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Research Article

Evaluation of Cardiac Functions Using Conventional and Tissue Doppler Echocardiography in Patients with Henoch-Schonlein Purpura

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Abstract

Introduction and Purpose: Henoch-Schönlein Purpura (HSP) is a self-limiting systemic vasculitis that involves the skin, joints, gastrointestinal system, and kidneys, and less frequently affects other organs. The purpose of the present study is to evaluate the cardiac functions in patients with HSP using conventional and tissue Doppler echocardiographic examinations.

Material and Methods: The study was performed at the pediatric cardiology department. The patient population consisted of 43 patients who were diagnosed with HSP in the Pediatric Nephrology Department. Thirty-two age, gender, height and weight matched cases were included as the control group. All patients underwent M-mode, two-dimensional echocardiography, Doppler, and tissue Doppler echocardiography.

Findings: While M-mode and two-dimensional echocardiography did not demonstrate statistically significantly different findings between the patient and control groups, the tissue Doppler examination enabled the detection of the left and right ventricular diastolic dysfunction findings.

Discussion and Conclusions: Cardiac involvement is a rare but life-threatening complication of HSP. Thus, cardiac scanning procedures should be performed at the early stages of the disease. In the presence of symptomatic cardiac involvement, early steroid and cytotoxic immune therapy can be helpful in preventing poor prognosis.

Keywords: *Henoch-Schönlein Purpura; Cardiac Involvement; Tissue Doppler; Diastolic Dysfunction*

Introduction and Purpose

HSP is a self-limiting systemic vasculitis that involves the skin, joints, gastrointestinal system, and kidneys, and less frequently affects other organs [1]. In 2006, Ozen., *et al.* classified childhood vasculitis and established the staging criteria for HSP [2]. Cardiac involvement of HSP is a very rare event and a limited number of cases resulting in serious mortality and morbidity were described in the literature. The present study aims to evaluate the conventional and tissue Doppler examinations for the assessment of cardiac systolic and diastolic functions in patients with HSP, and to demonstrate the potential value of tissue Doppler echocardiography in the assessment of clinical or subclinical cardiac involvement at the early stages of the disease, and accordingly to improve prognosis through early diagnosis and treatment of cardiac complications.

While cardiac involvement is not considered as a characteristic of HSP, a majority of the previously reported rare cases followed a fatal course. Laboratory abnormalities (troponin T or CK-MB elevations) and/or arrhythmias can indicate cardiac involvement. In addition, rare cases associated with outcomes such as rhythm disorders, myocardial necrosis, endocardial vascular inflammation, vasculitis, necrosis, and death have been reported in the literature.

Material and Methods

The study was performed at the Pediatric Cardiology Department. The study was planned as a prospective study including two populations: the patient (Group 1) and control group (Group 2). Patient group consisted of 43 patients who had been diagnosed by HSP at the Pediatric Nephrology Department. Thirty-two healthy children, whose age, gender, height, and weight distribution were similar to the patient group, and who had been investigated in the pediatric cardiology polyclinics due to cardiac murmur, but were not diagnosed with any systemic or cardiologic disease, were included in the study as the control group.

The entire study group underwent regular polyclinic examinations including a physical examination, blood pressure measurements, ECG, and echocardiography. Blood pressure measurements were obtained from the left arm at rest.

Electrocardiographic examinations

A 12-lead ECG of all patients and controls was recorded using an EDAN SE-1200 Express (Edan Instruments, Inc., China) device. Heart rate, rhythm, QRS, and p axes, PR interval, QRS, and QTc time, presence of atrial dilatation or ventricular hypertrophy, ST segment and T wave changes in electrocardiography were recorded for all patients and controls.

Echocardiographic Examinations

All echocardiographic examinations were performed using a two-dimensional, M-mode, Doppler, and tissue Doppler equipped General Electric Vivid S-6 (Vingmed Ultrasound, Norway) echocardiography device with 4-6 MHz phase transducer and in accordance with the standard imaging techniques recommended by the American Society of Echocardiography. Echocardiographic examinations of all subjects were performed by the same researcher. Measurements were recorded in the left lateral decubital position, from the short and long-axis parasternal and apical windows at the 4th and 5th intercostal spaces. Left ventricular end-systolic diameter, left ventricle end-diastolic diameter, interventricular septum end-diastolic thickness, left ventricle posterior wall end-diastolic thickness, aortic annulus diameter, fractional contraction, and ejection fraction were measured from the parasternal long-axis views in the M-mode images.

Statistical Analysis

Statistical analyses were performed using SPSS 16.0 package software (SPSS Inc. Chicago, Illinois). Values were shown as mean ± standard deviations. Between-group comparisons of the parameters were done using the student's t-test for normally distributed parameters, and the Mann-Whitney U-test for nonparametric measurements. For all statistical findings, p values < 0.05 were considered statistically significant.

This study was approved by the chairmanship of non-interventional clinical trials ethics committee of Yuzuncu Yil University Medical Faculty Dursun Odabas Medical Center.

Findings

A total of 43 patients diagnosed with HSP, including 22 males and 21 females (Group 1), and 32 healthy children, including 16 males and 16 females, (Group 2) were enrolled in the study. The mean age and body weight of the patient group were 9.13 ± 3.61 years and 30.13 ± 10.24 kg, respectively. The mean age and body weight of the control group were 9.16 ± 3.71 years and 26.71 ± 8.18 kg, respectively. No statistically significant difference was detected between the study groups in terms of the mean age, gender distribution, mean body weight, systolic and diastolic blood pressures, and heart rate measurements ($p > 0.05$) (Table 1).

	Patient group (Group 1) (n = 43)	Control group (Group 2) (n = 32)	P value
Age (year)	9,13 ± 3,61	9,16 ± 3,71	0,614
Gender (male, %)	55, n = 24	53, n = 17	0,78
Gender (female %)	45, n = 19	47, n = 15	0,80
Weight (kg)	30,13 ± 10,24	26,71 ± 8,18	0,125
Systolic BP (mmHg)	108 ± 10,6	102 ± 9,8	0,64
Diastolic BP (mmHg)	78 ± 5,7	80 ± 6,4	0,586
Heart rate (pulse/min)	107,26 ± 8,13	103,88 ± 6,81	0,61

Table 1: *Basic characteristic features of the groups.*
BP: Blood Pressure; min: Minute

Electrocardiographic examinations of both groups showed that all patients had normal sinus rhythm and no statistically significant difference was noted between the two groups in terms of heart rate, QRS, and p axis, PR interval, or QRS and QTc time. Atrial dilatation or ventricular hypertrophy, ST segment, or T wave changes were not detected in either of the groups.

A comparison of the M-mode measurements between the two groups did not indicate any statistically significant difference in the left atrium diameter, left ventricular end diastolic diameter, left ventricular end systolic diameter, diastolic diameter of the interventricular septum, diastolic diameter of the left ventricle posterior wall, ejection fraction, and contraction fraction ($p > 0.05$) (Table 2).

	Group 1	Group 2	P value
Ao (mm)	16,62 ± 2,27	16,03 ± 2,38	0,276
LA (mm)	20,46 ± 2,82	19,62 ± 2,84	0,208
LVEDD (mm)	35,11 ± 3,13	33,37 ± 5,99	0,107
LVESD (mm)	21,09 ± 2,63	20,03 ± 2,22	0,069
IVS (mm)	7,55 ± 1,31	7,56 ± 1,74	0,99
LVPWD (mm)	6,88 ± 1,00	6,62 ± 1,31	0,337
EF (%)	70,37 ± 3,87	71,56 ± 3,17	0,16
SF (%)	38,65 ± 2,88	39,12 ± 1,99	0,307

Table 2: *M-mode measurements of the groups.*
Ao: Aorta Diameter; LA: Left Atrium Diameter; LVEDD: Left Ventricle End Diastolic Diameter; LVESD: Left Ventricle End Systolic Diameter; IVS: Interventricular Septum End Diastolic Diameter; LVPWD: Left Ventricle Posterior Wall End Diastolic Diameter; EF: Ejection Fraction SF: Shortening Fraction

A comparison of the mitral valve PW Doppler measurements between the two study groups demonstrated that the E and A waves were significantly elongated in the patient group ($p < 0.001$); however, E/A ratio values were not significantly different between the two groups ($p > 0.05$). While no significant difference was noted between the two groups in IVCT and ET values ($p > 0.05$), the patient group had significantly longer DT and IVRT ($p < 0.001$) and significantly increased MPI ($p < 0.05$) compared to the control group (Table 3).

	Group 1	Group 2	P value
E (cm/sn)	94,37 ± 8,68	83,09 ± 11,95	< 0,001
A (cm/sn)	63,11 ± 8,49	56,33 ± 8,10	< 0,001
E/A	1,51 ± 0,20	1,48 ± 0,17	0,507
DZ (msn)	190,56 ± 20,24	174,44 ± 15,82	< 0,001
IVRT (msn)	63,93 ± 7,66	58,12 ± 6,12	< 0,001
IVCT (msn)	72,18 ± 6,21	70,15 ± 5,51	0,168
ET (msn)	340,42 ± 15,32	336,12 ± 13,29	0,209
MPI	0,40 ± 0,028	0,38 ± 0,029	0,009

Table 3: *Mitral valve PW Doppler measurements.*
E: Early Diastolic Flow; A: Late Diastolic Flow; DT: Deceleration Time; IVRT: Isovolumetric Relaxation Time; IVCT: Isovolumetric Contraction Time; ET: Ejection Time; MPI: Myocardial Performance İndex

When mitral valve lateral annulus PW tissue Doppler measurements of the two groups were compared, Em and Em/Am values were significantly decreased, while the Am value was significantly elevated in the patient group ($p < 0.05$). Compared to the control group, the patient group had significantly longer IVRT ($p < 0.001$) and significantly increased MPI ($p < 0.05$) (Table 4).

	Group 1	Group 2	P value
Em (cm/sn)	11,27 ± 1,86	12,62 ± 1,72	0,002
Am (cm/sn)	8,11 ± 1,62	7,28 ± 0,95	0,019
Em/Am	1,40 ± 0,14	1,72 ± 0,16	< 0,001
Sm (cm/sn)	10,21 ± 2,61	9,98 ± 1,58	0,665
IVRT (msn)	56,30 ± 7,15	50,90 ± 6,20	0,001
IVCT (msn)	62,41 ± 7,07	59,81 ± 6.70	0,111
ET (msn)	316,33 ± 24,10	319,94 ± 22,05	0,508
MPI	0,37 ± 0,045	0,34 ± 0,042	0,005

Table 4: *Mitral valve lateral annulus PW Tissue Doppler measurements of the groups.*
Em: Early Diastolic Flow; Am: Late Diastolic Flow; Sm: Systolic Flow Rate; IVRT: Isovolumetric Relaxation Time; IVCT: Isovolumetric Contraction Time; ET: Ejection Time; MPI: Myocardial Performance İndex.

A comparison of septal PW Tissue Doppler measurements did not indicate any significant difference between the two groups in Es, As, Es/As ratio, Ss, IVCT, and ET values ($p > 0.05$), while the patient group had significantly longer IVRT and significantly increased MPI than the control group ($p < 0.05$) (Table 5).

	Grup 1	Group 2	P value
Es (cm/sn)	11,58 ± 1,48	11,32 ± 1,35	0,451
As(cm/sn)	7,05 ± 1,12	6,75 ± 0,72	0,363
Es/As	1,67 ± 0,20	1,67 ± 0,15	0,868
Ss (cm/sn)	8,49 ± 1,18	8,30 ± 0,85	0,446
IVRT (msn)	58,32 ± 5,2	53,46 ± 6,18	< 0,001
IVCT (msn)	64,02 ± 5,27	64,53 ± 5,44	0,685
ET (msn)	316,60 ± 20,27	323,22 ± 17,08	0,14
MPI	0,38 ± 0,033	0,36 ± 0,030	0,002

Table 5: *Interventricular septum PW Tissue Doppler measurements of the groups.*
Es: Early Diastolic Flow; As: Late Diastolic Flow; Ss: Systolic Flow Rate; IVRT: Isovolumetric Relaxation Time; IVCT: Isovolumetric Contraction Time; ET: Ejection Time; MPI: Myocardial Performance İndex.

When tricuspid valve PW Doppler measurements were compared between the two groups, IVRT was significantly longer and MPI was significantly elevated in the patient group compared to the controls ($p < 0.05$), while IVCT, St and ET values were not significantly different between the groups ($p > 0.05$) (Table 6).

	Group 1	Group 2	P value
E (cm/sn)	67,51 ± 8,81	64,53 ± 7,52	0,128
A (cm/sn)	45,44 ± 5,86	45,31 ± 7,59	0,934
E/A	1,48 ± 0,16	1,44 ± 0,17	0,222
DT (msn)	160,70 ± 45,80	147,34 ± 9,12	0,109
IVRT (msn)	56,53 ± 5,92	51,18 ± 5,37	< 0,001
IVCT (msn)	58,16 ± 6,48	57,21 ± 3,51	0,459
ET (msn)	318,91 ± 17,75	321,91 ± 15,22	0,445
MPI	0,35 ± 0,025	0,33 ± 0,023	< 0,001

Table 6: *Tricuspid valve PW Doppler measurements of the groups.*
E: Early Diastolic Flow; A: Late Diastolic Flow; DT: Deceleration Time; IVRT: Isovolumetric Relaxation Time; IVCT: Isovolumetric Contraction Time; ET: Ejection Time; MPI: Myocardial Performance İndex

When tricuspid valve lateral annulus PW tissue Doppler measurements of the two groups were compared, Et and Et/At values were significantly decreased, while the At value was significantly elevated in the patient group ($p < 0.05$). Compared to the control group, the patient group had significantly longer IVRT ($p < 0.001$) and significantly increased MPI ($p < 0.05$) (Table 7).

	Group 1	Group 2	P value
Et (cm/sn)	10,58 ± 1,90	12,40 ± 1,43	< 0,001
At (cm/sn)	8,27 ± 1,24	7,40 ± 1,34	0,005
Et/At	1,46 ± 0,22	1,62 ± 0,22	0,004
St (cm/sn)	13,69 ± 1,95	13,32 ± 0,80	0,319
IVRT (msn)	57,27 ± 7,60	52,59 ± 6,11	0,005
IVCT (msn)	66,04 ± 8,27	67,06 ± 7,61	0,588
ET (msn)	316,60 ± 22,51	326,91 ± 22,74	0,078
MPI	0,39 ± 0,037	0,36 ± 0,040	0,001

Table 7: *Tricuspid valve lateral annulus PW Tissue Doppler measurements of the groups. Et: Early Diastolic Flow; At: Late Diastolic Flow; St: Systolic Flow Rate; IVRT: Isovolumetric Relaxation Time; IVCT: Isovolumetric Contraction Time; ET: Ejection Time; MPI: Myocardial Performance İndex.*

For the mitral valve, the E/Em ratio was significantly higher in the patient group compared to the control group ($p < 0.001$). Similarly, E/Et for the tricuspid valve was significantly elevated in the patient group compared to the controls ($p < 0.001$) (Table 8).

	Group 1	Group 2	P value
Left Ventricle E/Em	8,36 ± 1,27	6,90 ± 0,81	< 0,001
Right Ventricle E/Et	6,66 ± 2,17	5,27 ± 0,95	0,001

Table 8: *Left and Right Ventricle E/Em and E/Et values of the groups.*

Discussion

HSP is a self-limiting systemic vasculitis that involves the skin, joints, gastrointestinal system and kidneys, and less frequently affects other organs [1]. It is the most frequently encountered condition among the rare systemic vasculitis syndromes of childhood, and it is the most common type of childhood vasculitis in our country, where the markedly increased frequency of HSP compared to other vasculitis among Turkish children is remarkable [3].

While cardiac involvement is not considered as a characteristic of HSP, a majority of the previously reported rare cases followed a fatal course. When the cases of HSP with cardiac involvement were reviewed, myocarditis events were more common than valvulitis [4,5]. Zaidi., et al. reported a case of HSP with multi-organ involvement including the heart, liver, kidneys, and the skin in a 17-year-old male patient [6]. Ocal., *et al.* described an 11-year-old female patient who received HSP diagnosis one week after a proven streptococcus infection, followed by skin rashes for two weeks along with recently developed rheumatoid carditis with moderate mitral and aortic valve insufficiency. The authors associated the consecutive development of HSP and rheumatoid carditis in their case with the previous streptococcus infection of the patient [7]. In the present study, ASO values were not statistically significantly different between the two groups.

Abdel-hadi., *et al.* previously reported the development of femoral artery and renal artery embolism and myocardial infarction two years after the diagnosis of HSP nephritis in a 27-year-old male patient [8].

Laboratory abnormalities (Troponin T or CK-MB elevations) and/or arrhythmias may indicate cardiac involvement. In addition, rare cases associated with outcomes such as rhythm disorders, myocardial necrosis, endocardial vascular inflammation, vasculitis, necrosis, and death have been reported in the literature [4,9-13]. Lutz., *et al.* reported cardiac involvement along with HSP in a 19-year-old male patient. Their case presented with T negativity in the DII, DIII, aVF, and V4-V6 leads in ECG, while the systolic and diastolic functions of the heart were normal in the echocardiography. The patient's skin rash completely resolved within three weeks under high-dose steroid therapy, while proteinuria and repolarization abnormalities in the ECG were still persistent after two months of follow-up. The patient's cardiac MRI showed posterior-inferior myocardial involvement and the patient had asymptomatic atrial ectopic pulses and grade II type 2 AV block in the ECG. A renal biopsy of the patient demonstrated a glomerular crescent, and since the patient also had cardiac involvement, he was given monthly 750 mg/m^2 cyclophosphamide therapy for six months and the ECG changes were normalized after the second cycle [14].

In the present study, we demonstrated findings consistent with type I diastolic dysfunction of the left and right ventricles, using PW Doppler and tissue Doppler imaging in patients with HSP.

PW Doppler findings in the present study indicated a decrease in the E wave time, an increase in the A wave time, and statistically significant increases in IVRT, deceleration time, and MPI in HSP patients compared to the control group. On the other hand, E/A wave ratio, IVCT and ejection time were not significantly different between the two groups. Tissue Doppler imaging of the mitral valve lateral annulus showed statistically significantly decreased E wave time, increased A wave time, decreased Em/Am wave ratio, and increase in IVRT and MPI in the HSP patients, whereas IVCT, ET, and Sm were not significantly different between the two groups. Septal PW tissue Doppler, as another technique reflecting left ventricular functions, showed statistically significant elevations only in IVRT and MPI in the patients with HSP, while there were no significant differences between the two groups in terms of E wave, A wave, E/A ratio, IVCT, ET and values. When mitral valve and septal tissue Doppler imaging were evaluated together, in line with the mitral valve tissue Doppler imaging findings, HSP patients had statistically significantly decreased E wave time, increased A wave time, decreased E/A ratio, and higher IVRT and MPI. In the present study, systolic dysfunction was not identified in any HSP patient or in any healthy control subject. The fact that we did not detect systolic dysfunction based on ejection fraction, contraction fraction, and Sm values of any patient in this study can be due to all patients who had diastolic dysfunction were asymptomatic, had type 1 diastolic dysfunction grade, and had a short disease duration.

The myocardial performance index reflects both systolic and diastolic functions. In children, MPI is below 0.4 [15]. MPI can be calculated based on both conventional Doppler and tissue Doppler measurements. The present study is the first in this regard. In this study, MPI values measured in the tissue Doppler investigations of the mitral valve, and septal and tricuspid valves of patients with HSP were significantly elevated compared to the control group. Among the values required for MPI measurement, only IVRT was elevated (IVCT and ET were within normal range). We believe that the increase in MPI value is a result of IVRT elongation; in other words, impaired diastolic functions, rather than impairment systolic functions.

We assessed the right ventricular functions of patients and controls using tricuspid valve PW Doppler and tissue Doppler in the present study. While PW Doppler showed significant increases only in IVRT and MPI values in the patient group, tissue Doppler also indicated a statistically significant decrease in E wave time, an increase in A wave time, a decrease in E/A ratio, and an increase in IVRT and MPI in HSP patients. However, IVCT, ET, and St were not significantly different between the two groups. These findings indicate that right ventricular diastolic functions were impaired in patients with HSP compared to healthy controls, while systolic functions were normal in both groups.

Cardiac involvement is a rare but life-threatening complication of HSP. Thus, cardiac screening procedures should be carried out at an early stage of the disease. In the presence of symptomatic cardiac involvement, early steroid and cytotoxic immune therapy can prevent poor prognosis. Based on previously published data, we believe that the investigation of arrhythmia development and cardiac involvement by serial ECG recordings, the investigation of concomitant streptococcal infections by ASO assays, assessment of cardiac enzymes such as troponin particularly in the presence of cardiac symptoms, abnormal cardiac physical examination and a pathological ECG, and the evaluation of cardiac structure and functions using conventional and tissue Doppler echocardiography can be helpful in the early detection of cardiac involvement, which may otherwise cause significant mortality and morbidity.

Conclusion

In conclusion, we believe that in addition to routine detailed cardiac examination, ASO, ECG, and troponin evaluations in selected patients, and obtaining conventional as well as tissue Doppler echocardiography in pediatric HSP patients can ensure the early detection of cardiac complications and thus significantly reduce mortality and morbidity in this patient group.

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