Early Online

The European Research Journal 2025 Original Article

DOI: https://doi.org/10.18621/eurj.1525171 *Internal Medicine*

Renal shear wave elastography in familial Mediterranean fever patients without nephropathy

Mehmet Kök[1], Ayşe Balkarlı Ayan[2], Sinan Ülgen[3]

[1]Departmant of Internal Medicine, University of Health Sciences, Antalya Training and Research Hospital, Antalya, Türkiye; [2]Departmant of Rheumatology, University of Health Sciences, Antalya Training and Research Hospital, Antalya, Türkiye; [3]Department of Radiology, University of Health Sciences, Antalya Training and Research Hospital Antalya, Türkiye

ABSTRACT

Objectives: Due to its lethal effects, early diagnosis of high risk patient groups for renal involvement especially amyloidosis is critical for Familial Mediterranean Fever (FMF). Amyloidosis, defined by the accumulation of extracellular amyloid protein material in the kidney, can reduce the elasticity of the renal parenchyma. Shear wave elastography (SWE) is a new ultrasonographic imaging modality that evaluates tissue elasticity. This pilot study assessed the renal parenchyma of FMF patients using SWE.

Methods: Fifty-three FMF patients and 51 age- and sex-matched healthy control participants were included in this study. Participants with amyloidosis, estimated glomerular filtration rate (eGFR) less than 60 mL/min and/or signs of nephropathy (proteinuria, hematuria, renal tubular acidosis) were excluded. Routine history, physical, laboratory examinations (blood urea nitrogen, creatinine, C-reactive protein, urine dipstick test, spot proteinuria) and renal ultrasound were performed. SWE imaging was performed to measure renal parenchymal stiffness.

Results: There was no significant correlation between SWE values (elasticity and velocity) and age, eGFR, serum blood urea nitrogen, and creatinine in the comparison of SWE findings of FMF patients and control groups. SWE values were statistically higher in FMF patients than in the control group ($P=0.002$ and $P< 0.001$ for elasticity and velocity, respectively).

Conclusions: Increased renal stiffness in FMF patients may indicate early renal involvement (especially amyloidosis), suggesting SWE as a potential non-invasive diagnostic tool for early detection.

Keywords: Familial Mediterranean fever, nephropathy, amyloidosis, shear wave elastography, renal cortical stiffness

Familial Mediterranean Fever (FMF) represents an autosomal recessive, autoinflammatory disorder distinguished by recurrent, self-limiting episodes of fever, concomitant with aseptic inflammation in serosal cavities, joints, and the skin [1, 2]. Acute attacks usually last 1 to 3 days and resolve spontaneously. Nevertheless, in certain individuals, these episodes may extend beyond the typical timeframe, lasting more than one week, with an occasional occurrence of up to one month. However, instances of even longer durations are exceedingly rare [3]. Despite being self-limiting, some FMF patients develop sec-

Corresponding author: Mehmet Kök, MD.,
Phone: +90 242 249 44 00, E-mail: dr.mehmetkok@hotmail.com

How to cite this article: Kök M, Balkarlı Ayan A, Ülgen S. Renal shear wave elastography in familial Mediterranean fever patients without nephropathy. Eur Res J. 2025. doi: 10.18621/eurj.1525171

Received: July 31, 2024
Accepted: September 12, 2024
Published Online: February 13, 2025

ondary amyloidosis, particularly AA type, which is the most severe complication of FMF [4].

Before colchicine therapy, renal amyloidosis was the main cause of death in those under the age of 40 years. In addition, according to more recent studies, 11-13% of FMF patients develop still amyloidosis despite receiving colchicine therapy [5]. This disease typically presents with heavy proteinuria, nephrotic syndrome, and eventually progresses to end-stage renal failure. Early diagnosis of renal amyloidosis is challenging because its symptoms become apparent only in the later stages, marked by significant amyloid deposition [6]. Currently, the diagnosis requires biopsy to show amyloid deposition. Therefore, many studies have concentrated on early identifying FMF patients at risk of amyloidosis.

In the past, conventional methods have been utilized to detect and evaluate renal disorders. These methods include computed tomography (CT) scans, magnetic resonance imaging (MRI), conventional ultrasound (USG), and biochemical analysis of blood samples. However, each method carries its own risks, such as radiation exposure and the administration of iodinated contrast medium in CT scans. Conventional renal USG is often used for initial evaluation because it is safe, easy, and inexpensive to perform. Renal USG can easily assess features such as increased parenchymal echogenicity and decreased renal size and parenchymal thickness. Parenchymal echogenicity is a commonly used marker for nephropathy. However, this marker is subjective, not quantitative, and often fails to detect renal abnormalities [7]. Elastography is a non-invasive, objective and cost-effective ultra-sonographic imaging modality that evaluates tissue elasticity [8]. Strain wave elastography, acoustic radiation force impulse imaging, shear wave elastography (SWE) and transient elastography are the different elastography techniques. The advantage of SWE over other USG elastography techniques is that it shows the true quantitative elasticity values of the tissues (kPa). It also does not require external compression and therefore allows to investigate the elasticity of the abdominal organs [7, 9]. Variations of SWE have been used to study many organs, including breast, thyroid, prostate, renal allografts and CKD [10-13]. Renal cortical stiffness, as assessed by SWE, exhibits a correlation with renal parenchymal disease and fibrosis. Importantly, this parameter remains unaffected by systemic and demographic variables [2].

In the kidney, amyloid can accumulate in the vascular space, glomeruli and interstitial space. The glomerulus is the most common and most severely involved renal compartment, but as mentioned above, it can be asymptomatic until the late stage [14]. Therefore, amyloid deposit in the renal parenchyma can be detected by SWE without any symptoms. As a matter of fact, in a few limited and small-scale studies on this subject, SWE values were found to be higher in FMF patients [15, 16]. This study aimed to evaluate renal elasticity in FMF patients with SWE

METHODS

Patient Population

In this cross-sectional pilot study, 53 FMF patients were recruited from the Department of Rheumatology at the Health Sciences University Antalya Training and Research Hospital, and 51 age- and sex-matched healthy control participants were enrolled in the study between June 2022 and June 2023.

The FMF diagnosis was made according to Tel-Hashomer criteria and all FMF patients were on colchicine treatment (1.5 mg/day) [17]. International severity scoring system for FMF (ISSF) was used to assess severity [18]. In this scoring system, parameters such as chronic sequelae, organ involvement and failure, and attack frequency are scored to determine the severity of the disease. A detailed history of the disease (duration of treatment, disease severity, etc.) was obtained from each patient, routine physical examination, laboratory examinations (blood urea nitrogen [BUN], creatinine, C-reactive protein [CRP], dipstick, spot urine protein/creatinine ratio) and conventional and doppler USG was performed followed by SWE imaging to measure renal stiffness. All participants in the healthy control group had normal laboratory parameters and no abnormal findings (echogenicity, kidney size, cortical blood flow, etc) on conventional doppler USG.

The exclusion criteria were as follows; participants with FMF-associated renal involvement, participants with diseases affecting the kidney other than FMF (such as chronic kidney disease [CKD], diabetes

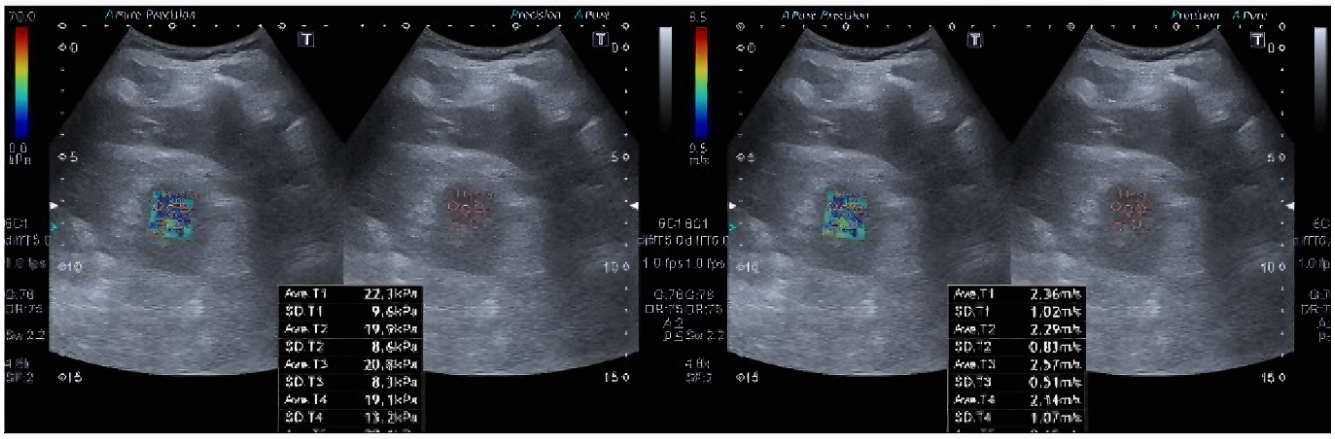

Fig. 1. Elasticity (kPa) and velocity (m/s) values in measurements obtained in the transverse plane from the lower pole parenchyma of the kidney in a FMD patient.

mellitus, hypertension, cardiovascular diseases, etc.), participants using nephrotoxic drugs such as nonsteroidal anti-inflammatory drugs, antibiotics in the past three months, participants with estimated glomerular filtration rate (eGFR) < 60 mL/min (It was calculated eGFR using KD-EPI Creatinine 2009) or markers of kidney damage such as haematuria and proteinuria), smokers, participants with CKD any findings on conventional and doppler USG, participants with body mass index (BMI) over 35 kg/m2, participants with pregnancy or nursing status, any condition that prevents visualization of the kidney by ultrasound. Participants over 18 years of age who did not fulfill any of the exclusion criteria were included in the study. This study was approved by the Clinical Research Ethics Committee of Health Sciences University Antalya Training and Research Hospital (Approval number: 8/9 and date: 08.06.2023) and was conducted in accordance with the ethical standards defined in the 1964 Helsinki Declaration. During the study execution, patients were informed about the study, and their written consents were obtained. All participants gave written informed consent before enrolment.

Shear Wave Elastography

SWE assessment was conducted using a convex abdominal probe operating at a frequency range of 5-1 MHz, utilizing the Toshiba Applio 500 ultrasound system based in Tokyo, Japan. SWE measurements were assessed from the left kidney while the patients

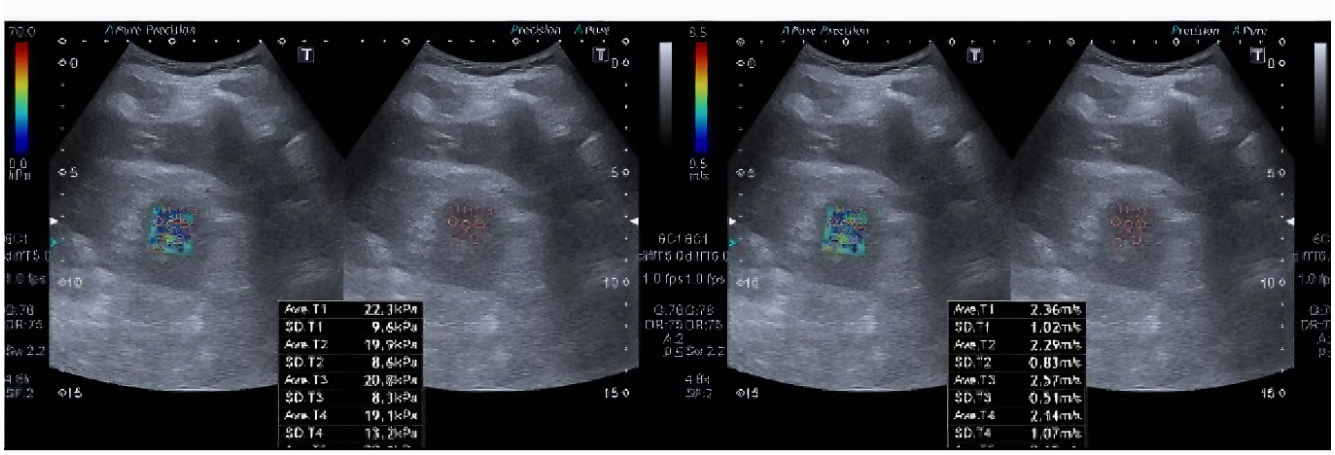

Fig. 2. Elasticity (kPa) and velocity (m/s) values in measurements obtained in the transverse plane from the pole parenchyma of the kidney in a healthy individual.

were lying in the lateral decubitus position. If the left kidney was deep or the acoustic window was deemed inadequate by the radiologist, measurements were taken from the right kidney. To minimize external pressure on the kidney, measurements were performed at the end-expiration. SWE evaluation was obtained at the lower renal pole, where the acoustic window was optimum. The measurement was performed in the transverse axis of the kidney so that the medulla segments do not enter the image area from the lower pole. Measurements were acquired subsequent to defining a region of interest (ROI) on specified targets within conventional renal USG images. ROI was positioned vertically within a renal cortex region devoid of vessels or cysts. The primary axis of the ROI was aligned in parallel with the axis of the renal pyramid, oriented vertically to the kidney surface. The maximum ROI target distance was 8 cm, and the ROI constant box size was 1-0.5 cm. We obtained five valid measurements from kidney and calculated the mean value. SWE stiffness values were presented as kPa, velocity values as m/sec (Figs. 1 and 2). Participants were assessed by a single radiologist with 5 years of experience in SWE. The radiologist was blinded to the groups.

Statistical Analysis

Descriptive analyses were depicted with measures such as mean ± standard deviation, median (minimum-maximum), or n (%), as deemed suitable. The normality of the data was assessed using the Shapiro–Wilk test, while categorical data were subjected to analysis using the Pearson chi-square test. The Mann-Whitney U test and Student's t-test were employed for the analysis of numerical data with non-normal and normal distributions, respectively. Receiver Operating Characteristic (ROC) curve analysis was utilized to ascertain the optimal cut-off point for elasticity and velocity in predicting FMF. The Area Under the Curve (AUC), sensitivity, and specificity were calculated and reported with 95% confidence intervals. The optimal threshold for measurements was identified as the value associated with the maximum Youden index. To explore relationships between variables, Spearman's correlation coefficient was computed. Statistical analysis was conducted using IBM SPSS Statistics for Windows, Version 23.0 (IBM Corp., Armonk, NY). A two-tailed p-value less than 0.05 was deemed statistically significant.

RESULTS

A cohort comprising 53 FMF patients (28 females) and 51 healthy participants (31 females) were included in this study. The average age among FMF patients was 39.98±11.56 years, while healthy participants had an average age of 41.63±16.07 years. There was no statistically significant age and BMI difference between the patient and control groups (Table 1).

We found that SWE values were statistically higher in FMF patients than in the control group. The mean values for elasticity were 17.66±3.77 kPa, 15.49±3.15 kPa, respectively (P= 0.002). The mean values for velocity were 2.31±0.25 m/sec and 2.12±0.26 m/sec, respectively (P<0.001) (Table 1).

Table 1. Demographic features and shear wave elastography imaging parameters in participants

Variables	FMF (n=53)	Control (n=51)	P value
Age (years)	39.98±11.56	41.63±16.07	0.551
Gender, n (%)			
Female	28(52.8)	31(60.8)	0.413
Male	25(47.2)	20(39.2)	
BMI (kg/m^2)	28±2.57	28±2.15	0.563
Elasticity (kPa)	17.66±3.77	15.49±3.15	**0.002**
Velocity (m/sec)	2.31±0.25	2.12±0.26	**<0.001**

Data are shown as mean±standard deviation or n (%). FMF=familial mediterranean fever BMI= body mass index

Table 2. Correlation of elastography findings with age and laboratory findings of FMF patients

Variables	Elasticity		Velocity	
	r	P value	r	P value
Age	-0.173	0.215	-0.067	0.631
BUN	0.036	0.806	-0.043	0.770
Creatinine	0.117	0.427	0.148	0.317
GFR	-0.064	0.667	-0.176	0.231
CRP	-0,008	0.959	-0.072	0.640

BUN=blood urea nitrogen, CRP=C-reactive protein, eGFR=estimated glomerular filtration rate, FMF=familial mediterranean fever

r=relationship coefficient

There is no significant correlation between SWE values and age, eGFR, BUN and creatinine (Table 2). Upon analyzing the correlation coefficients of mean elasticity and mean velocity values in relation to treatment duration and disease severity, it was observed that the correlation coefficients for both mean elasticity and velocity values with treatment duration were neither significant nor high (P>0.05). Conversely, a strong, direct, and significant correlation was identified between SWE value and disease severity (ISSF score) (elasticity: r=0.853, P<0.001; velocity: r =0.801, P<0.001,) (Table 3).

Using a cut-off value >15.8 kPa for mean values for elasticity, the area under the ROC curve to diagnose FMF was 0.674 (95%CI: 0.575-0.763, P=0.001) with a sensitivity and specificity of 67.92 and 62.75, respectively (Fig. 3). These values indicate that the test has a certain accuracy, although not perfect, in showing renal involvement, and that velocity has a slightly higher accuracy than elasticity. Using optimal cut-off value > 2.25 m/s for velocity, the area under the ROC curve was found 0.707 to diagnose FMF (95%CI: 0.609-0.792, P<0.001) with a sensitivity and specificity of 67.92% and 74.51, respectively (Fig. 4).

DISCUSSION

Early detection of amyloidosis in high-risk FMF patients is crucial due to its lethal consequences. In this preliminary study, we conducted an assessment of the renal parenchyma in FMF patients using SWE early. Our findings revealed that the recorded SWE values exhibited a higher magnitude within the patient group as compared to the control group. Moreover a strong, direct and significant correlation was found between mean elasticity and velocity and disease severity.

SWE values, like conventional USG, may be affected by age and laboratory parameters such as urea, creatinine, and BUN. Yu *et al*. [19] and Hassan *et al*. [20] and Leong *et al*. [21] founded significantly correlated with age and this laboratory parameters. This may be due to the development of glomerulosclerosis, interstitial fibrosis, tubular atrophy, and arteriosclerosis as the kidneys age. However, Samir *et al*. [10] reported no significant correlation between elastography values and age. Much like the findings of Samir *et al*. [10] our study also did not reveal any significant correlation between these parameters. This lack of correlation could potentially be attributed to variations in

Table 3. Correlation of elastography findings with treatment duration and disease severity score

Variables	Treatment duration		Disease severity score	
	r	P value	r	P value
Elasticity (kPa)	0.083	0.531	0.853	**<0.001**
Velocity (m/sec)	0.142	0.278	0.801	**<0.001**

r=relationship coefficient

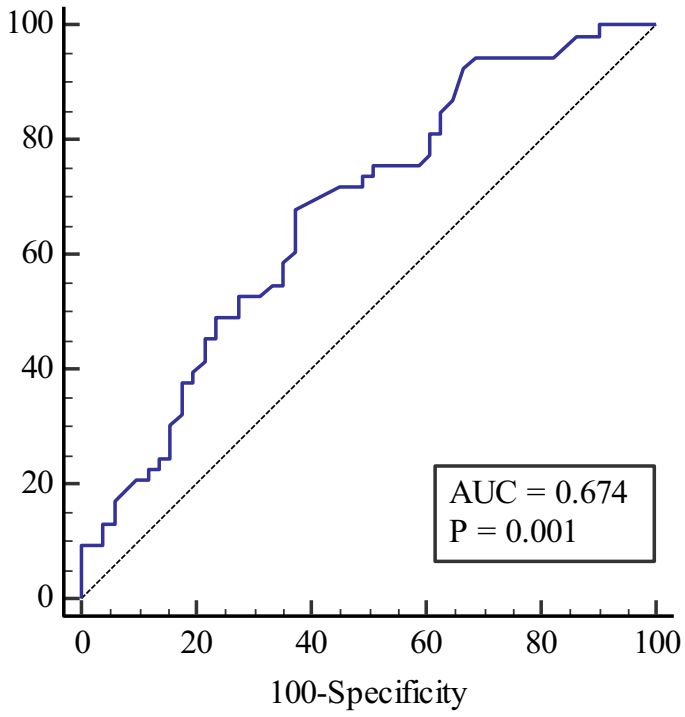

Fig. 3. ROC analysis for elasticity in predicting diagnosis of FMF. In the ROC analysis with a cut-off value of >15.8 kPa for elasticity, the AUC was 0.674. The sensitivity and specificity of the elasticity parameter was 67.92% and 62.75%, respectively.

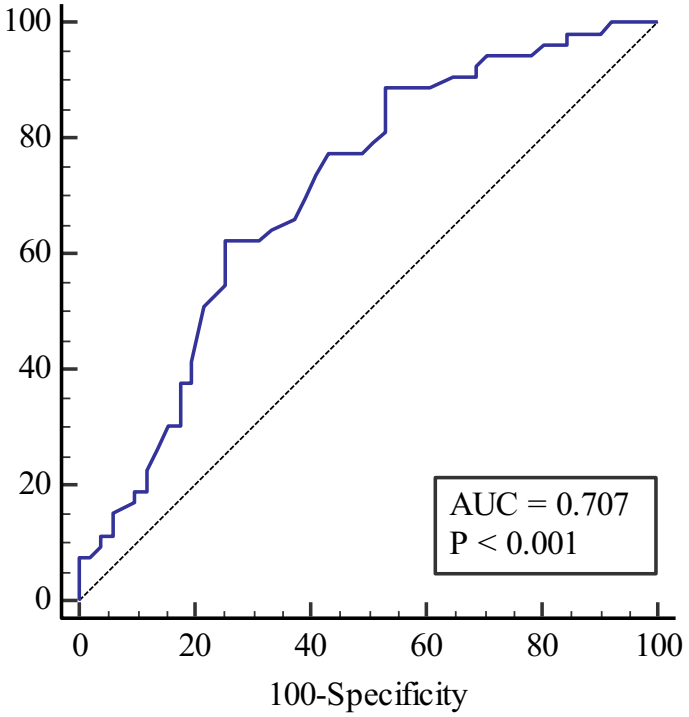

Fig. 4. ROC analysis for velocity in predicting diagnosis of FMF. In the ROC analysis performed with a cut-off value of >2.25 m/s for velocity, the AUC was calculated as 0.707. The sensitivity and specificity of the velocity parameter was 67.92% and 74.51, respectively.

the sample type and sample size we selected. Participants with renal dysfunction were not included in our study. Intrarenal fibrosis represents the ultimate shared pathway across all CKD, and the degree of fibrosis has been observed to correlate with the severity of the disease [22, 23] . As of the present clinical practices, renal biopsy stands as the sole method available for the assessment of renal fibrosis. Since renal biopsy is an invasive and expensive method, new methods such as elastography are being investigated. For instance, Leong *et al*. [21] and Samir *et al*. [10] evaluated renal parenchymal stiffness with SWE in adults with CKD, they reported that the patient group had higher SWE values than the control group. In addition, Hu *et al*. [24] investigated the relationship between SWE scores and renal biopsy scores in CKD patients. In this study, it was determined that as the fibrosis score increased in the biopsy and the elasticity score also increased. As a result of these studies, it has been shown that SWE is a cost-effective and non-invasive method that provides additional diagnostic information in the diagnosis and follow-up of CKD [24].

CKD incidence and prevalence are increasing, particularly diabetes and hypertension-related nephropathies [25]. It is crucial to ascertain alterations in mesangial, endothelial, and epithelial cells during the early stages of fibrosis, preceding the onset of nephropathy. In studies conducted for this purpose, the SWE values of patients with primary hypertension or diabetes mellitus without signs of nephropathy were observed to be greater than the control groups [26, 27]. In addition, increased SWE levels in patients with diabetic nephropathy correlated with BUN, creatinine, eGFR, urinary albumin/creatinine ratio, and urinary micro albumin level in these studies [18, 19, 28]. Similar to these studies, we found SWE values were higher in patients with FMF without nephropathy. However, we did not detect significant correlation between SWE values and eGFR, BUN, creatinine. It may result from exclusion of patients with eGFR <60 mL/min and/or those with signs of nephropathy such as microalbuminuria. In conclusion, SWE can be em-

ployed as a new method in the early diagnosis and follow-up of nephropathy.

There are few studies in the literature investigatıng renal elastography in FMF patients Bayramoğlu *et al*. [15] compared the changes in lung, spleen, pancreas and kidney elasticity in prediatric FMF patients with and without amyloidosis with healthy control group. They found that liver, spleen, kidney and pancreas elasticity values were significantly higher in the amyloidosis group compared to the control group. SWE values were significantly higher in the FMF group with or without amyloidosis compared to control subjects. In this study, the age range of the participants was very wide. Factors that may affect SWE values such as BMI, hypertension, diabetes mellitus and smoking were not excluded. In addition, participants were not evaluated for other renal pathologies such as cysts and lipomas before elastography. In a study conducted by Özmen *et al*. [16] in children with FMF, SWE values were found to be higher in FMF patients compared to healthy control group. However, in this study, the participants were not evaluated in terms of nephropathy (hematuria, proteinuria, creatinine). Additionally, the relationship between disease severity, duration of treatment, treatment regimen, age at diagnosis, and SWE values was not examined. Albayrak *et al*. [29] compared the renal elasticity value of adult FMF patients with and without proteinuria with the control group. They found that SWE values of FMF patients were higher than the control group. In addition, SWE values of patients with proteinuria were higher than the control group and FMF patients without proteinuria. However, although FMF patients with proteinuria were included in the study, biopsy was not performed in these patients, so the cause of proteinuria may be due to causes other than amyloidosis. In the study conducted by Kayalı *et al*. [30] on adult FMF patients, higher SWE values were also found compared to healthy control group. However, this study included a small number of patients, some of whom had nephropathy (e.g., proteinuria). Morover, factors that may affect SWE values, such as BMI, smoking, hypertension and diabetes, have not been excluded. In our current study, similar to previous research, we found higher SWE values in FMF patients. Unlike other studies, our research included a larger number of adult patients and excluded volunteers with any evidence of nephropathy to ensure a more objective and homogeneous sample.

Currently, there are no standardized renal SWE values available for FMF patients. In their comparison of renal velocity and elasticity values between FMF patients and the control group, Kayalı *et al*. [30] established cut-off values of 7.37 kPa for elasticity (sensitivity=76%, specificity=93%) and 1.42 m/s for velocity (sensitivity=70%, specificity=89%) [30]. In our study we have suggested that a cut-off value 15.8 kPa for mean values for elasticity (sensitivity and specificity of 67.92 and 62.75, respectively) and cut-off value 2.25 m/s for velocity (sensitivity and specificity of 67.92% and 74.51, respectively). While these values may not be adequate for diagnosing FMF patients, they indicate that SWE could serve as a valuable method for monitoring renal involvement in FMF patients. Extensive studies in this area may contribute to the standardization of SWE values and further augment their diagnostic utility.

Amyloidosis is characterized by the deposition of extracellular protein material known as amyloid in various organs, including the heart and kidneys. This condition can result in a gradual decline in organ function, potentially culminating in a fatal outcome. The clinical and imaging characteristics of the disease are not pathognomonic. Currently, a biopsy is needed to demonstrate the deposition of amyloid. Elastography is a novel imaging technique for assessing tissue elasticity. Elestosonographic findings have been demonstrated that amyloid material increases the tissue stiffness of the affected organ [28]. For instance, numerous case reports have demonstrated elevated liver stiffness in patients with hepatic amyloidosis [31-33]. Amyloidosis is seen more often in patients in the severe disease group. ISSF is the most commonly used scoring system to determine the severity of the disease in the follow-up of FMF patients. Kayalı *et al*. [30] found that as ISSF scores increased, SWE values also increased, but this positive correlation was not statistically significant. In our study, we observed a strong correlation was found between SWE values and disease severity score. Long-term prospective studies with larger cohorts are necessary to understand the future implications of these results for FMF patients.

Limitations

This study has same limitations: (1) The number

of patients enrolled in this study was low and further studies with larger number patients are required. (2) In our study, there are two groups of individuals with normal kidney function with or without FMF. We recommend further studies including FMF patients with amyloidosis as a third group. (3) Since kidney biopsy is not clinically indicated for patients with FMF, no biopsy data were included for histological measurement. (4) We did not measure the variance between observations as all SWE studies were performed by a single radiologist.

CONCLUSION

We observed that the SWE values were higher in the patient group than in the control group. In additon, a strong correlation was found between elasticity and velocity and disease severity. Recently, SWE has been found to be a useful method in the early diagnosis and follow-up of renal involvement (especially amyloidosis). SWE may be also a cost-effective, non-invasive method to diagnose and follow up renal involvement (especially amyloidosis) in FMF patients.

Ethical Statement

This study was approved by the Clinical Research Ethics Committee of Health Sciences University Antalya Training and Research Hospital (Approval number: 8/9 and date: 08.06.2023) and was conducted in accordance with the ethical standards defined in the 1964 Helsinki Declaration. During the study execution, patients were informed about the study, and their written consents were obtained.

Authors' Contribution

Study Conception: MK, ABA; Study Design: MK, ABA, SÜ; Supervision MK, ABA; Funding: MK, SÜ; Materials: MK, ABA, SÜ; Data Collection and/or Processing: MK, ABA, SÜ; Statistical Analysis and/or Data Interpretation: MK, ABA; Literature Review: MK, ABA; Manuscript Preparation: MK, ABA, SÜ and Critical Review: MK, ABA, SÜ

Conflict of interest

The authors disclosed no conflict of interest during the preparation or publication of this manuscript.

Financing

The authors disclosed that they did not receive any grant during conduction or writing of this study.

REFERENCES

1. Alghamdi M. Familial Mediterranean fever, review of the literature. Clin Rheumatol. 2017;36(8):1707-1713. doi: 10.1007/s10067-017-3715-5.
2. Lancieri M, Bustaffa M, Palmeri S, et al. An Update on Familial Mediterranean Fever. Int J Mol Sci. 2023;24(11):9584. doi: 10.3390/ijms24119584.
3. Livneh A, Langevitz P, Zemer D, et al. The changing face of familial Mediterranean fever. Semin Arthritis Rheum. 1996;26(3):612-627. doi: 10.1016/s0049-0172(96)80012-6.
4. Andronesi AG, Ismail G, Gherghiceanu M, Mitroi G, Hârza MC. Familial Mediterranean fever-associated renal amyloidosis: case report and review of the literature. Rom J Morphol Embryol. 2019;60(4):1299-1303.
5. Kasifoglu T, Bilge SY, Sari I, et al. Amyloidosis and its related factors in Turkish patients with familial Mediterranean fever: a multicentre study. Rheumatology (Oxford). 2014;53(4):741-745. doi: 10.1093/rheumatology/ket400.
6. Gupta N, Kaur H, Wajid S. Renal amyloidosis: an update on diagnosis and pathogenesis. Protoplasma. 2020;257(5):1259-1276. doi: 10.1007/s00709-020-01513-0.
7. Fiorini F, Barozzi L. The role of ultrasonography in the study of medical nephropathy. J Ultrasound. 2007;10(4):161-167. doi: 10.1016/j.jus.2007.09.001.
8. Dewall RJ. Ultrasound elastography: principles, techniques, and clinical applications. Crit Rev Biomed Eng. 2013;41(1):1-19. doi: 10.1615/critrevbiomedeng.2013006991.
9. Garra BS. Elastography: history, principles, and technique comparison. Abdom Imaging. 2015;40(4):680-697. doi: 10.1007/s00261-014-0305-8.
10. Samir AE, Allegretti AS, Zhu Q, et al. Shear wave elastography in chronic kidney disease: a pilot experience in native kidneys. BMC Nephrol. 2015;16:119. doi: 10.1186/s12882-015-0120-7.
11. Zheng XZ, Ji P, Mao HW, et al. A novel approach to assessing changes in prostate stiffness with age using virtual touch tissue quantification. J Ultrasound Med. 2011;30(3):387-390. doi: 10.7863/jum.2011.30.3.387.
12. Bai M, Du L, Gu J, Li F, Jia X. Virtual touch tissue quantification using acoustic radiation force impulse technology: initial clinical experience with solid breast masses. J Ultrasound Med. 2012;31(2):289-294. doi: 10.7863/jum.2012.31.2.289.
13. Zhang YF, Xu HX, He Y, et al. Virtual touch tissue quantification of acoustic radiation force impulse: a new ultrasound elastic imaging in the diagnosis of thyroid nodules. PLoS One. 2012;7(11):e49094. doi: 10.1371/journal.pone.0049094. Epub 2012 Nov 13.
14. Castano E, Palmer MB, Vigneault C, Luciano R, Wong S, Moeckel G. Comparison of amyloid deposition in human kidney

biopsies as predictor of poor patient outcome. BMC Nephrol. 2015;16:64. doi: 10.1186/s12882-015-0046-0.
15. Bayramoglu Z, Akyol Sari ZN, Koker O, Adaletli I, Eker Omeroglu R. Shear wave elastography evaluation of liver, pancreas, spleen and kidneys in patients with familial mediterranean fever and amyloidosis. Br J Radiol. 2021;94(1128):20210237. doi: 10.1259/bjr.20210237.
16. Ozmen Z, Kasap T, Aktas F, Ozmen ZC. Shear wave elastography evaluation of kidneys in children with familial mediterranean fever. Niger J Clin Pract. 2023;26(7):957-962. doi: 10.4103/njcp.njcp_698_22.
17. Polat Z, Kilciler G, Ozel AM, Kara M, Kantarcioglu M, Uygun A, Bagci S. Plasma ghrelin levels in patients with familial Mediterranean fever. Dig Dis Sci. 2012 Jun;57(6):1660-1663. doi: 10.1007/s10620-012-2049-z.
18. Demirkaya E, Acikel C, Hashkes P, et al. Development and initial validation of international severity scoring system for familial Mediterranean fever (ISSF). Ann Rheum Dis. 2016;75(6):1051-1056. doi: 10.1136/annrheumdis-2015-208671.
19. Yu N, Zhang Y, Xu Y. Value of virtual touch tissue quantification in stages of diabetic kidney disease. J Ultrasound Med. 2014;33(5):787-792. doi: 10.7863/ultra.33.5.787.
20. Hassan K, Loberant N, Abbas N, Fadi H, Shadia H, Khazim K. Shear wave elastography imaging for assessing the chronic pathologic changes in advanced diabetic kidney disease. Ther Clin Risk Manag. 2016;12:1615-1622. doi: 10.2147/TCRM.S118465.
21. Leong SS, Wong JHD, Md Shah MN, Vijayananthan A, Jalalonmuhali M, Ng KH. Shear wave elastography in the evaluation of renal parenchymal stiffness in patients with chronic kidney disease. Br J Radiol. 2018;91(1089):20180235. doi: 10.1259/bjr.20180235.
22. Eddy AA. Experimental insights into the tubulointerstitial disease accompanying primary glomerular lesions. J Am Soc Nephrol. 1994;5(6):1273-87. doi: 10.1681/ASN.V561273.
23. Hewitson TD. Fibrosis in the kidney: is a problem shared a problem halved? Fibrogenesis Tissue Repair. 2012;5(Suppl 1):S14. doi: 10.1186/1755-1536-5-S1-S14.
24. Hu Q, Wang XY, He HG, Wei HM, Kang LK, Qin GC. Acoustic radiation force impulse imaging for non-invasive assessment of renal histopathology in chronic kidney disease. PLoS One. 2014;9(12):e115051. doi: 10.1371/journal.pone.0115051.
25. El Nahas M. The global challenge of chronic kidney disease. Kidney Int. 2005;68(6):2918-2929. doi: 10.1111/j.1523-1755.2005.00774.x.
26. Ağyar A. [Evaluation of renal parenchyma by ultrasound elastography in patients with primary hypertension]. Thesis, 2018. [Article in Turkish]. https://tez.yok.gov.tr/UlusalTezMerkezi/tezSorguSonucYeni.jsp.
27. Koc AS, Sumbul HE. Renal cortical stiffness obtained by shear wave elastography imaging is increased in patients with type 2 diabetes mellitus without diabetic nephropathy. J Ultrasound. 2018;21(4):279-285. doi: 10.1007/s40477-018-0315-4.
28. Goya C, Kilinc F, Hamidi C, et al. Acoustic radiation force impulse imaging for evaluation of renal parenchyma elasticity in diabetic nephropathy. AJR Am J Roentgenol. 2015;204(2):324-329. doi: 10.2214/AJR.14.12493.
29. Albayrak E, Akbas MG. Diagnostic Efficacy of Renal 2-D Shear Wave Elastography in Familial Mediterranean Fever Disease. Ultrasound Q. 2023;39(3):171-178. doi: 10.1097/RUQ.0000000000000640.
30. Kayalı A, Öztürk Keleş F, Seyfettin A, Dirican E, Çelik MM. An evaluation with shear wave elastography of kidney elasticity in patients with familial Mediterranean fever. J Clin Ultrasound. 2023;51(1):177-183. doi: 10.1002/jcu.23375.
31. Trifanov DS, Dhyani M, Bledsoe JR, et al. Amyloidosis of the liver on shear wave elastography: case report and review of literature. Abdom Imaging. 2015;40(8):3078-783. doi: 10.1007/s00261-015-0519-4.
32. Srinivasan S, Tan YQ, Teh HS, Lee PJ, Khoo RN. Primary hepatic amyloidosis presenting as nodular masses on the background of diffuse infiltration and extreme liver stiffness on MR elastography. J Gastrointestin Liver Dis. 2014;23(4):437-440. doi: 10.15403/jgld.2014.1121.234.hamy.
33. Janssens F, Spahr L, Rubbia-Brandt L, Giostra E, Bihl F. Hepatic amyloidosis increases liver stiffness measured by transient