Published in final edited form as:

Am J Cardiol. 2010 July 15; 106(2): 243–248. doi:10.1016/j.amjcard.2010.02.035.

Evaluation of Papillary Muscle Function Using Cardiovascular Magnetic Resonance Imaging in Mitral Valve Prolapse

Yuchi Han, MD^a, Dana C. Peters, PhD^a, Kraig V. Kissinger, RT(R)(MR)^a, Beth Goddu, RT(R)(MR)^a, Susan B. Yeon, MD, JD^a, Warren J. Manning, MD^{a,b}, and Reza Nezafat, PhD^a

^aDepartment of Medicine (Cardiovascular Division)

^bDepartment of Radiology, Beth Israel Deaconess Medical Center, Harvard Medical School, Boston, MA 02215

Abstract

Abnormal traction and excursion of the papillary muscle (PM) can be observed in patients with mitral valve prolapse (MVP), which may adversely affect the electrophysiological stability of the underlying myocardium. Cardiovascular magnetic resonance (CMR) techniques can directly measure the excursion and velocity of PM tips during ventricular systole. In addition, high resolution late gadolinium enhancement (LGE)-CMR allows for visualization of underlying potentially arrhythmogenic PM fibrosis substrate. We prospectively studied 16 MVP and 9 healthy adult subjects with PC-CMR and cine-CMR to assess PM velocity and excursion. LGE-CMR was performed in 13 (81%) MVP subjects. Peak PM systolic velocity and maximum PM excursion were significantly increased in MVP subjects (12 ± 5 cm/s vs. 5 ± 2 cm/s and 15 ± 5 mm vs. 2 ± 3 mm, both $p < 0.001$). Definite PM LGE was found in 6 (46%) patients, but did not correlate with PM velocity or excursion. In conclusion, functional CMR imaging demonstrated increased peak PM systolic velocity and excursion distance in MVP patients. These parameters, however, did not relate to underlying PM fibrosis.

Keywords

cardiovascular magnetic resonance imaging; papillary muscle; mitral valve prolapse; late gadolinium enhancement

Phase contrast (PC) velocity imaging is a cardiovascular magnetic resonance (CMR) technique commonly used to measure blood flow within the cardiovascular system¹. In addition to blood flow, PC-CMR has been used to measure myocardial motion through cardiac cycle with high temporal and spatial resolution^{2–6}. Unlike tissue Doppler imaging in echocardiography, there is no angle dependence with PC-CMR methods. We sought to use 3-directional 2-dimensional PC-CMR in addition to cine-CMR to assess the motion of the papillary muscle (PM) in otherwise healthy mitral valve prolapse (MVP) subjects as well as a group of healthy controls. In addition, we sought to examine the relationship of PM motion and PM fibrosis.

© 2010 Excerpta Medica, Inc. All rights reserved

Corresponding author: Yuchi Han, MD Cardiovascular Division, E/SH-457 Beth Israel Deaconess Medical Center 330 Brookline Ave Boston, MA 02215 Phone: 617-667-4430 yhan@bidmc.harvard.edu FAX: 617- 667- 4833.

Publisher's Disclaimer: This is a PDF file of an unedited manuscript that has been accepted for publication. As a service to our customers we are providing this early version of the manuscript. The manuscript will undergo copyediting, typesetting, and review of the resulting proof before it is published in its final citable form. Please note that during the production process errors may be discovered which could affect the content, and all legal disclaimers that apply to the journal pertain.

METHODS

Nineteen adult MVP subjects with no history of coronary artery disease and 12 healthy (no history of hypertension, diabetes, coronary artery disease, and not on any cardiac medications) age and gender matched subjects were studied. Three subjects from each group was excluded from analysis due to poor CMR image quality (either the PM was not adequately visible or there were severe motion artifacts). Our final cohort consisted of 16 MVP subjects (50 ± 14 years, 10 males) and 9 healthy subjects (47 ± 13 years, 6 males). 13 of the 16 (81%) MVP subjects had LGE-CMR imaging (one declined contrast injection, two were not injected due to minimally elevated creatinine). Four healthy control subjects returned 6 months later for a second study to evaluate test-retest variability with the same imaging protocol. The study was approved by our institutional review board and written consent was obtained in all MVP and control subjects.

CMR imaging was performed on a 1.5 T Philips Achieva MR scanner (Philips HealthCare, Best, NL), using either a 5-channel phased-array coil or a 32-channel cardiac array coil (In Vivo Corporation, Gainesville, FL) for which an electronic signal combiner was used to form a 16-channel signal (8 anterior and 8 posterior) from the 32-channel coil array. Left ventricular (LV) function and aortic flow were evaluated in each subject by acquiring breath-hold cine short axis steady state free precession slices covering the entire LV and a free-breathing PC velocity map in the ascending aorta as previously described^{7,8}.

A single 2-dimensional slice was chosen from the stack of breath-hold cine steady state free precession images of the LV outflow tract as previously described⁹, which captures the inferomedial PM during the entire systole (Figure 1). A stack of three free-breathing cine steady state free precession images was acquired at this slice level to determine the visibility of the PM during free breathing. Subsequently, a free-breathing 2-dimensional PC-CMR sequence with sensitivity to motion in all three directions was acquired. The imaging parameters were as follows: repetition time/echo time/flip angle = 6.8 ms/4.5 ms/15°, field-of-view = 330×309 mm², slice thickness of 8 mm, voxel size of 1.8×1.8×8 mm³, temporal resolution of 27–44 ms, maximum velocity encoding of 30 cm/s with three signal averages. Typical image acquisition time was 5–8 minutes.

LGE images were acquired using a high resolution 3-dimensional ECG-gated free breathing, respiratory navigator-gated inversion recovery-spoiled gradient echo sequence in the short axis orientation 20 minutes after intravenous administration of 0.2 mmol/kg gadolinium-diethylenetriamine penta-acetic acid (Magnevist, Berlex/Schering AG, Berlin, Germany) as previously described¹⁰. Imaging parameters: repetition time/echo time/flip angle = 5.6 ms/2.7 ms/25°, field-of-view = 320×320 mm², 23 to 32 partition-encoded lines, spatial resolution 1.3 × 1.3 × 5 mm³, reconstructed to 0.6 × 0.6 × 2.5 mm³. Due to the non-isotropic resolution of the images, the same sequence was acquired along the 4-chamber orientation immediately after the short-axis LGE acquisition to confirm its findings. Typical image acquisition time was 6 – 10 minutes for both sequences.

Volumetric and aortic flow data was analyzed on a ViewForum (Philips Health Care, Best, Netherlands. Release 4.0) workstation using the modified Simpson's method. End diastole/onset of systole was determined by the first phase of the cine-CMR image after ECG trigger. The end of systole was determined by aortic valve closure as demonstrated on the LV outflow view or the cessation of forward blood flow in aortic flow curves, whichever was earlier. Prolapsed distance was measured as the maximum prolapsed distance during peak systole beyond the mitral annulus as previously described⁹. Mitral regurgitation (MR) volume was determined by LV stroke volume subtracted by aortic flow volume. MR fraction was calculated as MR volume divided by LV stroke volume. Based on MR fraction,

five categories of MR were determined: none (<5%), mild (5–16%), moderate (16–25%), moderate to severe (25–48%), and severe (>48%)⁸.

PM PC-CMR were analyzed using MATLAB (The MathWorks, Natick, MA). A region of interest on the tip of PM was drawn on the magnitude image (Figure 2A) for each cardiac phase and its location was copied into all three velocity maps for each cardiac phase (Figure 2 B–D). Three directions of motion were measured in inferomedial PM with predominant motion in up-down orientation in the imaging slice orientation. Only systolic motion was analyzed because the stretch on the PM occurs during systole and blood flow contamination was prominent during diastole.

PM tip to mitral annular distance was measured at the beginning of systole and then again at peak systole with maximum prolapse (Figure 3) as previously described in transthoracic echocardiography¹¹. The difference was the PM excursion distance. The LV length (from the tip of the apex to the mitral annulus) in the LV outflow view was also measured.

The presence or absence of LGE was assessed by two independent experienced reviewers blinded to patient information and rated as no PM fibrosis (score 1), possible PM fibrosis (score 2) (if chordal enhancement at the insertion point into the PM and unclear if it was entirely chordal or with PM involvement), and definite PM fibrosis (score 3). After independent reviews, the two raters also performed a consensus review together.

Data are presented as mean $\pm$ SD. Data were analyzed using the two-tailed Student's t-test to compare continuous variables and the Wilcoxon rank sum test to compare categorical variables. A p-value of <0.05 was considered significant. Univariate analysis was performed on the volumetric variables with PM velocity and PM excursion as the outcome variables. All statistical analyses were performed with STATA Version 10 (STATcorp, TX, USA).

RESULTS

By design, MVP subjects and healthy control subjects had similar age, gender proportions, and body surface area (Table 1). MVP subjects had higher LV volumes but similar LVEF. The indexed LV mass was significantly higher in MVP subjects as were the MR volume and fraction.

MVP subjects demonstrated a different velocity profile through systole with peak velocity occurring in mid to late systole while the control subjects had low velocity throughout systole (Figure 4A). In MVP subjects, there was an increased mid to late systolic peak velocity of the PM tip (12 ± 5 cm/s vs. 5 ± 2 cm/s, $p < 0.001$) (Figure 4B). The test-retest reliability was assessed in four control subjects with repeat PC-CMR imaging using the same protocol 6 months later. It showed excellent reliability with a first test mean of 5.7 ± 1.7 cm/s and a second test mean of 5.7 ± 2.3 cm/s ($p = 0.96$).

Univariate linear regression analysis showed that PM velocity was correlated with MVP status ($p = 0.002$), male gender ($p = 0.01$), aortic flow volume ($p = 0.048$), posterior leaflet prolapsed distance ($p = 0.002$), anterior leaflet prolapsed distance ($p = 0.004$), MR volume ($p = 0.047$), MR fraction ($p = 0.014$), MR category ($p = 0.025$), and PM excursion ($p = 0.004$).

MVP patients had increased PM excursion compared to controls (15 ± 5 mm vs. 2 ± 3 mm, $p < 0.001$). The duration of systole between the MVP and control subjects was similar (316 ± 35 ms vs. 344 ± 36 ms, $p = 0.27$). There was no significant difference in LV length or PM to mitral annular distance at peak systole, but the PM to mitral annular distance was significantly higher at the onset of systole compared to controls (41 ± 7 mm vs. 31 ± 7 mm,

$p = 0.002$) (Figure 5). The PM excursion distance was significantly correlated with MVP status ($p < 0.001$), indexed LV end diastolic volume ($p = 0.039$), posterior leaflet prolapsed distance ($p < 0.001$), anterior leaflet prolapsed distance ($p < 0.001$), MR volume ($p = 0.011$), MR fraction ($p = 0.001$), MR category ($p < 0.001$), and PM velocity ($p = 0.004$) on univariate linear regression.

By consensus review, PM LGE was absent in 2/13 (15%) patients, possibly present in 5/13 (38%) patients, and definitely present in 6/13 (46%) patients. All patients showed chordal enhancement. The kappa statistic of the two raters was limited with $\kappa = 0.125$ and a confidence interval of $[0, 0.565]$. None of the single rater scores, combined LGE scores from both raters, or consensus scores showed significant correlation to PM velocity or PM excursion. A possible positive and a definite positive (agreed by both raters) PM-LGE images (both short axis and long axis images are shown in Figure 6).

DISCUSSION

In this study of MVP subjects, we demonstrated that PC-CMR could be used to directly quantify motion of the PM in 3 directions. MVP subjects were found to have increased peak PM tip velocity during mid to late ventricular systole as compared to normal subjects as well as increased distance between the tip of the PM and mitral annulus at the onset of systole.

PM tip to mitral annulus excursion distance was initially performed in transthoracic echocardiography and our findings are consistent with echocardiographic findings of 9 ± 3 mm (MVP) vs. 1 ± 1 mm (control)¹¹. With a longer distance to travel in a similar systolic duration, it is not surprising the PM moves at a higher velocity during mid to late systole when prolapse occurs.

In addition to the abnormal leaflet, our data also suggest that the chordae tendineae may be an important player in the pathophysiology of MVP. The primary chordae tendineae are lengthened in MVP patients as evidenced by the increased PM to mitral annular distance at the beginning of systole without significantly increased LV lengths. The chordae tendineae are also thickened as evidenced by universal enhancement on LGE images. The interpretation of PM tip LGE was complicated by chordal insertion enhancement. It was not clear how much of the late enhancement was chordal versus the involvement of the PM beyond the chords. In a few cases, it was clear that the PM was involved in addition to the chords when the enhanced area was extensive and LGE had replaced visualized PM on steady state free precession short axis images. Among the 13 patients that we studied, the two raters identified 6 such patients by consensus. The lack of correlation of LGE to PM velocity and excursion could be due to image resolution or imaging different patients at different points of their disease process in a cross-sectional study. For some patients, the increased PM velocity might be the onset of LGE development; while for others, the development of LGE may lead to an eventual decrease in PM velocity. Better image resolution and longitudinal follow up would be required to further delineate the relationship between LGE and PM velocity and excursion.

Our study is limited by optimal PC-CMR image acquisition. Almost 20% (6 out of 31) studies could not be evaluated due to poor image quality. The PM moves at a relatively low velocity with a range of 3 cm/s to 22 cm/s in our cohort of 25 subjects. Three-dimensional acquisition was attempted but abandoned due to poor image quality and lengthy acquisition duration. Breath-hold image acquisition was not possible due to inconsistent breath-hold positions and non-simultaneous data acquisitions.

Acknowledgments

Grant support: The project was supported in part by Grant Number UL1 RR025758- Harvard Clinical and Translational Science Center, from the National Center for Research Resources. The content is solely the responsibility of the authors and does not necessarily represent the official views of the National Center for Research Resources or the National Institutes of Health. Dr. Han was supported by American College of Cardiology Foundation/GE Health Care Career Development Award in Cardiovascular Imaging and the Clinical Investigator Training Program: Beth Israel Deaconess Medical Center - Harvard/MIT Health Sciences and Technology, in collaboration with Pfizer Inc. and Merck & Co. Dr. Peters was supported by American Heart Association SDG 0530061N and National Institutes of Health NIBIB K01 EB004434-01A1. Dr. Nezafat was supported by NIH R01-EB008743-01A2.

References

1. Pelc NJ, Herfkens RJ, Shimakawa A, Enzmann DR. Phase contrast cine magnetic resonance imaging. *Magn Reson Q*. 1991; 7:229–254. [PubMed: 1790111]
2. Arai AE, Gaither CC 3rd, Epstein FH, Balaban RS, Wolff SD. Myocardial velocity gradient imaging by phase contrast MRI with application to regional function in myocardial ischemia. *Magn Reson Med*. 1999; 42:98–109. [PubMed: 10398955]
3. Pelc LR, Sayre J, Yun K, Castro LJ, Herfkens RJ, Miller DC, Pelc NJ. Evaluation of myocardial motion tracking with cine-phase contrast magnetic resonance imaging. *Invest Radiol*. 1994; 29:1038–1042. [PubMed: 7721545]
4. Pelc NJ, Drangova M, Pelc LR, Zhu Y, Noll DC, Bowman BS, Herfkens RJ. Tracking of cyclic motion with phase-contrast cine MR velocity data. *J Magn Reson Imaging*. 1995; 5:339–345. [PubMed: 7633112]
5. Jung B, Foll D, Bottler P, Petersen S, Hennig J, Markl M. Detailed analysis of myocardial motion in volunteers and patients using high-temporal-resolution MR tissue phase mapping. *J Magn Reson Imaging*. 2006; 24:1033–1039. [PubMed: 16947325]
6. Foll D, Jung B, Staehle F, Schilli E, Bode C, Hennig J, Markl M. Visualization of multidirectional regional left ventricular dynamics by high-temporal-resolution tissue phase mapping. *J Magn Reson Imaging*. 2009; 29:1043–1052. [PubMed: 19388130]
7. Salton CJ, Chuang ML, O'Donnell CJ, Kupka MJ, Larson MG, Kissinger KV, Edelman RR, Levy D, Manning WJ. Gender differences and normal left ventricular anatomy in an adult population free of hypertension. A cardiovascular magnetic resonance study of the Framingham Heart Study Offspring cohort. *J Am Coll Cardiol*. 2002; 39:1055–1060. [PubMed: 11897450]
8. Gelfand EV, Hughes S, Hauser TH, Yeon SB, Goepfert L, Kissinger KV, Rofsky NM, Manning WJ. Severity of mitral and aortic regurgitation as assessed by cardiovascular magnetic resonance: optimizing correlation with Doppler echocardiography. *J Cardiovasc Magn Reson*. 2006; 8:503–507. [PubMed: 16755839]
9. Han Y, Peters DC, Salton CJ, Bzymek D, Nezafat R, Goddu B, Kissinger KV, Zimetbaum PJ, Manning WJ, Yeon SB. Cardiovascular magnetic resonance characterization of mitral valve prolapse. *JACC Cardiovasc Imaging*. 2008; 1:294–303. [PubMed: 19356441]
10. Peters DC, Wylie JV, Hauser TH, Kissinger KV, Botnar RM, Essebag V, Josephson ME, Manning WJ. Detection of pulmonary vein and left atrial scar after catheter ablation with three-dimensional navigator-gated delayed enhancement MR imaging: initial experience. *Radiology*. 2007; 243:690–695. [PubMed: 17517928]
11. Sanfilippo AJ, Harrigan P, Popovic AD, Weyman AE, Levine RA. Papillary muscle traction in mitral valve prolapse: quantitation by two-dimensional echocardiography. *J Am Coll Cardiol*. 1992; 19:564–571. [PubMed: 1538011]

Figure 1. LV outflow track view of the papillary muscle. A. Beginning of systole. B. Peak systole. Papillary muscle is seen during the entire systole. Arrows point to PM (papillary muscle). Ao = aorta. LV = left ventricle.

Figure 2. Papillary muscle 3-directional phase contrast velocity imaging can provide velocity measurements in 3 directions. A region of interest is drawn at the tip of the papillary muscle (arrow) on the magnitude image (A) and copied on to all 3 velocity images for analysis (B, C, D). This is repeated for each cardiac phase in systole.

Figure 3.

Papillary muscle excursion. The distance between the tip of the papillary muscle and the mitral annular plane is measured at the beginning of systole (A) and at the peak systole (B). The difference is papillary muscle excursion.

Figure 4.

Papillary muscle tip peak systolic velocity in MVP subjects compared to healthy control subjects. A. The representative velocity curves are drawn in three directions (Right-Left, Up-Down, and Through-Plane) on the top panels. The magnitude of the PM velocity is plotted in the bottom panels. B. Significantly higher peak mid to late systolic PM velocity of MVP subjects compared to healthy subjects.

Figure 5.

Comparisons of LV length, papillary muscle to mitral annular distance at beginning of systole, peak systole, and the papillary muscle excursion distance. The PM to mitral annular distance at beginning of systole and the PM excursion distance are significantly increased in MVP subjects.

Figure 6. LGE images of papillary muscle possible enhancement (A and B) and definite enhancement (C and D) in both short axis (A and C) and 4-chamber long axis (B and D) views. Circles indicate the area of interest. In A and B, the enhancement is at the chordal insertion. In C and D, the enhancement extends beyond the chordal insertion.

Table 1

Subject characteristics.

Variable	MVP (n=16)	Control (n=9)	p-value
Age (years)	50 ± 14	47 ± 13	0.61
Gender (male, %)	10 (63%)	6 (66%)	0.84
Body surface area (m ²)	1.8 ± 0.2	1.8 ± 0.1	0.95
Left ventricular end diastolic volume (ml)	192 ± 53	138 ± 22	0.002
Left ventricular end diastolic volume index (ml/m ²)	103 ± 22	75 ± 7	<0.001
Left ventricular end systolic volume (ml)	78 ± 27	54 ± 9	0.003
Left ventricular stroke volume (ml)	114 ± 42	85 ± 15	0.02
Left ventricular ejection fraction (%)	64 ± 5	61 ± 3	0.14
Left ventricular mass (g)	116 ± 39	91 ± 24	0.05
Left ventricular mass index (g/m ²)	62 ± 17	49 ± 11	0.03
Left ventricular end diastolic volume (ml)	151 ± 35	147 ± 31	0.78
Aortic flow (ml)	77 ± 11	81 ± 14	0.516
Mitral regurgitation volume (ml)	45 ± 29	4 ± 6	< 0.001
Posterior leaflet prolapsed distance (mm)	6 ± 3	0	< 0.001
Anterior leaflet prolapsed distance (mm)	3 ± 3	0	0.005
Mitral regurgitation fraction (%)	34 ± 14	5 ± 6	< 0.001
Mitral regurgitation category (median) [interquartile range]	3 [2, 3]	0 [0, 1]	< 0.001