ESOPHAGEAL MOTILITY DISORDERS IN PATIENTS WITH MITRAL VALVE PROLAPSE

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ABSTRACT

Background: The cause of chest discomfort in patients with primary mitral valve prolapse (MVP) remains unknown.

Aim: our aim was to determine prospectively the incidence of esophageal disorders and abnormal responses to esophageal acid infusions in patients with primary MVP with and without chest pain.

Patients and Methods: 28 patients with primary MVP diagnosed by echocardiography underwent esophageal motility study and provocative testing with acid infusion. Ten healthy subjects served as control group; they also underwent the same studies.

Results: Esophageal manometry revealed esophageal disorders in 14 patients: diffuse esophageal spasm in 9 patients, hypotensive lower esophageal sphincter (LES) in 4, hypertensive LES in 3, nonspecific motor disorders in 2 and no patient with nutcracker esophagus. Acid infusion tests (Bernstein tests) evoked typical chest discomfort in 11 of 28; most of them were in group III with severe MVP, on the other hand, acid infusion test evoked chest discomfort in only one of 10 control subjects.

Conclusion: Esophageal disorders were common and may account for chest discomfort in some patients with primary MVP and persistent chest pain syndromes.

INTRODUCTION

Nonischemic angina-like chest discomfort is often a challenging diagnostic and therapeutic problem that is
frequently frustrating for the patient and the physician. After a thorough cardiologic evaluation for the cause of typical or atypical angina pectoris, the only notable positive finding may be mitral valve prolapse (MVP). Although an association between MVP and chest discomfort has been accepted in clinical practice and a variety of cardiac mechanisms have been proposed, the etiology of such pain remains uncertain and disputed (1, 2).

Thus, non-cardiac causes for chest discomfort should be considered in patients with MVP in whom ischemic heart disease has been excluded.

Disorders of esophageal motility have been implicated as an important and common cause of angina-like chest pain in patients with normal coronary arteriograms (3, 4). Spears and Koch (5) reported a high incidence of esophageal motility disorders in a group of patients with MVP who were referred to a tertiary care center for persistent chest pain syndromes. Furthermore, esophageal manometry revealed diffuse esophageal spasm in a young woman with MVP, and provocative testing with edrophonium and acid infusion reproduced typical chest discomfort in this patient with MVP (6).

Our aim was to determine the incidence of esophageal disorders and abnormal responses to esophageal acid infusions in patients with MVP.

MATERIAL AND METHODS

Our study included, 28 patients with primary MVP (19 females and 9 males) with their age ranging from 14 to 35 years and 10 normal individuals matched for age (3 males and 7 females) as a control group. Patients with MVP were classified into 3 groups according to the degree of MVP into: group I with mild mitral valve prolapse (14 cases), group II with moderate MVP (8 cases) and group III with severe MVP (6 cases). They were also classified according to the presence or absence of chest pain into: group A with no chest pain (13 cases) and group B with chest pain (15 cases). We excluded from the study patients with rheumatic heart disease, congenital heart disease, ischemic heart disease, hypertension, cardiomyopathy, chronic obstructive lung disease and previous upper gastrointestinal operations.

Echocardiography:

Standard M-mode and two-dimensional echocardiography was performed using STM 7000 instru-
ment with 3.0 MHz transducer. The diagnosis of MVP by two-dimensional echocardiography was made if billowing of one or both mitral leaflets or systolic coaptation behind the plane of the mitral valve annulus, or both, were demonstrated in the parasternal long-axis view. Systolic superior displacement of the mitral valve in the apical four-chamber was considered diagnostic of MVP only if moderate to severe (7). The degree of MVP was assessed as follows: Mild MVP, where the coaptation point is on the ventricular side of the mitral annulus plane; moderate MVP, where the coaptation point is on the level of the mitral annulus plane; severe MVP, where the coaptation point is on the atrial side of the mitral annulus plane.

**Esophageal manometry:**

Each patient fasted overnight and received no medications for at least 12 hours before esophageal manometry was performed. The measurement of esophageal motility is performed using a direct intravesophageal microtransducers (distal transducer system) consisting of a flexible solid probe containing three small pressure transducers with lateral openings spaced 5 cm apart. These transducers have a frequency response as flat to approximately 5000 Hz. Pressures were graphed on a multirecording system.

Xylocaine spray 10% was used as topical anaesthetic in the interior of the nare used. The transducers are passed nasally down to the stomach with the patient lying in supine position. The gastric pressure is recorded firstly. The three transducers are verified to be in the stomach where their readings are similar and in phase with respiratory wave form. Now, the probe will be withdrawn slowly 1 cm incrementally "using the slow pull-through technique". The lower esophageal sphincter (LES) will appear firstly by the upper transducer and be known by the increase of the pressure measured. The LES is a 3-5 cm long, the transducers will traverse it in a sequential manner and the readings will be recorded each on a separate channel. The probe is continued to be pulled up passing the sphincter after studying the LES length, position, resting tone and properties of relaxation. During the middle transducer transit, three unique traces are recorded while the distal transducer is still in the stomach. Continues on inspiration, the middle transducer records the traversing of the sphincter.
and the proximal orifice measures esophageal pressure with its mean pressure and negative excursions up on inspiration. When all the three probe transducers are located in the esophageal body, the study of gastroesophageal junction is ended.

Diagnostic criteria for esophageal motility disorders used in this study have been published by Benjamin et al. (8) and Richter & Castell (9). Hypotensive LES was present when the average pressure was \( \geq 10 \text{ mmHg} \); the presence of an accompanying motor disorder of the esophageal body did not affect assignment to this diagnostic category. Diffuse esophageal spasm (DES) was diagnosed if peristaltic contractions were present and if \( > 20\% \) of the total contractions were repetitive and/or simultaneous; increased amplitude (\( > 120 \text{ mmHg} \)) and/or duration (\( > 5.5s \)) of contractions added support for this diagnosis (9). Hypertensive LES was diagnosed when LES P was \( \geq 30 \text{ mmHg} \), with normal LES relaxation and normal motor activity in the esophageal body.

Nutmeg esophagus was present if wave forms in the esophageal body were single-peaked and peristaltic and the average amplitude of 10 consecutive wave forms in the distal esophageal body was \( \geq 140 \text{ mmHg} \). Achalasia was diagnosed when LES pressure was \( \geq 30 \text{ mmHg} \), the LES failed to relax completely after swallows, and peristaltic activity in the esophageal body was absent. A nonspecific motor disorder was diagnosed if contraction abnormalities such as isolated simultaneous or spontaneous contractions or low amplitude contractions were present in the body but failed to meet criteria listed above.

**Acid infusion (Bernstein test):**

Routine Bernstein acid infusion tests were then performed with the catheter withdrawn until the distal part was located 10 cm above the LES. Either 0.1 N hydrochloric acid or saline was infused for 30 minutes (120gtts/minute) in a single-blind fashion. Onset of typical chest discomfort during acid infusion and resolution of discomfort during saline infusion were necessary criteria for a positive test result (10).

**RESULTS**

Twenty eight patients (19 women and 9 men, mean age 23.21 ± 6.02 years) were identified with MVP. Fif-
teen patients (53.57%) described chest pain in the substernal and left chest areas of different characters (heavy, pressure, tight, gripping, sharp, stabbing). Twelve patients (42.86%) described heartburn.

Fourteen patients (50%) had esophageal abnormalities including DES in nine (32.14%), hypertensive LES pressure in three (10.71%), non-specific motor disorders in two (7.14%), hypotensive LES pressure in four (14.28%). Two persons of the control group (20%) had esophageal abnormalities in the form of DES (table 2). Thirteen of fifteen patients with chest pain (subgroup B) had esophageal motility abnormalities mainly in the form of DES (table 3). Six of thirteen patients without chest pain (subgroup B) had esophageal motility disorders mainly in the form of DES (table 3). Eleven patients (39.28%) had positive Bernstein test and 17 (60.72%) had negative Bernstein test (table 4). Most of the patients with positive Bernstein test (66.66%) were in group III (severe MVP) (table 4). Eight of eleven patients with positive Bernstein test (72.72%) had esophageal motility disorders while ten of 17 patients with negative Bernstein test (58.82%) had esophageal motility disorders (table 5).

Comparative analysis of esophageal body motility study in control versus whole test group revealed significant increase in proximal amplitude (P < 0.05), increase in distal duration (P < 0.05), and significant increase in lower esophageal sphincter pressure (P < 0.05), (table 6).
Table (1): Percentage of clinical symptoms in studied groups.

<table>
<thead>
<tr>
<th>Clinical symptoms</th>
<th>Whole test group (n = 28)</th>
<th>Group I (n = 14)</th>
<th>Group II (n = 8)</th>
<th>Group III (n = 6)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>No</td>
<td>%</td>
<td>No</td>
<td>%</td>
</tr>
<tr>
<td>Chest pain</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>15</td>
<td>53.57</td>
<td>9</td>
<td>64.28</td>
</tr>
<tr>
<td>No</td>
<td>13</td>
<td>46.43</td>
<td>5</td>
<td>35.71</td>
</tr>
<tr>
<td>Heartburn</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>12</td>
<td>42.86</td>
<td>6</td>
<td>42.85</td>
</tr>
<tr>
<td>No</td>
<td>16</td>
<td>57.14</td>
<td>8</td>
<td>57.15</td>
</tr>
</tbody>
</table>

Table (2): Clinical types of esophageal motility disorders in the whole test and control groups.

<table>
<thead>
<tr>
<th></th>
<th>HP. LES</th>
<th>Hr. LES</th>
<th>DES</th>
<th>Nutcracker</th>
<th>NS.MD</th>
<th>Normal motility</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>No</td>
<td>%</td>
<td>No</td>
<td>%</td>
<td>No</td>
<td>%</td>
</tr>
<tr>
<td>Whole test group n=28</td>
<td>4</td>
<td>14.28</td>
<td>3</td>
<td>10.71</td>
<td>9</td>
<td>32.14</td>
</tr>
<tr>
<td>Control group n=10</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>2</td>
<td>20</td>
</tr>
</tbody>
</table>

LES = lower esophageal sphincter. NS.MD = nonspecific disorder. Hr. LES = hypertensive LES. DES = diffuse esophageal spasm. HP. LES = hypotensive LES.
N.B. The same patient may show more than one motility disorder.

Table (3): Clinical types of esophageal motility disorders in subgroup (A) and subgroup (B).

<table>
<thead>
<tr>
<th>Groups</th>
<th>HP. LES</th>
<th>Hr. LES</th>
<th>DES</th>
<th>Nutcracker</th>
<th>NS.MD</th>
<th>Normal motility</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>No</td>
<td>%</td>
<td>No</td>
<td>%</td>
<td>No</td>
<td>%</td>
</tr>
<tr>
<td>Subgroup (A) n=13</td>
<td>2</td>
<td>15.38</td>
<td>0</td>
<td>0</td>
<td>4</td>
<td>30.76</td>
</tr>
<tr>
<td>Subgroup (B) n=15</td>
<td>2</td>
<td>13.33</td>
<td>3</td>
<td>20.0</td>
<td>6</td>
<td>40.0</td>
</tr>
</tbody>
</table>

Subgroup (A) = no chest pain group. Subgroup (B) = chest pain group.

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Table (4): Incidence percentage of the Bernstein test results in the whole test group and subgroups.

<table>
<thead>
<tr>
<th>Bernstein test</th>
<th>Control group no=10</th>
<th>Whole test group no=28</th>
<th>Group I no=14</th>
<th>Group II no=8</th>
<th>Group III no=6</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>No</td>
<td>%</td>
<td>No</td>
<td>%</td>
<td>No</td>
</tr>
<tr>
<td>Positive</td>
<td>1</td>
<td>10</td>
<td>11</td>
<td>39.28</td>
<td>4</td>
</tr>
<tr>
<td>Negative</td>
<td>9</td>
<td>90</td>
<td>17</td>
<td>60.72</td>
<td>10</td>
</tr>
</tbody>
</table>

Table (5): Incidence percentage of esophageal motility disorders and chest pain in Bernstein –ve and +ve patients.

<table>
<thead>
<tr>
<th>Esophageal motility disorders</th>
<th>Bernstein +ve n = 11</th>
<th>Bernstein –ve n = 17</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>No</td>
<td>%</td>
</tr>
<tr>
<td>With chest pain</td>
<td>5</td>
<td>45.45</td>
</tr>
<tr>
<td>Without chest pain</td>
<td>6</td>
<td>54.54</td>
</tr>
<tr>
<td>HP.LES</td>
<td>2</td>
<td>18.18</td>
</tr>
<tr>
<td>Hr.LES</td>
<td>2</td>
<td>18.18</td>
</tr>
<tr>
<td>DES</td>
<td>2</td>
<td>18.18</td>
</tr>
<tr>
<td>NS.MD</td>
<td>2</td>
<td>18.18</td>
</tr>
<tr>
<td>Total</td>
<td>8</td>
<td>72.72</td>
</tr>
</tbody>
</table>
Table (6): Comparative analysis of esophageal body motility study in control versus whole test group.

<table>
<thead>
<tr>
<th>Groups</th>
<th>Value</th>
<th>Amplitude</th>
<th>Duration</th>
<th>%tertiary waves</th>
<th>%Normal waves</th>
<th>LESP</th>
<th>%Relaxation</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Prox</td>
<td>Mid</td>
<td>Dis</td>
<td>Prox</td>
<td>Mid</td>
<td>Dis</td>
</tr>
<tr>
<td>Control</td>
<td>Mean</td>
<td>61.0</td>
<td>70.1</td>
<td>84.4</td>
<td>26.1</td>
<td>2.62</td>
<td>3.12</td>
</tr>
<tr>
<td>n=10</td>
<td>SD</td>
<td>23.74</td>
<td>27.03</td>
<td>23.54</td>
<td>0.49</td>
<td>0.50</td>
<td>0.45</td>
</tr>
<tr>
<td>Test</td>
<td>Mean</td>
<td>44.07</td>
<td>57.28</td>
<td>82.07</td>
<td>2.2</td>
<td>2.37</td>
<td>2.54</td>
</tr>
<tr>
<td>group n=28</td>
<td>SD</td>
<td>17.91</td>
<td>27.8</td>
<td>28.4</td>
<td>0.58</td>
<td>0.49</td>
<td>0.42</td>
</tr>
<tr>
<td>P</td>
<td></td>
<td>&lt;0.05</td>
<td>&gt;0.05</td>
<td>&gt;0.05</td>
<td>&gt;0.05</td>
<td>&gt;0.05</td>
<td>&gt;0.05</td>
</tr>
</tbody>
</table>

Prox = Proximal  
Ret = Retrograde  
Nitr = Nontransmitted  
Dis = Distal  
Mid = Middle  
Sim = Simultaneous  
LESP = Lower esophageal sphincter pressure.

DISCUSSION

In this study, the diagnosis of MVP was supported by physical examination combined with objective evidence from echocardiography.

The current study indicates that the 53.57% patients with MVP had chest pain. Chest pain was reported by 33-60% of patients with MVP (11). Chest discomfort is often poorly localized, unrelated to exertion, sharp in quality, either transient or prolonged, and unrelieved by nitroglycerin (12).

Such atypical chest pain has ascribed to several factors, including local myocardial ischemia due to increased myocardial wall tensions resulting from prolapse of the mitral valve leaflets (13). Esophageal disorders such as diffuse esophageal spasm, gastroesophageal reflux, "nutcracker esophagus", and hypertensive lower esophageal sphincter have been associated with typical and atypical angina-like chest pain syndromes (14).

In the present study, 12 out of the
28 patients with primary mitral valve prolapse (42.86%) reported frequent heartburn. These results are nearly similar to those of Spears and Koch (5) whom reported frequent heartburn in six of 12 mitral valve prolapse patients. Results of the questionnaire done by Koch et al. (10) showed that 8 of 20 subjects with MVP experienced heartburn.

Disorders of esophageal motility have been implicated as an important and common cause of angina-like chest pain in patients with normal coronary arteriograms (3, 4). In the present study half of the patients with MVP has esophageal disorders. The frequency of esophageal motility disorders in patients with mitral valve prolapse, chest pain, and normal coronary arteriograms is over 50% (15), ranging from 4% to 78% (5, 16). In studies of patients with angina-like pain and normal cardiac catheterization results (and no MVP), 30 to 60 percent of patients had disorders of esophageal motility, the majority of which were nutcracker esophagus (4). However, in our study, most of the esophageal motility disorders in patients with primary MVP were in the form of diffuse esophageal spasm. In a similar study conducted by Koch et al. (10) on a more homogeneous population of subjects with MVP and chest discomfort, the majority of patients has diffuse esophageal spasm. Thus, it appears that esophageal contraction abnormalities, which comprise diffuse esophageal spasm (DES), are common in this select population. The increased incidence of diffuse esophageal spasm in MVP patients with chest discomfort was also found in a retrospective study done by Spears and Koch (5). In several other series, 2 to 36% of patients with noncardiac chest pain (not selected for MVP) had DES (17). Different incidences of DES reflect variable diagnostic criteria for DES (9) and the variable use of provocative agents among laboratories. Nutcracker esophagus, a frequently diagnosed cause of noncardiac chest pain (14), was not found in the present series as well as the series of Spears and Koch (5). Gastroesophageal reflux, with or without documented hypotensive lower esophageal sphincter, is another cause of angina-like chest pain (18) and the potential mechanism of chest discomfort in the patients with hypotensive lower esophageal sphincter (LES) and positive Bernstein tests. Four patients in our study had a hypotensive LES nearly similar to the find-
ings of Spears and Koch (5). Provoca-
tive testing with Bernstein acid infu-
sion or the use of esophageal pH pro-
bes to correlate symptoms with re-
flux episodes may further clarify the
origin of chest pain symptoms in pa-
tients with hypotensive LES and MVP.
In our study 11 of 28 patients with
MVP had positive Bernstein test, most
of them were in group III (with severe
MVP) (66.66%). A minority of our pa-
tients with primary MVP had nonspe-
cific motor esophageal disorders
(7.14%) and hypertensive LES
(10.71%).

An increased frequency in the
diagnosis of irritable bowel syndrome
in patients with MVP has been noted
(19). It is of interest that several of
the MVP patients with the present
as well as previous series reported
intermittent constipation and diarrhea
consistent with the diagnosis of irri-
table bowel syndrome. These findings
suggest a more generalized motility
disorders may be present in some
patients with MVP. MVP has been
associated with disorders of mesen-
chymal migration (20). Since smooth
muscle of the digestive tract is also
derived from embryonal mesenchyma
(21), the association of MVP and
gastrointestinal motility disorders may
relate in some way to the embryologic
development of these organs. The
high incidence of DES in this study
also raises the issue of a true associa-
tion between esophageal spasm and
MVP. On the other hand, two of ten
patients without MVP had DES and
only one had positive responses to
the provocative agents. These find-
ings suggested that esophageal disor-
ders were responsible for chest dis-
comfort in patients with symptomatic
MVP.

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حركية المرئي في مرضى إرتخاء الصمام الميترالي

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أقسام الباطنة العامة والجراحة العامة* - بكلية طب المنصورة

هدف البحث:

تقديم حركية المرئي وعلاقتها بارتخاء الصمام الميترالي الأولي.

أجري هذا البحث على 28 مريضاً بارتخاء الصمام الميترالي الأولي (9 من الإناث و19 من الذكور) تراحت أعمارهم بين 14 و53 سنة. كما شملت الدراسة 10 أفراد أصحاء لهم نفس العمر كمجموعة ضابطة. تم إخضاع كل المرضى والمجموعة الضابطة لنفحص القلب بالموجات فوق الصوتية، وظائف حركة المرئي واختيار برتبطين.

نتائج البحث:

وجود إضطرابات في حركة المرئي عند 14 من مرضى المجموعة الاختبارية، 9 منهم أظهروا تقلص عام بالمرئي، 4 نقص ضغط العضلة السفلية العاصرة، 2 زيادة ضغط العضلة السفلية العاصرة.

إضطرابات حركية غير محددة كما تبين عدم إصابة أي من المرضى بمرئي كسارة البنين.

أظهر اختبار برتبطين ألم بالصدر عند 11 من 28 مريض معظمهم ضمن المجموعة الثالثة المصابة بارتخاء شديد بالصمام الميترالي ومن ناحية أخرى لم يظهر اختبار برتبطين ألم الصدر إلا في حالة واحدة من بين العشرة أفراد الذين يكونون المجموعة الضابطة.

الإجمالى:

مساءً تبين أن إضطرابات حركة المرئي منتشرة ومستقلة عن ألم الصدر في مرضى إرتخاء الصمام الميترالي الأولي.

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بالسماح، أقترح أن نحن في حاجة إلى إجهاض هذه القضية.

وأخيراً، ربما يكون من الأفضل أن نبحث عن حلول أخرى.

فيما يتعلق بزيادة العمل، فإن القاء مضجعات العمل أو تجنبها يأتي في الاعتبار.

شكراً،

[署名]