

Real-Time Ultrasound Elastographic Features and Color Doppler Imaging of Mitral Valve Prolapse

Dursun Topal¹ , Mehmet Erol Can² , Evrim Karadag Tekin³ ,
Berat Uguz¹ , Mehmet Fatih Kocamaz² , Mehmet Emin Aslanci⁵ 

¹Department of Cardiology, Bursa Sehir Training and Research Hospital, Bursa, Turkey

²Department of Ophthalmology, Bursa Sehir Training and Research Hospital, Bursa, Turkey

³Departments of Radiology, Bursa Sehir Training and Research Hospital, Bursa, Turkey

⁴Department of Ophthalmology, Bursa Yuksek Ihtisas Training and Research Hospital, Bursa, Turkey

ABSTRACT

Background The aim of this study was to investigate the elasticity of ocular structures in patients with mitral valve prolapse (MVP).

Material and Methods This prospective study included a total of 35 patients with MVP (study group) and 35 healthy volunteers (control group). The elastography value of the ratio of orbital fat-sclera (ROF/S) was measured with real-time ultrasound elastography. For each eye, central retinal artery (CRA), posterior ciliary artery (PCA), and ophthalmic artery (OA) were evaluated, respectively.

Results The mean ages of the patients in the study and the control groups were 31.77 ± 11.40 years, and 30.65 ± 7.45 years, respectively ($p=0.511$). Mean ROF/S were 1.95 ± 0.81 and 1.37 ± 1.06 ($p=0.001$) in the study groups and control, respectively. The mean resistance index (RI) of the OA was 0.67 ± 0.05 in the control group, 0.67 ± 0.05 (0.55; 0.87) in study group. The mean RI of the PCA was 0.66 ± 0.05 in the control group, 0.68 ± 0.06 in study group. The mean RI of the CRA was 0.66 ± 0.05 in the control group, 0.66 ± 0.06 in study group. The RI value was not a significant difference between control and study group ($p>0.05$).

Conclusions Scleral elasticity was significantly increased in MVP patients. These could be related to ocular pathologies such as glaucouma, kerataconus in MVP.

Turk J Int Med 2022;4(4):148-154

DOI: [10.46310/tjim.1167465](https://doi.org/10.46310/tjim.1167465)

Keywords: Mitral valve prolapse, glaucouma, ocular elasticity, ultrasound elastography.



Introduction

Mitral valve prolapse (MVP) is a common valvular disease, seen in 2-6% of cases, characterized by the bulging of one or both mitral leaves into the left atrium more than 2 mm above the plane of the mitral annulus during systole, due to progressive myxomatous degeneration of the mitral valve leaflets and chorda tendinea.¹ Kerataconus is associated with most of ocular manifestations described in MVP.^{2,3} In some studies, retinal vascular occlusion, retinal emboli and glaucoma are also related with MVP.⁴⁻⁶

Real-time elastography (RTE) performed in the differential diagnosis of tumour, inflammation, and normal tissue is a relatively new imaging technique that provides a noninvasive and painless assessment of tissue stiffness and elasticity.⁷ Ultrasound elastography show changed elasticity of tissues resulting from from radiofrequency signals during externally applied compression-relaxation cycles.⁸ Color doppler imaging (CDI) also is a non-invasive and painless technique that used to evaluated of blood flow velocity.⁹ Assessment of blood flow and the retrobulbar vascular parameters (central retinal artery, posterior ciliary artery, and ophthalmic artery) have been researched with CDI in many studies.¹⁰ In this study, we aimed to evaluate the ocular elasticity and retrobulbar vascular properties in patients with MVP by comparing them with the stiffness in the eyes of age and sex-matched healthy controls using ocular real-time ultrasound elastography and doppler ultrasonography.

Material and Methods

Ethical considerations

The study protocol was approved by the local ethics committee. The study followed the tenets of the Declaration of Helsinki. Written informed consent was obtained from all participants.

Study population and design

This prospective cross-sectional study was conducted at the departments of cardiology ophthalmology, and radiology of a tertiary referral hospital in Turkey. A total of 70 participants without any major comorbidities were enrolled to the study. Of them 35 patients with a diagnosis

of MVP consisted of the study group while 35 healthy subjects consisted of the control group. Participants' basic demographic characteristics, elastography value of the ratio of orbital fat-sclera (ROF/S) as well as central retinal artery (CRA), posterior ciliary artery (PCA), and ophthalmic artery (OA) were assessed and then compared between the groups. Patients who had a history of significant ocular disease, intraocular pressure readings greater than 21 mmHg, glaucoma, ocular trauma, or tumor, ocular inflammatory disease, history of uveitis, retinal disease, diabetes, hypertension were excluded from the study.

Measurements of transthoracic echocardiography

All procedures of transthoracic echocardiography using a 1-5 MHz transducer (Vivid 7, GE Vingmed Sound Horten, Norway) were performed by two experienced cardiologist. All volunteers were investigated using parasternal long-axis and short-axis approaches and apical four- and two-chamber views in supine and left lateral positions. According to the suggestions of the American Society of Echocardiography primary MVP was diagnosed when at least 1 mitral leaflet was prolapsed into the left atrium and passed the mitral annulus by at least 2 mm along the parasternal long axis during the systolic phase.¹¹

Ocular ultrasound elastography measurement

The image analyzes were performed by the same radiologist who carried out the ultrasound (USG) examinations. All measurements were acquired in the supine position. All images were obtained from both eyes of both groups. Freehand RTE measurement was carried out with a high frequency linear probe (13-15 MHz) on a Hitachi Arietta 65 ultrasound machine (Hitachi Aloka Medical, Ltd, Japan) by the same radiologist experienced on B-scan USG and elastography.

The all ocular measurements were assessed in the same direction as the blood flow with in an angle (<60°). The measurements have been carried out by the same experienced radiologist and the method was previously described.^{12,13} The peak systolic velocity (PSV) and the end-diastolic velocity (EDV) values were recorded for each artery. Then, the vascular resistance index (RI) was calculated ($RI = \frac{PSV - EDV}{PSV}$). After assessment of orbit with conventional USG, the

probe was put onto the lids of the patient and elastography was carried out with the existing elasto software. Elasticity images were obtained by moving the probe continuously and obtaining compression and relaxation waveforms. After 8-10 compression and relaxation cycles, the elastographic examination was finalized, and strain rate measurements were acquired. We performed at a relatively slow speed, very gentle compression/release 3 to 5 times in intervals of 1 to 2 seconds and repeated measurements. At least 10 attempted elastography examinations were made for each eye until the color displayed in the ROI was completely stable to allow reliable measurement results. The strain images were put over gray-scale images in a color layout: red (largest strain, softest tissue), green (mean strain, intermediate tissue) and blue (lowest strain; hardest tissue). The ratio of orbital fat to sclera (S) was measured according to the semi-quantitative evaluation of the elastographic images. The region of interest (ROI) of the sclera was drawn, and the corresponding ROI in the adjacent normal fatty tissue was later drawn as a control for the measuring ROF/S (ratio of orbital fat-sclera) (Figure 1). The analyzed region in the sclera was the same dimension for all subjects and it was placed at a fixed distance from the surface. Higher elastography ratio values indicated stiffer tissue, while lower elastography ratio values showed increased elasticity. The image analyses were performed by the same radiologist who carried out the USG examinations. All measurements were acquired in the supine position. All images were obtained from both eyes of both groups.

Statistical analysis

All statistical analyses were applied using SPSS version 26 software (SPSS Inc., Chicago, IL, USA). The conformity to normal distribution of each continuous variable was assessed using the Kolmogorov-Smirnov test. The Chi-square test were used to analyze the categorical variables between the groups. An independent *t* test was used to compare continuous variables. Continuous variables were presented as mean±standard deviation while categorical variables were presented as number (percentage). A value of $p<0.05$ was accepted as statistically significant.

Results

Demographic characteristics

The mean age was 31.77 ± 11.40 years in the study group and 30.65 ± 7.45 years in the control group. There was no statistically significant difference between the two groups in respect of mean age ($p=0.511$). The female-to-male ratio was 20:15 in the study group and 20:15 in the control group, with no significant difference between the groups ($p>0.05$).

USG elastography results

The mean ROF/S was 1.95 ± 0.81 in the study group, 1.37 ± 1.06 in the control group ($p=0.001$). The mean ROF/S was significantly higher in the study group than the control group. The mean RI of the OA was 0.67 ± 0.05 in the control group, 0.67 ± 0.05 (0.55;0.87) in study group. The mean RI of the PCA was 0.66 ± 0.05 in the control group, 0.68 ± 0.06 in study group. The mean RI of the CRA was 0.66 ± 0.05 in the control group, 0.66 ± 0.06 in study group. The RI value was not a significant difference between control and study group ($p>0.05$). The RTE and CDI measurements of both control and study are summarized in Table 1.

Discussion

Our study evaluated the blood flow rates of retrobulbar vascular structures and elasticity of the eye in MVP patients. The results indicated that MVP patients had higher ROF/S values compared with the healthy participants. In the comparison of the MVP patients with a control group, statistically significant differences were found in the EDV, and PSV values of the PCA and CRA. A significant relationship was related with ocular elasticity. MVP may occur as a result of various pathological mechanisms involving any of the functional components of the mitral valve apparatus. Primary MVP, which is seen as a result of valvular collagen disruption and myxomatous infiltration, is the prominent condition among them. MVP may be familial, sporadic, non-syndromic, or part of a well-defined syndrome of heritable connective tissue disorders, such as Marfan syndrome, Ehlers-Danlos syndrome, polycystic kidney disease among others.¹⁴

Table 1. Comparison of the ratio of sclera to orbital fat and retrobulbar hemodynamics measurements between the groups.

	Study Group	Control Group	P-value ^a
ROF/S	1.95±0.81	1.37±1.06	0.001
Ophthalmic artery			
RI	0.67±0.05	0.67±0.05	0.975
PSV (cm/s)	17.30±9.53	20.60±8.79	0.051
EDV (cm/s)	5.69±4.01	6.62±3.20	0.171
Posterior ciliary arteries			
RI	0.68±0.06	0.66±0.05	0.069
PSV (cm/s)	18.04±8.59	23.50±9.36	0.001
EDV (cm/s)	5.67±3.28	7.98±3.72	<0.001
Central retinal artery			
RI	0.66±0.06	0.66±0.05	0.978
PSV (cm/s)	19.66±8.60	26.17±9.13	0.004
EDV (cm/s)	5.80±2.52	8.53±3.41	<0.001

RI; resistance index, PSV; peak systolic velocity, EDV; end-diastolic velocity.

^aIndependent samples t-test.

Patients with primary MVP have excessive connective tissue, which causes thickening of the spongiosa layer due to the excess of dermatan sulfate, which is a glycosaminoglycan. This condition weakens the structure of the mitral leaflets and adjacent tissues, resulting in elongation of the chordae tendineae.⁶

Ocular involvement can potentially lead to vision threatening disease. MVP can be associated with ophthalmological diseases such as keratoconus (KC), glaucoma, chronic progressive external ophthalmoplegia, and retinal

artery embolism.¹⁵ According to the literature information some studies showing a relationship between MVP and ocular involvement. Duru et al.² reported thinning of Bowman layer in the inferior half of the cornea in patients with MVP. Lichter et al.³ found 22.2% keratoconus patients with MVP. Akcay et al.¹⁵ reported that KC prevalence is higher than control individuals in MVP patients and the biomechanical properties of the cornea are altered in patients with MVP.

Chiang et al.⁶ reported that MVP is a significant predictor for the development of open angle

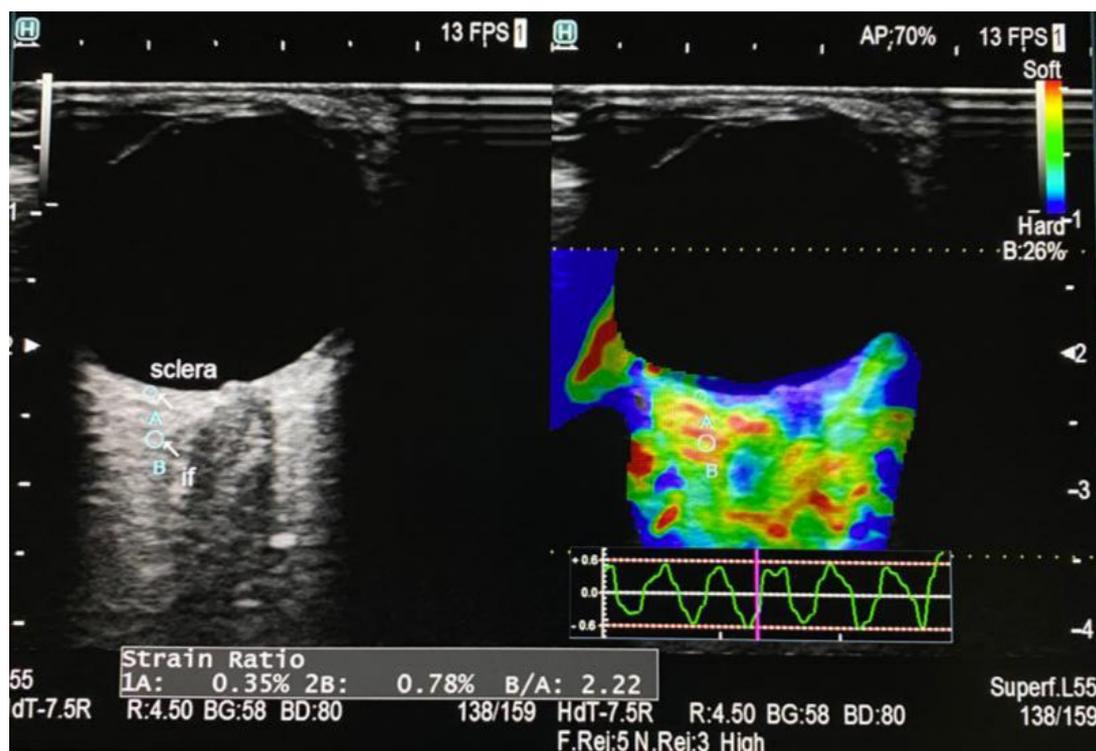


Figure 1. B-mode ultrasonography image (1) and the related elastography image (2) of scleral tissue (A) versus intraconal fat (B). The circles (A and B) indicate where the elastographic measurements were taken. B intraconal fat, A sclera tissue.

glaucoma, after adjusting for possible confounding factors. In MVP, the disease duration induces scleral tissue alterations which can lead to scleral destruction. Thus can be related with ocular involvement in MVP disease.

Previous studies have demonstrated the elastographic characteristics of ocular tissue. Unal et al.¹⁶ investigated the optic nerve head (ONH) characteristics in patients with primary open angle glaucoma (POAG) using real-time elastography. They found that human scleral rigidity of POAG patients was greater than the control eyes. Agladioglu et al.¹⁷ reported the correlation between primary open angle glaucoma and ocular elasticity in adults and demonstrated that anterior vitreous/posterior vitreous strain ratio increases in glaucoma patients. Kazemi et al.¹⁸ found that ocular rigidity was significantly lower in glaucomatous eyes than control eyes.

In addition to these associated with ophthalmological diseases, involvement of retinal vascular manifestations retinal embolism and retinal vascular occlusive disorders. Previous studies have reported abnormal elastic properties of the vascular systems in MVP. Kardesoglu et al.¹⁹

found that the aortic stiffness index was increased. Erolu et al.¹ reported that increased elasticity of the aorta in childhood.

Limitations of the study

The present study had several important limitations. The main limitations of the study were relatively small number of participants in the groups and its single-centered design. Another main limitation was that the evaluated medical data was limited.

Conclusions

To the best of our knowledge, our study is the first to compare the blood flow rates of retrobulbar vascular structures and elasticity of the eye at the same time in MVP patients. This study demonstrated that MVP patients has a statistically significant difference scleral elasticity. The mean ROF/S values were significantly increased in patients with MVP as compared to the control group. The results of this study showed a significant difference between the control, and MVP groups

in respect of the EDV and PSV values of PCA, and CRA. From these results, it can be said that vascular extracellular matrix changing in the vessels feeding the eye. This histological alteration can cause the feeding of tissues will be impaired with a reduced flow and consequently more ocular complications will be seen such as retinal vascular occlusive disorders. Nevertheless, there is a need for further studies to evaluate the importance of early determination of ocular vascular damage in MVP with CDI and RTE.

Acknowledgements

We would like to thank Medicine department and our lab staff for their assistance in this research.

Conflict of interest

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

Funding Sources

The author(s) received no financial support for the research, authorship, and/or publication of this article.

Ethical Approval

Bursa City Hospital Clinical Research Ethics Committee approved the study protocol (Decision number: 2020-8/5, date: 07.10.2020).

Authors' Contribution

Study Conception: DT, MEC, EKT; Study Design: DT, MEC, EKT, BU; Supervision: DT, MEC, EKT, BU, MFK, MEA; Literature Review: DT, BU, MFK, MEA; Critical Review: EKT, BU, MFK, MEA; Data Collection and/or Processing: DT, MEC, EKT, BU, MFK, MEA; Statistical Analysis and/or Data Interpretation: DT, MEC, BU; Manuscript preparing: DT, MEC. Echocardiography: DT, BU; Ocular ultrasound elastography: EKT; Ocular measurements: CRA, PCA, OA.

References

1. Erolu E, Akalın F, Çetiner N, Şaylan Çevik B. Aortic elasticity and carotid intima-media thickness in children with mitral valve prolapse. *Cardiol Young*. 2018 Feb;28(2):292-301. doi: 10.1017/S1047951117001950.
2. Duru N, Haşhaş OE, Göktaş E, Duru Z, Arifoğlu HB, Ulusoy DM, Karatepe Haşhaş AS, Ataş M. Corneal sublayers thickness in patients with mitral valve prolapse. *Eye Contact Lens*. 2018 Jan;44(1):55-9. doi: 10.1097/ICL.0000000000000300.
3. Lichter H, Loya N, Sagie A, Cohen N, Muzmacher L, Yassur Y, Weinberger D. Keratoconus and mitral valve prolapse. *Am J Ophthalmol*. 2000 May;129(5):667-8. doi: 10.1016/s0002-9394(00)00371-8.
4. van Rhee F, Blecher TE, DeLepeleire KA, Galloway NR. Bilateral retinal artery occlusion due to mitral valve prolapse. *Br J Ophthalmol*. 1991 Jul;75(7):436-7. doi: 10.1136/bjo.75.7.436.
5. Caltrider ND, Irvine AR, Kline HJ, Rosenblatt A. Retinal emboli in patients with mitral valve prolapse. *Am J Ophthalmol*. 1980 Oct;90(4):534-9. doi: 10.1016/s0002-9394(14)75024-x.
6. Chiang SJ, Daimon M, Wang LH, Hung MJ, Chang NC, Lin HC. Association between mitral valve prolapse and open-angle glaucoma. *Heart*. 2015 Apr;101(8):609-15. doi: 10.1136/heartjnl-2014-306198.
7. Sigrist RMS, Liao J, Kaffas AE, Chammas MC, Willmann JK. Ultrasound elastography: Review of techniques and clinical applications. *Theranostics*. 2017 Mar 7;7(5):1303-29. doi: 10.7150/thno.18650.
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. Baxter GM, Williamson TH. Color Doppler imaging of the eye: normal ranges, reproducibility, and observer variation. *J Ultrasound Med*. 1995 Feb;14(2):91-6. doi: 10.7863/jum.1995.14.2.91.
10. Lieb WE. Color Doppler ultrasonography of the eye and orbit. *Curr Opin Ophthalmol*. 1993 Jun;4(3):68-75. doi: 10.1097/00055735-199306000-00012.
11. Liu PY, Tsai KZ, Lin YP, Lin CS, Zeng HC, Takimoto E, Lin GM. Prevalence and characteristics of mitral valve prolapse in military young adults in Taiwan of the CHIEF Heart Study. *Sci Rep*. 2021 Feb 1;11(1):2719. doi: 10.1038/s41598-021-81648-z.
12. Williamson TH, Harris A. Color Doppler ultrasound imaging of the eye and orbit. *Surv Ophthalmol*. 1996 Jan-Feb;40(4):255-67. doi: 10.1016/s0039-6257(96)82001-7.
13. Harris A, Williamson TH, Martin B, Shoemaker JA, Sergott RC, Spaeth GL, Katz JL. Test/Retest reproducibility of color Doppler imaging assessment of blood flow velocity in orbital vessels. *J Glaucoma*. 1995 Aug;4(4):281-6.
14. Pollack CV, eds. *Differential Diagnosis of Cardiopulmonary Disease*. Switzerland AG: Springer Nature; 2019.
15. Kalkan Akcay E, Akcay M, Uysal BS, Kosekahya P, Aslan AN, Caglayan M, Koseoglu C, Yulek F, Cagil N. Impaired corneal biomechanical properties and the prevalence of keratoconus in mitral valve prolapse. *J Ophthalmol*. 2014;2014:402193. doi: 10.1155/2014/402193.
16. Unal O, Cay N, Yulek F, Taslipinar AG, Bozkurt S, Gumus M. Real-time ultrasound elastographic features of primary open angle glaucoma. *Ultrasound Q*. 2016 Dec;32(4):333-7. doi: 10.1097/RUQ.0000000000000250.

17. Agladioglu K, Pekel G, Altintas Kasikci S, Yagci R, Kiroglu Y. An evaluation of ocular elasticity using real-time ultrasound elastography in primary open-angle glaucoma. *Br J Radiol.* 2016;89(1060):20150429. doi: 10.1259/bjr.20150429.
18. Kazemi A, Zhou B, Zhang X, Sit AJ. Comparison of corneal wave speed and ocular rigidity in normal and glaucomatous eyes. *J Glaucoma.* 2021 Oct 1;30(10):932-40. doi: 10.1097/IJG.0000000000001901.
19. Kardesoglu E, Ozmen N, Aparci M, Cebeci BS, Uz O, Dincturk M. Abnormal elastic properties of the aorta in the mitral valve prolapse syndrome. *Acta Cardiol.* 2007 Apr;62(2):151-5. doi: 10.2143/AC.62.2.2020235.

