Prevalence of Esophageal Disorders in Patients With Chest Pain Newly Referred to the Cardiologist*

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**Study objective:** The prevalence of esophageal disorders (dysmotility and/or gastroesophageal reflux) in patients with chest pain newly referred to a cardiologic clinic is unknown. The aims of our study were to investigate the prevalence of esophageal abnormalities in these patients and to assess the value of medical history in predicting the origin of the patient’s chest pain.

**Design:** We evaluated 28 consecutive patients who were newly referred to the cardiologist because of angina-like chest pain. Patients with evidence of severe myocardial ischemia were excluded. Cardiologic evaluation included medical history, physical examination, ECG, and exercise testing; further cardiologic workup was carried out only when considered necessary. Gastroenterologic evaluation consisted of medical history, esophageal manometry, endoscopy, and 24-h ambulatory monitoring of esophageal pH and pressure.

**Measurements and results:** In five patients a diagnosis of ischemic coronary artery disease was made. In only two of these five patients, the cardiologic history strongly suggested a cardiac origin of the pain. Twelve patients had a pathologic 24-h pH profile, four of whom also had reflux esophagitis. Ten patients had symptomatic reflux. In only three of these ten patients, the history was judged to be indicative of an esophageal origin of the chest pain. No motility disorders were found.

**Conclusions:** Thirty-six percent of the patients with chest pain newly referred to a cardiologic outpatient clinic have symptomatic gastroesophageal reflux. Neither cardiologic nor gastroenterologic history data have a high predictive value with respect to the origin of the chest pain.

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**Key words:** esophageal monitoring; gastroesophageal reflux disease; noncardiac chest pain

**Abbreviations:** GER=gastroesophageal reflux; GERD=gastroesophageal reflux disease; LES=lower esophageal sphincter; SAP=symptom association probability; SI=symptom index

Most patients with angina-like chest pain consult a cardiologist to have a cardiac origin of the pain identified and treated. However, angina-like retrosternal chest pain is not always caused by cardiac disease.

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Esophageal motility abnormalities and gastroesophageal reflux (GER) are likely to play an etiologic role in those patients in whom cardiac disease has been excluded.

These esophageal abnormalities can be detected by endoscopy, manometry, 24-h ambulatory esophageal monitoring, and provocation tests. Since 1986, many studies on esophageal monitoring in patients with noncardiac chest pain were reported. The proportion of patients in whom a correlation was found between esophageal abnormalities and pain varied from 10 to 90%, differences in yield depending on differences in patient selection and diagnostic criteria.

Until now, most studies have been performed in patients referred to the gastroenterologist in a late phase of the diagnostic pathway, after a cardiac origin of the symptoms had been excluded.

In a recent study by Lam et al., patients were studied in an early phase of the diagnostic pathway, ie, within 1 h after admission to a coronary care unit with acute chest pain. In 27 of 30 patients (90%) in whom cardiac ischemia was excluded, one or more chest pain events without ECG changes were found to be correlated with an esophageal abnormality.

We hypothesized that the prevalence of an esophageal abnormality in unselected patients who were referred for the first time to the cardiologic outpatient clinic of a large general hospital because of angina-like
chest pain could also be substantial. If this hypothesis would be correct, this could have implications for the “standard” workup of these patients.

Therefore, the first aim of this study was to investigate the prevalence of esophageal abnormalities in a very early phase in the diagnostic workup of patients referred for the first time to the cardiology department of our hospital because of angina-like chest pain, immediately after life-threatening cardiac ischemia was excluded. The secondary aim of our study was to assess the value of medical history in predicting the origin of the patient’s chest pain.

**Materials and Methods**

We studied 30 consecutive patients with angina-like chest pain who had been newly referred to the outpatient cardiology department of our hospital. The patients were 16 men and 14 women, with a median age of 53 years (range, 33 to 69 years). Patients with severe cardiac ischemia, congestive heart failure, previous cardiology history, thoracic trauma, or thoracic surgery were excluded. Patients with known esophageal or gastric disorders or surgery were also excluded. The study protocol was approved by the medical ethics committee of our hospital. All patients gave written informed consent.

In all patients, the cardiology history was taken by one and the same investigator (M.J.C.). The incidence, duration, severity and character of the chest pain, and its relation to exercise, emotion, and temperature changes were assessed. In addition, the frequency of occurrence and the severity of the symptoms orthopnea, dyspnea, and palpitations were assessed. Furthermore, use of medication and the existence of cardiovascular risk factors were evaluated. Based on these history data, the probability of a cardiac origin of the patient’s chest pain was scored on a scale ranging from 1 to 5 (1=very low, 2=low, 3=indifferent, 4=probable, 5=highly probable). Further cardiology workup consisted of bicycle exercise testing. Additional evaluation such as cardiac ultrasound, myocardial perfusion scintigraphy, or coronary angiography was carried out only when considered necessary by the patient’s cardiologist.

Within 3 days after the first visit to the cardiologist, the gastroenterologic history was taken in all patients. All patients were interviewed by one and the same investigator (J.H.V.). The incidence, duration, severity and character of the chest pain, and its relation to exercise, emotion, and consumption of meals and/or beverages were assessed. In addition, the frequency of occurrence and the severity of the symptoms heartburn, regurgitation, dysphagia for solid and/or liquid food, and odynophagia were assessed. Furthermore, the patient’s actions to relieve the symptoms (ie, rest, change of position, eating or drinking, and the use of antacids) were assessed. The interviewer then scored the probability of an esophageal origin of the patient’s symptoms on a scale ranging from 1 to 5 (low to high).

Immediately after the interview, esophageal manometry, upper GI endoscopy and 24-h ambulatory esophageal pH and pressure monitoring were performed. At least 72 h before esophageal manometry and 24-h ambulatory monitoring, treatment with any medication that could interfere with acid secretion or esophageal motility was stopped. A low-compliance perfusion pump with a three-lumen catheter with openings 5 cm apart and oriented in three different directions was used for conventional manometry. The lower esophageal sphincter (LES) was localized by the stationary pull-through method. Thereafter, the catheter was placed with the distal opening 5 cm above the upper border of the LES and ten wet swallows were given, 20 to 30 s apart. Amplitude, duration, and propagation of contractions at 5, 10, and 15 cm above the LES were assessed.

A video endoscopic system (Pentax) was used for esophageal endoscopy. Reflux esophagitis was described according to the Savary-Miller grading system (grades I through IV). Directly afterwards, a 24-h ambulatory pressure and pH recording system was installed. Intraesophageal pH was recorded with a glass electrode with incorporated reference (Ingold AG; Uerdingen, Switzerland). Intraesophageal pressure was recorded using a 5F polyurethane pressure catheter with three pressure sensors 5 cm apart (Sentron 205; Sentron; Roden, the Netherlands). The pH electrode and the distal pressure transducer were positioned 5 cm above the upper border of the LES. The signals were recorded with a digital portable data logger (UPS 2020 GS; MMS; Enschede, the Netherlands).

The three pressure signals were sampled at a rate of 4 Hz and the pH signal was sampled at a rate of 0.2 Hz. The data logger used allows the recording of five marker signals, of which only one was used, to indicate the episodes of chest pain.

During the 24-h monitoring, periods of eating and drinking and periods spent in the supine position were registered by the patient in a diary. Episodes of chest pain were registered by pushing the event marker and writing down the time, nature, and characteristics of the symptoms.

When the 24-h study period was ended, the recorded data were transferred to the computer, stored on a floppy disk, and analyzed in a fully automatic way using previously validated algorithms.7

Esophageal acid exposure was calculated for the upright and supine positions separately and for the total time of registration. GER disease (GERD) was diagnosed when the percentage of time of pH below 4 exceeded the upper limit (95th percentile) of normal, according to the criteria proposed by Richter et al.8 pH less than 4, percent upright—8.15; pH less than 4, percent supine—3.45; and pH less than 4, percent total—5.78.

In patients experiencing pain during the recording, an additional computerized analysis of the symptom episode was done using a 2-min window starting 2 min before pain onset and ending at the onset of pain.9 In the analysis of motility disorders, the patient’s symptom-free episodes were used as his or her own control. In the analysis of reflux, a symptom episode was considered to be associated with reflux when a pH drop of more than 1 U occurred within 5 s, or when the pH fell below 4, or when both criteria were met during that episode. This computerized analysis of the symptom episode was published in detail elsewhere.5 The last step in the analysis consisted of the calculation of the symptom index (SI) for abnormal motility, and the symptom association probability (SAP) for reflux. The SI was calculated according to Wiener et al.10 A patient was considered to have a positive correlation between his or her pain and motor abnormality when the SI was more than 50%. The SAP was calculated as described by Weusten et al.11 The SAP expresses the strength of the association between symptoms and reflux episodes taking all relevant variables (number of reflux episodes, number of symptom episodes, number of associated symptom episodes) into account. A patient was considered to have a positive correlation between his or her pain and reflux when the SAP was 95% or greater.

Therapy with acid-secretion inhibitors (omeprazole, 40 mg daily) was started when the diagnosis of GERD, with or without reflux esophagitis, was made. A patient was considered to suffer from symptomatic GERD when there was a relief in chest pain after initiating therapy. Finally, the chest pain of all patients was classified as cardiac (as proved by exercise test, scintigraphy, coronary angiography, or myocardial event), esophageal (as proved by a positive SI for dysmotility, a SAP of 95% or greater, and/or relief in chest pain after initiating therapy in patients with GERD), cardiac and esophageal, or unidentified (noncardiac, nonesophageal) in origin.

Obviously, we performed a “routine” cardiology workup compared with a more extensive gastroenterologic investigation. This was done to prove our hypothesis that the prevalence of esophageal disorders in angina-like chest pain is substantial.

The statistical significance of differences in history scores be-
The median time interval between the first visit to the cardiologist and gastroenterologic evaluation was 3 days (range, 1 to 20 days). The gastroenterologic assessment of all 25 patients is described in Table 1. In all patients, baseline esophageal manometric findings were within normal limits. At endoscopy, four patients were found to have a grade I reflux esophagitis (Savary-Miller). One of these patients also had Barrett’s metaplasia. Seven patients had a sliding hiatal hernia. Eighteen patients had no abnormalities.

As can be seen in Table 1, five patients suffered from severe ischemic coronary artery disease (proved by scintigraphy and/or coronary angiography; one patient had a myocardial infarction during ambulatory esophageal monitoring). In only two of these five patients, the history was considered highly indicative of a cardiac origin of the chest pain (score 4 to 5). In only three of the seven patients with a cardiologic history score of 4 to 5, the chest pain was eventually diagnosed as cardiac (Fig 1). The cardiologic follow-up period of all patients was at least 6 months.
patients tolerated the 24-h monitoring procedure well. Twelve of the 28 patients showed pathologic GER during pH monitoring; 4 of these had reflux esophagitis, the other 8 had no abnormalities at endoscopy. Ten of the 12 patients with pathologic reflux (including all patients with reflux esophagitis) were treated with omeprazole shortly after the 24-h monitoring. Nine patients were free of chest pain thereafter. Two of these patients were not treated with acid inhibition: one patient was already free of symptoms with beta-blocking medication, and one patient developed a myocardial infarction during 24-h esophageal monitoring.

Eleven patients experienced one or more periods of pain during ambulatory monitoring of esophageal pH and pressure. In four of these patients, the pain episodes and GER were associated, as reflected by a positive SAP. There were no motility-related pain episodes during 24-h pressure monitoring in any of the 28 patients. Based on the symptom relief upon acid inhibition, in nine patients the chest pain was considered to be due to pathologic reflux.

In only three of the ten patients with symptomatic reflux, the interviewing gastroenterologist classified the history as highly indicative of an esophageal origin of the chest pain (score 4 to 5). In only three of the six patients with a gastroenterologic history score of 4 or 5, the chest pain was finally diagnosed as esophageal (Fig 2). The history score for an esophageal origin was not significantly higher in patients finally diagnosed as having esophageal chest pain than in the patients diagnosed otherwise (Wilcoxon test, p=0.18).

In 2 of the 28 patients, a combination of both symptomatic cardiac and esophageal abnormalities was found.

**Discussion**

It has long been recognized that the differential diagnosis of retrosternal chest pain can create difficulties. The “classic” symptoms of angina pectoris can also be found in patients with esophageal causes of retrosternal chest pain. This can be explained by the fact that the esophagus and the heart have a similar innervation. Based on history only, it is difficult to distinguish between cardiac and esophageal abnormalities.\(^\text{12,13}\)

In our study, the medical history was taken by a cardiologist and a gastroenterologist separately. Based on history alone, the probability of either a cardiac or an esophageal origin of the patient’s chest pain was assessed. The results were astonishing: in only 40% (two of five) of the patients with severe ischemic coronary artery disease the probability of a cardiac origin of the chest pain was scored as “high” (score 4 to 5). In only 37% (three of eight) of the patients with esophageal abnormalities the esophageal cause of the chest pain was predicted correctly on the basis of the history.

All patients in our study were newly referred, by their general practitioner, with angina-like chest pain to the outpatient cardiologic department. These patients represent a large proportion of the patients seen in daily practice. The results of our study confirm the notion that medical history often provides insufficient information to allow reliable differentiation between cardiac and esophageal causes and that further diagnostic workup is always necessary. Common clinical practice is that gastroenterologic evaluation is started only after a cardiac origin of the symptoms has been excluded beyond reasonable doubt, requiring extensive cardiologic workup in some cases.

To our knowledge, this study is the first in which gastroenterologic evaluation was performed in a very early phase in the routine diagnostic workup of outpatients with angina-like chest pain referred to a cardiologic department. We would like to stress the fact...
that our study was deliberately meant not to interfere with normal daily practice in the cardiologic workup. Therefore, the cardiologic evaluation ended when the cardiologist believed there was sufficient proof for the diagnosis. To perform a coronary angiography in every patient would, in our opinion, not have been ethical. However, this approach might have led to a slight underestimation of the number of patients with cardiac and overlapping cardiac/esophageal problems.

The results show that in a population of patients with chest pain, the prevalence of reflux-related disease is high: 43% (12 of 28) of the patients showed pathologic reflux during 24-h ambulatory pH monitoring. In 36% (10 of 28), the reflux was symptomatic, as proved by a relief of symptoms after acid inhibition (omeprazole) or an SAP of 95% or more.

In this study, only 39% (11 of 28) of the patients experienced symptoms during the 24-h esophageal monitoring. This finding limits the value of the analysis of the association between symptoms and reflux. Therefore, we considered the chest pain also to be reflux related in case of symptom relief after acid inhibition.

The results of this study indicate that it is both feasible and worthwhile to perform a diagnostic workup for esophageal causes of chest pain in patients newly referred with angina-like chest pain to a cardiologic department. In our study population, the prevalence of reflux-related disease was high (43%). Therefore, the combination of endoscopy and 24-h ambulatory pH monitoring is probably the most cost-effective approach in this condition. One could argue that endoscopy did not contribute to the final outcome, since all four patients with esophagitis had pathologic reflux and symptom relief with omeprazole. However, it is well known that esophagitis, pathologic reflux, and symptomatic response to treatment do not correlate perfectly. Furthermore, endoscopy serves to exclude other esophageal causes of chest pain, such as a tumor. Therefore, we believe that endoscopy is a mandatory part of the workup in these patients.

The prevalence of motility disorders in patients with noncardiac chest pain is notoriously low. The prevalence in our study (0%) confirms this low prevalence. This result is in contrast to the study by Lam et al. who found similar prevalences of motility disorders and reflux in a group of patients who were admitted to a coronary care unit because of chest pain. Possibly, part of the motility disorders observed were secondary to the stress of the coronary care unit admission. The discrepancy might also be explained by the difference in time interval between first presentation and esophageal evaluation; in the study by Lam et al., the evaluation was performed within 1 h after hospital admission, whereas in our study, this period varied between 1 and 20 days. The fact that Lam et al. also found a substantially higher prevalence of pain episodes during registration supports the latter hypothesis.

Based on the low prevalence of motility disorders, we conclude that conventional manometry does not contribute much to the diagnostic workup. However, conventional manometry is the best technique to localize the upper border of the LES.

In this study, possible or definite signs of coronary artery disease were ultimately diagnosed only in the group of patients with either abnormal or nonconclusive results of the exercise test. Therefore, we propose that the diagnostic search for an esophageal cause should begin early in patients with chest pain who have relatively normal resting ECG, normal results of cardiac enzyme tests, and a normal result of an exercise test.

References