Esophageal Function in Patients with Angina-Type Chest Pain and Normal Coronary Angiograms

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Ten per cent of patients with angina pectoris have normal coronary arteries and cardiac function and, despite this reassurance, continue to have chest pain. Since pain of cardiac or esophageal origin is clinically difficult to differentiate, 50 patients with severe chest pain, normal cardiac function, and normal coronary arteriography with ergotamine provocation were evaluated with a symptomatic questionnaire and esophageal function test. On 24-hour esophageal pH monitoring, 23 patients had abnormal reflux, and 27 were normal. There was no difference in the incidence and severity of chest pain, esophageal symptoms, or medication taken between refluxers and nonrefluxers. Ten refluxers and ten nonrefluxers had chest pain on exercise electrocardiography. Thirteen refluxers documented chest pain during the pH monitoring period, and in 12 it coincided with a reflux episode. Fifteen nonrefluxers documented chest pain during the monitoring period, and in only one did it coincide with a reflux episode. Of the 23 refluxers, 12 were treated with medical therapy and 11 by a surgical antireflux procedure, and all followed for two to three years. Ten (91%) of the 11 surgically treated patients are totally free of chest pain compared with five (42%) of the 12 medically treated patients. All 12 patients who had chest pain coincide with a documented reflux episode responded positively to antireflux therapy, eight surgical and four medical. It is concluded that 46% of patients complaining of angina pectoris with normal cardiac function and coronary arteriography have gastroesophageal reflux as a possible etiology. Seventy-three per cent of these patients have total abolition of chest pain by either surgical or medical antireflux therapy. Patients whose experience of chest pain coincided with a documented reflux episode on 24-hour esophageal pH monitoring had a 100% response to medical or surgical therapy. Overall, surgical therapy gave better results (91%) but was associated with an 18% temporary morbidity. Objective evaluation of reflux status and its correlation to the symptom of chest pain by 24-hour pH monitoring allows for selective therapy in these difficult to manage patients.

A CLINICAL DIAGNOSIS of angina pectoris no longer implies myocardial ischemia, since approximately 10% of individuals with this complaint have on investigation angiographically normal coronary arteries and an expected mortality similar to normal cohorts matched for age and sex.[1,2,3] In a careful follow-up study of 86 women with normal coronary arteriograms and angina-type pain, Waxler et al.[4] found no incidence of sudden death or myocardial infarction. He concluded that the syndrome had a benign prognosis and that those afflicted do not have a serious cardiac problem.

From a functional point of view, however, many of these patients do poorly. Follow-up studies by Ocken et al.[5] and by Levy and Winkle[6] show that 58–82% of these patients continued to have pain of equal or greater severity to that present at the time of their initial presentation. Reassurance that cardiac function and coronary arteries were normal did not have a favorable impact on their life style, as most of these patients continued to report an inability to work and persisted in seeing their physician regularly.[5]

For the patients whose symptoms continued unabated, little relief from treatment can be expected. Nifedipine is often used on the assumption that coronary artery spasm is involved but is not particularly effective.[7] Similarly, the response to Propranolol is poor and far below that obtained for coronary artery stenosis.[8] Nitrate therapy is often ineffective and when it does work, often takes many minutes to relieve the pain. It was the authors' belief that to improve on this ineffective therapy requires, first of all, a clarification of the etiology of this condition.

An esophageal abnormality is a reasonable consideration for the cause of chest pain in these patients since the differentiation between pain of cardiac or esophageal origin can be clinically difficult. Both diseases are common, may occur simultaneously, and may have overlapping symptomatology. Pain originating from either the myocardium or the esophagus can be of similar intensity and character, share a common distribution, oc-

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cur frequently at night, and be accompanied by acute attacks of breathlessness.[9] Pain from either organ may be precipitated by effort, emotion, exposure to cold, or ingestion of food. Similarily, pain from either organ can be relieved by nitroglycerine therapy. Because of these similarities the authors prospectively studied esophageal function in 50 patients who were originally considered to have angina pectoris but eventually had myocardial ischemia excluded by coronary arteriography with ergotomine provocation. All of these patients had esophageal function evaluated by esophageal manometry and 24-hour esophageal pH monitoring. Arising from this study was the recognition that many of these patients have pain originating from the esophagus and benefit substantially from appropriate therapy.

TABLE 1. *Symptoms of Gastroesophageal Reflux*

Heartburn		
None	-0-	No heartburn
Minimal	-1-	Occasional episodes
Moderate	-2-	Reason for medical visit
Severe	-3-	Interference with daily activities
Regurgitation		
None	-0-	No regurgitation
Minimal	-1-	Occasional episodes
Moderate	-2-	Predictable on position or straining
Severe	-3-	Episodes of pulmonary aspiration manifested by chronic nocturnal cough or recurrent pneumonias
Dysphagia		
None	-0-	No dysphagia
Minimal	-1-	Occasional episodes
Moderate	-2-	Required liquids to clear
Severe	-3-	Episodes of esophageal obstruction manifested by vomiting

Studied Population

The population studied consisted of 50 consecutive patients who were evaluated for angina type chest pain, and were found to be free of cardiac disease on the basis of a normal cardiac catheterization and normal coronary arteriography. None of the patients had a history of esophageal surgery or were previously investigated for an esophageal disorder. There were 34 females and 16 males with an age range between 33 and 77 years.

Cardiac Investigations

In each patient the attending physician believed that the clinical examination and resting electrocardiogram either suggested or could not exclude the presence of coronary artery disease, and that further investigation of the complaint was indicated. All of the patients were seen by at least two physicians primarily interested in cardiac diseases who assessed the quality and character of their chest pain as to aggravating factors, radiation patterns, and response to medication. Those patients with pain indistinguishable from angina pectoris were selected for further investigation.

Prior to coronary angiography, maximal exercise electrocardiography was performed on a treadmill with constant electrocardiographic monitoring using the Bruce protocol.[10] The end-point of the test was (1) symptom-limited by fatigue, dyspnea, or ischemic chest pain, (2) the occurrence of clinical signs of inadequate cardiac output, or (3) the development of electrocardiographic abnormalities. The test was stopped when 85–90% of the age-predicted maximal heart rate was achieved, or when symptoms, signs, or electrocardiographic changes dictated earlier cessation.

Invasive cardiac investigations consisted of right and left heart chamber catheterizations with ventricular angiographic studies and selective coronary cineangiography performed by Judkins techniques.[11] Patients with minimal coronary artery irregularities, ventriculographic abnormalities, valvular stenosis or insufficiency, or evidence of hypertrophic obstructive cardiomyopathy were excluded. Patients with mitral valve prolapse without hemodynamic abnormalities were not excluded, since an esophageal etiology for their pain was possible. All patients with normal coronary arteriograms and normal cardiac function had repeat injection with cinecoronary arteriography during ergotomine provocation to exclude coronary artery spasm as a possible cause of their symptoms. The first 50 consecutive patients to complete these studies with normal cardiac function and normal coronary arteriography were accepted for esophageal investigation.

Esophageal Investigations

All of the patients accepted for esophageal investigation were evaluated by a clinical questionnaire, upper G.I. barium study, cholecystography, skeletal survey, esophagoscopy, esophageal manometry, and 24-hour pH monitoring of the distal esophagus. All current cardiac or gastrointestinal medication were discontinued one day prior to and for the duration of the esophageal study. Normal controls were investigated similarly with the exception of cholecystography and endoscopy and have been the subject of previous communications.[12,13]

Prior to the performance of any esophageal study, each patient was graded on a scale of 0–3 for symptoms of heartburn, regurgitation, and dysphagia using a symptomatic questionnaire completed by a physician primarily interested in esophageal disease (Table 1).

The esophagus, stomach, and duodenum were visualized using the fiberoptic endoscope. When esophagitis was present the severity was scored as follows: Grade I for erythema and friable mucosa, Grade II for linear

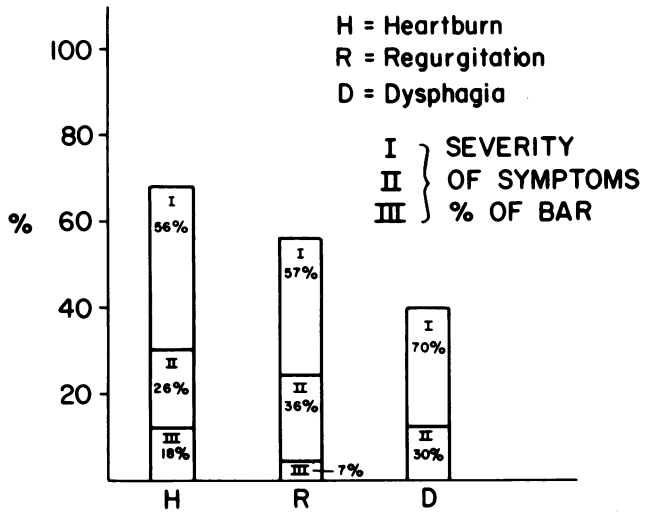


FIG. 1. Incidence and severity of esophageal symptoms in 50 patients presenting with severe chest pain and normal coronary angiography.

erosions, Grade III for ulceration and "cobblestone" deformity, and Grade IV for the presence of a fibrous stricture. The stomach mucosa was examined for the presence of florid gastritis, peptic ulceration, or tumor.

Esophageal manometry was performed using a catheter containing three intraluminal transducers set 5 cm apart in its distal end. The catheter was passed into the stomach and withdrawn in 1 cm intervals back into the esophagus and up into the pharynx. Using this technique the location, resting pressure, and degree of relaxation of the lower esophageal sphincter was measured and the presence of abnormal motility in the body of the esophagus noted. The height of the lower esophageal sphincter pressure was measured as the difference in mm of mercury between the resting inspiratory gastric pressure and the pressure at the respiratory inversion point. A motility disorder was signified by the recording of repetitive, spontaneous, simultaneous, or broad-based powerful esophageal contractions following pharyngeal swallows.

The 24-hour pH monitoring of the distal esophagus was performed using a technique previously described by two of the authors.[12] A pH electrode was placed 5 cm above the upper border of the lower esophageal sphincter located by manometry and a reference lead on the skin of the nondominant forearm using a method that assures good electrical contact. Both the pH probe and reference lead were connected via a pH meter to a strip chart recorder running at a speed of six inches per hour. A normal diet was served during the monitored period unique only in the absence of food and beverages having a pH value of less than five or more than six. All patients were requested to write on the chart recorder their subjective symptoms and their body position, that is whether upright or supine. A reflux episode was defined as a drop in the esophageal pH to less than four. Using the 24-hour pH record, the per cent time the pH was less than four in the distal esophagus was determined for the full 24 hours and for the time spent in the upright and supine positions. In addition the total number of reflux episodes, the number of episodes lasting five minutes or longer, and the length of the longest reflux episode was obtained from the tracing. The reflux status of each individual patient was assessed by calculating the 24-hour pH composite score from these six components of the pH record. A mean normal value for each component of the 24-hour pH test and the composite score was obtained from 15 control volunteers and has been previously reported.[12,13]

Results

Quality and Character of the Chest Pain

All studied patients complained a of squeezing-type chest pain with radiation to the left soulders in 26, left arm in 29, left neck in 12, and back in nine patients. The pain was documented to be induced by effort during maximum exercise electrocardiography in 20 patients. Twenty-four patients were regularly taking nitrate therapy, nine antacids, and six propranolol therapy. Six other patients were regularly taking miscellaneous combinations of drugs including minor analgesics or tranquilizers. Five patients were not on any medication. None of the patients considered their medication effective in controlling their chest pain.

On resting electrocardiogram 42 patients had S-T depression or T-wave inversion. Forty-one patients had a maximum exercise electrocardiography test, and in nine patients it was omitted because of severe S-T depression on the resting electrocardiogram and concern over a recent infarction. The test was stopped in twenty patients because of pain. In 14 of these patients the electrocardiogram was unchanged; in two, premature ventricular contractions developed, and in four, S-T segment depression occurred. In 13 patients the exercise test was discontinued because of fatigue or dyspnea. In one of these patients S-T depression occurred, and in three premature ventricular contractions developed. In five patients the exercise test was discontinued because of the development of significant S-T segment depression on the electrocardiogram without symptoms. Three patients completed the test without developing electrocardiographic changes or limiting symptoms, but because of the presence of S-T segment depression or T-wave inversion on the resting electrocardiogram and a history of persistent chest pain, a coronary angiogram was considered indicated.

Incidence of Esophageal Symptoms

Thirty-four of the 50 patients studied complained of one or more esophageal symptoms. The majority of the

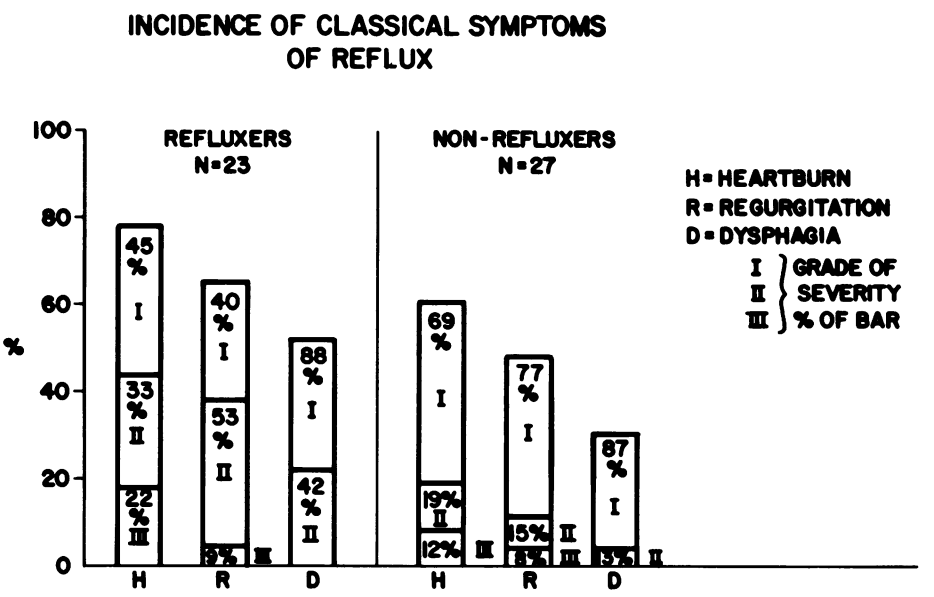


FIG. 2. Incidence and severity of esophageal symptoms in patients with reflux compared with those without based on the results of 24-hour esophageal pH monitoring. The similarity of esophageal symptoms between the two groups shows that symptoms alone are not a reliable guide to the presence of reflux.

symptoms were mild in severity and overshadowed by the patient's preoccupation with his chest pain (Fig. 1).

Relationship of Chest Pain and Esophageal Symptoms to Gastroesophageal Reflux

Based on the 24-hour esophageal pH monitoring score, 23 patients were classified as refluxers and 27 as nonrefluxers. There was no difference in the incidence and severity of the classical symptoms of gastroesophageal reflux between patients who refluxed and those who did not (Fig. 2.) Similarly, there was no difference in the quality and character of the chest pain between the two groups. Ten of the patients with reflux and ten who did not reflux had chest pain induced during exercise electrocardiography. Consumption of nitroglycerine, propranolol, and/or antacid therapy was similar for both groups. (Table 2).

Fifteen of the 23 patients who refluxed recorded symptoms during 24-hour pH monitoring. Thirteen of these patients documented the symptom of chest pain, and in 12 the onset of chest pain coincided with a reflux episode on the 24-hour pH record (Figs. 3a, b, c). Seven of these 12 patients had exercise electrocardiography, and in five, chest pain was induced of the severity that necessitated cessation of the test. Five of the 12 patients did not have an exercise test because of severe S-T segment changes on the resting electrocardiogram and concern over a possible recent infarction. The remaining two of the 15 patients with reflux who recorded symptoms during 24-hour pH monitoring documented wheezing that coincided with a reflux episode in both.

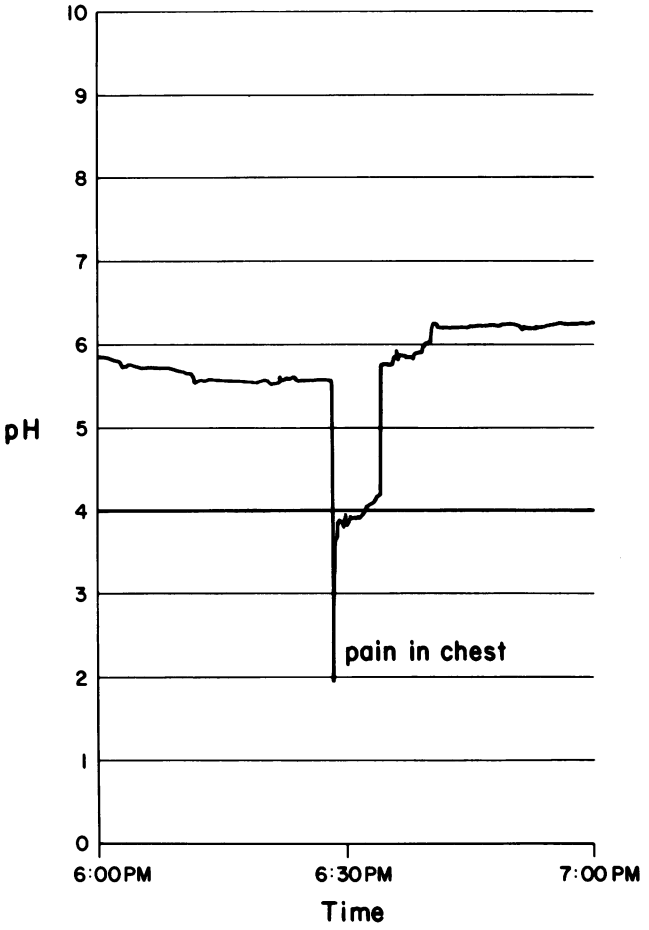
Fifteen, of the 27 patients who did not reflux, documented chest pain during 24-hour pH monitoring, and in only one did the onset of chest pain coincide with a reflux episode. None of the four patients with a mild mitral valve prolapse were found to have significant reflux, nor did their symptoms of chest pain coincide with a reflux episode. Twenty-two patients, ten with reflux and 12 without, did not experience chest pain during the monitored period.

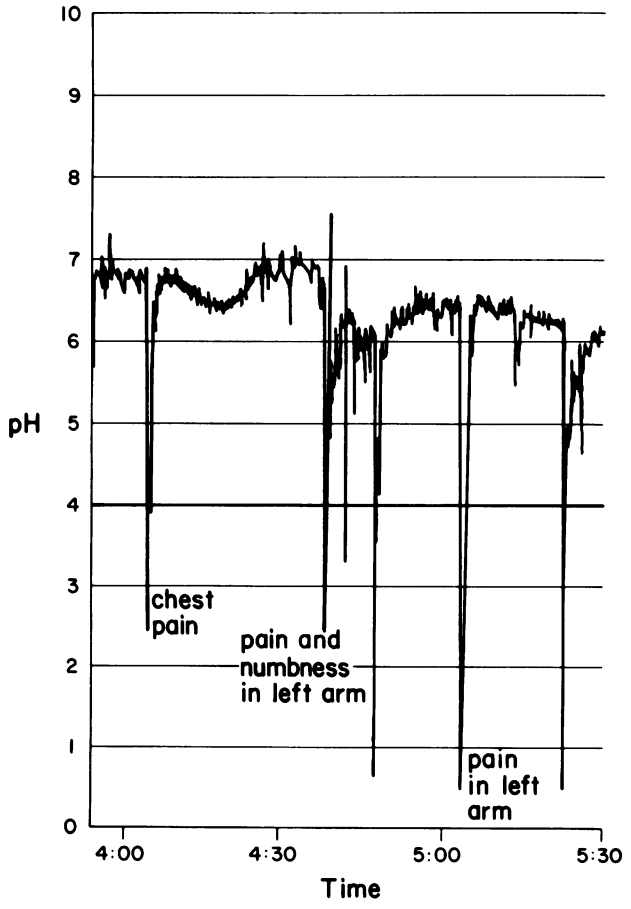
Quantitation and Pattern of Gastroesophageal Reflux

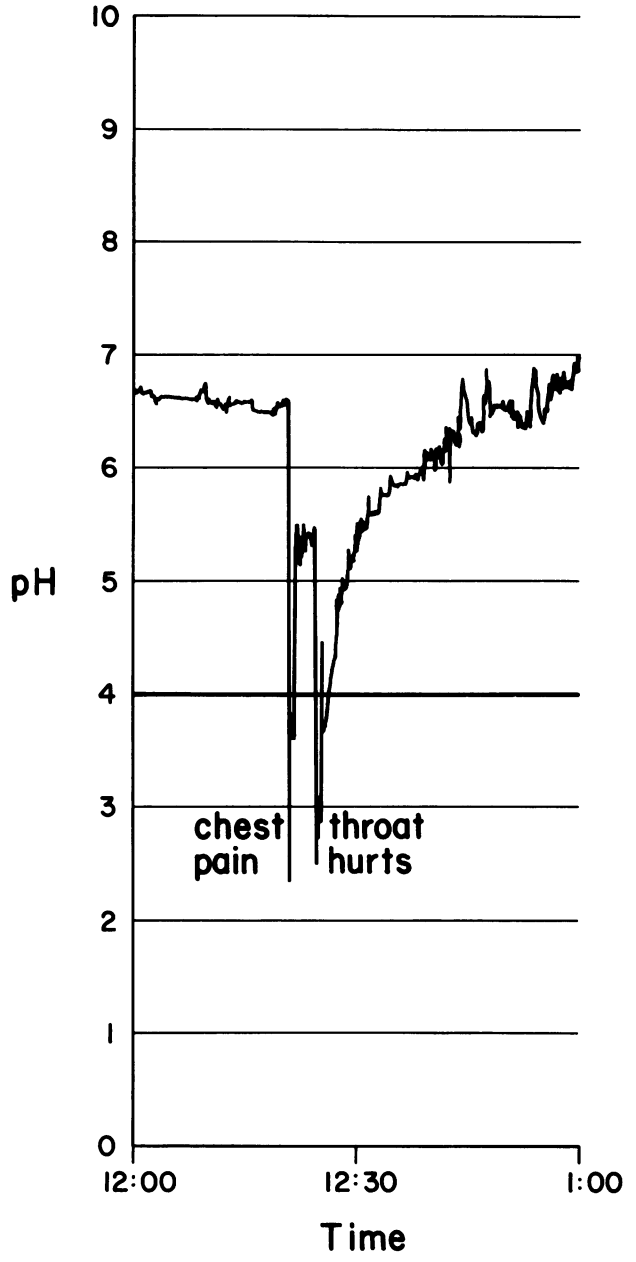
Table 3 shows that the group of patients, considered on the basis of an abnormal 24-hour esophageal pH score to be refluxing, had statistically more acid exposure to their esophagus during 24 hours than patients who did not reflux, or control subjects. Patients with abnormal gastroesophageal reflux were classified as to the patterns of reflux (*i.e.*, reflux in the upright, supine, or both positions). Fifteen patients had abnormal gastroesophageal reflux in both the upright and supine positions (bipositional refluxers). Two patients had abnormal reflux only while lying supine (supine refluxers). Six patients had reflux only while upright (upright refluxers). The number of reflux episodes greater than five minutes

TABLE 2. *Comparison of Chest Pain Between Refluxers and Nonrefluxers*

	Refluxers N = 23		Nonrefluxers N = 27	
Effort pain on stress EKG	10/19	53%	10/22	45%
Pain radiation				
Shoulder	13	57%	13	48%
Left arm	6	26%	13	48%
Neck	9	39%	3	11%
Back	4	17%	5	19%
Medication				
Antacids	4	17%	5	19%
Nitrates	12	52%	12	44%
Propranolol	2	9%	0	0%







FIGS. 3a, b, and c. Portions of a 24-hour pH tracing from three patients with reflux induced chest pain demonstrating the onset of chest pain coinciding with a reflux episode, identified by a drop in esophageal pH to below 4.

TABLE 3. *Twenty-four-hour pH Data*

Subjects	% Time pH <4			Duration of Reflux Episodes	
	Total	Upright	Supine	No. >5 Min.	Longest in Minutes
Refluxers N = 23	14.59 ± 18.46 *	17.77 ± 24 †	11.08 ± 18.3 †	8.9 ± 10.67 *	56.8 ± 87.58 †
Nonrefluxers N = 27	0.82 ± 0.72	1.2 ± 1.3	0.27 ± 0.52	0.48 ± 0.97	3.48 ± 3.68
Controls N = 15	1.5 ± 1.42	2.3 ± 0.2	0.3 ± 0.5	0.6 ± 1.2	3.89 ± 2.63

Differ from nonrefluxers and control values.

* = $P < .01$.
†* = $P < .025$.

and the duration of the longest reflux episode are measures of esophageal clearance.[14] Based on these parameters, patients who refluxed had impaired esophageal clearance compared with controls.

Esophageal manometry. The distal esophageal sphincter pressure was lower in patients who refluxed than in those who did not ($p < .01$). In the reflux group motility was normal in 15 and showed a nonspecific motility disorder in six patients. One patient had findings compatible with diffuse spasm, and another had aperistalsis of the lower half of the esophagus with a hypotensive sphincter suggesting scleroderma. In the nonreflux group motility was normal in 20 and showed a nonspecific motility disorder in seven patients. On the basis of esophageal manometry alone, only two of the 50 patients studied, one with diffuse spasm and one with scleroderma, would be suspected to have an esophageal abnormality as the cause of their chest pain. (Table 4).

Radiographic and endoscopic findings. Seven patients had a previous cholecystectomy, four of whom were refluxers. In the remaining 43 patients all cholecystograms were normal. Of the 23 patients who refluxed, nine had normal upper G.I. barium studies. One patient had radiographic reflux without evidence of a hiatal hernia, and two others had tertiary waves without evidence of a hiatal hernia. Eleven of the 23 patients had a radiographic hiatal hernia, four of whom had radiographic reflux, three tertiary waves, and two a Schatzky's ring. In the 27 patients who did not reflux the barium examination was normal in 21, showed a mid-esophageal diverticulum in two and a hiatal hernia in four. The latter was associated with tertiary waves in one patient and radiographic reflux in one patient.

Endoscopy was performed only in the patients with documented reflux. Equivocal Grade I esophagitis was present in nine patients. Four patients had an endoscopic hiatal hernia: three without esophagitis, and one with esophagitis and a patulous cardia. Three patients had a patulous cardia without any other abnormality.

Therapy of Reflux Induced Angina-Type Chest Pain

As stated previously, 12 patients who refluxed were documented on 24-hour pH monitoring to have the onset of angina-type chest pain coincide with an episode of gastroesophageal reflux. Eight of these patients had relief of this symptom following surgery, and four responded well to medical therapy.

The remaining 11 patients with reflux were unable to document the experience of chest pain during the monitored period. In these patients the complaint of chest pain was relieved by surgery in two and medical therapy in three. In one patient, the chest pain was initially relieved by surgery but reoccurred after a breakdown of a Nissen fundoplication confirmed roentgenographically by 24-hour pH monitoring. In five patients medical therapy has failed to control both the chest pain and esophageal symptoms.

All together, 11 of the patients who refluxed were treated surgically (Fig. 4). Ten had a Nissen antireflux procedure and one an esophagomyotomy with a Belsey antireflux operation. In all of the patients, the symptom of chest pain was clinically identical to angina pectoris and indistinguishable from the chest pain that occurred in the other studied patients. Eight of the surgically treated patients had the onset of chest pain coincide with a documented reflux episode on 24-hour pH monitoring, and of these, seven developed effort pain on exercise electrocardiography. All 11 patients have been followed for two to three years. Ten patients have remained totally free from chest pain without medication. Two patients have had complication secondary to surgery, and repeat studies showed a positive 24-hour pH test in one, implicating a failure of the antireflux procedure as the cause for the single chest pain recurrence. The other

TABLE 4. *Manometric Data*

	DES Pressure mmHg	Motility	Number of Patients
Refluxers N = 23	9.4 ± 5.2	Nonspecific abn.	6
		Diffuse spasm	1
		Scleroderma	1
		Normal	15
Nonrefluxers N = 27	13.3 ± 5.4	Nonspecific abn.	7
		Normal	20
	$P < .01$		

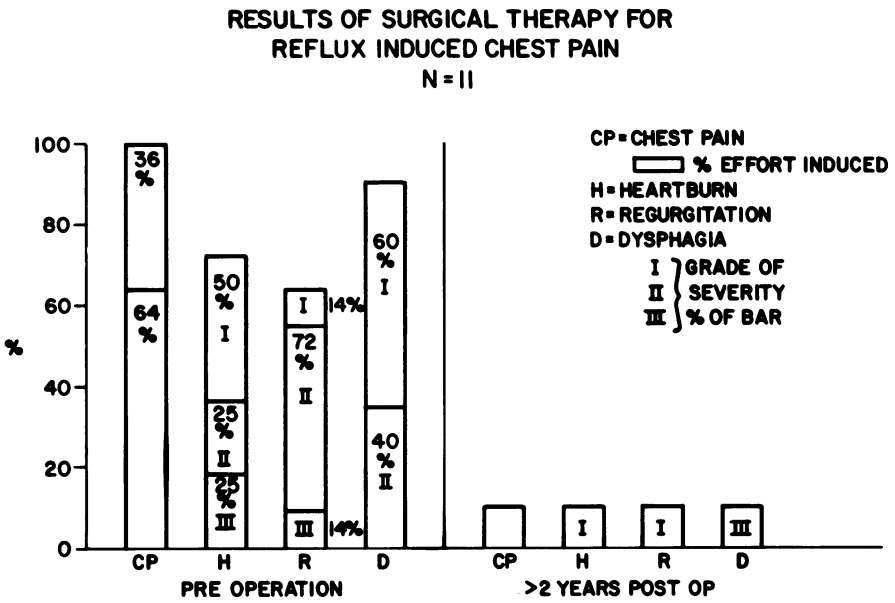


FIG. 4. Preoperative and postoperative symptomatic evaluation of patients following surgical therapy for reflux induced chest pain. See text for detailed explanation.

patient suffered from severe postoperative dysphagia necessitating a distal esophageal resection and a colon interposition. She is currently free of her dysphagia.

All together, 12 of the patients who refluxed were treated medically with antacids, cimetidine, and postural and dietary instructions (Fig. 5). As with the surgically treated group, the symptom of chest pain was clinically identical to angina pectoris and indistinguishable from other patients in the study. Four of the medically treated patients had the onset of chest pain coincide with a documented reflux episode on 24-hour pH monitoring, and none were tested for exercise induced pain because of severe changes on the resting electrocardiogram and concern over a recent infarction. All 12 patients have been followed for two to three years. Seven patients have remained free from their chest pain when taking their medication, but two of the seven continue to have esophageal symptoms. Five patients continue to complain of chest pain and esophageal symptoms despite intensive medical therapy.

Discussion

Since the introduction of coronary angiography a syndrome of angina-type chest pain with abnormal resting or exercise electrocardiography in the presence of normal coronary arteriography has been well documented. Most studies, including the authors', have noted a female preponderance, persistence of symptoms with functional disability, and continued use of nitrate and/or antacid therapy with a variable symptomatic response.

In order to establish that esophageal disease causes angina-type chest pain, four criteria must be fulfilled: (1) the patient must have symptoms typical of angina pectoris, (2) a cardiac basis for symptoms must be excluded, (3) a cause and effect relationship between episodes of chest pain and the esophageal abnormality should be established, and (4) the correction of the esophageal abnormality should result in relief from the chest pain.

All patients selected for this study gave a history of retrosternal squeezing-type chest pain that radiated either to the shoulder, left arm, or both, and when assessed by two physicians interested in cardiac disease, was considered identical to angina pectoris. Like angina, the pain was documented to occur during exercise electrocardiography in 20 patients. The observation that 30 patients were already on nitrate or propranolol therapy and only nine were regularly taking antacids indicates that in the majority of the patients, the attending physician thought the cause of the chest pain was cardiac.

A cardiac origin of the chest pain, caused by abnormal oxyhemoglobin dissociation curves, small vessel disease, coronary artery spasm, misinterpretation of arteriograms, or cardiomyopathy, has been suggested but has not been established. In this study patients with cardiomegaly, hypertension, and elevated left ventricular end diastolic pressure were excluded. Four patients with angiographic and echocardiographic evidence of mild mitral valve prolapse were not excluded from the study since the physicians involved had held the opinion that this lesion was rarely symptomatic, and an esophageal etiology for the chest pain was possible. All four patients had negative 24-hour pH tests, and an esophageal basis for symptoms could not be established. It seems then that these patients had a cardiac cause for their angina.

Myocardial lactate production has been noted in 20–

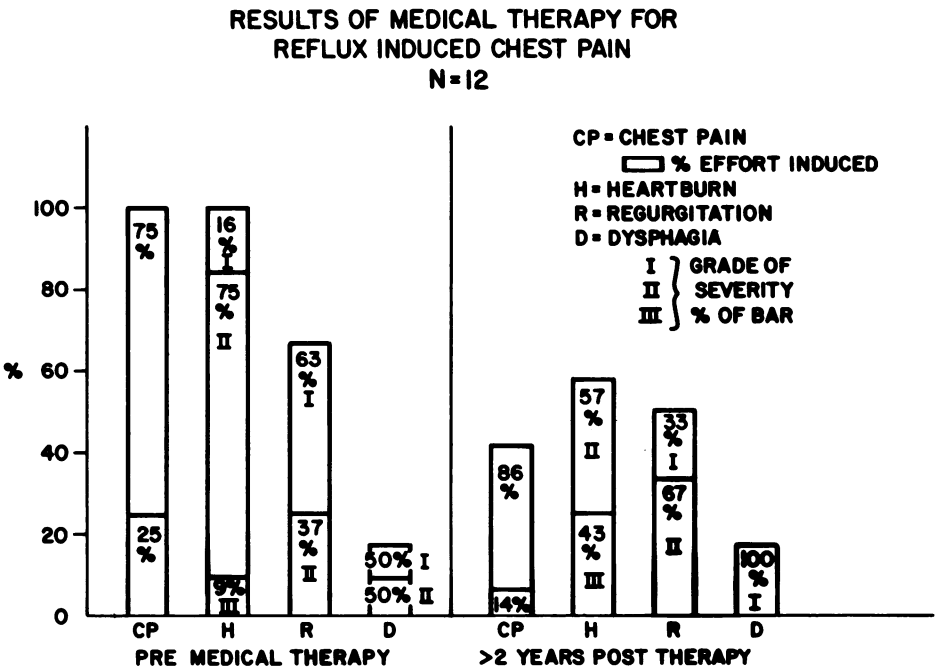


FIG. 5. Symptomatic evaluation before and after medical therapy for reflux induced chest pain. See text for detailed explanation.

30% of patients with angina-type chest pain and normal coronary arteriography. Such patients are thought to have pain of ischemic origin secondary to coronary artery spasm. In the present study an attempt was made to exclude coronary artery spasm, in that all patients with normal coronary angiography and cardiac function had immediate repeat coronary cineangiography with ergotamine provocation. It seems reasonable to conclude then that a cardiac basis for pain could not be established in the majority of the patients studied.

To establish that the complaint of chest pain is related to an esophageal disorder requires that the onset of a typical attack of chest pain coincides with an observed manometric abnormality[1] or a reflux episode[13], and that the chest pain is relieved by a specific therapy directed toward the esophageal abnormality. None of the patients in our study complained of pain during manometric evaluation of the esophagus. Eight of the patients had the onset of chest pain coincided with a documented reflux episode, and all had total relief of all chest pain following antireflux surgery. An additional four patients with a similar correlation between their chest pain and a recorded reflux episode received complete symptomatic relief with medical antacid therapy. On the basis of these observations, a strong argument can be made to implicate gastroesophageal reflux as the cause of the chest pain experienced by these patients.

In the other eleven reflux patients a less definitive conclusion must be made since they were asymptomatic during the monitored period and had a normal esophageal manometry and endoscopy. Yet five of these patients reported relief from their presenting complaint of chest pain, two after an antireflux procedure and three with medical antacid therapy. It seems reasonable to assume that this pain was also of esophageal origin. The eight remaining patients continue to have pain, one after a known failure of a surgical antireflux procedure and seven while receiving medical antacid therapy. All continue to have mild esophageal symptoms of reflux as well, suggesting inadequate therapy rather than another etiology, as the cause for their continued episodes of chest pain.

Twenty-seven patients had a normal 24-hour pH test. Four of these patients had mild, mitral valve prolapse which may explain their chest pain. In only one of the remaining 23 patients could it be said that the pain was esophageal in origin since the symptoms correlated with a physiologic reflux episode. The significance of the nonspecific motility disorders recorded in seven of these patients during manometry is unclear since these are frequently seen in patients over 50 years of age who are otherwise asymptomatic.

Of interest in this study was the observation that chest pain was frequently induced with effort and was documented during exercise electrocardiography in 49% of the patients who had the study. Although it is understandable that an incompetent cardia would allow gastroesophageal reflux during exercise and at rest, the question arises, would exercise-induced reflux occur through a competent cardia and be responsible for chest pain in patients who otherwise did not reflux during periods of inactivity. Using radioisotope methods the authors studied a patient in whom reflux could not be induced at rest by postural maneuvers or by abdominal

belt compression. After exercise, reflux was clearly measurable within the esophagus. This suggests that exercise-induced reflux may be the trigger mechanism for pain in some of the patients who did not reflux when relatively inactive during 24-hour esophageal pH monitoring. Stimulated by this observation the authors have monitored esophageal pH in eight patients during exercise electrocardiography and have documented reflux occuring during the test in three. One of these patients was normal and the other two were abnormal on subsequent 24-hour esophageal pH monitoring at rest. Continued study is warranted in this area to clarify the influence of exercise on esophageal function and to determine if it can induce chest pain of an esophageal origin.

The angina-type chest pain of esophageal origin is theoretically caused by reflux-induced, esophageal muscle spasm causing wall ischemia. That such a mechanism is possible is supported by the occasional ability to measure episodes of sustained luminal pressures in excess of 200 mmHg during esophageal manometry. Such pressures are sufficient to interrupt arteriolar flow and cause temporary ischemia of the segment of esophageal wall involved. Furthermore the pain is frequently relieved by nitroglycerine therapy,[15] as would be suspected if the ischemic theory were true. In addition, acid-induced, esophageal spasm has been well documented during spontaneous reflux episodes[16] or during acid perfusion of the esophagus.[17] All of these observations support the ischemic theory, but why the esophageal response to acidification is spastic in some patients while in others this rarely occurs, is not, at present, clear.

It is not surprising that esophageal spasm causes pain in a cardiac distribution. Certainly, similar type pain is frequently seen in patients with diffuse spasm or vigorous achalasia.[18] Kramer et al., when studying esophageal sensation, found that balloon distension of the mid esophagus caused retrosternal chest pain that frequently radiated to the shoulder or arms and could not be differentiated from angina by seven of 22 patients with angina pectoris of cardiac origin.[19] The similar distribution of esophageal and myocardial pain is presumably caused by the sharing of a common sensory pathway since both organs have a common innervation.

In this study there was a high incidence of pure upright refluxers (6/23 or 26%) when compared with the 11% incidence in the populations referred because of primarily esophageal pathology.[20] In previous studies the authors have reported that upright reflux is associated with excessive aerophagia, irritable colon syndrome, and rapid gastric emptying, but is rarely associated with esophagitis.[14] These patients frequently have a severe gas-bloat syndrome after antireflux repair, and consequently, the authors persist with medical therapy in such patients even though the symptomatic response is variable.[20] Despite this philosophy, five of the patients with pure upright reflux in this study had surgical therapy, and the two complications, *i.e.*, breakdown of a repair and severe postoperative dysphagia, occurred in these patients. Only one of the upright refluxers received medical therapy and responded well. This experience has served to confirm the authors' thoughts about nonoperative therapy for upright refluxers.

Opinions vary as to the best method of separating pain of cardiac from that of esophageal origin. This is particularly important in that a physician skilled in the diagnosis of esophageal abnormalities can detect esophageal symptoms in 60 to 80% of patients. Others less skilled are overcome by the patient's focus on their chest pain, and the less important esophageal symptoms go unnoticed. Even if esophageal symptoms are appreciated, a problem develops as to whether they are caused by reflux or a motility abnormality and whether the esophagus is the origin of the chest pain. Many of the previous studies made of this problem have been retrospective in design and relied upon barium studies or endoscopy to detect the presence of esophageal disease.[20] Such investigative methods, while relevant, are insensitive and have a poor correlation with the patient's reflux status. Twenty-four-hour pH monitoring of the esophagus is particularly useful in this regard because it is known to have a high sensitivity in detecting reflux in patients with esophagitis, a high specificity in excluding pathologic reflux in normals,[21] and allows objective timing of a patient's complaints with the occurrence of a reflux episode.[20] The physician can therefore be confident that reflux is indeed present and is effecting the chest pain if the occurrence of the symptom coincides with a reflux episode.

The absence of a correlation between chest pain and a reflux episode excludes gastroesophageal reflux as an etiology, but the pain may still be of esophageal origin if the symptoms occur during a recorded motility abnormality on a standard esophageal manometry study. This chance occurrence is unlikely in the majority of the patients studied because of the shortness of the observation period. Until prolonged esophageal manometry becomes technically convenient, the diagnosis of chest pain related to manometric abnormalities will be hampered. Indeed, in only two of the 50 patients studied was a specific motor disorder uncovered. If this was the only test done, then just one of the 50 patients would be suspected of having chest pain from an esophageal origin. As it turned out, both of the patients with a specific motility abnormality were refluxing as well, and, as a consequence, it is difficult to exclude reflux as the underlying cause of the patient's chest pain.

It is possible that the patient will not experience an

episode of chest pain during the monitored period as occurred in 22 of the patients in the present study. In this situation the reflux status of the patient can be determined, but no conclusion can be drawn concerning the relationship of the chest pain to a reflux episode other than the probability that it is unrelated if the patient does not have reflux. The authors have found that monitoring for a more prolonged period or during exercise can be helpful in this situation. Recently, the development of a portable esophageal pH monitoring device has made the monitoring of outpatients possible. It is hoped that such equipment that can monitor the patient during activities of daily living will help to clarify the etiology of effort precipitated chest pain.

The clinical situation becomes more difficult to sort out in patients with both conditions, *i.e.*, sufficient coronary artery pathology to account for ischemic chest pain and abnormal reflux on 24-hour esophageal pH monitoring. In this situation the chest pain may be caused by reflux, myocardial ischemia, or both. Treatment of the angina with long-acting nitrates can reduce the distal esophageal sphincter pressure and make the reflux worse. If this is not recognized, the reported increased incidence of chest pain, or a worsening in the severity of the chest pain, can be interpreted as a medical failure to control the angina and initiate a recommendation for coronary bypass surgery. The subsequent failure of surgery to give complete symptomatic improvement under these conditions is often accredited to inadequate revascularization until it is recognized that the patient has another disease. Esophageal evaluation should be performed in any patient who does not have a satisfactory explanation for persistent postoperative symptoms after coronary artery bypass. If possible, both abnormalities should be recognized before operation and a combined procedure performed.

This study suggests that determining the reflux status of the patient with chest pain and normal coronary angiography can uncover a treatable etiology about 50% of the time. In the present study fifteen such patients had total abolition of their chest pain and esophageal symptoms by either surgical or medical therapy. Of the remaining eight patients, seven were treated medically, and their response to antacid therapy was variable. Whether this represents a true failure of medical therapy to control reflux, or excludes an esophageal origin for the pain, cannot be determined until the response to antireflux surgery has been evaluated in these patients. It is probable that medical therapy, since it is administered intermittently and designed to alleviate symptoms rather than correct the underlying abnormality, may not be as effective as surgery in providing constant protection against reflux and its consequences during the activities of daily living.

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Discussion

DR. HIRAM C. POLK, JR. (Louisville, Kentucky): Those of us who see patients with complicated esophageal problems are seeing a steady trickle of patients who are precisely characterized by the signs and symptoms that Dr. DeMeester has talked about. Very often, they will have been worked up in detail, and have all the usual tests indicating