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Original Article

Assessment of Ventricular Functions by Tissue Doppler Echocardiography in Follow-up of Patients with Kawasaki Disease

Kawasaki Hastalığı Olan Hastaların Takibinde Doku Doppler Ekokardiyografi ile Ventriküler Fonksiyonların Değerlendirilmesi

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ABSTRACT

Objective: To evaluate ventricular functions using tissue Doppler echocardiography in long-term follow-up of children with Kawasaki disease after acute phase treatment.

Method: Thirty patients (16 boys, 14 girls; mean age 4.41±3.07 years) treated for Kawasaki disease at our unit between September 1999 and June 2009 were compared with 24 healthy controls of similar age and gender. All subjects underwent standard and tissue Doppler echocardiographic evaluations. Systolic (S') and diastolic (E', A') myocardial velocities were measured from left ventricular basal segments, and myocardial performance indices (MPIs) were calculated.

Results: Mean follow-up period was 24.53±19.06 months. Coronary artery involvement occurred in 13 (43.3%) patients during acute phase, but no aneurysms persisted during follow-up period. Standard echocardiographic parameters including left ventricular ejection fraction, shortening fraction, mitral flow velocities, and aortic velocity showed no significant differences between groups (p>0.05). Tissue Doppler echocardiography measurements of lateral wall velocities and time intervals were comparable. However, left ventricular MPIs were significantly higher in patients (0.518±0.028) compared to controls (0.497±0.028) (p=0.01).

Conclusions: Despite normal conventional echocardiography findings after average 2-year follow-up period, elevated myocardial performance indices indicated subclinical global ventricular dysfunction in children with Kawasaki disease. Tissue Doppler-derived MPI represents a valuable non-invasive parameter for long-term cardiac surveillance in these patients.

Keywords: Kawasaki disease, tissue Doppler echocardiography, myocardial performance index, ventricular function

ÖZ

Amaç: Kawasaki hastalığı olan çocukların akut faz tedavisi sonrası uzun dönem takibinde doku Doppler ekokardiyografi ile ventriküler fonksiyonların değerlendirilmesi.

Yöntem: Ünitemizde Kawasaki hastalığı nedeniyle tedavi edilen 30 hasta (16 erkek, 14 kız; ortalama yaş 4,41±3,07 yıl) (Eylül 1999-Haziran 2009) benzer yaş ve cinsiyetteki 24 sağlıklı kontrol ile karşılaştırıldı. Tüm olgulara standart ekokardiyografi ve doku Doppler değerlendirmesi yapıldı. Sol ventrikül bazal segmentlerinden sistolik (S') ve diyastolik (E', A') miyokardiyal hızlar ölçüldü ve miyokardiyal performans indeksi (MPİ) hesaplandı.

Bulgular: Ortalama takip süresi 24,53±19,06 ay idi. Akut fazda 13 hastada (%43,3) koroner arter tutulumu görüldü, ancak takipte anevrizma saptanmadı. Sol ventrikül ejeksiyon fraksiyonu, kısalma fraksiyonu, mitral akım hızları ve aortik hız dahil standart ekokardiyografik parametreler gruplar arasında anlamlı fark göstermedi (p>0,05). Lateral duvar hızları ve zaman aralıklarının doku Doppler ölçümleri benzerdi. Ancak, sol ventrikül MPİ hasta grubunda (0,518±0,028) kontrol grubuna (0,497±0,028) göre anlamlı olarak yüksek bulundu (p=0,01).

Sonuç: Ortalama 2 yıllık takip sonrası konvansiyonel ekokardiyografi bulgularının normal olmasına rağmen, artmış miyokardiyal performans indeksi Kawasaki hastalığı olan çocuklarda subklinik global ventriküler disfonksiyonu göstermektedir. Doku Doppler ile elde edilen MPİ, bu hastaların uzun dönem kardiyak izleminde değerli bir non-invaziv parametre olarak kullanılabilir.

Anahtar kelimeler: Kawasaki hastalığı, doku Doppler ekokardiyografisi, miyokart performans indeksi, ventrikül fonksiyonu

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INTRODUCTION

Kawasaki disease (KD) is an acute inflammatory vasculopathy characterized by its predilection for medium-sized vessels, with its peak incidence observed in the pediatric population under five years of age[1,2]. The pathological involvement of coronary vasculature represents the most clinically significant sequela of KD, with potential risks including aneurysmal formation, ischemic myocardial injury, and potentially fatal cardiac events[3].

The diagnosis of KD depends on clinical assessment demonstrating fever persisting for five days or longer in conjunction with at least four of five characteristic clinical features including bilateral bulbar conjunctival hyperemia without exudate, mucocutaneous changes affecting the oral cavity and lips, polymorphous truncal rash, peripheral extremity manifestations, and enlarged cervical lymphadenopathy[4,5]. Early initiation of therapy using intravenous immunoglobulin (IVIG) together with aspirin has proven instrumental in substantially diminishing the incidence of coronary complications[6].

Despite effective therapeutic interventions in KD, ongoing cardiovascular complications necessitate further research. Recent studies have revealed that patients without visible coronary artery abnormalities may still experience latent myocardial dysfunction after resolution of the initial disease[7,8]. Routine echocardiographic examinations do not adequately capture the intricate cardiac structural and functional shifts present in affected patients[9].

Tissue Doppler echocardiography (TDE) offers a quantitative approach to evaluate myocardial function through direct measurement of tissue velocities[10]. Among its derived parameters, the myocardial performance index (MPI)—often referred to as the Tei index incorporates both systolic and diastolic components, making it particularly valuable for assessing overall ventricular function[11]. Evidence suggests that TDE-based MPI measurements can identify subtle myocardial abnormalities that conventional echocardiographic methods may overlook[12].

In this study we have aimed to evaluate ventricular functions using TDE in long-term follow-up of children with KD after acute phase treatment and to compare findings with those of a healthy control group.

MATERIALS and METHODS

Study Population

This study was designed as a retrospective cohort with cross-sectional follow-up. We included 30 patients (16 boys, 14 girls; mean age 4.41±3.07 years) who were diagnosed and treated for KD at our unit between September 1999 and June 2009. All patients attended regular cardiology follow-up visits and were in the convalescent phase of the disease. The diagnosis of KD was established according to the criteria of the American Heart Association[13], which remain consistent with recent Japanese diagnostic guidelines[5].

The control group consisted of 24 healthy children (14 boys, 10 girls) of similar age and gender without any cardiac pathology, systemic disease, or family history of cardiovascular disease. All control subjects had normal physical examination and electrocardiographic findings.

Patients and control subjects with congenital heart disease, acquired heart disease other than KD, systemic diseases affecting cardiovascular system, and those with poor echocardiographic image quality were excluded from the analyses.

Echocardiographic Examination

All echocardiographic examinations were performed using a Vivid 7 ultrasound system (GE Healthcare, Milwaukee, WI, USA) equipped with 2.5-5 MHz transducers. Standard two-dimensional, M-mode, and Doppler echocardiographic studies were performed according to the recommendations of the American Society of Echocardiography[14].

TDE

Tissue Doppler imaging was performed in the apical four-chamber view. Pulsed-wave tissue Doppler sample volume was placed at the basal segments of the left ventricular lateral wall and interventricular septum. The following parameters were measured (Figure 1):

- Systolic myocardial velocity (S')
- Early diastolic myocardial velocity (E')
- Late diastolic myocardial velocity (A')
- E'/A' ratio
- Isovolumetric relaxation time (IVRT)
- Deceleration time (DT)
- Isovolumetric contraction time (IVCT).

Calculation of MPI

The MPI was calculated using the formula: MPI = (IVCT + IVRT) / ET, where ET is the ejection time. All measurements were averaged over three consecutive cardiac cycles. For the final statistical analysis, MPI values

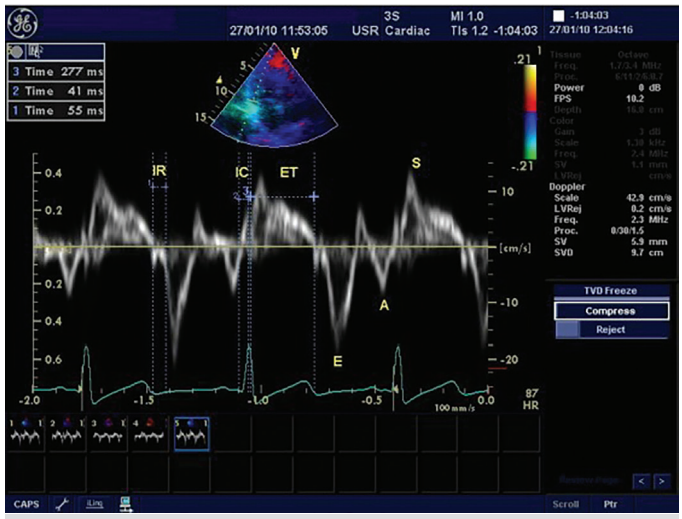

Figure 1. Representative pulsed wave tissue Doppler echocardiography tracing from the left ventricular septal wall showing myocardial velocity patterns

S: Systolic velocity, E: Early diastolic velocity, A: Late diastolic velocity, DT: Deceleration time, IVRT (IR): Isovolumetric relaxation time, IVCT (IC): Isovolumetric contraction time, LVET: Left ventricular ejection time

derived from the (lateral wall/septal wall/average of both walls) were utilized.

Statistical Analysis

Statistical analysis was performed using SPSS version 15.0 (SPSS Inc., Chicago, IL, USA). Continuous variables were expressed as mean ± standard deviation. The normality of data distribution was assessed using the Kolmogorov-Smirnov test. Independent samples t-test was used to compare continuous variables between groups. Chi-square test was used for categorical variables. A p-value <0.05 was considered statistically significant.

The study was approved by Local Non-Drug Ethics Committee of Ege University (decision no: 09-7/63, date: 28.06.2009). Written informed consent was obtained from parents or legal guardians of all participants.

RESULTS

Baseline Characteristics

The mean follow-up period of the study group was 24.53±19.06 months (range: 6-72 months). During the acute phase of KD, coronary artery involvement was detected in 13 (43.3%) patients. However, no coronary aneurysm was found in any patient during the follow-up period. All patients received standard treatment with IVIG and aspirin during the acute phase.

There were no significant differences between the patient and control groups regarding the parameters of age, gender, body weight, height, heart rate, and blood pressure (Table 1).

Standard Echocardiographic Findings

Standard echocardiographic parameters including left ventricular ejection fraction, left ventricular shortening fraction, mitral flow velocities (E, A, E/A ratio), and aortic maximum velocity showed no significant differences between the patient and control groups (p>0.05) (Table 2).

Tissue Doppler Echocardiographic Findings

Analysis of tissue Doppler echocardiographic findings of the left ventricular lateral wall showed no significant differences in terms of S', E', A', E'/A' ratio, IVRT, DT, and IVCT values between the groups (Table 3). Similarly, septal wall tissue Doppler echocardiographic parameters showed no significant differences between the patient and control groups (Table 4).

MPI

The most significant finding of the study was that left ventricular MPI in the patient group (0.518±0.028) was statistically significantly higher compared to the control group (0.497±0.028) (p=0.01) (Figure 2).

Table 1. Demographic and clinical characteristics of the study population

Parameter	Kawasaki patients Mean ± SD	Control Mean ± SD	p
Age (years)	4.41±3.07	4.6±3.34	0.826
Body weight (kg)	18.91±10.27	17.67±7.3	0.617
Height (cm)	99.6±20.89	102±23.87	0.403
Heart rate (bpm)	102.2±10.1	97.1±9.44	0.064
Systolic blood pressure (mmHg)	88.26±8.31	90.29±9.73	0.414
Diastolic blood pressure (mmHg)	62.4±6.14	63.83±5.69	0.383

SD: Standard deviation

Table 2. Conventional echocardiographic parameters			
Parameter	**Kawasaki patients Mean ± SD**	**Control Mean ± SD**	**p**
Mitral E (cm/s)	102.73±12.12	106.96±13.46	0.231
Mitral A (cm/s)	64.03±9.23	62.62±11.58	0.621
Mitral E/A ratio	1.63	1.75	0.139
DT (ms)	143.5±18.6	133.8±16.97	0.802
Aortic peak velocity (cm/s)	113.8±15.63	110.41±12.62	0.390
LVEF (%)	68.34±3.69	65.12±4.80	0.443
LVFS (%)	31.94±2.67	29.72±3.08	0.452
DT: Deceleration time, LVEF: Left ventricular ejection fraction, LVFS: Left ventricular fractional shortening, SD: Standard deviation, E: Early diastolic velocity, A: Late diastolic velocity			

Table 3. Tissue Doppler echocardiographic findings of the LV lateral wall in the study group			
Parameter	**Kawasaki patients Mean ± SD**	**Control Mean ± SD**	**p**
S' lateral (cm/s)	7.97±1.37	7.95±1.0	0.990
E' lateral (cm/s)	16.83±3.43	16.62±11.58	0.109
A' lateral (cm/s)	7.66±1.37	7.92±1.24	0.309
E'/A' lateral	2.24±0.5	2.38±0.41	0.692
IVRT lateral (cm/s)	55.46±3.08	55.5±2.70	0.945
DT lateral (cm/s)	65.81±5.14	60.41±2.68	0.900
IVCT lateral (cm/s)	55.9±4.54	55.95±3.54	0.909
SD: Standard deviation, IVCT: Isovolumetric contraction time, IVRT: Isovolumetric relaxation time, LV: Left ventricle, S': Systolic velocity, E': Early diastolic velocity, A': Late diastolic velocity, DT: Deceleration time			

Table 4. Tissue Doppler echocardiographic findings of the LV septal wall in the study group			
Parameter	**Kawasaki patients Mean ± SD**	**Control Mean ± SD**	**p**
S' septal (cm/s)	7.16±1.41	7.83±1.3	0.269
E' septal (cm/s)	13.63±2.12	15.95±1.73	0.050
A' septal (cm/s)	6.66±1.02	7.58±1.05	0.050
E'/A' septal	2.07±0.036	2.12±0.26	0.927
IVRT septal (cm/s)	51.43±3.82	53.66±3.14	0.676
DT septal (cm/s)	57.73±3.82	59.37±3.67	0.850
IVCT septal (cm/s)	54.5±5.0	55.83±3.98	0.405
SD: Standard deviation, IVCT: Isovolumetric contraction time, IVRT: Isovolumetric relaxation time, LV: Left ventricle, S': Systolic velocity, E': Early diastolic velocity, A': Late diastolic velocity, DT: Deceleration time			

DISCUSSION

This study demonstrates that children with a history of KD may have subclinical global ventricular dysfunction detectable by tissue Doppler-derived MPI, even when conventional echocardiographic parameters appear normal during an average 2-year follow-up after the onset of acute phase. The significantly elevated MPIs in the patient group suggests that the myocardial effects of KD may persist beyond the acute inflammatory phase.

The MPI is a Doppler-derived parameter that provides information on global ventricular performance[15]. An elevated MPI indicates impaired ventricular function, and its prognostic value has been documented to be correlated with clinical outcomes in various cardiac conditions[16].

Previous studies have reported conflicting results regarding long-term cardiac function in KD patients. Several investigators have found that cardiac function was preserved in long-term follow-up [17,18], yet others have

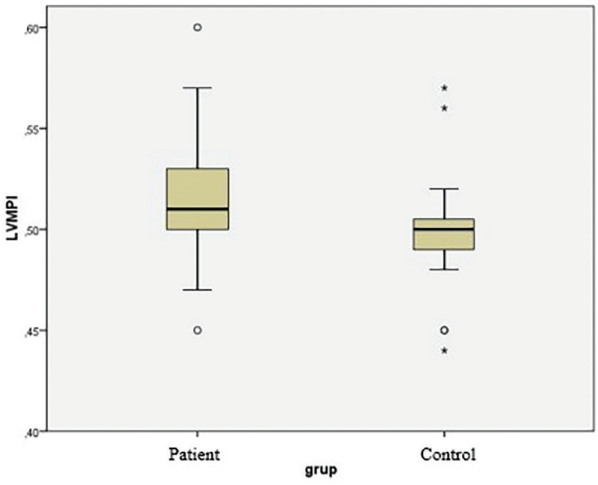

Figure 2. Left ventricular MPI values in patient and control groups

MPI: Myocardial performance index, LVMPI: Left ventricular myocardial performance index

identified persistent abnormalities[19-21]. These conflicting findings may be due to variability in patient population, the length of observation periods, and methods used for evaluation.

TDE has shown greater sensitivity for detection of early myocardial dysfunction than conventional echocardiography. Although standard indices—ejection fraction and shortening fraction—were within normal ranges in our cohort, an elevated MPI indicated subclinical impairment that these conventional measures would not detect.

KD is characterized by systemic inflammation of blood vessels, affecting coronary arteries and heart tissue, although the long-term impact on myocardial function remains incompletely understood[22]. Studies of tissue samples have revealed that KD patients experience persistent myocardial inflammation and scarring, hinting that these adverse effects may last beyond the early phase and lead to enduring functional disabilities[23].

Our finding of elevated MPI in KD patients is consistent with prior studies which have used tissue Doppler imaging to assess myocardial function in this population of patients with KD[24,25]. Selamet Tierney et al.[26] reported diastolic dysfunction in children with KD using tissue Doppler imaging. Likewise, other studies have found evidence of subclinical myocardial dysfunction using various advanced imaging techniques[27,28]. The clinical significance of subclinical myocardial dysfunction in KD patients remains to be determined. It is hard to say whether these changes represent a benign finding or a precursor to clinically significant cardiac dysfunction in later life. Therefore, long-term prospective studies are needed to determine the natural history and clinical implications of these findings.

The 2017 American Heart Association scientific statement on the diagnosis, treatment, and long-term management of KD emphasizes the importance of long-term cardiac surveillance in all KD patients, including those without documented coronary artery abnormalities. The statement recognizes that myocardial involvement may persist beyond the acute phase and recommends periodic cardiac evaluation, though specific guidance on tissue Doppler-based parameters for follow-up remains limited[2].

The most notable finding of this study is the significantly elevated tissue Doppler-derived MPIs in children with a history of KD (0.518±0.028) compared to healthy controls (0.497±0.028; p=0.010), despite normal conventional echocardiographic parameters. Although the absolute difference of 0.021 may appear numerically modest, MPI is a dimensionless index with a narrow physiological range, and Tei et al.[11] established that values exceeding 0.50 indicate impaired global ventricular performance. The mean MPI of our patient cohort (0.518) crosses this validated threshold into the range of subclinical dysfunction, whereas the MPI of the control group (0.497) remains within normal limits.

Study Limitations

This study has several limitations that should be acknowledged. First, the sample size was relatively small (n=30), which restricted statistical power and the generalizability of findings. The wide heterogeneity in follow-up duration (range: 6-72 months) introduces variability that may affect the interpretation of MPI values, as myocardial recovery or progression may differ at various time points after the acute phase. As a single-center study, the results may not be representative of broader KD populations with varying ethnic backgrounds and treatment practices. The cross-sectional design of the study did not allow for assessment of changes in cardiac function over time.

Although echocardiographic assessments were prospectively performed during follow-up visits, the identification of patients was performed using a retrospective study design covering a 10-year period (1999-2009), during which treatment protocols and diagnostic criteria may have evolved. The cross-sectional

nature of the follow-up evaluation did not allow for assessment of temporal changes in MPI or longitudinal trajectories of ventricular function.

We did not perform speckle-tracking strain analysis or cardiac magnetic resonance imaging. Strain would have shown whether the dysfunction is regional or diffuse; CMR would have indicated whether it reflects fibrosis or oedema. We also recorded no clinical outcomes—cardiac events, heart failure symptoms, exercise capacity—so we cannot say whether an elevated MPI matters to the patient. That second gap is the more consequential one. A multicentre cohort followed with serial imaging into adolescence would establish whether these values predict later events or simply normalise on their own.

CONCLUSION

MPI was higher in our KD group than in controls despite normal conventional echocardiographic indices, which suggests that routine measurements are not sensitive enough to exclude residual myocardial involvement at a mean of two years after the acute phase. Tissue Doppler-derived MPI is quick to obtain and requires no additional equipment, so it can reasonably be added to long-term follow-up echocardiography in these children. Whether the abnormality we detected progresses, resolves, or predicts later events is not answerable from a cross-sectional design; prospective follow-up into adolescence would be needed to establish that.

Ethics

Ethics Committee Approval: The study was approved by Local Non-Drug Ethics Committee of Ege University (decision no: 09-7/63, date: 28.06.2009).

Informed Consent: Written informed consent was obtained from parents or legal guardians of all participants.

Declaration of AI Use: No artificial intelligence tools were used in the preparation of this manuscript.

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Footnotes

Authorship Contributions

Surgical and Medical Practices: M.O.B., Concept: M.O.B., Design: M.O.B., Data Collection or Processing: M.O.B., M.D., B.A., Analysis or Interpretation: Z.Ü., E.L., A.R.Ö., Literature Search: M.O.B., Writing: M.O.B., Z.Ü., E.L.

Conflict of Interest: No conflict of interest was declared by the authors.

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