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ORIGINAL ARTICLE

Unveiling subclinical myocardial dysfunction in pediatric *Helicobacter pylori* infection via speckle tracking echocardiography

Helicobacter pylori enfeksiyonu olan çocuklarda subklinik miyokardiyal disfonksiyonun ortaya çıkarılması: Speckle tracking ekokardiyografi ile değerlendirme

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ABSTRACT • **Background and Aims:** *Helicobacter pylori* is among the most prevalent infectious agents globally. Recent evidence has highlighted its potential impact beyond the gastrointestinal tract, including possible effects on the cardiovascular system. This study aimed to evaluate myocardial function in children with *Helicobacter pylori* infection using advanced echocardiographic modalities, particularly two-dimensional speckle tracking echocardiography. **Materials and Methods:** A total of 54 children diagnosed with *Helicobacter pylori* infection (mean age: 14 ± 3.1 years) and 37 age-matched healthy controls (mean age: 13.6 ± 2.2 years) were enrolled. Conventional echocardiography, tissue Doppler imaging, and two-dimensional speckle tracking echocardiography were performed to assess left ventricular function. **Results:** No significant differences were found in traditional echocardiographic parameters between the groups. However, the myocardial performance index measured via tissue Doppler imaging was significantly higher, and mitral S', A', and E'/A' values were significantly lower in the *Helicobacter pylori* group ($p < 0.05$). Furthermore, both global longitudinal strain and circumferential strain values obtained from two-dimensional speckle tracking echocardiography were significantly reduced in the patient group (global longitudinal strain: -18.1 ± 0.8 vs. -19.6 ± 1.1; circumferential strain: -19.2 ± 1.2 vs. -21.2 ± 1.0; $p < 0.001$). **Conclusion:** *Helicobacter pylori* infection in children is associated with subclinical alterations in myocardial function, which can be detected using two-dimensional speckle tracking echocardiography and tissue Doppler imaging -derived myocardial performance index. These findings underscore the importance of cardiac follow-up in children diagnosed with *Helicobacter pylori* infection.

Key words: *Helicobacter pylori,* myocardial dysfunction, subclinical cardiomyopathy, tissue Doppler imaging, strain echocardiography

ÖZET • **Giriş ve Amaç:** *Helicobacter pylori,* dünya çapında en yaygın enfeksiyon etkenlerinden biridir. Son bulgular, gastrointestinal sistemin ötesinde, kardiyovasküler sistem üzerindeki olası etkileri de dahil olmak üzere potansiyel etkisini vurgulamaktadır. Bu çalışma, Helicobacter pylori enfeksiyonu olan çocuklarda miyokardiyal fonksiyonu, özellikle iki boyutlu speckle tracking ekokardiyografi olmak üzere gelişmiş ekokardiyografik yöntemler kullanarak değerlendirmeyi amaçlamaktadır. **Gereç ve Yöntem:** Helicobacter pylori enfeksiyonu tanısı almış toplam 54 çocuk (ortalama yaş: 14 ± 3.1 yıl) ve yaşları eşleştirilmiş 37 sağlıklı kontrol (ortalama yaş: 13.6 ± 2.2 yıl) çalışmaya dahil edildi. Sol ventrikül fonksiyonunu değerlendirmek için konvansiyonel ekokardiyografi, doku Doppler görüntüleme ve iki boyutlu speckle tracking ekokardiyografi uygulandı. **Bulgular:** Gruplar arasında geleneksel ekokardiyografik parametrelerde anlamlı bir fark bulunmadı. Ancak, doku Doppler görüntüleme ile ölçülen miyokardiyal performans indeksi Helicobacter pylori grubunda anlamlı derecede yüksek, mitral S', A' ve E'/A' değerleri ise anlamlı derecede düşüktü ($p < 0.05$). Ayrıca, iki boyutlu speckle tracking ekokardiyografi ile elde edilen hem global longitudinal strain hem de circumferential strain değerleri hasta grubunda istatiksel anlamlı düşük saptandı (global longitudinal strain: -18.1 ± 0.8 vs. -19.6 ± 1.1; circumferential strain: -19.2 ± 1.2 vs. -21.2 ± 1.0; $p < 0.001$). **Sonuç:** Çocuklarda Helicobacter pylori enfeksiyonu, iki boyutlu speckle tracking ekokardiyografi ve doku Doppler görüntüleme türevli miyokardiyal performans indeksi kullanılarak tespit edilebilen miyokardiyal fonksiyonda subklinik değişikliklerle ilişkilidir. Bu bulgular, Helicobacter pylori enfeksiyonu tanısı alan çocuklarda kardiyak takibin önemini vurgulamaktadır.

Anahtar kelimeler: Helicobacter pylori, miyokardiyal disfonksiyon, subklinik kardiyomiyopati, doku Doppler görüntüleme, strain ekokardiyografi

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INTRODUCTION

Helicobacter pylori (H. pylori) is a gram-negative, microaerophilic, spiral-shaped bacterium that colonizes the gastric mucosa and is recognized as one of the most widespread infectious agents globally (1). Beyond its established role in gastrointestinal pathologies, growing evidence suggests that *H. pylori* infection may also contribute to extra-gastrointestinal disorders, including those affecting the cardiovascular and neurological systems (2).

Recent adult studies have demonstrated a possible association between *H. pylori* infection and ischemic heart disease, increased arterial stiffness, and elevated carotid intima-media thickness, suggesting a potential link between this infection and cardiovascular morbidity (3-7). However, data on pediatric populations remain scarce, and no studies to date have systematically assessed the impact of *H. pylori* infection on myocardial function in children.

Specifically, the study sought to determine whether advanced echocardiographic techniques -such as Tissue Doppler Imaging (TDI) and two-dimensional speckle tracking echocardiography (2D-STE)- could detect myocardial dysfunction not apparent on conventional echocardiography.

Given the possibility that persistent *H. pylori* -related inflammation and metabolic disruptions could subtly affect the myocardium, this study aimed to investigate early subclinical myocardial changes in pediatric patients with confirmed *H. pylori* infection absent overt cardiac disease or classical cardiovascular risk factors.

MATERIALS and METHODS

Study Design and Population

This cross-sectional study was conducted between August 2020 and April 2021 at the Pediatric Gastroenterology and Pediatric Cardiology outpatient clinics of Gülhane Training and Research Hospital, Ankara, Türkiye. The study population comprised children aged 2 to 18 years who presented with chronic epigastric pain, nausea, vomiting, or dyspeptic symptoms and were newly diagnosed with *H. pylori* infection according to the 2016 ESPGHAN guidelines for upper gastrointestinal endoscopy (8).

Upper GI endoscopy was performed by an experienced pediatric gastroenterologist under deep sedation administered by an anesthesiologist, using an Olympus X260 endoscope (Olympus Optical Corporation, Japan). *H. pylori* infection was confirmed through a combination of rapid urease testing and histopathological examination. Gastric mucosal biopsies were evaluated according to the updated Sydney classification system, which includes grading of *H. pylori* density (colonization degree), chronic inflammation, activity, atrophy, intestinal metaplasia, and presence of lymphoid follicles (9).

The control group consisted of healthy, age- and sex-matched children with no gastrointestinal or cardiovascular complaints, findings, or medical history. *H. pylori* testing was not routinely performed in controls, but all were asymptomatic and had no history of suggesting chronic infection. Demographic data, physical examinations, electrocardiograms, and echocardiographic evaluations were recorded for all participants. C-reactive protein (CRP) was measured only in the patient group, as it is a routinely indicated marker of inflammation during diagnostic work-up for gastrointestinal complaints. This study was approved by the Ethics Committee of Health Sciences University Gulhane Training and Research Hospital (Approval No: 2020-389). Written informed consent was obtained from the parents or legal guardians of all participating children, and assent was obtained from children when appropriate, in accordance with the Declaration of Helsinki.

Echocardiographic Evaluation

All echocardiographic assessments were performed by a single pediatric cardiologist blinded to group allocation, using a Philips EPIC 7C ultrasound system (Philips, Andover, MA, USA) with a 5S-1 probe. Examinations were conducted under electrocardiographic monitoring. Left ventricular (LV) systolic and diastolic functions were evaluated using three modalities: conventional echocardiography, tissue Doppler imaging (TDI), and two-dimensional speckle tracking echocardiography (2D-STE).

Conventional Echocardiography

Standard two-dimensional (2D) and M-mode echocardiographic measurements were performed according to the recommendations of the American Society of Echocardiography (10). Left ventricular ejection fraction (EF) and shortening fraction (SF) were obtained from the parasternal long-axis view using M-mode imaging. Mitral inflow velocities during early (E) and late (A) diastole, along with the E/A ratio, were calculated from pulsed-wave Doppler recordings in the apical four-chamber view.

Tissue Doppler Imaging

Tissue Doppler Imaging (TDI) measurements were obtained from the apical four-chamber view by placing the sample volume at the junction of the LV posterior wall and the mitral annulus. Peak myocardial velocities during systole (S′), early diastole (E′), and late diastole (A′) were recorded. The myocardial performance index (MPI) was calculated as the ratio of the sum of isovolumic contraction time (IVCT) and isovolumic relaxation time (IVRT) to ejection time (ET) (11).

Speckle Tracking Echocardiography

For speckle tracking analysis, echocardiographic cine-loops from apical four-chamber and parasternal short-axis views were recorded over 3–4 cardiac cycles. The LV myocardium was segmented into 17 regions in accordance with the American Heart Association guidelines (12). Global longitudinal strain (GLS) and global circumferential strain (GCS) values were calculated after manual tracing of the endocardial border and automatic speckle tracking analysis.

Statistical Analysis

Statistical analysis was conducted using IBM SPSS Statistics version 23.0 (IBM Corp., Armonk, NY, USA). The Shapiro–Wilk test was used to assess the normality of distribution. Continuous variables were expressed as mean ± standard deviation (SD) or median (min–max), and categorical variables as counts and percentages. Between-group comparisons were performed using the independent samples t-test or Mann–Whitney U test, depending on data distribution. Chi-square test was used for categorical data. Pearson's correlation analysis was employed to examine relationships between echocardiographic parameters and clinical variables. A p-value < 0.05 was considered statistically significant.

RESULTS

A total of 91 participants were included in the study: 54 children with confirmed *H. pylori* infection (68.5% female, 31.5% male) and 37 healthy controls (75.7% female, 24.3% male). The mean age of the patient group was 14.0 ± 3.1 years, and that of the control group was 13.6 ± 2.2 years. There were no statistically significant differences between the groups in terms of age, height, weight, body mass index (BMI), BMI z-score, heart rate, or systolic and diastolic blood pressure ($p > 0.05$ for all variables) (Table 1).

The median duration of gastrointestinal symptoms in the patient group was 12.7 months (range: 1 - 48 months), with epigastric pain (55%) and dyspepsia (47%) being the most frequently reported com-

plaints. The median C-reactive protein (CRP) level was 3.7 mg/L (range: 0.1 - 22). Histopathological analysis indicated moderate disease activity in 79.6% of patients and moderate *H. pylori* colonization in 41.2%. Although no cases of atrophy or intestinal metaplasia were observed, marked inflammatory infiltration was reported in 16.7% of the biopsy samples.

Conventional Echocardiographic Findings

Conventional echocardiographic measurements, including ejection fraction (EF), shortening fraction (SF), left ventricular end-diastolic diameter (LVEDd), and left ventricular mass, showed no statistically significant differences between the patient and control groups ($p > 0.05$) (Table 2).

Table 1 Demographical and baseline clinical characteristics of study participants

Variable	*H. pylori* Group (n = 54)	Control Group (n = 37)	p Value
Age (years)	14.0 ± 3.1	13.6 ± 2.2	0.40
Height (cm)	158.4 ± 15.6	157.7 ± 10.8	0.70
Weight (kg)	50.4 ± 16.4	51.2 ± 12.0	0.80
BMI (kg/m²)	19.5 ± 3.6	20.3 ± 3.1	0.30
BMI z-score	–0.5 ± 1.3	–0.02 ± 0.98	0.07
Heart rate (bpm)	83.1 ± 16.4	86.6 ± 13.9	0.36
Systolic BP (mmHg)	106.7 ± 9.9	108.2 ± 6.0	0.45
Diastolic BP (mmHg)	70.8 ± 6.9	73.8 ± 7.5	0.08
CRP (mg/L)*	1.0 (0.1–22)	—	—

*Values are presented as mean ± SD unless otherwise specified.
BMI: Body mass index; BP: Blood pressure; CRP: C-reactive protein.

Table 2 Comparison of conventional echocardiographic parameters

	H. pylori Group (n = 54)	Control Group (n: 37)	p Value
M Mode - 2D parameters			
EF (%)	74.7 ± 5.9	76 ± 5.9	0.3
SF (%)	43.6 ± 5.6	44.9 ± 5.4	0.27
LVEDd (mm)	43.1 ± 5.6	43.5 ± 5	0.7
LVEDs (mm)	24 ± 3.9	24.1 ± 3.9	0.87
IVSD (mm)	7.9 ± 0.8	8.3 ± 0.9	0.06
IVSS (mm)	12 ± 3.4	11.8 ± 1.5	0.71
LPWd (mm)	7.5 ± 1.8	7.9 ± 1.2	0.16
LV mass (gr)	101.8 ± 28.1	113.3 ± 28.5	0.06
PW Doppler measurements			
E mitral (mitral inflow, cm/sn)	85.1 ± 11.5	84.2 ± 13.3	0.7
A mitral (mitral inflow, cm/sn)	55.2 ± 10.6	58.4 ± 9.7	0.1
E/E'	5.4 ± 1.1	4.9 ± 1.1	0.06
E/A	1.5 ± 0.2	1.4 ± 0.1	0.06

EF: Ejection fraction; SF: Shortening fraction; LV: Left ventricular; LVEDd/s: LV end-diastolic/systolic diameter; IVSd/s: Interventricular septum thickness; LVPWd: LV posterior wall thickness.

Tissue Doppler Imaging Results

Tissue Doppler Imaging (TDI)-derived parameters revealed significant alterations in the *H. pylori* group. Specifically, the patient group exhibited significantly lower mitral annular systolic velocity (S′), early diastolic velocity (E′), and late diastolic velocity (A′) compared to controls. Furthermore, the E′/A′ ratio was significantly reduced, while the myocardial performance index (MPI) was significantly elevated in the *H. pylori* -positive group ($p < 0.05$ for all) (Table 3).

Speckle Tracking Echocardiography Findings

Speckle Tracking Echocardiography (2D-STE) analysis demonstrated that global longitudinal strain (GLS) and global circumferential strain (GCS) values were significantly lower in the *H. pylori* group than in the healthy controls (GLS: –18.1 ± 0.8 vs. –19.6 ± 1.1; GCS: –19.2 ± 1.2 vs. –21.2 ± 1.0; $p < 0.001$ for both) (Table 3).

Correlation Analysis

No significant correlations were found between LV GLS or GCS and the duration of gastrointestinal symptoms or histopathological severity ($p > 0.05$). Moreover, no correlation was found between GLS/GCS and symptom duration or CRP levels ($p > 0.05$ for all). A subgroup comparison of patients with symptom durations ≤ 6 months vs. > 6 months also revealed no significant differences in strain or MPI values.

However, both GLS and GCS values were positively correlated with MPI (r: 0.35 p: 0.004, r: 0.65, $p < 0.001$, respectively), suggesting a consistent relationship between impaired strain parameters and overall myocardial performance.

DISCUSSION

Cardiovascular diseases (CVD) continue to be the leading global cause of morbidity and mortality across all age groups (13). While traditional risk factors such as hypertension, dyslipidemia, and diabetes mellitus are well-established contributors, accumulating evidence suggests that chronic infections—particularly Helicobacter pylori—may also play a role in cardiovascular pathophysiology (14).

Although the majority of studies exploring the relationship between *H. pylori* infection and CVD have been conducted in adults, pediatric data remain limited. However, given that *H. pylori* infection often begins during childhood—particularly

Table 3 Comparison of echocardiographic parameters derived from TDI and 2D STE among groups

	H. pylori Group (n = 54)	Control Group (n: 37)	p Value
TDI			
E′ (cm/sn)	16 ± 3	17.3 ± 3.2	0.07
A′ (cm/sn)	7.3 ± 1.7	8.9 ± 1.6	**< 0.001**
E′/A′	1.9 ± 0.3	2.1 ± 0.3	0.03
S (cm/sn)	9.9 ± 1.9	11.7 ± 2.3	**< 0.001**
ET (ms)	254.8 ± 26.2	262.1 ± 22.1	0.2
MPI	0.61 ± 0.08	0.48 ± 0.07	**< 0.001**
2D- STE			
LV GLS	-18.1 ± 0.8	-19.6 ± 1.1	**< 0.001**
LV GCS	-19.2 ± 1.2	-21.2 ± 1	**< 0.001**

TDI: Tissue Doppler imaging; STE: Speckle tracking echocardiography; LV: Left ventricular; GLS: Global longitudinal strain; GCS: Global circumferential strain; ET: Ejection time; MPI: Myocardial performance index.

in developing countries—it is important to investigate its potential long-term consequences on cardiovascular health from an early age (15).

Several pathophysiological mechanisms have been proposed to explain how *H. pylori* infection may affect the cardiovascular system. Although the precise mechanisms remain incompletely understood, several hypotheses have been proposed regarding the cardiovascular implications of *H. pylori* . These include chronic low-grade inflammation, oxidative stress, lipid metabolism disorders, and immune system dysregulation—factors that are all closely linked to the pathogenesis of endothelial dysfunction and early atherosclerosis (16-19).

Elevated pro-inflammatory cytokines and acute-phase reactants resulting from persistent gastric colonization can promote endothelial activation and procoagulant states, while molecular mimicry may initiate autoimmune responses that target vascular or myocardial tissues (16,20). Additionally, associations between *H. pylori* and dyslipidemia, insulin resistance, and impaired glucose metabolism have also been reported (21).

These mechanisms may extend beyond the vasculature and influence myocardial structure and function. Indeed, myocardial dysfunction has been demonstrated in other chronic inflammatory or autoimmune disorders, such as systemic lupus erythematosus, rheumatoid arthritis, and inflammatory bowel disease. Moreover, chronic inflammation-associated malnutrition and micronutrient deficiencies may further compromise myocardial performance. In accordance with this perspective, although no clinical studies have directly assessed myocardial function even in adults with *H. pylori* infection, evidence linking *H. pylori* -associated arrhythmias to subclinical myocarditis in adults has been reported and is consistent with our hypothesis of subclinical myocardial involvement in pediatric patients (22).

The present study provides novel insights into early myocardial alterations in children with *H. pylori* infection, using advanced echocardiographic techniques to detect subclinical dysfunction. Notably, while conventional echocardiographic parameters—including ejection fraction and fractional shortening—were within normal limits, significant differences were observed in tissue Doppler and strain echocardiographic indices between patients and controls.

Specifically, children with *H. pylori* infection exhibited significantly lower mitral S′, A′, and E′/A′ values, and elevated MPI on TDI, indicative of both systolic and diastolic dysfunction. Furthermore, 2D-STE revealed impaired global longitudinal and circumferential strain values, which were also correlated with MPI, reinforcing the evidence of subtle myocardial involvement.

These findings align with studies in other pediatric populations with chronic gastrointestinal inflammation. For example, El Amrousy et al. reported reduced GLS in children with celiac disease, and similar results have been observed in patients with inflammatory bowel disease and other chronic inflammatory conditions (23,24-28). These studies, like the present one, consistently demonstrate the superiority of advanced myocardial deformation imaging over conventional techniques in detecting early cardiac dysfunction (29).

Interestingly, no correlation was found in our study between histopathological severity of gastric inflammation or symptom duration and myocardial strain parameters. This may reflect the heterogeneous distribution of pathology and the relatively limited sample size within histological subgroups. Further studies are warranted to clarify whether specific inflammatory or histological features of *H. pylori* infection are predictive of myocardial involvement.

This study has several limitations. The relatively small sample size and the absence of stress echocardiography limit the generalizability and depth of myocardial assessment. Additionally, the cross-sectional design precludes evaluation of long-term cardiac outcomes. Future longitudinal studies with larger cohorts and incorporation of other imaging modalities are essential to better understand the cardiovascular implications of *H. pylori* in children.

In conclusion, the findings of this study suggest that *H. pylori* infection in children is associated with subtle yet significant alterations in myocardial function. To the best of our knowledge, this is the inaugural study to utilize 2D-STE for the evaluation of subclinical myocardial involvement in children infected with *H. pylori* , thereby contributing novel insights with significant implications for early cardiovascular risk stratification and intervention. While conventional echocardiographic parameters may remain within normal ranges, tissue Doppler imaging and speckle tracking echocardiography can detect early subclinical changes in both systolic and diastolic function.

The observed impairments in myocardial strain and elevated myocardial performance index (MPI) indicate that even in the absence of overt cardiac symptoms or established cardiovascular disease, children with *H. pylori* infection may exhibit early myocardial involvement. These changes are likely multifactorial, involving inflammation, immune dysregulation, and possibly nutritional deficiencies linked to chronic infection.

Given these findings, routine cardiovascular monitoring may be advisable in pediatric patients diagnosed with *H. pylori* , particularly in those with chronic or recurrent symptoms. Early identification of myocardial impairment may allow timely intervention and prevention of potential long-term cardiac consequences.

Future prospective studies with larger sample sizes and extended follow-up are warranted to validate these observations and to clarify the clinical significance of subclinical myocardial dysfunction in this population.

Ethics approval and consent to participate: *This study was approved by the Ethics Committee of Health Sciences University Gülhane Training and Research Hospital (Approval No: 2020-389). Written informed consent was obtained from all participants' parents or legal guardians, and assent was obtained from children when appropriate.*

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