

Color M-Mode Mitral Propagation Velocity in Patients with Mitral Stenosis

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Abstract

- Aim:** Our aim was to evaluate the use of mitral color M-mode flow propagation velocity (Vp) as a novel approach to assessing the severity of MS.
- Patients and Methods:** We prospectively examined 65 consecutive patients with MS. Pressure Half Time (PHT) and Planimetry was used as the reference method due to invasive nature of catheterization. According to planimetry, MS was mild in 25 patients (38.5%), moderate in 27 (41.5%) and severe in 13 (20%). Vp was obtained by measuring the slope of the blue jet with the first aliasing velocity.
- Results:** The mean Vp was 43.3 ± 9.05 cm/s in mild MS, 52.09 ± 9.22 cm/s in moderate MS and 73.93 ± 15.75 cm/s in severe MS ($p1-2=0.002$, $p2-3<0.001$, $p1-3<0.001$), demonstrating statistically significant correlation between severity of MS and Vp. When PHT was used, a similar correlation was observed between MS severity and Vp ($p1-2=0.002$, $p2-3<0.001$, $p1-3<0.001$). With planimetric valve area as reference, a Vp threshold of 48 cm/s allowed to distinguish mild MS from moderate/severe MS (sensitivity - 77.5%, specificity - 80%, positive predictive value - 86.1%, negative predictive value - 69%), while a threshold of 60 cm/s distinguished severe MS from mild/moderate MS (sensitivity - 92.3%, specificity - 88.5%, positive predictive value - 66.7%, negative predictive value - 97.9%).
- Conclusion:** Our results indicate that Vp may be a simple, non-invasive and reliable method for determining the severity of MS.
- Keywords:** Mitral stenosis, planimetry, mitral color M-mode propagation velocity.

Özet

- Amaç:** Bu çalışmanın amacı mitral darlığı ciddiyetini belirlemede yeni bir yöntem olarak mitral M-mod akım yayılma hızı (Vp) kullanımını değerlendirmektir.
- Yöntem:** Prospektif olarak mitral darlığı (MD) olan 65 hasta incelendi. Hastalarda MD planimetri, PHT ve ortalama gradilyent kullanılarak ayrı ayrı derecelendirildi. Kardiyak kateterizasyon yapılmadığından referans ölçüm olarak kabul edilen planimetriye göre 25 hastada hafif MD (%38.5), 27 hastada orta MD (%41.5), 13 hastada ciddi MD (%20) mevcuttu. Vp ilk aliasing velosite ile mavi jet eğimini ölçerek elde edildi.
- Bulgular:** Hafif MD'de ortalama Vp 43.3 ± 9.05 cm/s, orta MD'de Vp 52.09 ± 9.22 cm/s, ciddi MD'de ise Vp 73.93 ± 15.75 cm/s olarak saptandı ($p1-2:0.002$ (hafif ile orta MD) $p2-3<0.001$ (orta ile ciddi MD) $p1-3<0.001$ (hafif ile ciddi MD)), yani planimetrik kapak alanı ciddiyeti ile Vp arasında istatistiksel anlamlı korelasyon saptandı. Benzer şekilde PHT kullanıldığında MD ciddiyeti ile Vp arasında anlamlı korelasyon gözlemlendi ($p1-2:0.002$ $p2-3<0.001$ $p1-3<0.001$). Planimetrik kapak alanı referans alındığında Vp için sınır değer 48 cm/s alınması hafif MD olanları, orta ve ciddi MD olanlardan ayırma sağladı (duyarlılık 77.5%, özgüllük 80%, pozitif tahmin değeri 86.1%, negatif tahmin değeri 69%). Vp için sınır değeri 60 cm/s alındığında ise ciddi MD olanlar, hafif ve orta derece MD olanlardan daha iyi bir şekilde ayrılabilir (duyarlılık 92.3%, özgüllük 88.5%, pozitif tahmin değeri 66.7%, negatif tahmin değeri 97.9%).
- Sonuç:** Vp, MD ciddiyetini belirlemede kullanılacak basit, girişimsel olmayan, güvenilir bir yöntem olabilir. Vp özellikle ciddi MD hastalarını ayırmada yüksek duyarlılık ve özgüllüğe sahiptir.
- Anahtar Kelimeler:** Mitral darlığı, planimetri, PHT, M-mod akım yayılma hızı.

Introduction

Echocardiography plays an essential role in confirmation of diagnosis, quantitation of mitral valve stenosis severity and its consequences, analysis of valve anatomy, decision making for medical therapy, percutaneous treatment and timing of surgery for mitral stenosis (MS)¹⁻³. The echocardiographic methods proposed for evaluation of MS severity are as follows: measuring the valve area using planimetry or pressure half-time (PHT) (Level 1 recommendation), continuity equation or proximal isovelocity surface area (PISA) calculation (Level 2), using mitral valve resistance as indicator (Level 3, rarely used), and using transmitral pressure gradient and estimated systolic pulmonary artery pressure as suggestive data. However, each of these methods has its limitations and may not be feasible in every case. Invasive cardiac catheterization is only recommended when echocardiography is inconclusive³.

Direct planimetric measurement of mitral valve area has the strongest correlation with anatomical valve area and is not influenced by flow conditions, chamber compliance or associated valvular lesions, making planimetry the reference measurement. Nevertheless, planimetry is not reliable when there is a poor acoustic window or significant distortion of valve anatomy, particularly with severe valve calcifications. In such cases, additional data may be needed in order to make a clinical decision such as PHT or PISA^{3,4}.

Mitral color M-mode flow propagation velocity (Vp) makes use of the high temporal resolution of M-mode echocardiography to examine the progress of diastolic flow from the mitral valve opening to the left ventricular apex. The flow propagates from the relatively narrow opening of the valve into the larger cavity of the ventricle, forming ring vortices. Vp is defined as the velocity of such a vortex as it propagates towards the apex^{5,6}.

Being relatively independent of preload, Vp has been used to evaluate left ventricular diastolic function⁷⁻¹³. While this method is not very widespread due to measurement differences, it has been used as mitral regurgitant flow propagation velocity for grading mitral regurgitation¹⁴⁻¹⁵ and as aortic regurgitant flow propagation velocity for grading aortic regurgitation^{16,17}. To the best of our knowledge, there is no information in the

literature regarding Vp as a means of evaluating MS severity. Our aim was to investigate the potential role of Vp, a parameter relatively independent of other variables, in determining the severity of MS, as well as its correlation to other parameters traditionally used to evaluate MS.

Patients and Methods

65 patients with mild, moderate or severe mitral valve stenosis those applied to the outpatient clinic of the Diskapi Yildirim Beyazit Training and Research Hospital. Ethical Committee was approved the study. After initial evaluation, all patients signed informed consent forms.

The patients were aged 18-80. Excluded from the sample were those with severe aortic valve disease, moderate and severe mitral regurgitation, moderate to severe mitral valvular calcification, severe mitral annular calcification, previous cardiac surgery patients, patients who had prosthetic valves, existence of congenital valvular stenosis, left ventricle hypertrophy, NYHA class III-IV heart failure and/or left ventricular systolic dysfunction (LVEF \leq 45%), as well as those with a history of ASD, VSD and cardiac surgery.

All patients underwent a complete 2D transthoracic echocardiographic and Doppler study from multiple windows in the left lateral decubitus position. Studies were performed using the Vingmed Vivid-3 system (General Electric, Haifa, Israel) and a 2.5 MHz transducer. The gain, depth, sector angles and Nyquist limit ranges were adjusted as needed for each case and zoom mode was used where necessary. The studies were performed with the patients at rest (heart rate of 60-100 bpm). 2D echocardiographic measurements were obtained in the parasternal long axis, short axis and apical four-chamber views. The measurements acquired were as follows: left ventricular systolic function, left ventricular end-diastolic and end-systolic diameters, mitral valve area according to planimetry, transmitral peak and mean gradient, mitral valve area according to pressure half-time, estimated systolic pulmonary artery pressure and mitral color M-mode flow propagation velocity. Left ventricular ejection fraction was calculated using the modified biplane Simpson's technique. Echocardiographic measurements were performed in accordance with the guidelines issued by The American Society of Echocardiography.

Based on these values, the Vp value was obtained from 2D apical four-chamber echocardiographic images using Doppler color flow imaging and M-mode method. The M-mode scan line was oriented along the center-line of inflow, from the mitral valve towards the apex. Before the color M-mode Doppler measurement, the Nyquist limit and color gain of the equipment were adjusted for aliasing (the central jet with the highest velocity was seen as blue). Vp was determined by measuring the slope of the blue jet with the first aliasing velocity formed during early diastole (Figure 1 A-B)¹⁸. In patients with sinus rhythm, we averaged at least 3 cardiac cycles, while in those with atrial fibrillation at least 5 cardiac cycles were averaged. Two investigators performed the quantitative echocardiographic grading of MS.

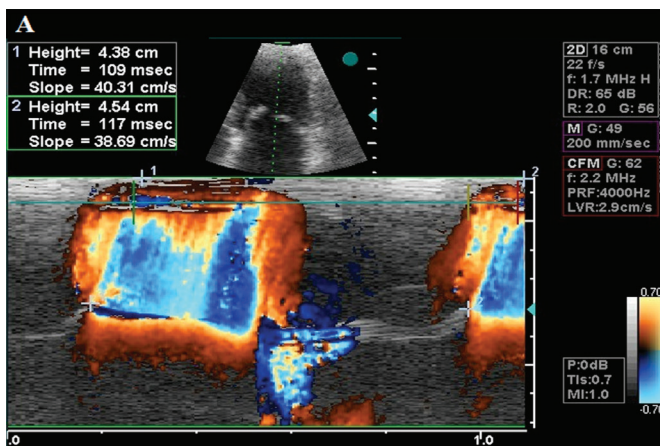
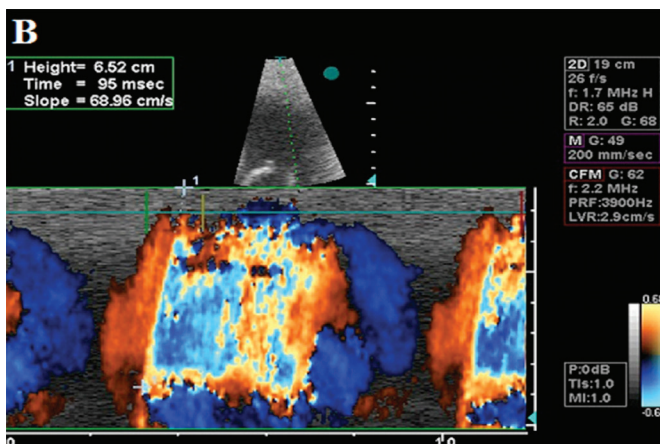


Figure 1a. Mitral color M-mode flow propagation velocity (Vp) recordings. A. Mild mitral stenosis.



B. Severe mitral stenosis. Vp was measured as the slope of the first aliasing velocity from the mitral valve to the left ventricular cavity

Probability of a type I error was set at $\alpha=0.05$, type II error at $\beta=0.05$, AUC at 0.825 and null hypothesis value at $H_0=0.5$ using MedCalc Version 11.1.0. Obtained data were analyzed using the SPSS 15.0 software package for Windows. Continuous variables were presented as mean \pm standard deviation, frequency tables and ratios. Correlation between mitral M-mode flow propagation velocity (Vp) and severity of MS measured by other methods was analyzed using the Kruskal-Wallis test and Spearman's correlation coefficient. Reference measurements for Vp were planimetry or PHT; ROC analysis was performed with a 95% confidence interval. The threshold of significance for all hypotheses was set at $p<0.05$.

Results

The patient sample was comprised of 65 patients with mild, moderate or severe mitral valve stenosis, aged 18-80. Stenosis developed secondary to rheumatic heart disease in all patients. Eighteen patients had hypertension (27.7%), 10 – coronary artery disease (15.4%) and 5 – diabetes mellitus (7.7%). Electrocardiography showed atrial fibrillation (AF) in 23 patients (35.4%) and a sinus rhythm in 42 (64.6%). Six patients had a history of percutaneous mitral balloon valvuloplasty (9.2%).

Evaluation of echocardiographic data showed a mean left atrium size of 4.5 ± 0.6 cm, mean left ventricular ejection fraction of $64.8\pm 4.6\%$, transmitral peak gradient of 16.7 ± 7 mmHg, transmitral mean gradient of 8.2 ± 4.2 mmHg, median mitral valve area (MVA) of 1.4 cm² according to PHT, median MVA of 1.4 cm² according to planimetry, mean estimated systolic pulmonary artery pressure of 41.1 ± 10.3 mmHg and mean mitral color M-mode flow propagation velocity (Vp) of 53.1 ± 15.4 cm/s. Mitral regurgitation was mild in 39 patients (60%), moderate in 7 (10.8%) and severe in none. Aortic regurgitation was mild in 29 patients (44.6%) and moderate in 5 (7.7%). All echocardiographic findings are presented in Table 1.

The severity of MS was quantitated using planimetry, PHT and mean transvalvular gradient in accordance with the Level 1 recommendation of the American and European Society of Echocardiography. As catheterization was not performed due to its invasive nature, planimetry was chosen as the reference measurement. According to planimetry, MS was mild in

25 patients (38.5%, $MVA > 1.5 \text{ cm}^2$), moderate in 27 (41.5%, $MVA = 1.0 - 1.5 \text{ cm}^2$) and severe in 13 (20%, $MVA < 1.0 \text{ cm}^2$). The mean Vp was $43.3 \pm 9.05 \text{ cm/s}$ in mild MS, $52.09 \pm 9.22 \text{ cm/s}$ in moderate MS and $73.93 \pm 15.75 \text{ cm/s}$ in severe MS. Thus, $p_{1-2} = 0.002$ for mild-moderate MS, $p_{2-3} < 0.001$ for moderate-severe MS, and $p_{1-3} = 0.001$ for mild-severe MS, demonstrating a statistically significant correlation between planimetric measurement and Vp.

A similarly significant correlation was detected between Vp and stenosis severity measured with PHT; the mean Vp was $43.99 \pm 8.6 \text{ cm/s}$ in mild MS, $52.92 \pm 11.45 \text{ cm/s}$ in moderate MS, and $75.52 \pm 16.77 \text{ cm/s}$ in severe MS ($p_{1-2} = 0.002$, $p_{2-3} < 0.001$, $p_{1-3} < 0.001$). However, as demonstrated in Table 2, there was no significant difference between patients with mild and moderate stenosis in terms of mean gradient.

ROC analysis was performed in order to assess the efficacy of Vp in differentiating between grades of stenosis severity. With planimetry as reference, Vp discriminated mild MS from moderate/severe MS with a threshold of 48 cm/s (sensitivity - 77.5%, specificity - 80.0%, positive predictive value - 86.1%, negative predictive value - 69%), while a threshold of 60 cm/s particularly discriminated severe MS from mild/moderate MS (sensitivity - 92.3%, specificity - 88.5%, positive predictive value - 66.7%, negative predictive value - 97.9%). Similarly, with PHT as reference, Vp discriminated severe MS from mild/moderate MS with a threshold of 60 cm/s (sensitivity - 90%, specificity - 83.6%, positive predictive value - 50%, negative predictive value - 97.9%). Table 3 demonstrates the relative efficacy of Vp in grading the MS of patients classified based on planimetry and PHT. The ROC curves in Figure 2 A-B and 3 A-B demonstrate the efficacy of Vp in patients classified based on planimetry and PHT.

Discussion

Results of this study showed that Vp may be a method for grading of MS as compared to PHT and planimetry methods. We found that Vp threshold of 48 cm/s allowed to distinguish mild MS from moderate/severe MS (sensitivity - 77.5%, specificity - 80%, positive predictive value - 86.1%, negative predictive value - 69%), while a threshold of 60 cm/s distinguished severe MS from mild/moderate MS (sensitivity - 92.3%,

specificity - 88.5%, positive predictive value - 66.7%, negative predictive value - 97.9%). This results are very important because that all the current diagnostic methods such as planimetry, PHT and PISA have limitations.

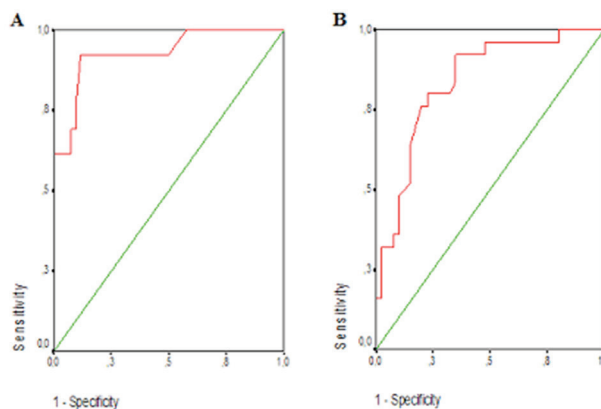


Figure 2. A. Sensitivity and specificity of Vp on the ROC curve plot for discriminating severe mitral stenosis from mild/moderate mitral stenosis measured with planimetry (threshold $\geq 60 \text{ cm/sec}$). B. Sensitivity and specificity of Vp on the ROC curve plot for discriminating mild mitral stenosis from moderate/severe mitral stenosis (threshold $\leq 48 \text{ cm/sec}$).

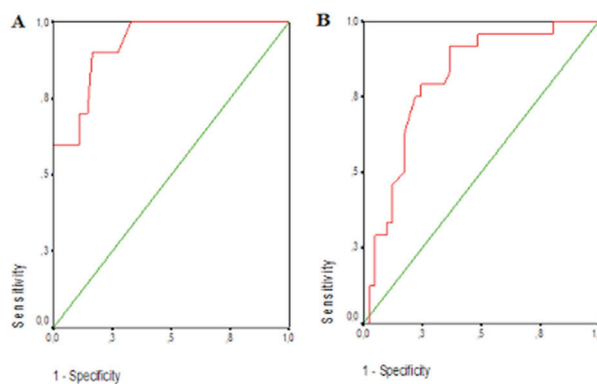


Figure 3. A. Sensitivity and specificity of Vp on the ROC curve plot for discriminating severe mitral stenosis from mild/moderate mitral stenosis measured with pressure half-time (threshold $\geq 60 \text{ cm/sec}$). B. Sensitivity and specificity of Vp on the ROC curve plot for discriminating mild MS from moderate/severe MS (threshold $\leq 48 \text{ cm/sec}$).

TABLE 1. Clinical, Doppler and Echocardiographic Variables for Grades of Mitral Stenosis

	Mean	Std Deviation	Median	Min.	Max.
Age	49,06	13,45	48	20	80
LA size	4,47	0,59	4,47	3	6
LVEDD	4,81	0,47	4,9	3,2	6,3
LVESD	3,01	0,40	3	2	3,9
LVEF	64,86	4,58	65	55	79
Peak Gradient	16,68	6,94	15	5	34,7
Mean Gradient	8,18	4,24	7	2	20
MVA Planimetry	1,38	0,30	1,4	0,8	2
MVA PHT	1,40	0,29	1,4	0,8	1,9
Vp	53,10	15,41	49	28	112
SPAB	41,13	10,26	40	25	60

LA: Left atrium, LVEDD: Left ventricle end-diastolic diameter, LVESD: Left ventricle end-systolic diameter, LVEF: Left ventricle ejection fraction, MVA: Mitral valve area, Vp: Mitral color M-mode flow propagation velocity, SPAB: Systolic pulmonary artery pressure.

TABLE 2. Vp in Groups that were Graded by Planimetry, PHT and mean gradient respectively

	Planimetry			p: 1-2	p: 1-3	p: 2-3
	Mild MS	Moderate MS	Severe MS			
Number of patients (n, %)	25(%38,5)	27(%41,5)	13(%20,0)			
Mean Vp	43,35	52,09	73,94	0,002	<0,001	<0,001
Std Deviation	9,05	9,22	15,75			
MVA PHT						
	Mild MS	Moderate MS	Severe MS	p: 1-2	p: 1-3	p: 2-3
Number of patients (n,%)	24(%36,9)	31(%47,7)	10(%15,4)			
Mean Vp	43,99	52,92	75,52	0,002	<0,001	<0,001
Std Deviation	8,65	11,45	16,78			
Mean Gradient						
	Mild MS	Moderate MS	Severe MS	p: 1-2	p: 1-3	p: 2-3
Number of patients (n,%)	19(%29,2)	31(%47,7)	15(%23,1)			
Mean Vp	45,20	50,32	68,86	0,13	<0,001	<0,001
Std Deviation	10,29	11,93	16,64			

MS: Mitral Stenosis, Std. Deviation: Standard Deviation, Vp: Mitral Color M-mode Flow Propagation Velocity (cm/s), MVA PHT: Mitral Valve Area calculated with pressure half time, p:1-2 ; Mild- moderate MS p:1-3 ; Mild-severe MS, p: 2-3 ; Moderate- severe MS

TABLE 3. Vp (cm/sec) by Mitral Color M-mode Flow Propagation Velocity, and Its Cut Points, Sensitivities, Specificities and Positive and Negative Predictive Values.

			Cut points (cm/sec)	Sensitivity %	Specificity %	Positive predictive value %	Negative predictive value%
Planimetry	Mild+Moderate vs Severe	Vp	60	92,3	88,5	66,7	97,9
	Mild vs Moderate+Severe Moderate+Severe	Vp	48	77,5	80,0	86,1	69,0
MVA PHT	Mild+Moderate vs Severe	Vp	60	90,0	83,6	50,0	97,9
	Mild vs Moderate+Severe	Vp	48	72,4	90,7	92,9	60,5

MVA PHT: Mitral valve area according to pressure half time, Vp: Mitral color M-mode flow propagation velocity

Five different methods of measuring Vp have been described to date^{6,19-24}. The Duval-Moulin-Garcia method, focusing instead on formation of overflow, or 'aliasing'^{20, 22}, with Vp defined as the slope of the brighter inner contour line (m/s). The fact that the vortex ring propagating towards the apex does not form at the very beginning of the diastole results in the biphasic filling pattern seen on color M-mode imaging. The first phase is the flow propagation during early filling, which reflects the sudden simultaneous entry of a big volume into the ventricle under the effect of the pressure wave. It has been noted that actual Vp must be measured during the second phase of flow propagation, which starts with the formation of the vortex^{6,19-24}. For this reason, we chose to use the Duval-Moulin-Garcia method in our study.

In a normal ventricle, the early filling wave rapidly propagates from the left atrium to the apex, triggered by the pressure gradient between the base and the apex. This gradient reflects ventricular relaxation and suction. Vp decreases in patients with impaired left ventricular relaxation¹⁸. In case of MS, generally have intact left ventricular systolic and diastolic function, the propagation of blood through the narrow valve towards the ventricular apex in MS is thought to have different velocity and dynamics. Besides the suggestive data provided by transmitral pressure gradient, a significant correlation was found between Vp and other parameters traditionally used to determine MS severity - planimetry and PHT. Vp was found to be positively correlated with MS severity. However, when only the mean gradient was taken into account, Vp did not discriminate mild and moderate MS well. This may be due to the mean gradient being affected by factors like preload, concomitant mitral regurgitation and heart rate outside the mitral valve.

A similar correlation has been reported in studies by Akdemir et al, Gaber et al and Tokgoz et al between mitral regurgitant flow propagation velocity (RFPV) and mitral regurgitation severity, and in a study by Onbasili et al. between aortic RFPV and aortic regurgitation severity¹⁴⁻¹⁷.

This study is the first by the fact that there are no data available regarding the use of Vp as indicator of MS severity. Compared to planimetric measurement of MVA, however, Vp thresh-

olds of 48 cm/s ve 60 cm/s showed strong discriminating ability. Similarly, compared to the PHT method, a Vp threshold of 60 cm/s had high sensitivity, specificity and negative predictive value for discrimination of severe and moderate/mild MS. In determining the severity of MS, these parameters should be evaluated not separately but combined. Vp may be a useful complementary method in cases where findings are inconsistent with clinical presentation or there are discrepancies between other parameters. Vp is particularly effective in distinguishing patients with severe stenosis.

The most important limitation of our study is the lack of a gold standard for invasive evaluation of mitral stenosis severity. Gorlin method is the reference method for MS definite calculations. But, we thought that it would be unethical to use Gorlin formula as the reference method in our study. Instead, we used planimetry and PHT which are also reference methods in many centers. When used properly, planimetry is the mostly-correlated method with direct measurements²⁵.

Conclusion

Mitral color M-mode flow propagation velocity may be used as a non-invasive 2D echocardiographic method of grading the severity of mitral valve stenosis. The Vp thresholds had particularly high sensitivity and specificity for discriminating patients with severe MS, which may help to improve treatment and follow-up of such patients. However, further research with larger patient samples and evaluation of MS grading before-after balloon valvotomy and heavily calcified mitral valves.

Acknowledgements

We do not have any acknowledgements.



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