control group consisted of 36 healthy children. The healthy children were of similar age to those in the patient group and exhibited innocent murmurs during routine examinations.

Patients who presented with respiratory distress and were diagnosed with bronchiolitis were administered oxygen by mask, inhaled salbutamol and budesonide, and systemic steroids. In patients with no improvement, intravenous magnesium was administered. In cases of persisting respiratory distress despite these treatment, patients were transitioned to High-flow Nasal Cannula (HFNC) therapy, which was administered using the Airvo2 system (Fisher & Paykel Healthcare). Initial FiO2 and flow were set as 1-2 L/kg/min by the clinicians. Inspired oxygen concentration was regulated to achieve SpO2 >94%.

Respiratory rate, saturation, body temperature, heart rate, blood pressure, venous blood gas, hemogram and CRP values of the patients at the time of admission were recorded. All patients underwent echocardiographic evaluation by the same clinician within the first 12 hours of admission. Echocardiographic studies were performed by a Philips Affiniti 70 ultrasound system. According to the age and weight of the cases, S4-2 cardiac sector (2-4 MHz, 80 elements, 5mm), S8-3 pediatric cardiac Sector (3-8 MHz, 96 elements, 15.4mm), S12-4 neonatal cardiac sector (4-12 MHz, 96 elements, 9.78mm) probes were used.

Transthoracic echocardiography was applied by a single pediatric cardiologist and the following parameters were monitored:

LVIDs: Left ventricular internal end-systolic diameter
LVIDd: Left ventricular internal end-diastolic diameter
LV EF teicholz: Left ventricular ejection fraction according to the Teicholz formula (Teicholz EF= (LVIDd-LVIDs)/(LVIDd)[10]
FS: Left ventricular shortening fraction
IVSd: End-diastolic interventricular septum diameter
LVPWd: End-diastolic left ventricular posterior wall diameter
EDV Teicholz: LV end-diastolic volume according to the Teicholz formula [EDV = ($LVIDd^3$ X 7)/(LVIDd + 2.4)]
ESV Teicholz: LV end-systolic volume according to the Teicholz formula [ESV = ($LVIDs^3$ X 7)/(LVIDs + 2.4)]
LV mass: Left ventricular mass calculated with the formula 1.05 ([LVIDd+ LVPWd + IVSd]^3- [LVIDd]^3)[11]
LV length D: Left ventricular internal diameter from mitral annulus (leaflet insertion to leaflet insertion) to the endocardium of *LV* apex in apical view at the end of the diastole.

LV area D: Left ventricular area at the end of the diastole.
LV length S: Left ventricular internal diameter from mitral annulus (leaflet insertion to leaflet insertion) to the endocardium of *LV* apex in apical view at the end of the systole.
LV area S: Left ventricular area at the end of the systole.
LV Vol D: LV end-diastolic volume at apical 4-chamber view with Simpson's method
LV Vol S: LV end-systolic volume at apical 4-chamber view with Simpson's method
EF modified simpson: Left ventricular ejection fraction according to the modified Simpson formula (Simpson EF=(LVEDV–LVESV)/(LVEDV)[12]
Mitral E (cm/s): Velocity of the passive blood flow from the left atrium to the left ventricle which is measured by pulsed wave Doppler placed on the mitral valve
Mitral A (cm/s): Velocity of the blood flow generated by active atrial contraction which is measured by pulsed wave Doppler placed on the mitral valve
E/A: The ratio between mitral E and mitral A.
Deceleration time: The time interval from the peak of the E-wave to its projected baseline
Lat IVRT: Isovolumic relaxation time is the time interval between the end of aortic ejection and the beginning of ventricular filling.
Lat IVCT: The isovolumic contraction time is defined as the interval between the closing of the atrioventricular valves and the opening of the semilunar valves.
LVOT diam: Left ventricle outflow tract diameter which was measured at parasternal 5-chamber view.
LVOT area: Left ventricular outflow tract cross-sectional area which is described in the formula "π.Diameter of $LVOT^2$"
LV SV: Sroke volume of the left ventricle which is defined as the difference between end diastole and end systole volumes of the left ventricle
LV CO: Cardiac output of the left ventricle which is calculated as stroke volume multiplied by heart beats per minute
RVOT: Right ventricle outflow tract diameter which was measured at parasternal 5-chamber view.
MAPSE: Mitral annular plane systolic excursion refers to the displacement of the mitral valvular plane in parasternal 4-chamber view in M-mode and is associated with LV systolic function in patients with heart failure with preserved ejection fraction
TAPSE: Tricuspid annular plane systolic excursion refers to the displacement of the tricuspid valvular plane in parasternal 4-chamber view in M-mode and is associated with right ventricle function.
The following parameters were monitored by TDI:
MV peak E vel: Early diastolic flow peak velocity of the mitral valve (E') which was measured by tissue Doppler mode at the apical four-chamber view.
Mitral e': Early diastolic peak velocity of mitral valve annulus (e') which was measured by tissue Doppler mode at the apical four-chamber view.
MV peak A vel: Diastolic flow peak velocity of the mitral valve (A') which was measured by tissue Doppler mode at the apical four-chamber view.
E'/A': The ratio between mitral E' and mitral A'.
LVOT VTI Vmax: Left ventricular outflow tract velocity time integral which is measured with pulsed-wave Doppler

Statistical Analysis

For the analysis of the data, version 25.0 of IBM SPSS (Statistical Package for the Social Sciences) was used. Shapiro-Wilk test and histogram were used to examine the normal distribution suitability of the variables. Descriptive statistics were presented as mean (±) standard deviation. The significance of differences between groups in terms of averages; independent t test, and Pearson correlation were used. Variables found to be significant at the $p<.2$ level in correlation and univariate analyses were analyzed with a multivariate linear regression (LR) backward model, and statistically significant variables are presented in the table. Results for $p<0.05$ were considered as statistically significant.

Result

The age range of the children was similar, 1-120 months in the case group and 2-120 months in the control group. While LV vol D (p=0.043), LV vol S (p=0.010) and heart rate (p=0.000) was increased, LVOT diameter (p=0.010), RVOT diameter (p=0.001) and LVOT area (p= 0.012) was decreased in children with bronchiolitis (Table 1).

Mitral E'(p=0.000) and mitral A' (p=0.000) was decreased, E'/A' (p=0.001) was increased in bronchiolitis group (Table 2).

There was a negative correlation with respiratory rate and E/A, DT, LV CO and LV SV. Heart rate was positively correlated with mitral E and A. SpO2 was positively correlated with LV vol S, LV vol D, LV SV and LV CO. Serum platelet level was negatively correlated with E/A, DT, LV SV and LV CO (Table 3).

Table 1. Left ventricular systolic function parameters in children with bronchiolitis

	Groups					
	Case (n=32)		Controls (n=36)			
	Mean	SD	Mean	SD	t	P
Age (month)	30,1	28,1	29,7	25,7	0.067	0.947
LVIDd (mm)	28.15	5.26	26.94	5.21	0.919	0.362
LVIDs (mm)	17.22	3.60	16.80	3.11	0.506	0.615
EF teicholz	70.70	6.38	67.28	11.65	1.398	0.167
FS	38.80	5.37	37.22	4.33	1.307	0.196
IVSd (mm)	5.45	0.85	5.15	0.76	1.463	0.148
LVPWd (mm)	5.39	1.26	5.30	0.70	0.345	0.732
EDV (mm) teich	31.67	15.20	28.41	13.08	0.922	0.360
ESV (mm) teich	9.38	5.57	8.70	4.00	0.571	0.570
LV mass (g)	33.95	17.39	29.33	11.76	1.264	0.211
LV length D (cm)	4.42	0.68	4.92	4.06	0.645	0.521
LV area D (cm^2)	10.10	3.32	8.72	2.66	1.849	0.069
LV length S (cm)	3.24	0.57	3.49	0.63	1.699	0.094
LV area S (cm^2)	4.92	1.58	4.36	1.36	1.539	0.129
LV vol D	19.96	10.65	15.34	7.26	2.062	**0.043**
LV vol S	6.50	3.18	4.67	2.33	2.669	**0.010**
LVOT diam (cm)	1.183	0.228	1.336	0.226	2.677	**0.010**
LVOT VTI Vmax (cm/s)	12.99	3.77	12.62	1.63	0.490	0.627
LVOT area (cm^2)	1.138	0.439	1.440	0.485	2.580	**0.012**
Heart rate (/min)	161.82	32.91	116.64	12.59	6.884	**0.000**
LV SV	15.176	8.331	18.299	7.202	1.607	0.113
LV CO	2.382	1.353	2.063	0.613	1.157	0.255
RVOT diam (cm)	1.087	0.224	1.266	0.173	3.597	**0.001**
MAPSE (mm)	12.93	3.11	12.58	2.17	0.512	0.611
TAPSE (mm)	11.73	2.97	10.93	1.95	1.244	0.220

LVIDs: Left ventricular internal end-systolic diameter, LVIDd: Left ventricular internal end-diastolic diameter, LV EF teicholz: Left ventricular ejection fraction according to the Teicholz formula, FS: Left ventricular shortening fraction, IVSd: End-diastolic interventricular septum diameter, LVPWd: End-diastolic left ventricular posterior wall diameter, EDV Teicholz: LV end-diastolic volume according to the Teicholz formula, ESV Teicholz: LV end-systolic volume according to the Teicholz formula, LV mass: Left ventricular mass, LV length D: Left ventricular internal diameter at the end of the diastole, LV area D: Left ventricular area at the end of the diastole. LV length S: Left ventricular internal diameter from mitral annulus to the endocardium of *LV* apex in apical view at the end of the systole. LV area S: Left ventricular area at the end of the systole, LV Vol D: LV end-diastolic volume, LV Vol S: LV end-systolic volume, Lat IVRT: Isovolumic relaxation, Lat IVCT: The isovolumic contraction time, LVOT diam: Left ventricle outflow tract diameter, LVOT VTI Vmax: Left ventricular outflow tract velocity time integral, LVOT area: Left ventricular outflow tract cross-sectional area, LV SV: Sroke volume of the left ventricle, LV CO: Cardiac output of the left ventricle, RVOT diam: Right ventricle outflow tract diameter, TAPSE: Tricuspid annular plane systolic excursion MAPSE: Mitral annular plane systolic excursion.

Table 2. Left ventricular diastolic function parameters in children with bronchiolitis

	Groups					
	Case (n=32)		Control (n=36)			
	Mean	SD	Mean	SD	t	P
Mitral E (cm/s)	99.92	19.96	134.14	158.77	1.131	0.262
Mitral A (cm/s)	66.80	13.60	66.50	5.50	0.141	0.889
E/A	1.503	0.147	2.063	2.673	1.105	0.273
Deceleration time (ms)	119.46	45.18	103.72	29.98	1.591	0.119
Mitral E' (cm/s)	11.27	2.69	14.01	1.09	5.092	**0.000**
Mitral E/e'	9.341	2.795	9.598	11.508	0.115	0.909
Mitral A' (cm/s)	6.26	1.48	8.82	0.69	8.464	**0.000**
E'/A'	1.83	0.31	1.59	0.10	3.8814	**0.001**
Lat IVRT (ms)	63.39	15.49	61.39	7.89	0.625	0.53
Lat IVCT (ms)	68.29	133.28	45.36	5.96	0.909	0.371

Lat IVRT: Isovolumic relaxation, Lat IVCT: The isovolumic contraction time

Table 3. Correlations between left ventricular cardiac functions and vitan signs and laboratory parameters in children with bronchiolitis

	Age (month)	Systolic blood pressure	Diastolic blood pressure	Respiratory rate	SpO2	Fever	Heart rate	pH	pCO2	lactat	WBC	Hb	Plt	CRP
EF teicholz	0,071	0,075	0,011	0,176	0,096	0,035	0,032	0,223	-0,155	0,043	**-,512****	0,192	-0,236	-0,251
FS	0,183	0,136	-0,005	0,125	0,127	0,045	-0,010	0,206	-0,137	0,032	**-,465***	0,193	-0,260	-0,217
LV vol D	,749**	**,486****	-0,146	-0,312	**,427***	0,159	-0,343	-0,158	0,238	-0,179	0,140	-0,331	-0,343	0,103
LV vol S	,692**	**,605****	-0,023	**-,400***	**,446***	0,007	**-,428***	-0,069	0,083	-0,185	0,154	-0,163	-0,269	0,071
EF simpson	0,075	-0,136	-0,072	0,147	0,004	0,350	0,209	-0,257	0,311	-0,088	0,108	-0,262	-0,053	0,146
Mitral E (cm/s)	-0,112	-0,128	-0,001	0,233	0,338	-0,121	**,387***	-0,297	0,277	0,303	-0,278	-0,194	-0,257	-0,287
Mitral A (cm/s)	-0,102	-0,265	0,034	**,427***	0,151	-0,039	**,535****	-0,311	0,224	0,277	-0,217	-0,211	-0,029	-0,325
E/A	-0,101	0,255	-0,047	**-,380***	0,357	-0,244	-0,246	0,067	0,068	0,023	-0,190	0,026	**-,494****	0,050
Deceleration time (ms)	,689**	**,663****	-0,154	**-,627****	0,315	0,255	**-,633****	0,100	-0,046	-0,009	0,302	-0,043	**-,427***	0,333
E'(cm/s)	0,005	0,060	-0,155	-0,112	0,316	-,392*	0,022	0,080	-0,214	0,115	-0,279	-0,177	-0,332	0,141
Mitral E/e'	-0,120	-0,163	0,143	0,281	0,008	0,185	0,249	-0,282	**,392***	0,145	0,006	0,028	0,124	-0,310
E'/A'	-0.434*	-0.338	-0.116	0.163	-0.129	-0.116	0.130	-0.047	0.102	0.033	-0.178	-0.282	0.039	-0.174
A'(cm/s)	0,133	0,289	-0,041	-0,189	**,390***	-0,324	-0,040	0,087	-0,280	0,089	-0,112	0,043	-0,345	0,280
Heart rate (/min)	-,364**	**-,494****	0,163	**,468***	-0,076	0,054	**,984****	-0,127	-0,089	0,165	-0,205	-0,164	0,151	-0,195
LV SV	,828**	**,575****	-0,010	**-,623****	**,553****	-0,178	-0,237	0,057	-0,168	0,000	0,208	0,006	**-,456***	0,290
LV CO	,668**	**,399***	0,038	**-,529****	**,506****	-0,135	0,015	0,037	-0,191	0,030	0,181	-0,068	**-,416***	0,263
MAPSE (mm)	,688**	**,478***	0,058	-0,258	0,122	0,050	-0,367	-0,019	0,131	-0,082	0,259	0,089	-0,127	0,276
TAPSE (mm)	,554**	**,442***	-0,117	**-,500****	0,098	0,036	**-,537****	0,101	-0,197	-0,107	0,178	0,039	0,015	0,120

**. Correlation is significant at the 0.01 level (2-tailed). *. Correlation is significant at the 0.05 level (2-tailed).
EF teicholz: Left ventricular ejection fraction according to the Teicholz formula, FS: Left ventricular shortening fraction, , LV Vol S: LV end-systolic volume, LV Vol D: LV end-diastolic volume, EF simpson: Left ventricular ejection fraction according to the modified Simpson formula, LV SV: Sroke volume of the left ventricle, LV CO: Cardiac output of the left ventricle, MAPSE: Mitral annular plane systolic excursion, TAPSE: Tricuspid annular plane systolic excursion, WBC: White blood cell, plt: platelet, Hb: hemoglobin, CRP: C reactive protein.

Discussion

Bronchiolitis, a lower respiratory tract disease most commonly caused by RSV, is most common in children under 2 years of age during winter months.[13] In recent years, HFNC therapy has gained widespread acceptance as a noninvasive respiratory support method for moderate to severe bronchiolitis in children.[14] We aimed to investigate LV functions in children diagnosed with bronchiolitis and undergoing HFNC therapy, utilizing conventional echocardiography and TDI.

Previous studies have predominantly concentrated on evaluating right ventricular (RV) dysfunction in children with bronchiolitis, with suggestions that this may be linked to pulmonary hypertension.[7,8] Thorburn[7] analyzed RV cardiac function in 34 children with severe bronchiolitis who were ventilated and found decreased RV functions.

While several studies have addressed right ventricular (RV) functions, there has been a limited focus on evaluating left ventricular (LV) functions in bronchiolitis cases. LV diastolic dysfunction in bronchiolitis may be attributed to factors such as pulmonary hypertension, the application of aggressive positive pressure ventilation, and potential direct myocardial damage induced by the virüs.[9,15]

Previous studies suggested that pulmonary hypertension may cause distortions in LV geometry, causing abnormal relaxation of the LV wall and impaired contraction of the wall, resulting in LV dysfunction.[16-18] Kimura et al[19] revealed that pulmonary hypertension detected by echocardiography during RSV infection was associated with increased morbidity and mortality. Several case studies have documented left ventricular (LV) dysfunction attributed to RSV infection. Erdogan[20] reported a case of a 7-year-old child infected by RSV, which showed LV dysfunction. Additionally, Miura[21] and Menchise[22] reported cases diagnosed with RSV myocarditis.

Rodrigez[15] studied on children with bronchiolitis caused RSV-B virus and found that LV myocardial dysfunction was observed in the early stages with TDI. LV myocardial dysfunction was associated with severe respiratory status, Pediatric Intensive Care admission, increased RV pressure, and RV myocardial dysfunction and they indicated the presence of adverse RV-LV interactions in severe RSVB cases.

Rosie[9] suggested that E and A waves may fuse in cases due to increased heart rate in acute illness and cause inaccurate measurements, and that measurements with TDI are more sensitive in measuring diastolic functions. They found LV systolic functions to be normal in patients with severe and moderate bronchiolitis, while LV diastolic functions were impaired similar with current study. In mild cases, they detected normal LV functions. In current study while LV diastolic functions were normal with conventional echocardiography, it was detected to be impaired by TDI (E',A'). Some studies in healthy infants with RSVB found no abnormalities when assessing LV myocardial dysfunction through conventional echocardiographic parameters consisted with our result.[7,15,23,24]

Similar to patients with bronchiolitis, LV dysfunction can be seen in patients with asthma secondary to hypoxia or pulmonary hypertension. In our previous study, we found LV diastolic functions were in normal limits while LV systolic functions were impaired in children with asthma.[25] Despite hypoxia and pulmonary hypertension in asthmatic children, LV diastolic functions remained normal, which suggests that the LV diastolic dysfunction in patients with bronchiolitis was likely attributable to viral exposure.

Considering the LV diastolic dysfunction in patients with severe bronchiolitis, caution should be exercised to prevent fluid overload, and the need for inotropic support may arise in such cases.

An inverse correlation was detected between admission respiratory rate and LV systolic (SV, CO) and diastolic (E/A) functions. As the respiratory rate increased, LV systolic and diastolic function was decreased. A positive correlation was detected between admission SpO2 and LV systolic functions. As the patient's saturation decreased during admission, systolic function also decreased. It is understood that the admission respiratory rate and saturation values were proportional to LV systolic and diastolic functions. As the severity of bronchiolitis increased, LV functions were more affected.

The correlation between cardiac functions and blood gas and hemogram values was examined. While there was no significant correlation with pCO2, pH and lactate, negative correlation was found between platelet value and LV systolic (CO, SV) and diastolic (E/A) functions. As platelet value increased, systolic and diastolic functions were decreased. So platelet level can give a clue about the severity of bronchiolitis.

This study was limited as a single-center study with a small sample. LV functions could be re-evaluated by echocardiography after patients recovered from HFNC treatment. It would be better to evaluate patients' RV functions and whether they have pulmonary hypertension and correlate them with vital signs and blood tests.

In conclusion, patients with bronchiolitis exhibited normal systolic functions, but their diastolic functions were impaired, potentially due to viral exposure. As the severity

of bronchiolitis increased, left ventricular (LV) functions were more significantly affected. Notably, there was an inverse correlation between the platelet count and the severity of LV systolic and diastolic functions.

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Conflicts of Interest

The author declares that there are no conflicts of interest.

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