Elastic properties of the abdominal aorta in the children with bicuspid aortic valve: an observational study

Biküspit aortik kapaklı çocuklarda abdominal aortun elastik özellikleri: Gözlemsel bir çalışma

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Abstract

Objective: Abnormalities of the aortic root and ascending aorta are common in patients with a bicuspid aortic valve (BAV). The aim of this study was to evaluate the stiffness of the abdominal aorta in children with BAV.

Methods: In this cross-sectional observational study, we evaluated 35 children with normally functioning or mildly regurgitant BAV and 35 healthy children as controls. All children were noninvasively evaluated with transthoracic echocardiography. Annulus of aorta and abdominal aorta diameters were measured. Aortic strain (S), pressure strain elastic modulus (Ep), pressure strain normalized by diastolic pressure (Ep*), aortic stiffness β index (β SI) and, aortic distensibility (DIS) were calculated using the measured data. In evaluation of the data Student's t-test, Chi-square test, Pearson's correlation and multivariate linear regression analysis were used.

Results: Diameter of the aortic annulus was found significantly larger in the children with BAV than the control group (p<0.05). The abdominal aorta systolic and diastolic diameters were similar in the two groups (p>0.05). The children with BAV exhibited significantly lower S (0.210±0.04/0.267±0.07, p<0.001) and DIS ($1.04\pm0.2/1.4\pm0.4$ 10⁻⁶ cm² dyne⁻¹, p<0.001); and higher Ep ($200\pm39/153\pm47$ N/m⁻², p<0.001), Ep* ($3.42\pm0.9/2.5\pm0.9$, p<0.001) and β SI ($1.1\pm0.3/0.84\pm0.3$, p<0.001) than the control group. There was no correlation between the systolic and diastolic diameters of abdominal aortic elasticity parameters (p>0.05).

Conclusion: Bicuspid aortic valve is associated with an increased abdominal aortic stiffness in children. However, impaired abdominal aortic elasticity is not due to abdominal aortic dilatation. These findings require validation by further studies.

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Key words: Bicuspid aortic valve, aortic elasticity, abdominal aorta, children, echocardiography, regression analysis

ÖZET

Amaç: Biküspit aortik kapaklı hastalarda aort anülüsü ve asendan aort anomalileri oldukça yaygın görülmektedir. Bu çalışmanın amacı biküspit aortik kapaklı çocuklarda abdominal aort sertliğini değerlendirmektir.

Yöntemler: Enine kesitli gözlemsel olan bu çalışmada, kapak fonksiyonu normal veya hafif derecede yetmezliği olan 35 biküspit aortik kapaklı çocuk ile kontrol grubu olarak alınan sağlıklı 35 çocuk değerlendirildi. Tüm çocuklar transtorasik ekokardiyografi ile noninvaziv olarak değerlendirildi. Aort anülüsü ve abdominal aorta çapları ölçüldü. Bu ölçümlerde alınan veriler ile aortik gerilme (G), gerilme elastik modülü (Ep), diyastolik basınç ile normalleştirilmiş gerilme elastik modülü (Ep^{*}), aortik sertlik indeksi (βSI) ve aortik esneklik (ES) hesaplandı. Verilerin istatistiksel değerlendirmesinde Student's t-testi, Ki-kare testi, Pearson's korelasyon analizi ve çoklu lineer regresyon analizi kullanıldı.

Bulgular: Aort anülüs çapı kontrol grubuna göre anlamlı olarak geniş bulundu (p<0.05). Abdominal aortun sistolik ve diyastolik çapları açısından farklılık saptanmadı (p>0.05). Biküspit aortik kapaklı çocuklarda G (0.210±0.04/0.267±0.07, p<0.001) ve ES (1.04±0.2/1.4±0.4 10⁻⁶ cm² dyne⁻¹, p<0.001) kontrol grubuna göre belirgin düşük; Ep (200±39/153±47 N/m⁻², p<0.001), Ep* (3.42±0.9/2.5±0.9, p<0.001) ve βSI (1.1±0.3/0.84±0.3, p<0.001) ise belirgin olarak yüksek bulundu. Abdominal aort sistolik ve diyastolik çapları ile aortik elastisite parametreleri arasında ilişki saptanmadı (p>0.05).

Sonuç: Biküspit aortik kapak, çocuklarda artmış aort sertliği ile ilişkilidir. Bununla birlikte abdominal aort elastisitesindeki bu bozulma aortik dilatasyondan kaynaklanmamaktadır. (Anadolu Kardiyol Derg 2012; 12: 413-9)

Anahtar kelimeler: Biküspit aortik kapak, aortik elastisite, abdominal aort, çocuk, ekokardiyografi, regresyon analizi

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Introduction

The bicuspid aortic valve (BAV) is the most common congenital cardiac malformation with an incidence of approximately 0.5 to 2.0% in the general population and a significant male predominance (1-3). BAV may be complicated by aortic stenosis, aortic regurgitation, and infective endocarditis. Additionally, the bicuspid aortic valve may be associated with abnormalities of the aortic wall such as coarctation of the aorta, aortic dissection, and aortic aneurysm (3, 4). Aortic annulus and ascending aorta dilatation have been shown in patients with normally functioning bicuspid aortic valve (5-7). Aortic wall abnormalities associated with bicuspid aortic valve are due to cystic medial necrosis. Extensive loss of elastic fibers in the tunica media caused by increased metalloproteinase activity and cystic medial necrosis is thought to play a role in the pathogenesis of associated aortic wall abnormalities (8). Aortic stiffness and aortic distensibility are important to assess the elastic properties of the abdominal aorta. Transthoracic echocardiography has been shown to be a reliable and highly accurate technique to assess the abdominal aortic elasticity (9, 10).

Recent studies reported that adult patients with BAV have abnormal elastic properties of the ascending aorta (11-15). Increase in aortic stiffness may also increase the risk for dissection (12). Dissection may reach aorta through the antegrade way (16-18). On the other hand, infrequent thoracic and abdominal aorta dissections have also been documented in patients with BAV (19-21). Presence of spontaneous coeliac artery dissection was reported in a BAV case and it was emphasized that this situation was due to a systemic disease rather than a local condition (22). Considering these facts, the present study was planned to investigate by transthoracic echocardiography whether the elastic properties of abdominal aorta were affected.

There is good evidence indicating that the elastic properties of the ascending aorta are affected but it is not clear yet if the elastic properties of the descendent aorta are also impaired. However, the elastic properties of the abdominal aorta have not been investigated before. We hypothesized that the diameters and elastic properties of the abdominal aorta may also be affected in patients with BAV.

In the present study, we evaluated whether the stiffness and distensibility of the abdominal aorta was altered in children with bicuspid aortic valve by using transthoracic echocardiography.

Methods

Study design and population

Our study was designed as cross-sectional observational in the Pediatric Cardiology Department of Ege University Hospital. The study group consisted of 35 patients with BAV and the control group consisted of 35 healthy with normal aortic valve who were matched for gender and age. The patients with isolated BAV without any aortic valve dysfunction except mild aortic regurgitation followed in outpatient clinic were enrolled in the study. Patients with aortic stenosis, more than mild regurgitation, or any other congenital heart diseases including aortic coarctation, mitral and tricuspid valve disease, aortic dissection, Marfan's or Turner's syndrome, a history of cardiovascular surgery, and systemic arterial hypertension were excluded. Local ethics committee approved the study. Informed consent was obtained from the parents of the all patients and control groups.

Baseline evaluation

Detailed medical history was obtained and physical examination was performed by the same pediatric cardiologist. The body height and weight were measured and the blood pressure was also recorded in all subjects.

Weight was measured with an electronic digital scale that was sensitive to 0.1 kg. Body mass index (BMI) was calculated as weight (kg)/height (m²). Plasma lipid levels were measured after 12 hours of fasting. Serum total cholesterol, triglyceride, high-density lipoprotein (HDL), and low-density lipoprotein (LDL) levels were measured with Alcyon 300 (Abbott Laboratories, USA) equipment by enzymatic method.

Blood pressure measurement

All subjects rested in the supine position for 15 minutes and then their right brachial artery pressure was measured by sphygmomanometer with appropriate cuff. Both systolic (Ps) and diastolic blood pressure (Pd) were measured and after three measurements the mean value was obtained.

Pulse pressure (PP) was calculated as PP=Ps-Pd.

Echocardiographic evaluation

All the patients and control group underwent 2D, M-Mode, and Doppler study using GE Vingmed Vivid 7- model echocardiography (GE Vingmed, Ultrasound AS, Horten, Norway) and multifrequency transducer (2.5-4 MHz), images were taken with children in left lateral decubitus position. The children did not receive sedation. Aortic valve morphology was evaluated in the parasternal long axis and short axis views. The diagnosis of BAV was based on the previously defined criteria (23, 24). Two morphologic phenotypes of BAVs were identified depending on the commissural orientation and cusp position in the parasternal short axis view (20); if cusp orientation was anterior and posterior as type 1 and cusp orientation was left and right as type 2. The presence of raphe was reported when visualized.

The aortic annulus diameter (Da) was measured from the left ventricle-aortic junction at end-diastole in the parasternal long axis view. Presence of aortic regurgitation and/or stenosis was investigated by using continuous wave-pulsed wave Doppler and color Doppler echocardiography. Peak aortic velocity was assessed by continuous wave Doppler from the apical approach. Aortic stenosis was defined in case of peak aortic velocity \geq 2.5 m/s (25). Grading of aortic regurgitation was done on the basis of previously defined algorithm (26). Patients were excluded if they had aortic stenosis or more than mild regurgitation. Fractional shortening (FS) was measured at the parasternal long axis view.

A long axis view of abdominal aorta of the subxiphoid area was recorded and maximum systolic (Ds) and minimum diastolic diameter (Dd) was measured by M-mode echocardiography.

Calculations

All aortic measurements were made as previously described by Lacombe et al. (27). Aortic strain (S) was calculated from the changes in aortic diameters and pressure strain elastic modules was also calculated from the aortic strain and the changes in brachial artery systolic and diastolic pressure using the formulas: S=(Ds-Dd)/Dd, Ep=(Ps-Pd)/S. Pressure strain normalized (Ep*) by diastolic pressure was calculated by the equation: Ep*=Ep/Pd. Aortic distensibility (DIS) and Aortic stiffness β index (β SI) were calculated according to the previously proposed and evaluated equations (28-31) as;

DIS=[2(Ds-Dd)/Dd(Ps-Pd)]x10⁻⁶ cm²dyne⁻¹

 β SI=In(Ps/Pd)/[(Ds-Dd)/Dd]

S and DIS represent the distensibility or elasticity of the aortic wall; Ep, Ep*, and β SI represent the stiffness of the aortic wall. Ep and Ep* are the mean stiffness of aorta.

Statistical analysis

All statistical analyses were performed using Systat statistical software (version 15.0 for Windows; SPSS Inc, Chicago, IL, USA). Data were tested for homogeneity of variance with Shapiro-Wilk test. The Student's t-test (unpaired) and Chisquare test were used for comparison of statistical difference between the groups. Correlations between the diameters of aorta and aortic elasticity parameters were evaluated with Pearson's correlation test. Multivariate regression analysis were performed to determine if gender, age, BMI and presence of BAV were significant predictors of aortic elasticity parameters. While dependent variables for multivariate regression analysis were gender, age, BMI and presence of BAV. Statistical significance was taken at p<0.05. All data were presented as the mean \pm SD.

Results

Baseline characteristics

The study was performed on 35 children with normally functioning or mildly regurgitant bicuspid aortic valve (22 males and 13 females) mean ages 10.3±2.3 years (range between 8-14 years), and 35 healthy children (21 males and 14 females) mean ages 10.7±1.9 years (range between 8-14 years) were considered as control group. The defining data of the patients and healthy controls were presented in Table 1. No differences were evident between the groups in age, gender, weight, height, BMI, systolic and diastolic blood pressure and, fractional shortening (p>0.05). Aortic stenosis (peak velocity \geq 2.5 m/s) was not detected in any subjects with BAV. Peak aortic velocity was significantly higher in the BAV group than the healthy control group (p<0.001). Peak aortic velocity was found in the study and control group 150.6±11.9 and, 126.9±14.7 cm/sec respectively. Serum total cholesterol, triglyceride, HDL, LDL levels were in normal ranges in the all subjects. The two study groups revealed indifferent lipid levels (Table 1).

Of the entire BAV group 15 patients (43%) had normally functioning valves, whereas 20 patients (57%) had mild aortic regurgitation (jet height/left ventricular outflow tract height ratio <24% and jet area/left ventricular outflow area <4%). The morphologic analysis of BAVs designated those 23 patients (66%) had type 1 and 12 patients (34%) had type 2 BAVs. Raphe was detected in 19 patients with BAV (54%).

Diameters of aorta

In the children with BAV, the diameter of the aortic annulus was larger compared to the control group (p<0.05). The mean diameters of aortic annulus were 18.1 ± 3 and 16.6 ± 2.5 mm, respectively in the study and control groups (Fig. 1). There was no significant difference in the mean abdominal aorta systolic and diastolic diameters between the two groups (p>0.05). The mean abdominal aorta systolic and diastolic diameters were 10.7 ± 2.4 and 8.9 ± 1.9 mm, respectively in the study group, whereas these values were 10.4 ± 1.6 and 8.2 ± 1.2 mm, respectively in the control group (Fig. 2).

Elastic properties of abdominal aorta

Although there was no significant difference between the two groups in the measurements of abdominal aorta systolic and dia-

Table 1. The clinical data of the study and control groups

Variables	Study group (n=35)	Control group (n=35)	*р
Mean age, years	10.3±2.3	10.7±1.9	0.436
Sex, M/F	22/13	21/14	0.806
Height, cm	138±17	143±14	0.223
Weight, kg	37±12	38±10	0.781
BMI, kg/m ²	18.8±2.3	18.1±2	0.191
Ps, mmHg	104±11.5	102±10	0.499
Pd, mmHg	60.5±9	63±8	0.314
PP, mmHg	42±6	39±6	0.058
Total cholesterol, mg/dL	133±17	129±15	0.349
HDL cholesterol, mg/dL	45±6	47±10	0.198
LDL cholesterol, mg/dL	69±19	65±8	0.108
FS, %	39±3	40±3.5	0.536
Peak aortic velocity, cm/sec	150.6±11.9	126.9±14.7	<0.001

*Unpaired Student's t and Chi-square tests

BMI - body mass index, FS - fractional shortening, HDL - high density lipoprotein, LDL - low density lipoprotein, Pd - diastolic blood pressure, Ps - systolic blood pressure, PP - pulse pressure stolic diameters; Strain (S:0.210±0.04/0.267±0.07, p<0.001) and distensibility (DIS:1.04±0.2/1.4±0.4 10⁻⁶ cm² dyne⁻¹, p<0.001) were significantly lower in the children with BAV compared to the control group. However, pressure strain elastic modulus (Ep:200±39/153±47 N/m⁻², p<0.001), pressure strain normalized by diastolic pressure (Ep*:3.42±0.9/2.5±0.9, p<0.001) and aortic stiffness β index (β SI: 1.1±0.3/0.84±0.3, p<0.001) were significantly higher in the children with BAV in comparison to the controls (Fig. 3). Using multivariate regression analyses, aortic elasticity parameters were significantly associated with the presence of a BAV (p<0.001) (Table 2). There was no correlation between the systolic and diastolic diameters of abdominal aorta and aortic elasticity parameters (p>0.05).

There was no significant difference in the mean aortic diameters and aortic elasticity parameters between the type 1 and type 2 BAVs (p>0.05) (Table 3).



Figure 1. Mean diameters of aortic annulus in the study and control groups





Figure 2. Mean systolic and diastolic diameters of the abdominal aorta in the study and control groups

Results are presented as mean±standard deviation, p>0.05

 BAV - bicuspid aortic valve, Dd - abdominal aorta diastolic diameter, Ds - abdominal aorta systolic diameter

Discussion

The present cross-sectional study was undertaken to comparatively evaluate the elastic properties of abdominal aorta in children with BAV. To the best of our knowledge, this is the first study reporting data on the elastic properties of the abdominal aorta. Our findings showed that the strain and distensibility which indicate the elasticity of the abdominal aortic wall were significantly lower in children with BAV. Moreover, the pressure strain elastic modulus, the pressure strain normalized by diastolic pressure, and the aortic stiffness β index were all significantly higher in this group of children with BAV. The present parameters are independent from the abdominal aorta diameters and represent the stiffness of the abdominal aortic wall.

Larger aortic annulus and ascending aorta dimensions have been reported in patients with normally functioning BAV (5-7). Cystic medial necrosis is demonstrated to play an important role in the pathogenesis underlying the aortic root abnormalities in patients with BAV. This process is associated with increased metalloproteinase activity and apoptosis of vascular smooth muscle cells (8). There is only one study evaluating both the ascending and descending aorta including the abdominal aorta diameters published by Cecconi et al. (32). They showed that despite the larger aortic root and ascending aorta dimensions descending and abdominal aorta dimensions were similar to the control group in patients with BAV without significant valve dysfunction. Similarly, we detected that the diameter of aortic annulus was larger in the children with BAV than the controls and there was no difference in the abdominal aorta diameter between the two groups. The results of our study confirmed that aortic dilatation in patients with BAV involved the aortic root and ascending aorta but not the abdominal aorta.



Figure 3. Aortic elasticity parameters in the study and control groups (p<0.001) $\,$

Results are presented as mean±standard deviation, p<0.001

BAV - bicuspid aortic valve, DIS - aortic distensibility and β , Ep - pressure strain elastic modulus, Ep*: pressure strain normalized by diastolic pressure, S - aortic strain, SI - aortic stiffness β index

		Presence of BAV	Age	Gender	BMI
S	*р	<0.001	0.86	0.59	0.95
	β	-0.44	-0.022	0.063	-0.008
	**95% CI	-0.088-0.028	-0.009-0.008	-0.23-0.04	-0.008-0.007
Ep, N/m ⁻²	*р	<0.001	0.68	0.69	0.83
	β	0.484	0.054	0.045	-0.027
	**95% CI	25.4-69.4	-4.7-7.2	-18.3-27.4	-6.1-4.9
Ep*	*р	<0.001	0.09	0.23	0.61
	β	0.423	-0.22	0.135	-0.63
	**95% CI	0.41-1.3	-0.23-0.017	-0.189-0.76	-0.146-0.086
DIS, 10 ⁻⁶ cm ² dyne ⁻¹	*р	<0.001	0.67	0.62	0.72
	β	-0.507	-0.053	-0.055	-0.044
	**95% CI	0.01-0.024	-0.001-0.0	-0.002-0.001	0.0-0.0
β SI 	*р	<0.001	0.15	0.38	0.56
	β	0.445	-0.183	0.098	-0.71
	**95% CI	0.136-0.406	-0.063-0.01	-0.079-0.202	-0.044-0.024

Table 2. Relationship between aortic elasticity parameters and presence of BAV gender, age and BMI

*Multivariate regression analysis. Dependent variables: aortic elasticity parameters. Independent variables: presence of BAV, age, gender, and BMI.

**95% confidence interval

BAV - bicuspid aortic valve, BMI - body mass index, DIS - aortic distensibility, Ep - pressure strain elastic modulus, Ep* - pressure strain normalized by diastolic pressure, S - aortic strain and β SI - aortic stiffness β index

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Variables	Type 1 (n=23)	Type 2 (n=12)	*р-
Mean age, years	10.3±2.2	10.6±2.4	0.697
Sex, M/F	13/10	9/3 18.9±2	0.463 0.96
BMI, kg/m²	18.8±2.6		
PP, mmHg	42±7	43±6	0.058
Peak aortic velocity, cm/sec	149.9±12.9	152±10.3	0.624
Da, mm	17.8±2.6	18.7±3.8	0.414
Ds, mm	11.1±2.5 9.1±2.2	10.2±1.9 8.5±1.5 0.196±0.05	0.279 0.361 0.147
Dd, mm			
S	0.217±0.04		
Ep, N/m ⁻²	190±32	218±49	0.055
Ep*	3.38±0.98	3.5±0.94	0.730
DIS, 10 ⁻⁶ cm ² dyne ⁻¹	1.07±0.2	0.9±0.3	0.157
β SI	1.09±0.2	1.2±0.3	0.516

Table 3 The clinical data of the natients with type 1 and type 2 BAVs sure an

Data are presented as mean±standard deviation and number/percentage

*Unpaired Student's t and Chi-square tests

BMI - body mass index, Da - diameters of aortic annulus, Dd - abdominal aorta diastolic diameter, DIS - aortic distensibility and β , Ds - abdominal aorta systolic diameter, Ep - pressure strain elastic modulus, Ep* - pressure strain normalized by diastolic pressure, PP - pulse pressure, S - aortic strain, SI - aortic stiffness β index

Transthoracic echocardiography provides a highly accurate and reliable evaluation of regional aortic elastic properties. Stiffness and distensibility assessment of abdominal aorta has a very important role in the evaluation of the arterial system elasticity. The increased stiffness causes an increase in pulse pressure and a decrease in diastolic blood pressure, thereby causing increased left ventricular afterload and increased fatigue arterial wall tissues. Aortic stiffness β index represents the stiffness, while strain and distensibility represent the elasticity of the abdominal aortic wall. Previous studies have shown that measurement of aortic stiffness helps early detection of arteriosclerosis and the abdominal aorta becomes stiffer with age, hypertension, atherosclerosis, tobacco-smoking, obesity, β thalassemia patients, and patients of Marfan syndrome and Kawasaki disease (9, 10, 33).

In a few recent studies, abnormal elastic properties of the aortic annulus and ascending aorta were detected in adult patients with BAV (11-15). However, the elastic properties of the abdominal aorta have not been investigated before in adults or children with BAV. Nistri et al. (11) have previously investigated the elastic properties of the ascending aorta in young male patients with normally functioning BAV and they found that distensibility was lower and aortic stiffness was higher in BAV patients compared to the controls. In another study, same authors reported a correlation between aortic size of the ascending aorta and aortic distensibility-stiffness in patients with BAV (12). Similarly, Yap et al. (13) stated that patients with stenotic BAV had higher aortic stiffness of the aortic root compared to the controls and they showed a relationship between end-diastolic diameter of aortic root and parameters of the aortic elasticity. They suggested that an increased aortic root dimension was associated with a decreased aortic elasticity. Our present study differs from the previous ones as the elastic

properties of the abdominal aorta were evaluated in children with normally functioning or mildly regurgitating BAV. The incidence of associated abnormalities of the aortic wall such as coarctation of the aorta, aortic aneurysm, and particularly aortic dissection is high in BAV patients and these abnormalities usually occur in previously asymptomatic adult patients (1, 3). Presence of dissection of thoracic and abdominal aorta has been documented in patients with BAV in a few reports (19-21). A case report documented spontaneous celiac artery dissection in a patient with BAV and suggested that this should be regarded as a systemic disease rather than a local disease (22). However, our present findings suggest that not only the ascending but also the descending aorta are involved and this involvement may start during the adolescent ages. To our knowledge, this is the first study to demonstrate the involvement of elastic properties of abdominal aorta in children with BAV. Considering this fact, the present findings provide further support for the need for strict prospective echocardiographic investigation including the abdominal aorta and follow up of BAV patients even in normally functioning or mildly regurgitant BAV patients.

Study limitations

There are numerous published studies focusing on the ascending aorta and the affects in the ascending aorta are well known. Therefore, our intention was to document the possible effects in the descending aorta. However, comparatively recording the data in both ascending and descending aorta may better clarify the elastic properties of aorta at all parts with BAV patients. Further studies including the both parts of the aorta should be performed.

Conclusion

Results of the present study confirmed that elasticity of the abdominal aortic wall was decreased and the stiffness of the abdominal aortic wall was increased in the children with normally functioning or mildly regurgitant BAV compared to the control group despite the lack of difference in the abdominal aortic diameters. We suggest that additional risk factors such as obesity, hypertension, and tobacco-smoking which increase aortic stiffness should be especially eliminated in patients with BAV. Further pathophysiological studies with larger size are required to confirm these findings and clarify the reasons of altered elastic properties of the abdominal aorta in patients with BAV.

Conflict of interest: None declared.

Authorship contributions. Concept - R.Ö., D.G.; Design - D.G.; Supervision - R.Ö., E.L.; Resource - R.Ö., E.L.; Data collection&/ or Processing - D.G., Z.Ü.; Analysis &/or interpretation- D.G.; Literature search - D.G.; Writing - D.G.; Critical review - Z.Ü., R.Ö., E.L.; Other-Z.Ü.

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