
Communications

Idiopathic Scoliosis and Mitral Valve Prolapse

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Mitral valve prolapse (MVP) is the most common congenital cardiac anomaly, occurring in 6 to 10 percent of the young female population.¹⁻³ The auscultatory findings of a midsystolic nonejection click and an apical late systolic murmur are due to redundant mitral leaflets and elongated chordae tendineae.⁴⁻⁷ The pathologic findings of myxomatous degeneration of the mitral leaflets suggest an underlying connective tissue abnormality.⁸ MVP has been described with increased frequency in such known connective tissue diseases as Marfan's syndrome,⁹ Ehlers-Danlos syndrome,¹⁰ osteogenesis imperfecta,¹¹ and pseudoxanthoma elasticum.¹²

Both MVP and idiopathic scoliosis occur predominantly in young women. Thoracic skeletal deformities are common in patients with MVP, occurring in 75 percent of one adult series.¹³ These facts suggest that MVP should occur frequently in patients with idiopathic scoliosis, important information for such patients, who may require major orthopedic surgery. This study was performed to determine prospectively the incidence of MVP in a population of patients with the diagnosis of idiopathic scoliosis.

Methods

From February 1982 to February 1983, all patients seen in the private practice of one of the authors (JPL) with a diagnosis of idiopathic scoliosis and curvature greater than 20 degrees were considered potential participants in the study. Their scoliosis evaluation consisted of

a physical examination and posteroanterior and lateral thoracolumbar spine roentgenograms. The roentgenograms were measured by the Cobb method.¹⁴ Hypokyphosis was defined as a thoracic kyphosis of less than 20 degrees. Letters that briefly described MVP and offered a free evaluation at the pediatric cardiology clinic were sent to 47 of the patients. Thirty-nine patients were reached by the pediatric cardiology clinic, and of these, 33 agreed to an evaluation.

Each patient was examined by a pediatric cardiologist and a pediatric resident. The examination was done in the sitting, standing, recumbent, and left lateral positions. The diagnosis of MVP was made on the basis of the presence of a midsystolic nonejection click with typical postural variation.¹⁵ The finding of a late systolic or holosystolic murmur, if present, was noted, but it was not necessary for the diagnosis. In addition, each patient had a review and examination of cardiovascular systems, a 12-lead electrocardiogram, and an M-mode echocardiogram (Figure 1). Echocardiographic confirmation of the diagnosis was based on the criteria of Meyer.¹⁶ The two examiners were blind to the results of each other's examinations and to the echocardiogram results.

Results

The study group consisted of 31 female and 2 male patients. Mean age was 14 years (range, 9 to 21 years). Fifteen had a family history of scoliosis. Twelve also had hypokyphosis. None of the group had any cardiovascular complaints. No patient was aware of any abnormal cardiac findings. The electrocardiograms were normal in all patients. The auscultatory diagnosis of MVP was made in 26 of the 33 (79 percent). Sixteen had an isolated

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IDIOPATHIC SCOLIOSIS

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Although most of the patients with serious bleeding were receiving concomitant therapy and had a history of peptic ulcer disease, the drug has the potential for causing gastrointestinal bleeding on its own. Administer to patients with active gastric and duodenal ulcers only under close supervision. **Precautions: General:** **NAPROSYN® (NAPROXEN) SHOULD NOT BE USED CONCOMITANTLY WITH THE RELATED DRUG ANAPROX® (NAPROXEN SODIUM) SINCE THEY BOTH CIRCULATE IN PLASMA AS THE NAPROXEN ANION.** Because anaphylactic reactions usually occur in patients with a history of such reactions, question patients for such things as asthma, nasal polyps, urticaria, and hypotension associated with NSAIDs before starting therapy. If such symptoms occur, discontinue the drug. In chronic studies in laboratory animals, the drug has caused nephritis. Glomerular nephritis, interstitial nephritis and nephrotic syndrome have been reported. Use with great caution in patients with significantly impaired renal function. Monitoring of serum creatinine and/or creatinine clearance is advised in these patients. Certain patients, including those with compromised renal blood flow and some elderly in whom impaired renal function may be expected, should have renal function assessed before and during therapy. Consider reducing daily dosage in these patients. With NSAIDs borderline elevations of liver tests may occur in up to 15% of patients. They may progress, remain unchanged, or be transient with continued therapy. The SGPT (ALT) test is probably the most sensitive indicator of liver dysfunction. Elevations (3 times the upper limit of normal) of SGPT or SGOT (AST) occurred in controlled clinical trials in less than 1% of patients. Evaluate patients with symptoms and/or signs suggesting liver dysfunction, or in whom an abnormal liver test has occurred, for evidence of more severe hepatic reaction. Severe hepatic reactions, including jaundice and cases of fatal hepatitis, have been reported rarely. If abnormal liver tests persist or worsen, if clinical signs and symptoms consistent with liver disease develop, or if systemic manifestations occur (e.g., eosinophilia or rash), discontinue therapy. If steroid dosage is reduced or eliminated during therapy, do so slowly and observe patients closely for adverse effects, including adrenal insufficiency and exacerbation of arthritis symptoms. Determine hemoglobin values frequently for patients with initial values of 10 grams or less who receive long-term therapy. Peripheral edema has been observed in some patients. Each tablet contains approximately 25 mg (1 mEq) sodium, which should be considered in patients whose overall intake of sodium must be markedly restricted. Use with caution in patients with fluid retention, hypertension or heart failure. The antipyretic and anti-inflammatory activities of the drug may reduce fever and inflammation, thus diminishing their utility as diagnostic signs. Conduct ophthalmic studies soon after starting therapy and at periodic intervals if the drug is used for an extended period. **Information for Patients:** Caution should be exercised by patients whose activities require alertness if they experience drowsiness, dizziness, vertigo or depression during therapy. **Drug Interactions:** Naproxen anion may displace other albumin-bound drugs from their binding sites and could likewise be displaced itself. Studies failed to show that the drug significantly affects prothrombin times when administered to individuals on coumarin-type anticoagulants, but use caution since interactions have been seen with other nonsteroidal agents of this class. Observe patients receiving the drug and a hydantoin, sulfonamide or sulfonyleurea for signs of toxicity to these drugs. Some drugs of this class inhibit the natriuretic effect of furosemide. Increased plasma lithium due to inhibition of renal lithium clearance has been reported. This drug and other NSAIDs can reduce the antihypertensive effect of beta-blockers. Probenecid given concurrently increases naproxen anion plasma levels and extends its plasma half-life significantly. **Drug/Laboratory Test Interactions:** The drug may decrease platelet aggregation and prolong bleeding time. The drug may result in increased urinary values for 17-ketosteroids because of an interaction between the drug and/or its metabolites with m-dinitrobenzene used in this assay. Temporarily discontinue therapy with the drug for 72 hours before adrenal function tests are performed. The drug may interfere with some urinary assays of 5-hydroxy indoleacetic acid (5HIAA). **Carcinogenesis:** A two-year study in rats to evaluate the carcinogenic potential of the drug showed no evidence of carcinogenicity. **Pregnancy: Teratogenic Effects:** Pregnancy Category B. Do not use during pregnancy unless clearly needed. Avoid use during late pregnancy. Non-teratogenic Effects: In rats, pregnancy was prolonged when the drug was given before the onset of labor; labor was protracted when the drug was given after labor had begun. **Nursing Mothers:** Avoid use in nursing mothers. **Pediatric Use:** Pediatric indications and dosage recommendations have not been established. **Adverse Reactions: Incidence Greater Than 1%: Gastrointestinal:** The most frequent complaints related to the gastrointestinal tract: constipation,* heartburn,* abdominal pain,* nausea,* dyspepsia, diarrhea, stomatitis. **Central Nervous System:** Headache,* dizziness,* drowsiness,* lightheadedness, vertigo. **Dermatologic:** Itching (pruritus),* skin eruptions,* ecchymoses,* sweating, purpura. **Special Senses:** Tinnitus,* hearing disturbances, visual disturbances. **Cardiovascular:** Edema,* dyspnea,* palpitations. **General:** Thirst. *Incidence of reported reaction 3%-9%. Reactions seen in less than 3% of the patients are unmarked. **Incidence Less Than 1%: Probable Causal Relationship:** The following adverse reactions were reported less frequently than 1% during controlled clinical trials and through voluntary reports since marketing. The probability of a causal relationship exists between the drug and these adverse reactions: Abnormal liver function tests, gastrointestinal bleeding, hematemesis, jaundice, melena, peptic ulceration with bleeding and/or perforation, vomiting, glomerular nephritis, hematuria, interstitial nephritis, nephrotic syndrome, renal disease, eosinophilia, granulocytopenia, leukopenia, thrombocytopenia, depression, dream abnormalities, inability to concentrate, insomnia, malaise, myalgia and muscle weakness, alopecia, skin rashes, hearing impairment, congestive heart failure, anaphylactoid reactions, menstrual disorders, pyrexia (chills and fever). **Causal Relationship Unknown:** Other reactions have been reported in circumstances in which a causal relationship could not be established. However, in these rarely reported events, the possibility cannot be excluded. Therefore these observations are being listed to serve as alerting information to the physicians: agranulocytosis, aplastic anemia, hemolytic anemia, urticaria, angioneurotic edema, hyperglycemia, hypoglycemia. **Overdosage:** May be characterized by drowsiness, heartburn, indigestion, nausea or vomiting. Life-threatening dose is not known. If patient ingests many tablets, empty stomach and employ usual supportive measures. Animal studies suggest that the prompt administration of 5 grams of activated charcoal would tend to reduce markedly drug absorption. It is not known if the drug is dialyzable. **Caution:** Federal law prohibits dispensing without prescription. See package insert for full prescribing information. August 1983 Rev. 24

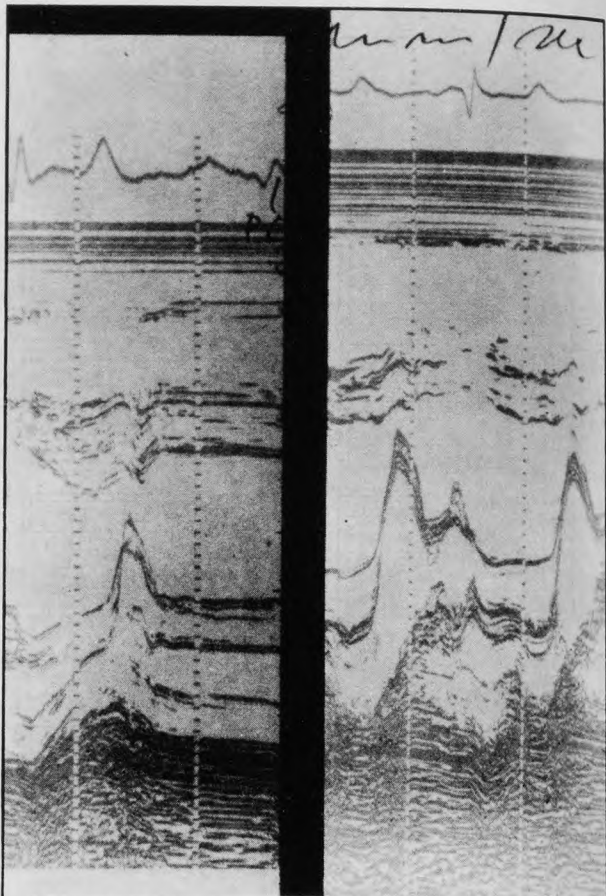


Figure 1. M-mode echocardiograms demonstrating normal mitral valve motion on the left, and mitral valve prolapse on the right. The electrocardiogram at the top of each frame identifies the onset of electrical systole. In the normal mitral valve, seen as an M-shape in diastole, the anterior and posterior leaflets move slowly anteriorly throughout systole (left-hand panel). With mitral valve prolapse, the leaflets remain horizontal rather than moving anteriorly, and there is an abrupt midsystolic posterior dip coincident with the auscultatory click

nonejection click, and 10 had a click with an associated late systolic murmur. The diagnosis of MVP was confirmed by M-mode echocardiography in 24 of these 26 patients (92 percent). All seven patients with normal physical examinations had normal echocardiograms. In four cases the diagnosis of MVP was made by only one examiner; in all four, echocardiography demonstrated typical findings of MVP.

Discussion

Although the association of mitral valve prolapse and thoracic skeletal deformities is well recognized, the incidence of MVP in patients with idiopathic scoliosis remains unclear. The frequency of 79 percent in this series is the highest yet reported. As only 70 percent of the target group was evaluated, perhaps some self-selection did occur despite the denial of symptoms on a cardiovascular review of systems. This frequency far exceeds that in the general population as well as the 29 percent incidence recently reported by Hirschfield et al¹⁷ in another series of patients with idiopathic scoliosis. There were no data on the severity of scoliosis in that study. All patients in this study had at least 20 degrees of curvature. Perhaps the connective tissue abnormality seen in MVP is seen more frequently in adolescents with more severe scoliosis.⁸

MVP is known to occur in a wide variety of connective tissue disorders.⁹⁻¹² The results of this study suggest that in some patients a pervasive developmental abnormality of connective tissue may underlie both idiopathic scoliosis and MVP. Further supporting this concept is the simultaneous development of the mitral valve and the thoracic vertebrae, ribs, and sternum early in the seventh week of embryonic life. The common familial patterns in idiopathic scoliosis¹⁸ and mitral valve prolapse¹⁹ suggest that a single collagenous abnormality may influence the development of both the mitral valve and the spine. That the configuration of the thorax does not appear to be a contributing factor was substantiated by the observation that the incidence of MVP in those with lumbar curves only was 80 percent (4/5).

The natural history of MVP is largely benign in children,¹⁵ although ventricular arrhythmias²⁰ and bacterial endocarditis^{15,21} have been reported. Bacterial endocarditis is an important consideration in the context of patients with idiopathic scoliosis, in that they frequently require surgery. If a diagnosis of mitral valve prolapse is made in a patient with idiopathic scoliosis, appropriate antibiotic prophylaxis would be necessary prior to instrumentation.

In no patient in this series was the diagnosis of MVP made prior to the study evaluation. One patient was excluded because of Marfan's syndrome, which was first noted during the cardiac evaluation. The majority of the patients considered fam-

ily physicians to be their primary care providers, and most had been referred to the orthopedist by these physicians. Study data suggest that careful screening for the presence of mitral valve prolapse is necessary in patients with idiopathic scoliosis.

References

1. McNamara D: Idiopathic benign mitral leaflet prolapse. *Am J Dis Child* 136:152, 1982
2. Markiewicz W, Stoner J, London E, et al: Mitral valve prolapse in 100 presumably healthy young females. *Circulation* 53:464, 1976
3. Procacci P, Savran S, Schreiter S, Bryson A: Prevalence of clinical mitral valve prolapse in 1,169 young women. *N Engl J Med* 294:1086, 1976
4. Barlow J, Pocock W: The significance of late systolic murmurs and mid-late systolic clicks. *Md State Med J* 12:76, 1963
5. Hancock E, Cohn K: The syndrome associated with midsystolic click and late systolic murmur. *Am J Med* 41:183, 1966
6. Criley J, Lewis K, Humphries J, Ross R: Prolapse of the mitral valve: Clinical and cine-angiographic findings. *Br Heart J* 28:488, 1966
7. Barlow J, Bosman C, Pocock W, Maschand P: Late systolic murmurs and non-ejection ("mid-late") systolic clicks. *Br Heart J* 30:203, 1968
8. Davies M, Moore B, Braimbridge M: The floppy mitral valve: Study of incidence, pathology and complications in surgical, necropsy and forensic material. *Br Heart J* 40:468, 1978
9. Brown O, Demots H, Kloster F, et al: Aortic root dilatation and mitral valve prolapse in Marfan's syndrome—An echocardiographic study. *Circulation* 52:651, 1975
10. Brandt K, Sumner R, Ryan T, Cohen A: Herniation of mitral leaflets in Ehlers-Danlos syndrome. *Am J Cardiol* 36:524, 1975
11. Wood S, Thomas J, Braimbridge M: Mitral valve disease and open heart surgery in osteogenesis imperfecta tarda. *Br Heart J* 35:103, 1973
12. Iebwohl M, Distefano D, Prioleau P, et al: Pseudo-xanthoma elasticum and mitral valve prolapse. *N Engl J Med* 307:228, 1982
13. Salomon J, Shah P, Heinle R: Thoracic skeletal abnormalities in idiopathic mitral valve prolapse. *Am J Cardiol* 36:32, 1975
14. Cobb JR: Outline in the study of scoliosis. *Am Acad Orthop Surg* 5:261, 1948
15. Bisset G, Schwartz D, Meyer R, et al: Clinical spectrum and long-term follow-up of isolated mitral valve prolapse in 119 children. *Circulation* 62:423, 1980
16. Meyer R: *Pediatric Echocardiography*. Philadelphia, Lea & Febiger, 1977, p 175
17. Hirschfield S, Rudner C, Nash C, et al: Incidence of mitral valve prolapse in adolescent scoliosis and thoracic hypokyphosis. *Pediatrics* 70:451, 1982
18. Wynne-Davies R: Familial (idiopathic) scoliosis—A family survey. *J Bone Joint Surg* 50:24, 1968
19. Pocock W, Barlow J: Etiology and electrocardiographic features of the billowing posterior mitral leaflet syndrome. *Am J Med* 51:731, 1971
20. Kavey REW, Sondheimer HM, Blackman MS: Detection of dysrhythmia in pediatric patients with mitral valve prolapse. *Circulation* 62:582, 1980
21. Gingell RL, Vlad P: Mitral valve prolapse. In Keith J, Rowe R, Vlad P (eds): *Heart Disease in Infancy and Childhood*. New York, Macmillan, 1978, p 810