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Spontaneous left atrial echo contrast, mitral annular systolic velocity, and left atrial appendage late emptying velocity in predicting improvement of left atrial function after percutaneous balloon mitral valvuloplasty

M.R.Abdelfattah, H.M.kabil, M.O.Hussein and M.S.Abdalnaby
Cardiology, Dept., Faculty of Medicine, Benha Univ., Benha, Egypt
E-mail: Dr_mahmoud.2008@hotmail.com

Abstract

LA/LAA dysfunction is a serious concern in patients with severe mitral stenosis, which may lead to blood stasis and thromboembolic consequences, as well as heart failure.

In this research, we aimed to examine the impact of PBMV on LA/LAA function, specifically focusing on mitral annulus Sa velocity, SEC grade and LAA TDI parameters, in order to identify the determinants of improved LA/LAA function. Methods: Preliminary research was undertaken between June 2020 and April 2022 at a Tertiary Care Hospital in the United States. At the National Heart Institute's Cardiology Department, a total of 50 patients with symptomatic, isolated, severe mitral stenosis underwent PBMV surgery. Dyspnea was a common symptom in more than half of our patients, most of whom were in their 30s and 40s (NYHA class II). An improved LA/LAA SEC grade, decreased mitral valve diastolic pressure gradient and decreased diastolic left atrial diameter were all seen following PBMV. After PBMV, mitral annular Sa velocity, LAAEV, and LAAFV were all significantly improved. " We also found that improvement in LA/LAA function after PBMV was significantly predicted by mitral annular Sa velocity. The SEC grade of the LA/LAA was shown to be a major predictor of improvement in LA/LAA function following PBMV. Our findings showed that the mital annular Sa velocity cutoff value was 5.5 cm/s was the ideal speed for predicting an inactive LAA.

The cutoff value for LAAEV in our investigation was 25 cm/sec for the prediction of inactive LA/LAA. Conclusion: Pre-PBMV inactivity was predicted by lower Sa-wave velocity; after PBMV inactivity was predicted by higher Sa-wave velocity, higher LAAEV, lower SEC grade, lower left atrial diameter, larger MVA and lower PASP. Specifically, lower left atrial diameter, larger MVA and lower PASP were associated with improved LA function after PBMV.

Key words: Spontaneous left atrial echo contrast - mitral annular systolic velocity - left atrial appendage late emptying velocity - improvement - left atrial function - percutaneous balloon mitral valvuloplasty.

1.Introduction

Cardiovascular mortality and morbidity in underdeveloped nations are exacerbated by rheumatic fever and its long-term consequences, Rheumatic heart disease (RHD).

In Western nations, despite a dramatic decline in its frequency, it remains a substantial concern and still accounts for 12% of native valvular heart disease [1].

Thromboembolic events have a crucial role in mitral stenosis patients' health and death (MS).

Stasis of blood, decreased LA and LAA ejection fraction, and atrial fibrillation are all symptoms of chronic pressure and volume overload imposed by multiple sclerosis (MS) (AF).

Because of this, MS patients are more likely to have thromboembolic events as a consequence of the development of LA and LAA thrombi [2].

The purpose of this research was to examine the influence of PBMV on the function of the LA/LAA, with particular focus on mitral annulus Sa velocity, SEC grade, and LAA TDI parameters.

2.Patients and Methods

This was a prospective single center study from a Tertiary care hospital conducted between june 2020 and april 2022. A total of 50 consecutive patients with symptomatic isolated severe mitral stenosis who underwent PBMV were recruited from the Cardiology Department of National heart institute .

Inclusion criteria:

- patients with severe (MVA<1cm 2) mitral stenosis of all age groups who are eligible for PMVB (3).
- Normal Sinus Rhythm
- willing to participate in the study with written informed conscent

Exclusion criteria:

- Patients with coronary artery disease
- Mitral regurgitation greater than 2/4
- severe aortic valve disease
- patients with Atial fibrillation ,
- pregnant patients are excluded
- patients who had hypertension, diabetes mellitus and congenital
  heart disease were excluded
- patients with left ventricular systolic dysfunction
- patients using antiplatelet or anticoagulant drugs
- patients unwilling to participate

Methods :

Every patient in this study was subjected to :

A-Full medical history

B- Full clinical examination:

C) 12 lead surface ECG

D) laboratory work up:

Routine laboratory work up including(CBC , coagulation profile , creatinine , liver profile) were done to all patients .

D) Transthoracic Echocardiography :
All study subjects were assessed before and 14 days after PBMV.
E) Tissue Doppler imaging :
TDI was performed to all patients befor PBMV and 14 days later.
F) Transesophageal echocardiography
G) percutaneous balloon mitral valvuloplasty
H) Standard TTE, TDI , and TEE examinations were repeated 14 days after PBMV.

Stattical analysis:

When it came to quantitative data, we used mean, SD, and range; when it came to qualitative data, we used frequency (number; No.) and percentage (percent).

The Shapiro-Wilk W test for normality was used to determine if the numerical data was distributed normally.

Prior to and after PBMV, cardiac parameters were compared using the paired t-test and the Wilcoxon signed rank test for both parametric and nonparametric data, respectively.

Different cardiac parameters were correlated using the relevant Pearson and Spearman correlation coefficients (rho and rho).

Logistic regression analysis were used to identify factors that might indicate whether or not a patient's lungs were inactive.

LAAEV and mitral annular Sa were subjected to Receiver Operator Characteristic (ROC) analysis in order to determine the best cutoff values for predicting LA inactivity, as well as the associated Area Under the Curve (AUC), Sensitivity, Specificity, Positive Predictive Value (PPV), and Negative Predictive Value (NPV).

A Windows version of STATA/SE 11.2 was used to perform all statistical analyses (STATA Corporation, College Station, Texas).

P 0.05 was judged statistically significant.

3. Results

There was significant reduction of left atrial diameter from 50.32±3.48 mm to 44.96±3.39 mm ($P < 0.001$) . There was increase in MVA (0.79 ± 0.14 cm^2

To 1.73±0.15 cm^2) ($P < 0.001$)

Mitral valve peak pressure gradient showed significant fall from 32.58±4.81mmhg

to 14.3±3.05 mmhg and mean pressure gradient from 19.12±3.84 mmhg

to 5.56±1.53 mmhg ($P < 0.001$)

the mean pulmonary artery systolic pressures was 57.98±8.31 mmhg before PMVP and was significantly decreased to 38.46±6.28 mmhg after PBMV ($P < 0.001$)

Table (1) TTE. Comparisons of cardiac parameters before and after PBMV.

	Mean ±SD Range		t	P
	Before PBMV	**After PBMV**		
LVEDD	46.08±4.92 35-55	45.82±4.69 35-54	0.86	0.39
LVESD	28.52±3.43 22-37	27.9±3.68 22-36	1.70	0.09
EF (%)	64.52±4.00 56-71	64.66±3.55 59-74	0.39	0.69
LA (mm)	50.32±3.48 44-60	44.96±3.39 39-52	21.27	**<0.001**
MVA (cm^2)	0.79±0.14 0.5-1.1	1.73±0.15 1.4-2.2	42.78	**<0.001**
MV MG (mm Hg)	19.12±3.84 12-30	5.56±1.53 3-10	26.65	**<0.001**
MV PG (mm Hg)	32.58±4.81 24-45	14.3±3.05 8-22	23.71	**<0.001**
PASP (mm Hg)	57.98±8.31 39-70	38.46±6.28 25-50	25.09	**<0.001**

t: Paired t-test; statistical significance at P<0.05

SEC was descresed from 2.06±0.81 to 0.2±0.40 ($p < 0.001$) and LAAEV was significantly increased from 22.7±4.09 to 43.12±6.19 cm/sec ($p < 0.001$), also LAA FV showed significant increase from 26.96±4.14 to 49.5±4.82 cm /sec ($p < 0.001$).

Table (2) Transthoracic echocardiographic variables.

	Mean ±SD Range Before PBMV	After PBMV	t	P
LAA SEC grade	2.06±0.81 0-3	0.2±0.40 0-1	Z=6.29	**<0.001**
LAA EV (cm/sec)	22.7±4.09 15-31	43.12±6.19 30-55	33.88	**<0.001**
LAA FV (cm/sec)	26.96±4.14 20-36	49.5±4.82 40-60	45.99	**<0.001**

t: Paired t-test; z: Wilcoxon signed-rank test; statistical significance at P<0.05

On TDI, mitral annular velocities showed significant improvement with PBMV as evidenced by significant increase in Sa from 5.61 ± 0.54 to 10.36 ± 0.74 cm/s, Ea from 5.64 ± 0.77 to 10.02 ± 1.20 cm/s, Aa from 4.50 ± 0.50 to 9.24±1.11 cm/s (P < 0.001) (Table 3)

Table (3) tissue Doppler imaging of mitral annular velocities Pre- and post- PBMV.

	Mean ±SD Range Before PBMV	After PBMV	t	P
Mitral annular Sa (cm/sec)	5.61±0.54 5-7	10.36±0.74 9-12	45.45	**<0.001**
Mitral annular Ea (cm/sec)	5.64±0.77 4.5-8.5	10.02±1.20 7-13	25.54	**<0.001**
Mitral annular Aa (cm/sec)	4.50±0.50 3.5-5.5	9.24±1.11 7-12	36.09	**<0.001**

t: Paired t-test; statistical significance at P<0.05

A-Univariate Regression Analysis

Univariate regression analysis showed that post –PMVB lower MV mean PG and lower LA/LAA SEC grade are associated with improvement of LA function (higher LAA EV) .

Also higher mitral annular Sa velocity , larger MV area and higher LAA FV are associated with improvemet of LA function

B-Multivariate regression analysis

Multivariate regression analysis showed that post -PBMV higher Sa-wave velocity, lower LAA SEC and lower LVEDD are associated with better LA function (improvement of LAAEV)

Table (4) Logistic Regression analysis predicting improvement of LA function after the PBMV (LAA EV as a dependent factor)

Predictors	**Univariate logistic regression**			**Multivariate logistic regression**		
(no.=50)	**OR**	**95% CI**	**P**	**OR**	**95% CI**	**P**
Age (years)	1.04	1.0-1.36	0.18			
Sex (Male vs female)	3.06	0.98-18.90	0.36			
Wilkins score	1.02	0.44-1.45	0.67			
LVED	0.95	0.30-1.10	0.06	0.71	0.56-0.91	**0.006**
LVESD	1.56	0.90-2.01	0.31			
EF (%)	1.20	0.87-1.90	0.23			
LA (mm)	0.87	0.90-1.65	0.18			
MVA (cm^2)	0.93	0.40- 2.95	**0.001**			
MV MG (mm Hg)	0.45	0.02-1.04	**0.02**			
MV PG (mm Hg)	0.13	0.30-1.24	0.12			
PASP (mm Hg)	1.0	0.94 -1.27	0.24			
LAA SEC grade	0.80	0.04-3.20	**0.001**	**0.87**	**0.24-2.20**	**0.002**
LAA FV (cm/sec)	2.40	1.12- 5.20	**0.004**			
Mitral annular Sa (cm/sec)	1.43	1.08-8.14	**0.001**	**3.60**	**1.90-12.51**	**0.01**
Mitral annular Ea (cm/sec)	1.01	0.49-1.16	0.48			
Mitral annular Aa (cm/sec)	1.76	0.80-4.90	0.43			

OR: Odd Ratio; 95% CI: 95% Confidence Interval; statistical significance at P<0.05

A-Univariate regression analysis

Univariate Regression Analysis Showed That Smaller La Diameter , Lower La/Laa Sec Grade , Larger Mva , Lower Mv Mean Pg And Higher Laa Ev Are Potential Predictors Of Improved La Function Post Pbmv (Higher Mitral Annulus Sa Velocity)

B-Multivariate regression analysis

multivariate regression analysis post PBMV showed that lower SEC grade, smaller LA diameter and higher LAAEV are associated with improvement of LA function

Table (5) Logistic Regression analysis predicting improvement of LA function after the PBMV (mitral valve annulus Sa velocity as a dependent factor)

Predictors	**Univariate logistic regression**			**Multivariate logistic regression**		
(no.=50)	**OR**	**95% CI**	**P**	**OR**	**95% CI**	**P**
Age (years)	1.28	1.10-2.55	0.14			
Sex(Male vs female)	4.50	1.01-22.0	0.86			
Wilkins score	0.98	0.23-1.80	0.21			
LVED	0.80	0.1-0.91	0.07			
LVESD	0.46	0.14- 1.94	0.20			
EF (%)	1.34	0.72-2.14	0.18			
LA (mm)	0.62	0.13-1.24	**0.002**	**0.49**	**0.22-1.60**	**0.002**
MVA (cm^2)	0.82	0.33- 2.01	**0.002**			
MV MG (mm Hg)	0.50	0.1-0.90	**0.01**			
MV PG (mm Hg)	0.26	0.18-1.47	0.32			
PASP (mm Hg)	0.90	0.82 -1.70	0.15			
LAA SEC grade	0.98	0.02-2.09	**0.006**	**0.90**	**0.71-2.67**	**0.01**
LAA FV (cm/sec)	2.33	1.20- 7.40	0.19			
LAA EV(cm/sec)	1.92	1.02-10.23	**0.001**	**1.79**	**1.60-5.44**	**0.002**
Mitral annular Ea (cm/sec)	1.14	0.56-1.34	0.47			
Mitral annular Aa (cm/sec)	1.40	1.0-4.50	0.28			

OR: Odd Ratio; 95% CI: 95% Confidence Interval; statistical significance at P<0.05

In ROC analysis of the tissue Doppler echocardiographic parameters, Sa-wave velocity showed largest area under the curve (AUC 0.6783 , CI 0.5107-0.8458 , P < 0.02) for prediction for inactive LAA. Optimal cut off value of Sa wave for prediction of inactive LAA was ≤5.5 cm/s with sensitivity of 72.73 %, specificity of 92.59 %, positive predictive value of 82.76 %, and negative predictive value of 83.14 % (table 6)

In ROC analysis , LAAEV showed largest area under the curve (AUC 0.6747 , CI 0.5227-0.8266 , P < 0.02) for prediction for inactive LAA. Optimal cut off value of LAAEV for prediction of inactive LAA (moderate to dense , SEC > II) was ≤ 25 cm/s with sensitivity of 78.79 %, specificity of 90.10 %, positive predictive value of 85.47 %, and negative predictive value of 79.25 % (table 6)

Table (6) ROC analyses of LAA SEC grade and Mitral annular Sa as predictors for inactive LA / LAA before PBMV.

Predictors	**Cut off**	**AUC**	**95% CI**	**Sensitivity (%)**	**Specificity (%)**	**PPV**	**NPV**	**Correctly classified**
LAA EV	25	0.6747	0.5227-0.8266	78.79	90.10	85.47	79.25	70.00
Mitral annular Sa (cm/sec)	5.5	0.6783	0.5107-0.8458	72.73	92.59	82.76	83.14	72.00
P				0.02(NS)				

AUC: Area Under the Curve; 95% CI: 95% Confidence Interval; PPV: Positive Predictive Value; NPV: Negative Predictive Value; statistical significance at P<0.05.

4. Discussion

After successful balloon mitral valvuloplasty (PBMV), our study found no significant changes in the left ventricle's internal dimensions (LVEDD and LVESD) or global function (EF) compared to Mahfouz et al., who studied the usefulness of non-Invasive right ventricular function assessment in predicting adverse events [4].

According to Güntürk et al., who studied the effects of successful percutaneous mitral balloon valvuloplasty (PMBV) on patients with moderate–severe mitral stenosis (MS) who had normal left ventricular systolic function, strain and strain rate echocardiography could not conclude significant changes in LVEDD and LVESD after PB in their study using conventional 2D transthoracic echocardiography and M mode.

After PBMV, a Doppler study indicated a considerable improvement in the overall function of the left ventricle [5].

Using cardiac MRI, Samaan and his colleagues showed substantial changes in left ventricle dimensions and global function at 6 and 12 month follow up following PBMV, contrasting to our findings, which were based on a different evaluation modality and a different follow up time [6].

When we looked at 30 patients with severe mitral stenosis to see what the immediate impact of successful percutaneous balloon mitral valvuloplasty on right and left ventricular functions was, we found that 70% of patients had a significant reduction in LA diameter after PBMV, which is consistent with what sowdagar and his co-workers found when they studied the same patients [7].

A study published by Ganeswara et al. found that PBMV had no immediate effect on LA diameter, which could be due to the inclusion of patients with atrial fibrillation in their study (they included AF patients), as well as the fact that their follow-up assessment was done on the third day after the procedure.

Our study found a significant reduction in mitral valve mean and peak pressure gradients and an increase in mitral valve area following PBMV, which is consistent with the findings of Sun and his coworkers who studied the short- and mid-term outcomes of percutaneous balloon mitral valvuloplasty under the guidance of ultrasound in a similar study [9].

Additionally, a study by Zhang and colleagues found that repeat percutaneous balloon mitral valvuloplasty had a long-term curative effect in patients with mitral restenosis, and that both the mitral valve gradient (MVG) and the mitral valve orifice area (MVA) improved significantly (1.05 0.19 cm for MVA vs. 2.23 0.22 cm for MVA, 17.03 4.52 mmHg for MVG and 7.79 4.07mmHg for M [10].

Our study observed a substantial decrease in PASP 48 hours and 15 days after PBMV, which is consistent with the findings of sakkuru and his colleagues who evaluated the immediate impact of PBMV on the right ventricular and pulmonary function on 52 patients with severe MS [11]

In agreement with Arava et al., who evaluated 100 patients with symptomatic MS with sinus rhythm who had undergone PBMV, our results demonstrated a substantial decrease in LA/LAA SEC and a large rise in LAAFV and LAAEV following PBMV [12].

Karakaya and his colleagues, on the other hand, reported no difference in LAAFV following PBMV in their study Effect of percutaneous mitral balloon valvuloplasty on left atrial appendage function [13].

A considerable improvement in the systolic and diastolic velocities of the mitral annulus following PBMV was seen in our research and is similar to that found by arava and colleagues in their analysis of mitral annulus tissue Doppler parameters in 100 MS patients who received the procedure [12].

This finding was also in line with that of Cayl and his colleagues, who used transthoracic and transesophageal echocardiography to examine the link between annular velocities and LAA function in 85 MS patients and 80 healthy controls [14].

In our study, we discovered a considerable rise in SEC, which is in agreement with karakaya et al., 2006, who studied the effect of percutaneous mitral balloon valvuloplasty on the left atrial appendage function in 20 severe MS patients [13].

The researchers that explored the relationship between NT-ProBNP and left atrial dysfunction in rheumatic mitral stenosis and how it correlates with left atrial function after PBMV discovered a substantial rise in LA SEC in conjunction with a decrease in LAA EV, as did Khare and coworkers [15].

However, in a study of 200 patients with severe rheumatic mitral stenosis, Goswami and his colleagues reported no significant influence of the mitral pressure gradient on LA SEC [16].

In a study comparing 20 consecutive MS patients to a control group of 20, Laufer –perl et al. found the same outcomes when examining the mechanisms of effort intolerance in patients with rheumatic mitral stenosis. They combined stress echocardiography and cardiopulmonary testing to evaluate cardiac function, hemodynamics, and oxygen extraction (A-Vo2 difference) [17].

These findings are in line with those of Li and his colleagues, who examined 39 patients with rheumatic mitral valve disease in sinus rhythm to compare echocardiographic and hemodynamic parameters between those with and those without spontaneous left atrial (LA) echo contrast [18].

Cianciulli and his co-workers, who performed a complete investigation of RAA and LAA contractile performance in patients with mitral stenosis and sinus rhythm in their research, found that these results were similar to their findings.

Group 1 (23 patients with severe MS, 38 +/- 11 years, 20 women), Group 2 (23 patients with moderate MS, 39 +/- 12 years, 19 women), and Group 3 (23 healthy individuals, 42 +/- 14 years, 16 women) comprised the total of 69 patients studied.

All patients had a multiplane transesophageal echocardiogram. Linear regression analysis demonstrated a link between the deterioration of systolic function of both appendages, pulmonary arterial pressure, valve area, and transmitral gradient [19].

After a six-month follow-up, Vijayvergiya and his coworkers discovered no significant influence of MVA and MV pressure gradient on the function of the LA/LAA, but these results were attributed to the ongoing structural remodelling of the LA/LAA after PBMV [20].

This study found that LA diameter is an independent predictor of LA/LAA function improvement after PBMV, which is consistent with xing and his coworkers who followed 96 MS patients who underwent PBMV for six years and found that LA diameter reduced from (44.6 +/- 6.6)cm before PBMV to (42.8 +/- 6.5)cm one week after PBMV and enlarged to (47.2 +/- 5.7)cm (all P 0.05) after PBMV

Preoperative left atrial diameter was shown to be an independent predictor of left atrial remodelling following PBMV over a four- to six-year follow-up period [21].

It was also consistent with the findings of Samrat and his colleagues who conducted a prospective study to evaluate the impact of successful percutaneous balloon mitral valvuloplasty on left atrial reservoir function and LA volume in patients with severe mitral stenosis using peak atrial longitudinal strain. They found that both LA volume and indexed LA volume reduced significantly immediately at 24 hours, as well as during follow-up, after the procedure and on regression [22].

LAAEV was a strong predictor of improvement in LA/LAA function after PBMV in the present study that was comparable to Ansari and his co-workers who aimed to evaluate the effect of PBMV on LAA function by trans-esophageal echocardiography (TEE) doppler and doppler tissue imaging, this study included 70 patients with severe MS and all the patients underwent clinical examination, ECG, detailed TTE and TEE before, immediately after and after [23].

A major independent predictor of improvement in LA/LAA function following PBMV was the mitral annular Sa velocity, which was congruent with kurakula and colleagues, who conducted TEE, D-dimer study, and transthoracic echocardiography in 104 severe MS patients and separated them into three groups:

No LA thrombus or SEC; LA SEC solely; and no thrombus or SEC in Group III.

Sa was shown to be a substantial independent predictor of LA thrombus in a multivariate analysis of their data [24].

LVEDD rose significantly after PBMV in our research and proved to be a major predictor of improvement in LA/LAA function after PBMV. This reflects greater left ventricular fullness and contractility and is mostly explained by mechanical relive of the right ventricle.Sowdagar and his colleagues evaluated 30 patients with severe MS to assess the immediate effect of a successful percutaneous balloon mitral valvuloplasty on right and left ventricular functioning. They came to the same conclusion [7].

As a result, Sengupta's research found no difference in longitudinal left ventricular dynamics after mitral commissure perforation, which may be attributable to the differing inclusion criteria used in Sengupta's study [25].

A strong correlation was found between LA/LAA SEC grade and improvement in LA/LAA function after PBMV, which was consistent with Wang and his co-workers' study on the relationship between SEC and left atrial appendage blood flow velocity using transesophageal echocardiography during percutaneous balloon mitral valvotomy (PBMV) in patients with atrial fibrillation and sinus rhythm.

A total of 35 patients with rheumatic mitral stenosis underwent PBMV with intraoperative transesophageal echocardiography monitoring for the purposes of measuring LAA blood flow velocities and checking the left atrium for various grades of SEC (from 0 = none to 4 = severe), before and after each balloon inflation. They discovered that a higher SEC grade was associated with worse LA/LAA function [26].

It was also found by Aslanabadi et al., who recruited 56 patients with severe mitral stenosis who had mitral valvuloplasty, as well as transesophageal echocardiography before and at least one month following PTMC [27].

In our results cut off value of mital annular Sa velocity was Optimal for prediction of inactive LAA was ≤ 5.5 cm/s that was consistent with Arava et al [12], but considered lower than cayli et al., who studied 105 patients with severe MS to investigate if the annular velocities obtained with tissue Doppler imaging can predict the presence of SEC in MS patients with Sinus Rhythm .

They uncovered aDue to various sample sizes and Cayli et al. not investigating Sa velocity after PBMV, the cutoff values for annular systolic velocity for prediction of the existence of any and dense SEC were 13.5 and 11.8 cm/s, respectively [28].

Using the LAAEV as a marker for inactive LAA, our study found that a value of 25 cm/sec was the cut-off point for inactive LAA, which is consistent with Mukhopadhyay et al. [29], who studied 100 patients with severe rheumatic mitral stenosis to determine the prevalence of inactive LAA, but this value is higher than Gawako et al. who defined the cut-off value of LAAEV to be 20 cm/sec, which could be a factor in predicting inactive LAA. Nonetheless, this difference could be an indicator of a different pathology [30]

5. Conclusion

Reduced Sa-wave velocity, decreased LAAEV, increased NYHA class, and increased mitral valve diastolic pressure gradients are all independent predictors of a non-functioning LA/LAA prior to PBMV, while factors favouring improvement in LA function after PBMV included increased Sa-wave velocity, decreased LAAEV and SEC grade, and decreased left atrial diameter, increased MVA, and decreased PASP.

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