Investigation of non-cardiac chest pain — which oesophageal test?

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SUMMARY

Five different tests were used to evaluate oesophageal function in 22 patients who presented to a cardiac unit with acute chest pain but whose cardiological investigations were negative. Eight patients had an abnormality on oesophagoscopy, 10 had an abnormal pH monitoring study, six had a positive acid infusion test, 10 had an abnormal manometric study and six had an abnormal oesophageal transit scintiscan. Concordance for the three tests of gastro-oesophageal reflux disease was low at 28%, and for the two tests of oesophageal motility only 55%. Only two patients had normal results in all five tests.

INTRODUCTION

Patients with typical angina pectoris but without demonstrable ischaemic heart disease are a small but important problem in a specialist cardiology unit, and may be more frequent in general medical practice. Between 10% and 30% of patients investigated because of chest pain appear to be free of ischaemic heart disease.\(^1\)\(^-\)\(^3\) Suggested cardiac reasons for their pain include coronary artery spasm, occult cardiomyopathy, myocardial bridging, small vessel disease of the myocardium, oxyhaemoglobin dissociation defects, or misinterpreted investigations.\(^4\)\(^-\)\(^5\) Follow-up studies of these patients indicate a uniformly good cardiac prognosis,\(^6\)\(^-\)\(^8\) and it is attractive to consider, therefore, that the cause of their pain lies outside the heart. Since the heart and oesophagus have a common sensory innervation, it is not surprising that pain from either organ is similar in nature and location.\(^9\)\(^,\)\(^10\)

Several reports have shown a high prevalence of gastro-oesophageal reflux,\(^2\)\(^,\)\(^9\)\(^,\)\(^11\) or oesophageal dysmotility\(^11\)\(^-\)\(^15\) in patients with 'non-cardiac' chest pain. We have
used five of the many techniques currently available to seek oesophageal abnormalities in a group of patients with no demonstrable cardiac disease who presented with typical anginal pain to the cardiac unit. We have compared the yield of oesophageal abnormalities detected by the different tests in an attempt to determine a practical approach to the investigation of these patients.

PATIENTS AND METHODS

Over a 30-month period, 22 patients were identified as having non-cardiac chest pain. There were nine men, 13 women, age range 39 to 67 years (mean 51.3 years). All had presented acutely to the cardiac unit with pain typical of cardiac ischaemia and were provisionally diagnosed as having unstable angina or myocardial infarction. No patient complained of typical oesophageal symptoms such as heartburn, regurgitation or dysphagia.

In all cases myocardial infarction was excluded by serial electrocardiography and cardiac enzyme assay. No patient had a previously documented myocardial infarct. In all cases the electrocardiograph on admission was normal or showed non-specific ST segment or T wave changes only. All patients underwent a maximal symptom-limited exercise test with combined thallium scintigraphy soon after admission. In every case the exercise electrocardiograph was negative (≥85% maximal predicted heart rate without ≥1 mm ST segment depression) or non-diagnostic (< 85% maximal predicted heart rate with < 1 mm ST segment depression). The thallium scans were assessed by two observers without knowledge of the clinical findings and all were considered normal. In six patients coronary arteriography was also performed and in all six this was normal.

Five tests were used to evaluate oesophageal function. Three tests—oesophagoscopy, prolonged ambulatory pH monitoring and an intra-oesophageal acid infusion test—were used to assess gastro-oesophageal reflux disease. Two tests—intraluminal oesophageal manometry and the oesophageal transit scintiscan—were used to assess oesophageal motility.

Oesophagoscopy: After administration of 5·10 mg diazepam intravenously the endoscopist intubated the fasting patient with an Olympus Q10 or D3 forward-viewing flexible endoscope. The mucosa of the lower oesophagus was assessed for erythema, linear streaking, erosions or gastric epithelialisation. The oesophago-gastric junction was noted and evidence of hiatus hernia sought by noting diaphragmatic ‘pinching’ of the gastric lumen during sniffing. Routine examination of the stomach and duodenum was also performed.

Prolonged ambulatory pH monitoring: A small pH sensitive radio-transmitter, similar in size to an antibiotic capsule, was suspended in the lower oesophagus, 5 cm above the oesophago-gastric junction. A portable radio receiver and recording device recorded oesophageal pH continuously while patients were fully mobile. All studies were conducted during an overnight stay in hospital. Food and drink of pH < 5 were excluded from the diet. The pH sensitive capsule was swallowed at approximately 3.30 pm and removed at 9.00 am the following morning so that 17-18 hours of recording were obtained. Details of the apparatus and the technique of pH monitoring used in this study have been published.16, 17 Reflux data from the patients both by day, when upright, and by night, when recumbent, were compared with normal values obtained from 27 control subjects (age 18-64 years) who were studied with the same apparatus under identical

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conditions.\textsuperscript{16} A reflux episode was defined arbitrarily as a fall in oesophageal pH to $< 4$ units.

\textit{Acid infusion test:}\textsuperscript{18} A nasogastric tube was placed with its distal end in the lower third of the oesophagus and connected by a T-piece to bottles of isotonic saline and 0.1 M hydrochloric acid. The control solution of saline was administered for up to 15 minutes, and then changed, without the patient's knowledge, to acid infusion. Both solutions were administered at a rate of $6 - 7\frac{1}{2}$ ml/min. Repetitive reproduction of the patient's usual chest pain, typical in site and intensity, with rapid relief on changing to saline infusion, which occurred on three consecutive occasions was considered a positive test. A test was negative when acid infusion for 30 minutes provoked no pain. A test was considered 'positive-unrelated' when acid provoked a new and unfamiliar pain.

\textit{Intraluminal manometry:} A four-lumen catheter was used, in which three lumina had side holes distally at different levels to measure intra-gastric, oesophagogastric sphincter and intra-oesophageal pressures, and the larger fourth lumen was available for the instillation or aspiration of material. Each of the manometry lumina was connected separately to pressure transducers by a Y connection, the other limb of each connection leading to an infusion pump adapted to take three 50 ml syringes. Deionised water was infused into each lumen at a rate of 0.42 ml/min. The pressure transducers were connected to an amplifier and recorder, and their output was displayed on heat sensitive paper. The lower oesophageal sphincter length and pressure were measured using a 'station pull through' technique. Here the end of the catheter was placed in the stomach and then pulled back, step by step, through the sphincter so that first the proximal and then the middle and distal side holes passed through. This allowed a record of mean sphincter pressure and length. In response to a wet swallow, both sphincter relaxation and oesophageal peristalsis were assessed. Spontaneous motor activity in the oesophagus was also recorded.

Normal values for lower oesophageal sphincter pressure were adopted from Calvert's work in healthy controls using the same apparatus.\textsuperscript{19} Normal values for mean sphincter length and degree of relaxation after a wet swallow were derived from the work of Benz et al.\textsuperscript{20} Spontaneous motor activity was abnormal if there were $> 3$ non propagating spikes per 5 cm of recording at 2.5 mm/sec (RAJ Spence, unpublished data).

\textit{Oesophageal transit scintiscan:}\textsuperscript{21, 22} The patient swallowed 5 ml water containing 18 MBq technetium 99m tin colloid. Nine consecutive images of the oesophagus at three-second intervals were collected by a gamma camera. The test was performed twice for each patient. In normal subjects the water progresses smoothly from mouth to stomach in less than 12 seconds. In subjects with disturbed oesophageal peristalsis, there is a delay in transit time, or the bolus of water is broken up in the lower oesophagus with failure of propulsion into the stomach. The test was reported as abnormal if one or both demonstrated any of these abnormal features.

\section*{RESULTS}

\textit{Oesophagoscopy:} Twenty-one patients underwent this investigation. Three (14\%) had a hiatus hernia, three (14\%) had oesophageal erosions and two (9\%) had both a hiatus hernia and oesophageal erosions. In the remaining 13 (63\%) patients no endoscopic abnormality was detected (Table).
## Table

**Oesophageal function tests in 22 patients with non-cardiac chest pain**

H = hiatus hernia, E = erosion of oesophageal mucosa, N = normal, A = abnormal

| Patient | Reflux Tests | Motility Tests |
|---------|--------------|----------------|
|         | Endoscopy | pH monitoring | Acid infusion | Manometry | Scintiscan |
| 1       | H + E      | N             | A             | A          | N          |
| 2       | N          | N             | N             | N          | N          |
| 3       | N          | N             | N             | N          | A          |
| 4       | H          | N             | N             | N          | A          |
| 5       | H + E      | N             | N             | A          | N          |
| 6       | N          | –             | N             | A          | A          |
| 7       | H          | A             | N             | A          | N          |
| 8       | N          | A             | N             | A          | N          |
| 9       | N          | A             | N             | N          | A          |
| 10      | E          | A             | A             | N          | N          |
| 11      | E          | A             | N             | N          | N          |
| 12      | N          | N             | N             | N          | A          |
| 13      | N          | N             | N             | A          | N          |
| 14      | N          | A             | A             | N          | N          |
| 15      | N          | A             | A             | N          | N          |
| 16      | N          | A             | N             | A          | A          |
| 17      | N          | N             | N             | A          | N          |
| 18      | N          | A             | N             | N          | A          |
| 19      | E          | –             | A             | –          | N          |
| 20      | N          | –             | N             | N          | A          |
| 21      | –          | –             | N             | A          | A          |
| 22      | N          | N             | A             | A          | –          |

**Prolonged ambulatory pH monitoring**: Two patients refused this test and in two others the apparatus failed. In the other 18 patients a technically satisfactory recording was obtained. Abnormal gastro-oesophageal reflux, mostly of a minor degree, was noted in 10 patients (56%). This was either an increase in the frequency (seven patients) or an increase both in frequency and duration (three patients) of reflux episodes (Figure). In nine of these patients, abnormal reflux only occurred whilst in the upright position, and in one patient it occurred in both the upright and the recumbent positions. In two patients typical chest pain occurred during the pH monitoring. One of these patients developed pain of such severity that admission to the coronary care unit was arranged. Oesophageal pH was noted to be normal while the patient had the pain before the probe was removed at the patient’s request. The other patient had two episodes of typical chest pain during monitoring, of which the first was associated with acid reflux and the second was not.
Non-cardiac chest pain

| Frequency (episodes/hr) | Duration (min/hr) |
|------------------------|------------------|
| 2.4                    | 6                |
| 2.0                    | 5                |
| 1.6                    | 4                |
| 1.2                    | 3                |
| 0.8                    | 2                |
| 0.4                    | 1                |
| 0                      | 0                |

Patients Controls

Figure. Reflux pattern (pH < 4) in chest pain patients and healthy controls

Acid infusion test: All patients underwent this investigation and in six (27%) a positive result was obtained. Two other patients had a 'positive unrelated' result and these were regarded as negative for oesophageal disease. No patient experienced acid-induced pain unrelieved by change to saline infusion.

Intraluminal manometry: This study was performed in 21 patients. In 10 (48%) an abnormality was noted. In two patients there was inadequate relaxation of the lower oesophageal sphincter and in one of these there was also inco-ordinated peristalsis in the oesophageal body. The other eight patients had increased spontaneous activity and inco-ordinated peristalsis of the oesophagus. All patients had a normal sphincter pressure and length. No patient experienced chest pain during the manometric evaluation.

Oesophageal transit scintiscan: This test was performed in 21 patients and in six (29%) patients one or both swallows were abnormal. No chest pain occurred during the scintiscan studies.

Concordance for all three reflux tests, either all normal or all abnormal, was very low at 28%. Between pairs of reflux tests concordance was also low. For endoscopy and pH monitoring concordance was 44%, for endoscopy and the acid infusion test 62% and for pH monitoring and acid infusion 50%. Concordance between the two tests of oesophageal motility was 55%.

DISCUSSION

Our results confirm the previously reported high prevalence of abnormalities which can be detected during oesophageal function testing in patients with non-cardiac chest pain,2, 9, 11-15 In only two of our 22 patients were all tests normal.

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The pattern of abnormalities found in the other 20 patients is disturbing in view of the low concordance between tests which purport to detect either gastro-oesophageal reflux disease or oesophageal motility disturbances. Differences in the sensitivity of these tests must account for some of the discrepancies in the results observed. It is also likely that disturbed oesophageal function is an intermittent phenomenon. If this is so, then caution is required in comparing tests used to detect such disturbances when they are not performed simultaneously. It is also necessary to consider the relevance of any detected abnormality to the chest pain which led to the patient's initial cardiological assessment.

Apart from the acid infusion test, which aims to provoke chest pain, only two patients experienced spontaneous chest pain during any of the other tests. For most of our patients, therefore, we cannot prove a causal link between the oesophageal abnormalities we detected and the chest pain they experienced. The two patients who developed spontaneous chest pain did so during prolonged pH monitoring. We suspect that more of our patients would have experienced pain if they had worn the apparatus at home or at work and had engaged in activities liable to provoke symptoms.\(^{23}\)

We found that oesophageal manometry was a sensitive test of disordered motility, but the interpretation of minor abnormalities in particular is difficult since their clinical relevance is not well established.\(^{24}\) The oesophageal scintiscan is a relatively unproven test of oesophageal dysmotility, but it is attractive as a screening procedure in view of its simplicity. Our finding of low concordance between these two tests carried out sequentially is disappointing. Studies using simultaneous manometry with the transit scintiscan are needed to determine the correlation between dysmotility and disordered bolus transit through the oesophagus. Further information may be derived from provocative studies using ergometrine\(^{25,26}\) or edrophonium,\(^{26}\) particularly if chest pain is provoked and coincides with disordered motility.

The intra-oesophageal acid infusion test, introduced by Bernstein,\(^{18}\) was useful in six patients in whom their usual chest pain was reproduced. In three of these patients there was no associated abnormality detected by endoscopy.

In conclusion, can we recommend oesophageal investigation routinely in patients with non-cardiac chest pain; and which of the tests should be performed? Fibreoptic endoscopy is widely available and allows examination not only of the lower oesophagus but also of the stomach and duodenum. We regard the high yield of erosive oesophagitis (five patients) in our study as justification for the use of endoscopy as the first line investigation in patients with non-cardiac chest pain. We do not share the view of some workers\(^{27}\) that oesophageal biopsy is a proven adjunct to endoscopy, particularly when other tests of reflux are available. In patients with a normal endoscopic appearance the acid infusion test or, if available, prolonged ambulatory pH monitoring are the logical next steps. The tests of oesophageal motor function — transit scintiscan and manometry — are of limited value unless they can be performed during a manoeuvre which reproduces pain.

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