

Clinical research

Isolated chordal shortening: a novel mechanism of functional mitral regurgitation

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Abstract

Introduction: Mitral regurgitation (MR) that occurs in the absence of primary leaflet disease is known as functional MR. MR that occurs in the absence of primary leaflet disease is known as functional MR. Functional MR generally results from left ventricular (LV) enlargement, altered geometry of the papillary muscles, and/or dilatation of the mitral valve annulus. At our institution, we noted a group of patients with surgical MR, who did not have either primary leaflet disease or obvious alteration in LV geometry. We present a cohort of patients with MR secondary to isolated chordal shortening.

Material and methods: The study population consisted of subjects with normal mitral leaflet appearance, left ventricular size and function, and mitral annular dimension by echocardiography. Valve morphology and appearance were confirmed by inspection during surgery and by pathological examination when available. Mitral valve tethering parameters were compared to sample subjects with normal valves, and to sample subjects with severe ischaemic functional MR. Both control groups were matched to the study cohort both by age, sex, and body surface area.

Results: Ten subjects met the inclusion criteria. On surgical inspection, chordal shortening or restriction was reported in six and chordal thickening or fibrosis was mentioned in two subjects. Compared to normal controls, the study group had shorter chordae, increased mitral tenting height, and smaller mitral annular diameter. Compared to the control group with severe ischaemic MR, the study group had shorter chordae, smaller leaflet tenting height, smaller tenting area, and smaller mitral annular diameter.

Conclusions: We report 10 subjects who underwent mitral valve surgery for severe MR attributable to pathologically short chordae. To the best of our knowledge, this is the first description of this mechanism of disease. Further work is needed to define the underlying factors that cause isolated mitral chordal disease.

Key words: mitral valve surgery, functional mitral regurgitation, chordal shortening.

Introduction

Mitral regurgitation (MR) that occurs in the absence of primary leaflet disease is known as function mitral regurgitation (FMR). FMR most commonly results from the left ventricular remodelling that occurs following

myocardial infarction or from primary cardiomyopathy [1–3]. Left ventricular (LV) enlargement often results in displacement of the papillary muscles, which can increase the distance from the papillary muscles to the mitral leaflets. When this distance is increased, chordal tethering of the mitral leaflets is frequently seen. Tethering limits leaflet closure and leaflet coaptation, causing regurgitation.

At our institution, we noted a cohort of subjects with severe MR, who had normal-appearing mitral valve leaflets and preserved LV size and function. On echocardiography these patients often appeared to have mitral leaflets with chordal tethering and restricted systolic closure despite having normal LV size. We hypothesised that primary shortening of the mitral chordae tendineae may be the mechanism of leaflet tethering and consequent regurgitation in this group. This case series describes subjects with FMR potentially attributable to chordal shortening, as supported by echocardiographic, intraoperative, and microscopic findings.

Material and methods

Study group

Our institution's cardiovascular database was queried for all subjects who underwent mitral valve surgery for regurgitation between 2006 and 2012 ($n = 658$). For subjects in whom the aetiology of regurgitation was not well delineated in the echocardiography report, the images were reviewed by a senior echocardiographer (D.S.) to identify a potential mechanism. The study population consisted of subjects thought to have normal mitral leaflet appearance, normal left ventricular size and function, with a normal mitral annular dimension that subsequently had surgical repair or replacement. A comprehensive chart review was performed to record medical history, laboratory data, cardiac angiography, operative reports, and pathology reports. Subjects were excluded if operative valve inspection or gross pathological findings supported an obvious mechanism for valve regurgitation.

Control groups

Because echocardiographic measurements of mitral chordal length and leaflet tethering are not standardised, we selected two control groups to compare these measures with our study sample. The first control group consisted of normal echocardiograms. Ten subjects were selected from a sample of echocardiograms acquired in our laboratory over a 2-week period in December 2014. Studies were reviewed to for subjects with normal chambers sizes, normal ventricular function, and normal valve function. Subjects were includ-

ed if they matched by age, sex, and body surface area to one of the study subjects. Ten additional control subjects with severe ischaemic MR were also selected. These controls were chosen from the same group of 658 subjects who underwent mitral surgery during the study period. Subjects were included in the ischaemic MR control group if the mitral leaflet appearance was normal, inferolateral LV infarction was present, and mitral leaflet tethering was reported. This control group was also matched by age, sex, and BSA to the study group.

Echocardiography

All study subjects had undergone transthoracic echocardiography (TTE) and transoesophageal echocardiography (TEE) within 60 days prior to surgery. Leaflets were assessed in both 2D and 3D planes for structural abnormalities. TTE was used to assess MR severity, LV size, LV wall motion, and LV ejection fraction. MR severity was classified by the American Society of Echocardiography (ASE) guidelines [2, 3]. Effective regurgitant orifice (ERO) and MR volume was assessed by PISA and VC methods using colour Doppler. Measurements of LV dimensions were performed at end diastole and systole in the parasternal long-axis view. LA volume and LV ejection fraction were obtained by biplane Simpson's method.

Leaflet tethering parameters

Mitral leaflet tethering parameters were measured by two different readers to allow assessment of inter-rater variability. Annular diameter, tenting height, and tenting area were obtained from TTE imaging in the PLAX view and end systole (Figure 1 A). Tenting height was measured as the distance between the coaptation point of mitral leaflets and the annular plane of the MV at mid-systole. Tenting area was measured as the area enclosed between the leaflets and the annular plane. Chordal length was assessed using TEE images and was measured from the papillary muscle tip to the leaflet margin on the P2 segment in both the transgastric long axis and mid-oesophageal four-chamber views. Posterior and apical papillary muscle displacement was measured using a method described by Dudzinski *et al.* [4–9].

Statistical analysis

Statistical analysis was done using Stata software, version 11.1 (College Station, TX). Normally distributed data were presented as the mean \pm standard deviation (SD). Non-normal data were presented as the median (interquartile range (IR)). Comparison of means was performed using the two-sample *t*-test. Comparison of categorical

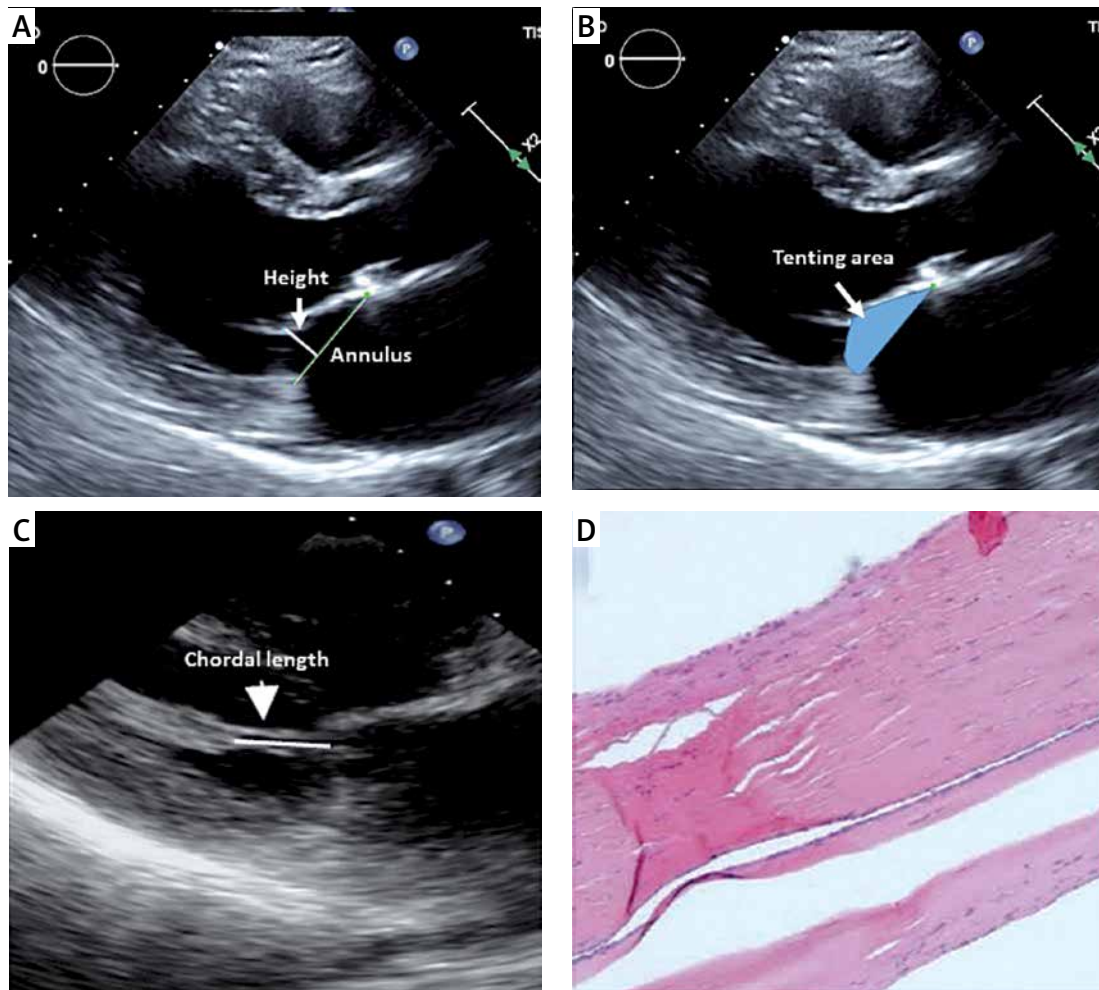


Figure 1. A, B – examples of mitral leaflet tethering parameters as measured on transthoracic echocardiography. C – an example of chordal measurement taken from transgastric view at 90°. D – haematoxylin and eosin staining of chordae tendineae removed at the time of mitral valve replacement. Pathological fibrosis is shown

data was performed using the chi-squared test. Comparison of medians was performed using the Mann-Whitney or Kruskal-Wallis tests as appropriate. *P*-values were considered significant if < 0.05 . Interobserver variability was compared using the mean and SD of the difference between the two readers' measurements. Paired *t*-test was used to compare measurements to check for measurement bias between readers.

Results

Patient demographics, echocardiographic, operative, and pathologic findings for the 10 included study subjects are presented in Tables I and II. Most of the cohort were female (9 of 10), with an average age of 63 years. None had history of rheumatic fever, endocarditis, malignancy, or other systemic inflammatory condition. Renal, hepatic, and thyroid function were normal in all study subjects. Electrolytes and troponin-T levels were also normal. Two subjects had single-vessel coronary disease, noted on perioperative angiography,

and underwent bypass during the MV surgery. Six subjects underwent MV replacement, while the remainder had MV repair.

On surgical inspection chordal shortening or restriction was reported in six and chordal thickening or fibrosis was mentioned in two subjects. For those who underwent valve replacement (6 of 10), the excised portions of the leaflets demonstrated generally normal gross appearance. Four valves showed either focal fibrous or focal myxoid changes on histopathological inspection.

Chordal length and geometric indices are presented in Table II. Compared to normal controls, the study group had shorter chordae, increased mitral tenting height, and smaller mitral annular diameter. Compared to controls with severe ischaemic MR, the study group had shorter chordae, smaller leaflet tenting height, smaller leaflet tenting area, and smaller mitral annular diameter.

Using paired analysis, no difference was noted between readers for measurement of mitral tenting area ($p = 0.9$), tenting height ($p = 0.8$), and

Table 1. Individual patient characteristics, echocardiographic findings, operative findings, and pathology findings

Patient	Age [year]	Sex	Height [cm]	Weight [kg]	BSA [m ²]	Comorbidity	Echo findings	Operative findings	Pathology
1	58	F	171	63	1.71	HTN HLD	Posterior leaflet tethering	Anterior and posterior chordal shortening with mild thickening of middle scallop. Reasonable leaflet motion. Normal posterior leaflet with shortened chordae	Gross: fragments of rubbery valvular tissue Micro: fragments of valvular tissue with focal myxoid degeneration and intimal thickening
2	79	M	208	64	2.00	HLD CKD	Symmetric tethering	Restricted chordae with normal appearing leaflets	No valve specimen obtained (min invasive)
3	38	F	170	73	1.85	HTN HLD	The leaflets are not thickened, do not prolapse, and there is no overt abnormality with subvalvular structures	Foreshortening of the chords to both anterior and posterior leaflets	Gross: rubbery tissue with a small focus of thickening Micro: valvular tissue with marked focal fibrosis and myxoid degenerative changes
4	68	F	167	61	1.62	HTN HLD	Mild leaflet thickening	Severe papillary muscle hypertrophy. Chordal restriction with normal appearing valve leaflets	No valve specimen
5	58	F	163	65	1.7	CAD	Restricted leaflet motion from thickened chordae	Intact normal appearing leaflets and chordae with central regurgitation	No valve specimen (MV repair)
6	74	F	160	62	1.59	HTN Atrial flutter	Thickening of the subvalvular apparatus without leaflet involvement	Calcified annulus with shortened and fibrotic chords	Gross: valve tissue without calcification or vegetation Micro: cardiac valve with fibromyxomatous changes
7	62	F	162	83	2.08	HTN	The tip of the posterior leaflet is thickened and severely restricted from chordal tethering	Posterior leaflet tethered by thickened secondary chords, normal appearing valve leaflets	Gross: small calcified portion of valve (0.2 × 0.3 mm) Micro: valvular tissue with fibrosis and calcification
8	64	F	154	78	1.81	HTN	Symmetric mitral leaflet tethering, but the reason for the apical tethering is unclear. The valve leaflets have normal thickness, the LV and annulus are not dilated. There is probably shortening of the chordae although the chordae tendineae are normal without thickening or calcification	There was no annular dilatation in fact, it was rather small. There was no significant leaflet calcification. There was bi-leaflet tethering and the chordal apparatus was not fibrotic	No valve specimen (MV repair)
9	57	F	168	95	2.04	HTN Atrial flutter	Thickened mitral valve chordae. Posterior mitral leaflet tethering with eccentric, posteriorly directed MR	The mitral valve leaflets appear grossly normal. There was mild chordal shortening without thickening	Gross: basal chords measuring 0.9 cm and 1.0 cm, respectively Micro: endocardial dense fibrous tissue c/w subvalvular apparatus. Negative staining for amyloid
10	77	F	159	63	1.63	CAD DMII	Normal leaflets with normal wall motion and EF	Mild anterior leaflet thickening otherwise normal valve leaflets	Gross: normal valvular tissue Micro: none

HTN – hypertension, HLD – hyperlipidaemia, DMII – diabetes type II, CAD – coronary artery disease.

Table II. Individual patient echocardiographic chamber measurements, LV function, mitral regurgitation parameters, and mitral chordal length

Patient	LVEF (%)	LAD [cm]	LVESD [cm]	LVEDD [cm]	EDV [ml]	ESV [ml]	VC [cm]	ERO [cm]	Chordal Length (AP4) [cm]	Chordal Length (SAX) [cm]
1	50	4.0	4.5	5.8	145	72	0.30	0.31	1.10	1.10
2	60	5.3	3.3	4.6	88	35	0.80	0.38	1.20	1.30
3	50	4.0	3.8	5.0	79	39	0.30	0.40	1.10	1.30
4	60	5.1	3.6	5.5	95	38	0.60	0.58	1.10	1.00
5	52	4.2	3.5	4.6	66	32	0.43	0.43	1.10	1.10
6	52	5.0	2.6	4.2	56	27	0.44	0.44	1.30	1.40
7	59	5.0	2.9	4.9	110	45	0.42	0.42	1.10	1.10
8	55	3.9	2.9	4.4	85	38	0.41	0.41	1.30	1.30
9	55	5.3	3.1	3.4	106	48	0.30	0.30	1.20	1.10
10	60	5.1	2.3	3.4	66	26	0.20	0.20	1.20	0.88

LVEF – left ventricular ejection fraction, LAD – left atrial diameter, LVESD – left ventricular end systolic dimension, LVEDD – left ventricular end diastolic dimension, EDV – end diastolic volume, ESV – end systolic volume, VC – vena contracta, ERO – effective regurgitant orifice.

chordal length ($p = 0.9$). Measurement of mitral annular diameter was different between readers (3.8 ± 0.3 vs. 3.4 ± 0.3 cm, $p = 0.04$).

Discussion

This report describes a series of subjects who underwent surgery for mitral regurgitation despite having normal leaflets, normal annular dimension, and normal LV size. We propose that the mechanism of regurgitation in this group is primarily related to shortened mitral chordae tendineae with consequent mitral leaflet tethering. To our knowledge this represents the first description of chordal shortening as an isolated mechanism for mitral regurgitation. Our results showed that chordal length was significantly shorter in the study population compared to healthy controls and also compared to those with ischaemic FMR.

The control subjects with ischaemic functional MR in our study had similar chordal length to those reported in prior works. In contrast, the study subjects in our report had shorter chordal length compared to historical controls (Figure 2) [10, 11].

Comparison of mitral geometry between the study group and controls revealed several important findings. Whereas increased leaflet tethering (tenting height toward the apex) was notable between the study subjects and the normal controls, tenting in the study group was not as pronounced as was observed in the controls with ischaemic FMR. In addition, we found that the study group had smaller mitral annuli compared to both the normal controls and the controls with ischaemic FMR. Although the measured tenting area was not demonstrated to be increased in the study group compared to normal controls, we suspect that this

was the result of measurement error, because apical tenting was evident with subjective visual inspection in all of the study subjects (Figure 1).

Histological evaluation of our study population was utilised to identify a potential common mechanism of the shortened chordae. In subjects for whom tissue analysis was available, we found mild abnormalities in the subvalvular apparatus; however, no common pathognomonic appearance could be identified. The most common abnormality noted was myxomatous change, but this was seen with approximately the same prevalence as in the general population [12].

Our study has several important limitations. One limitation is the lack of *in vivo* intraoperative measurement of the chordae. Because the study subjects were enrolled retrospectively, this measurement could not be obtained. However, use of TEE to measure the chordal length in the beating heart had good interobserver agreement in our

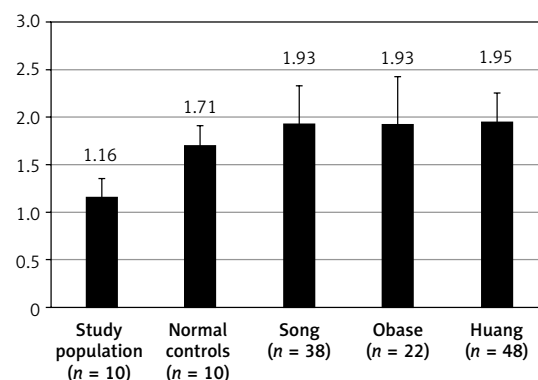


Figure 2. Chordal lengths measured in our study population, in our normal controls, and in several other published series

study and showed good agreement with historical controls. The histological evaluation was limited by the retrospective analysis because we were not able to stain the fixed slides post hoc. Use of 3D TEE would also have been helpful to measure mitral leaflet area. Since mitral leaflet remodeling is a common feature in FMR, examination for this phenomenon in the study group would help give more insight into the mechanism of regurgitation [13–15]. Future studies are needed with a larger dataset and prospective planning of tissue analysis to better characterise our findings.

Conflict of interest

The authors declare no conflict of interest.

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