Cardiovascular Topics

# Evaluation of cardiac function in paediatric Wilson's disease patients with advanced echocardiographic modalities (strain and strain rate echocardiography)

Kerem Ertaş, Özlem Gül, Fatma Demirbaş

## Abstract

**Objective:** In Wilson's disease (WD), copper accumulation in the organs and/or damage caused by oxygen free radicals occurs due to disturbances in copper excretion. In our study, we aimed to evaluate cardiac involvement with advanced echocardiographic modalities (tissue Doppler echocardiography, strain and strain-rate echocardiography).

**Methods:** Twenty WD patients and 20 healthy children from the Pediatric Gastroenterology Department of Diyarbakır Children's Hospital were included in the study between 2022 and 2023.

**Results:** The mean age of the WD patients was 12.89 ± 3.79 years. Left ventricular wall thicknesses and diameters (diastolic interventricular septum thickness, diastolic left ventricular posterior wall thickness, left ventricular end-diastolic diameter), left ventricular diastolic function parameters (E, A, E/A, deceleration time) and left ventricular ejection fraction and tricuspid annular plane systolic excursion were similar and not statistically significantly different in the WD and control groups. Mitral lateral e′, mitral septal e′ and tricuspid lateral e′ velocities were lower in the WD patients and statistically significantly different from the controls ($p$ = 0.02, 0.04 and 0.005, respectively), as assessed by tissue Doppler echocardiography. Global longitudinal systolic strain was similar in the WD and control groups and no statistically significant difference was detected. Longitudinal early diastolic strain rate was lower in the WD patients and statistically significantly different ($p$ = 0.002).

**Conclusion:** Subclinical early diastolic dysfunction and segmental systolic dysfunction were detected in WD patients with advanced echocardiographic modalities, in addition to normal cardiac function as assessed by conventional echocardiography. Advanced echocardiographic modalities can be used in the follow up of WD patients.

**Keywords:** Wilson's disease, strain, strain-rate echocardiography

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Wilson's disease (WD) is a genetic disorder that is inherited in an autosomal recessive manner. It is caused by mutations in the protein that transports copper in the liver cells (ATP7B), which leads to the accumulation of copper in the body and damage to organs such as the liver, central nervous system and heart. The incidence of the disease in the general population is 1/30 000. The dysfunction in copper excretion mainly affects the liver, as well as other organs such as the central nervous system and cardiovascular system.[1] The damage in the heart is thought to be related to copper accumulation and/or oxygen free radicals.[2,3] The damage can result in cardiomyopathy and arrhythmias.[4]

Asymptomatic patients may be overlooked when conventional methods are used for cardiac evaluation of their WD. Advanced echocardiographic (echo) imaging techniques allow early evaluation of asymptomatic patients.[5] For this purpose, we aimed to evaluate the cardiac involvement of WD patients using advanced echo imaging techniques such as tissue Doppler echocardiography (TDE), strain echocardiography (SE), and strain-rate echocardiography (SRE) derived from speckle tracking.

## Methods

The study was a prospective case–control study. It included 20 children diagnosed with WD who were followed up at the Pediatric Gastroenterology Department and consulted at the Pediatric Cardiology Department, and 20 healthy children matched for gender and age. Age is expressed in years, body weight in kilograms, height in centimetres and body surface area (BSA) in square metres.[6]

After informing all the parents of the patients, signed consent was obtained. Ethics board approval was obtained from the local ethics board (decision no: 2022/171) for this study.

A paediatric gastroenterologist diagnosed WD based on the diagnostic criteria.[7] WD was diagnosed in all patients by liver biopsy. The WD patients had only liver involvement and no central nervous system involvement. There were no deaths in any patients in our study. All patients were under follow up by the Pediatric Gastroenterology Department, and our patients

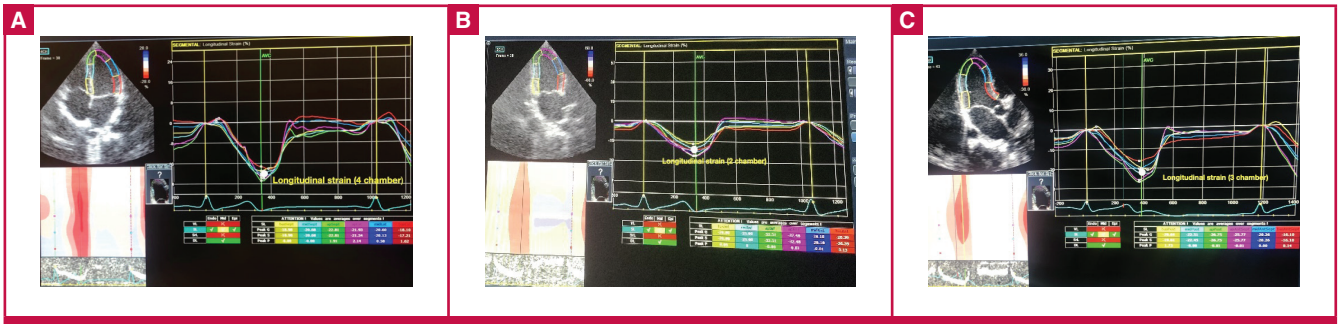


**Fig. 1.** Apical four- (A), three- (B) and two-chamber (C) longitudinal strain curve in a patient with a diagnosis of WD.

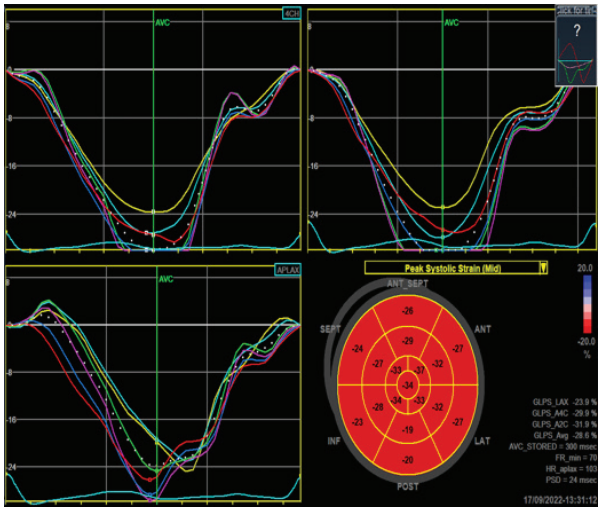


**Fig. 2.** Bull's-eye view of the 17th segment of the left ventricle in a patient diagnosed with WD.

visited our Pediatric Cardiology out-patient clinic for check-ups periodically. All patients were evaluated by the same paediatric cardiologist, who took a detailed medical history and performed a thorough physical examination.

Echocardiographic evaluations were performed with patients lying on their left side (Vivid S60, General Electric Healthcare, GE Vingmed, Norway). Using the appropriate transducer, the following standard images were obtained in apical and parasternal positions: left ventricular wall thickness [diastolic interventricular septum thickness (IVSd), diastolic left ventricular posterior wall thickness (LVPWd)], left ventricular diameter [left ventricular end-diastolic diameter (LVEDd)], left ventricular ejection fraction (LVEF) and fractional shortening (FS). Left ventricular mass (LVmass) was derived from left ventricular wall thickness and diameters. LVmass-index (LVmass-i) was derived from LVmass and body surface area (LVmass/BSA). Tricuspid annular plane systolic excursion (TAPSE) was also obtained.[7-10]

Mitral E and A velocities, deceleration time (DT), isovolumetric contraction time (ICT), isovolumetric relaxation time (IRT) and ejection time (ET) were determined, and myocardial performance index [MPI = (ICT + IRT)/ET], derived from these intervals, was obtained using pulse-wave (PW) Doppler in the apical position.[11] Systolic (s′), early (e′), and late (a′) velocities were obtained by evaluating TDE from the mitral and tricuspid lateral annulus. The myocardial performance index was calculated as:

$$mpi' = (ict' + irt')/et'.$$[12]

Strain and strain-rate echocardiography analyses were performed offline using the Echo Pac (Vivid, GE Vingmed, Horton, Norway) program. With speckle-tracking echocardiography, the deformation rate was expressed as the strain, and the systolic and diastolic velocities of deformation were expressed as the strain rate. Strain was measured globally and segmentally, and strain rate was measured globally. Left ventricular strain was evaluated longitudinally, circumferentially and radially, whereas

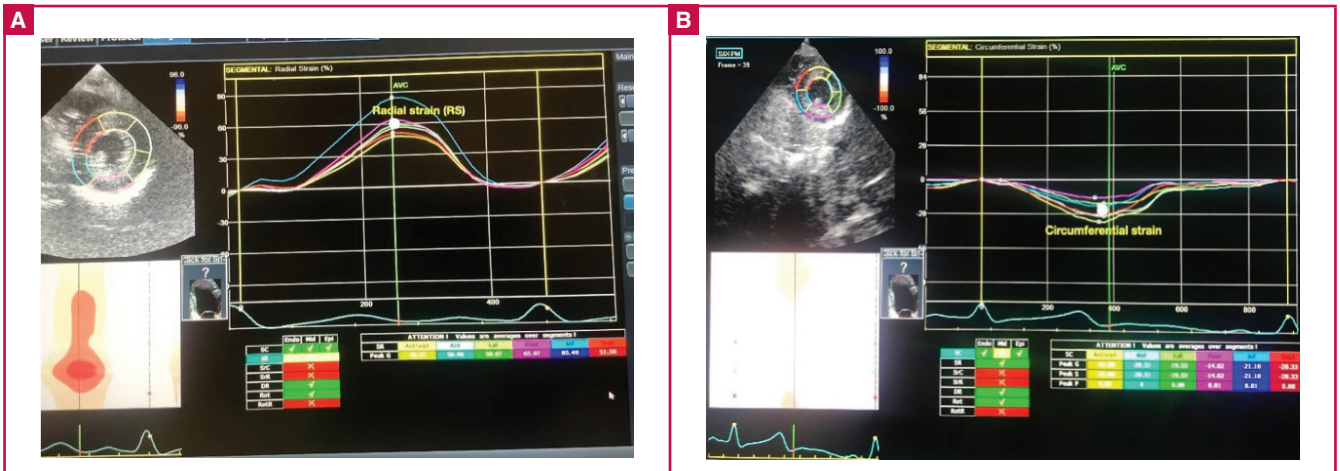


**Fig. 3.** Radial (A) and circumferential (B) strain curves.

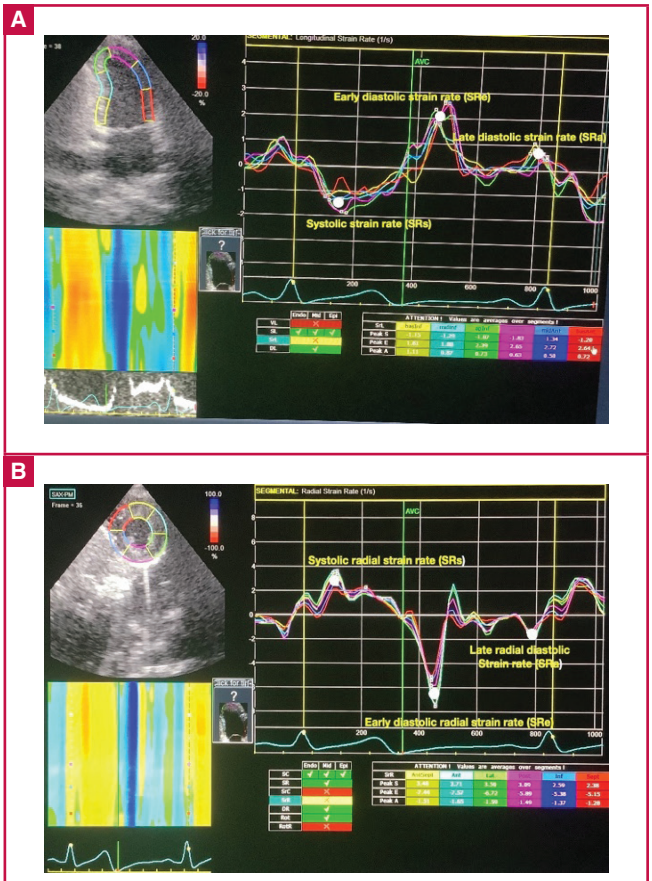


**Fig. 4.** Longitudinal (A) and radial (B) systolic (SRs), early diastolic (SRe), late diastolic (SRa) strain rate curves.

right ventricular strain was evaluated only in the longitudinal plane. Longitudinal (L), circumferential (C) and radial (R) deformations were obtained using strain echocardiography, and systolic (SRs), early (SRe) and late (SRa) diastolic deformation rates in these planes were obtained using strain-rate echocardiography (Figs 1–4).[13,14]

## Statistical analysis

Statistical analysis was performed using IBM SPSS 17 (SPSS, Chicago). The Kolmogorov–Smirnov test was used to evaluate normal distribution. Continuous variables are expressed as mean ± standard deviation or median (minimum–maximum), and categorical variables are expressed as percentages. The Chi-square test was used to compare categorical variables and the Student's *t*-test and Mann–Whitney *U*-test were used to compare continuous variables, depending on whether the parameters showed normal distribution or not. In the correlation analysis, Pearson's and Spearman's correlation tests were used, depending on whether the distribution of parameters was normal or not. A *p*-value of $< 0.05$ was considered statistically significant.

## Results

Twenty children diagnosed with WD by a paediatric gastroenterologist and 20 healthy children with similar characteristics in terms of age, weight, height and BSA were included in the study (Table 1). The ECGs of all our patients were normal. The mean age was 12.72 years (± 3.46) in the WD group and 12.93 years (± 2.97) in the control group, and 45% of the WD group and 50% of the control group were male.

During cardiac evaluation, patients with WD had normal hepatic function and were stable. The WD group of patients were receiving D-penicillamine treatment.

LVEDd, IVSd, LVPWd, EF, LVmass, LVmass-i, TAPSE, mitral E and A velocities, DT, E/A ratio and Tei index were similar in the groups and no statistically significant difference was found (Table 1). Mitral lateral a′ and s′ velocities, irt′ interval, mpi′ ratio and tricuspid lateral a′ and s′ velocities and

**Table 1. Demographic data, transthoracic echocardiography and tissue Doppler echocardiography (TDE) data**

| *Parameters* | *WD group (n = 20)* | *Control group (n = 20)* | p-*value* |
|---|---|---|---|
| Gender, M/F (%) | 9/11 (45/55) | 10/10 (50/50) | 1.0[3] |
| Age, year (± SD) | 12.72 (3.46) | 12.93 (2.97) | 0.96[1] |
| Weight, kg (± SD) | 40.32 (15.38) | 43.68 (14.72) | 0.73[1] |
| Height, cm (± SD) | 147.21 ( 18.32) | 154.31 ( 14.52) | 0.19[1] |
| BSA, $m^2$ (± SD) | 1.27 ( 0.31) | 1.35 ( 0.28) | 0.55[1] |
| IVSd, mm, median (min–max) | 7.00 (5.00–9.00) | 6.00 (4.90–7.60) | 0.12[2] |
| LVPWd, mm, median (min–max) | 6.00 (4.00–9.00) | 5.30 (4.00–7.00) | 0.10[2] |
| LVEDd, mm (± SD) | 41.57 ( 5.41) | 44.20 (4.71) | 0.14[1] |
| LVEF, % (± SD) | 66.82 ( 6.87) | 69.64 ( 5.62) | 0.20[1] |
| LVmass, g, median (min–max) | 68.23 (39.44–158.21) | 70.90 (43.20–123.78) | 0.94[2] |
| LVmass index, $g/m^2$, median (min–max) | 55.97 (40.90–106.90) | 52.33 (44.30–79.14) | 0.22[2] |
| E wave, m/s, median (min–max) | 0.87 (0.66–1.28) | 1.01 (0.75–1.25) | 0.12[2] |
| A wave, m/s (± SD) | 0.60 (± 0.16) | 0.59 (± 0.13) | 0.75[1] |
| E/A ratio (± SD) | 1.57 (± 0.47) | 1.71 (± 0.33) | 0.34[1] |
| DT, ms (± SD) | 143.0 (± 16.08) | 142.52 (± 27.43) | 0.95[1] |
| Tei index, median (min–max) | 0.25 (0.19–0.61) | 0.30 (0.23–0.39) | 0.054[2] |
| E/e, median (min–max) | 4.00 (3.67–7.14) | 4.66 (3–6.94) | 0.63[2] |
| TAPSE, mm (± SD) | 22.43 (± 2.24) | 22.78 (± 2.97) | 0.70[1] |
| Mitral lateral | | | |
| e, m/s (± SD) | 0.19 (± 0.02) | 0.22 (± 0.02) | 0.02[1] |
| a, m/s, median (min–max) | 0.08 (0.07–0.09) | 0.08 (0.05–0.10) | 0.51[2] |
| s, m/s, median (min–max) | 0.12 (0.10–0.16) | 0.12 (0.09–0.19) | 0.86[2] |
| e/a (± SD) | 2.53 (± 0.40) | 3.04 (± 0.88) | 0.04[1] |
| IRT, ms (± SD) | 45.00 (± 8.57) | 41.35 (± 7.07) | 0.96[1] |
| Tei index (± SD) | 0.34 (± 0.06) | 0.36 (± 0.05) | 0.45[1] |
| Mitral septal | | | |
| e, m/s (± SD) | 0.15 (± 0.02) | 0.16 (± 0.02) | 0.04[1] |
| a, m/s, median (min–max) | 0.08 (0.05–0.17) | 0.09 (0.06–0.12) | 0.47[2] |
| s, m/s (± SD) | 0.08 (± 0.01) | 0.14 (± 0.02) | 0.15[1] |
| e/a, median (min–max) | 1.70 (1.06-3.40) | 2.00 (1.42–3.17) | 0.20[2] |
| IRT, ms (± SD) | 51.41 (± 13.29) | 36.82 (± 7.69) | 0.92[1] |
| Tei index (± SD) | 0.39 (± 0.10) | 0.45 (± 0.09) | 0.25[1] |
| Tricuspid lateral | | | |
| e, m/s, median (min–max) | 0.14 (0.09–0.18) | 0.16 (0.10–0.22) | 0.005[2] |
| a, m/s (± SD) | 0.12 (± 0.05) | 0.12 (± 0.02) | 0.81[1] |
| s, m/s (± SD) | 0.14 (± 0.02) | 0.14 (± 0.02) | 0.57[1] |
| e/a, median (min–max) | 1.15 (0.62–2.80) | 1.33 (0.82–2.29) | 0.30[2] |
| IRT, ms (± SD) | 42.23 (± 9.90) | 36.82 (± 7.69) | 0.08[1] |
| Tei index (± SD) | 0.40 (± 0.11) | 0.45 (± 0.09) | 0.19[1] |

[1]Student's *t*-test, [2]Mann–Whitney *U*-test, [3]Chi-square test.
BSA: body surface area, IVSd: diastolic interventricular septum thickness, LVPWd: diastolic left ventricular posterior wall thickness, LVEDd: left ventricular end-diastolic diameter, LVEF: left ventricular ejection fraction, DT: deceleration time, IRT: isovolumetric relaxation time, L: longitudinal, C: circumferential, R: radial, s: systolic velocity, e: early diastolic velocity, a: late diastolic velocity.

**Table 2. Global strain and global strain rate**

| *Parameters* | *WD group (n = 20)* | *Control group (n = 20)* | p-*value* |
|---|---|---|---|
| GLS, % (± SD) | –22.27 (± 4.19) | –23.62 (± 2.79) | 0.13[1] |
| L-SRs, 1/s (± SD) | 1.43 (± 0.27) | 1.38 (± 0.21) | 0.69[1] |
| L-SRe, 1/s (± SD) | 2.07 (± 0.41) | 2.57 (± 0.43) | 0.002[1] |
| L-SRa, 1/s, median (min–max) | 0.80 (0.56–0.96) | 0.78 (0.47–1.11) | 0.23[2] |
| CS, % (± SD) | –15.07 (± 4.87) | –17.35 (± 5.60) | 0.18[1] |
| C-SRs, 1/s, median (min–max) | 1.09 (0.77–1.58) | 1.10 (0.77–1.55) | 0.66[2] |
| C-SRe, 1/s, median (min–max) | 1.20 (0.70–2.08) | 1.36 (1.00–2.71) | 0.07[2] |
| C-SRa, 1/s (± SD) | 0.35 (± 0.19) | 0.50 (± 0.17) | 0.07[1] |
| RS, % (± SD) | 45.62 (± 17.72) | 42.18 (± 19.76) | 0.42[1] |
| R-SRs, 1/s (± SD) | 2.38 (± 0.80) | 2.33 (± 0.70) | 0.70[1] |
| R-SRe, 1/s (± SD) | 3.25 (± 1.28) | 3.51 (± 1.41) | 0.91[1] |
| R-SRa, 1/s (± SD) | 2.65 (± 1.87) | 2.54 (± 1.41) | 0.54[1] |
| RV-LS (± SD) | –24.10 (± 5.17) | –25.22 (± 4.47) | 0.53[1] |
| RV-SRs (± SD) | 1.42 (± 0.36) | 1.49 (± 0.35) | 0.58[1] |
| RV-SRe (± SD) | 1.94 (± 0.51) | 2.28 (± 0.71) | 0.14[1] |
| RV-SRa (± SD) | 0.96 (± 0.63) | 0.88 (± 0.52) | 0.70[1] |

[1]Student's *t*-test, [2]Mann–Whitney *U*-test.
GLS: global longitudinal strain, L: longitudinal, SRs: systolic deformation, SRe: early diastolic strain rate, SRa: late diastolic deformation, C: circumferential, CS: circumferential strain, R: radial, RS: radial strain, RV: right ventricular, LS: longitudinal strain, s: systolic velocity, e: early diastolic velocity, a: late diastolic velocity.

**Table 3. Correlation between GLS strain and EF**

| *GLS* | r-*value* | p-*value* |
|---|---|---|
| EF | 0.48 | 0.004[1] |

[1]Pearson's correlation test.
GLS: global longitudinal systolic strain, EF: ejection fraction.

e′/a′ ratio, were similar in the two groups and no statistically significant difference was found. Mitral lateral e′ and triscuspid lateral e′ velocities were lower in the WD group compared to the control group and were statistically significantly different ($p$ = 0.02, 0.005, respectively). Mitral lateral e/a ratio was also lower in the WD group compared to the control group and was statistically significantly different ($p$ = 0.04) (Table 1).

Global strain values (L, C, R) were similar in the groups and no statistically significant difference was found. Except for the longitudinal early diastolic strain rate (L-SRe), systolic and diastolic (early, late) strain rate (L, C, R) values were similar in the groups and there was no statistically significant difference. L-SRe was lower in the WD group compared to the control group and was statistically significantly different ($p$ = 0.002) (Table 2).

TAPSE, triscuspid a′ and s′ velocities, right ventricular strain, and strain rate values were similar in the groups, with no statistically significant difference. The tricuspid lateral e velocity was found to be lower in the WD patients and was statistically significantly different ($p$ = 0.005) (Table 1).

A moderate correlation was found between global longitudinal strain and LVEF ($p$ = 0.004) (Table 3). In the segmental strain evaluation, while the longitudinal and radial segments had similar values in both groups, the strain value in the circumferential inferolateral segment was found to be significantly lower in the WD group (Table 4).

**Table 4. Segmental longitudinal, circumferential and radial systolic strain**

| *Parameters* | *WD group (n = 20)* | *Control group (n = 20)* | p-*value* |
|---|---|---|---|
| Longitudinal | | | |
| Basal septal, % (± SD) | –20.07 (± 3.04) | –20.28 (± 2.34) | 0.66[1] |
| Mid septal, % (± SD) | –22.61 (± 3.41) | –22.00 (± 2.70) | 0.96[1] |
| Apical septal, % (± SD) | –27.30 (± 5.77) | –26.34 (± 4.33) | 0.89[1] |
| Apical lateral, % (± SD) | –27.02 (± 6.65) | –25.57 (± 5.62) | 0.87[1] |
| Mid lateral, % (± SD) | –22.56 (± 5.32) | –21.22 (± 5.12) | 0.75[1] |
| Basal lateral, % (± SD) | –19.87 (± 4.72) | –19.49 (± 5.40) | 0.99[1] |
| Basal inferior, %, median (min–max) | –20.30 (14.81–26.18) | –23.14 (17.84–25.20) | 0.07[2] |
| Mid inferior, % (± SD) | –22.83 (± 3.59) | –24.38 (± 3.33) | 0.16[1] |
| Apical inferior , % (± SD) | –28.47 (± 6.21) | –28.13 (± 5.72) | 0.83[1] |
| Apical anterior, % (± SD) | –28.81 (± 6.53) | –27.68 (± 6.22) | 0.91[1] |
| Mid anterior, % (± SD) | –24.61 (± 5.39) | –22.63 (± 4.48) | 0.42[1] |
| Basal anterior, % (± SD) | –21.61 (± 7.41) | –20.87 (± 4.48) | 0.85[1] |
| Basal posterior, % (± SD) | –19.05 (± 4.82) | –21.14 (± 3.69) | 0.38[1] |
| Mid posterior, % (± SD) | –20.35 (± 5.01) | –22.18 (± 4.47) | 0.19[1] |
| Apical posterior, % (± SD) | –24.99 (± 5.70) | –26.26 (± 4.99) | 0.21[1] |
| Apical anteroseptal, % (± SD) | –27.84 (± 5.55) | –28.04 (± 4.38) | 0.30[1] |
| Mid anteroseptal, % (± SD) | –24.41 (± 3.74) | –24.19 (± 3.55) | 0.87[1] |
| Basal anteroseptal, % (± SD) | –21.86 (± 3.68) | –20.48 (± 3.47) | 0.18[1] |
| Circumferential | | | |
| Anteroseptal, %, median (min–max) | –24.56 (19.82–34.82) | –23.90 (18.63–37.00) | 0.45[2] |
| Anterior, % (± SD) | –20.35 (± 6.87) | –20.54 (± 7.22) | 0.90[1] |
| Lateral, % (± SD) | –15.06 (± 5.51) | –17.58 (± 4.67) | 0.03[1] |
| Posterior, % (± SD) | –13.71 (± 5.26) | –16.01 (± 4.12) | 0.07[1] |
| Inferior, % (± SD) | –15.50 (± 4.47) | –19.82 (± 4.16) | 0.003[1] |
| Septal, % (± SD) | –23.53 (± 3.42) | –26.94 (± 4.50) | 0.04[1] |
| Radial | | | |
| Anteroseptal, % (± SD) | 59.23 (± 24.39) | 46.36 (± 19.30) | 0.20[1] |
| Anterior, % (± SD) | 61.84 (± 22.90) | 45.45 (± 17.17) | 0.056[1] |
| Lateral, % (± SD) | 54.97 (± 15.55) | 47.29 (± 17.37) | 0.19[1] |
| Posterior, % (± SD) | 60.99 (± 20.15) | 48.24 (± 20.57) | 0.15[1] |
| Inferior, % (± SD) | 57.98 (± 22.01) | 49.46 (± 21.84) | 0.33[1] |
| Septal, % (± SD) | 54.17 (± 22.77) | 48.11 (± 19.38) | 0.55[1] |

[1]Student's *t*-test, [2]Mann–Whitney *U*-test.

## Discussion

WD is an autosomal recessive, hereditary, genetic, metabolic liver disease in which damage is formed by copper accumulation in organs such as the liver, central nervous system and heart, associated with mutation in the *ATP7B* gene, which provides transport of copper from the hepatocytes.[15]

The damage seen in WD is thought to be caused by copper accumulation[2] and oxygen free radicals.[3] Cardiomyopathy can occur as a result of damage in the heart. In autopsy studies of WD patients, histopathologically there have been findings of hypertrophy, interstitial fibrosis, intramyocardial vascular sclerosis, atrioventricular node degeneration and severe sclerosis in the left main coronary artery.[16]

Without doubt, histopathological examinations with invasive methods such as biopsy[17] provide objective findings in the follow up of diseases such as WD, which progress with especially myocardial deposition. However, as the morbidity and mortality rates are high for invasive methods such as biopsy,[18] the evaluation of histopathological findings with non-invasive methods has become more prominent. In the evaluation of these patients in clinical practice, this point requires echocardiographic evaluation in addition to physical examination.

In studies conducted on WD cases,[19,20] left ventricular hypertrophy has been determined in WD. When WD patients were classified to have hepatic and neurological WD, it was reported

that left ventricular hypertrophy was prominent in neurological WD patients,[19] and in another study,[20] left ventricular wall thicknesses increased significantly in WD patients compared to the control group. Studies of paediatric WD patients have found the values of left ventricular wall thickness to be similar to those of the control group.[21-23]

In our study, the left ventricular wall thicknesses (LVSd, LVPWd), LVmass and LVmass-i values of the WD patients were found to be higher than those of the control group, but not statistically significantly different. In addition, there was no central nervous system involvement in any of these study patients. That there were no clear findings of left ventricular hypertrophy in this study can be explained by the relatively young age of these patients and therefore, shorter disease duration. It can be considered that left ventricular hypertrophy findings may become evident later, especially in untreated patients.

Studies of paediatric WD patients showing diastolic function in WD have found mitral E velocity to be significantly lower compared to the control group.[22,23] When ventricular relaxation is impaired, mitral E velocity decreases, A velocity increases, E/A decreases and DT increases.[22] Consistent with the data in the literature, the current study results showed low mitral E velocity, increased DT, increased A velocity and decreased E/A compared to the control group. However, no statistically significant difference was determined between the two groups.

Collagen and elastin in the myocardial extracellular matrix play a role in relaxation.[24] Collagen functions as a copper co-factor in elastin synthesis.[25] Although myocardial damage in WD patients is thought to be the result of copper accumulation and damage by oxygen free radicals,[2,3] there may also be another mechanism resulting in impaired relaxation caused by impaired copper metabolism and disruption in the synthesis of collagen and elastin, which are components of the extracellular matrix. There is a need for more studies on this subject.

The current study results of increased left ventricle wall thickness (IVSd, LVPWd), LVmass and LVmass-i, and decreased left ventricular diastolic function compared to the control group support the notion that there is fibrosis in the extracellular matrix and subclinical relaxation disorder in the early period of myocardial damage. However, the mechanism of myocardial damage could not be fully explained in this study. There is a need for more-detailed research on this subject.

In our study, the TAPSE value was found to be similar to that of the literature,[26] and similar values were found in the WD and control groups. Low tricuspid lateral e′ velocity with TDE indicate subclinical diastolic dysfunction in WD.

There are few studies in the literature on advanced echo imaging techniques in paediatric WD. Subclinical diastolic dysfunction[21] and subclinical systolic dysfunction[27] have been reported in studies of WD using advanced echocardiographic imaging techniques. In our study, in parallel with the study by Karakurt *et al*.,[21] we found that WD patients had subclinical dysfunction with SRE. Contrary to the study by Ahmet *et al*.,[23] in parallel with other studies,[21,26] we found normal systolic function with SE and SRE. In the study in which subclinical systolic dysfunction was found in WD,[27] the Doppler technique could be improved by angle dependence. This brings up the use of SE and SRE, which is the most basic argument in our study.

SE and SRE derived from speckle tracking can show early myocardial dysfunction.[5] The greatest disadvantage of Doppler modality measurements is that they are angle-dependent, whereas the advantage of speckle-tracking imaging obtained from two-dimensional data is that it is independent of the angle and not affected by adjacent segments.[28,29] In the current study, despite the normal systolic and diastolic function with conventional echocardiography, there was seen to be early left ventricular diastolic dysfunction with advanced echocardiography modalities (TDE, SRE) and early right ventricular diastolic dysfunction with TDE, independent of the mechanism of myocardial damage.

In the evaluation of WD patients, the determination of subclinical diastolic dysfunction with advanced echocardiography methods (TDE, SE, SRE) in contrast to the determination of normal systolic and diastolic function with conventional echocardiography brings the routine use of advanced echocardiography methods to the agenda. Therefore, determining subclinical diastolic dysfunction in the early period may be a marker that can be used in the treatment and follow up of lowering serum copper levels in WD cases.

The main limitations of this study were the relatively low number of patients and that it was conducted in a single centre. Another limitation was that cardiac magnetic resonance imaging examinations were not performed. In addition, blood and urine copper levels of the patients were not examined in the evaluations, and therefore the correlation of the findings with blood and urine copper levels could not be analysed. There is a need for further multicentre studies with larger patient populations, and including cardiac magnetic resonance imaging examinations and blood and urine copper levels, to shed further light on this subject.

## Conclusion

This study showed that, despite normal systolic and diastolic function with conventional methods, advanced echocardiography methods showed there was both left and right ventricular subclinical diastolic dysfunction in the early period. Based on these findings, it can be said that diastolic dysfunction develops more prominently than systolic dysfunction in the early stages of WD. Therefore, WD patients need to be evaluated with advanced echocardiography in their follow up. The determination of subclinical diastolic dysfunction in WD using advanced echocardiography modalities (TDE, SE, SRE) suggests that its routine use in the treatment and follow up of these patients may affect the prognosis of the disease.

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