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The evaluation of gastro-oesophageal reflux and oesophagocardiac reflex in patients with angina-like chest pain following cardiologic investigations

András Rosztóczy [a,*], Andrea Vass [b], Ferenc Izbéki [a], Attila Nemes [b], László Rudas [b], Miklós Csanády [b], János Lonovics [a], Tamás Forster [b], Tibor Wittmann [a]

[a] *First Department of Medicine, Albert Szent-Györgyi Medical, Centre, University of Szeged, Hungary*
[b] *Second Department of Medicine and Centre of Cardiology, Albert, Szent-Györgyi Medical Centre, University of Szeged, Hungary*

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Abstract

The *aims* of the study were to assess pathogenetic role of gastro-oesophageal reflux and the oesophago-cardiac reflex in subjects with chest pain. To evaluate the prevalence of gastro-oesophageal reflux disease and the oesophago-cardiac reflex in patients with different coronary artery diseases and in coronary spasm.

Patients, methods: Fifty-one patients with chest pain were enrolled after detailed cardiologic evaluation including coronary angiography. The prevalence of gastrooesophageal reflux disease was established by symptom analysis, upper gastrointestinal endoscopy, 24-h oesophageal pH monitoring, and oesophageal manometry. The oesophago-cardiac reflex was established by oesophageal acid perfusion test (0.1 N HCl and 0.9% NaCl, 120–120 ml/10 min in a blinded manner) combined with transoesophageal Doppler echocardiographic coronary flow measurement in the left anterior descending artery.

Results: Gastro-oesophageal reflux disease was established in 45% (23/51) of the patients. Oesophageal acid perfusion decreased the coronary flow velocity in 49% (25/51) of the patients indicating the presence of oesophago-cardiac reflex. Oesophago-cardiac reflex was present more frequently in patients with coronary spasm, than in patients with either epicardial coronary artery disease or microvascular coronary disease ($p<0.02$). Patients with oesophago-cardiac reflex had higher DeMeester scores, increased number of reflux episodes, fraction time below pH 4, and prolonged acid reflux episodes ($p<0.05$ for each parameter).

Conclusions: Gastro-oesophageal reflux disease is frequently established in patients with either epicardial or microvascular coronary artery disease or with coronary spasm. The oesophago-cardiac reflex was more frequently observed in patients with coronary spasm. The combination of oesophageal acid perfusion test and transoesophageal Doppler echocardiographic coronary flow measurement seems to be a useful method for the detection of this reflex. Patients with prolonged gastro-oesophageal acid reflux episodes, erosive oesophagitis and coronary spasm may be at higher risk for the development of linked-angina.

Keywords: Acid-related diseases; Gastro-oesophageal reflux disease; Coronary artery; Disease; Oesophago-cardiac reflex; Non-cardiac chest pain

1. Introduction

It has been almost 50 years since Bernstein and Baker demonstrated that episodes of chest pain can be provoked by oesophageal acid perfusion. [1] Both Bernstein and later Bennett [2] believed that chest pain episodes of oesophageal and cardiac origin could be clearly distinguished. The time that has subsequently passed has revealed that the differential

Abbreviations: CFR, coronary flow reserve; ECG, electrocardiogram; LAD, left anterior descending artery; NCCP, non-cardiac chest pain.

* Corresponding author. Present address: H-6720 Szeged, Korányi fasor 8, Hungary. Tel./fax: +36 62 54 59 97.
E-mail address: air@in1st.szote.u-szeged.hu (A. Rosztóczy).

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diagnosis of chest pain is often difficult. In consequence of this the evaluation of the symptoms themselves is not sufficient to predict the underlying disease. It has been shown that up to 40% of the patients, admitted to a coronary care unit with typical angina-like chest pain have a normal coronary anatomy [3]. The majority of their chest pain events might, however, be caused by gastro-oesophageal reflux disease or other oesophageal motility disorders as it has been established by functional oesophageal testing [4–10]. Furthermore, oesophageal causes of non-cardiac chest pain can also be observed in patients with coronary artery disease with a similar incidence [11–13]. This large overlap between patients with cardiac and non-cardiac chest pain events has raised the question whether this is only a coincidence or a causative link exists between them [14]. Since the oesophagus and the heart share their innervation, mechanical or chemical stimulation of the oesophagus may evoke myocardial ischemia leading to chest pain both in experimental animals and in humans. This phenomenon has been designated as linked-angina [15–21].

Data on the prevalence of the oesophageal acid exposure induced oesophagocardiac reflex are still missing in humans; and only a few studies have evaluated the incidence of linked-angina, i.e. the oesophageal acid exposure-induced myocardial ischaemia mediated by the oesophago-cardiac reflex [14,22,23]. Therefore in the present study we aimed to evaluate the prevalence of this reflex, and to examine its relationship to different coronary artery diseases and gastro-oesophageal reflux disease by means of transesophageal echocardiographic coronary flow velocity measurement combined with oesophageal acid stimulation test in patients with angina-like chest pain.

2. Patients, methods

Fifty-one patients (24 males, 27 females, mean age 55 ± 13 years, range: 36–74 years) with class II chest pain according to Canadian Cardiovascular Society were enrolled after a detailed cardiologic evaluation including coronary angiography.

Nineteen patients had significant epicardial coronary artery disease. Eleven of them had the involvement of the left anterior descending artery, and 8 had stenosis of other large vessels. Thirteen patients had microvascular disease and normal epicardial coronary arteries. Ten patients had coronary spasm, 7/10 had spontaneous spasm resolved by intracoronarial nitrate administration, and 3/10 had provokable spasm by ergonovine testing. Nine patients had negative cardiologic evaluation. These were considered to have non-cardiac chest pain. Patients with autonomic neuropathy (diabetics, chronic alcohol consumers, etc.), or with an impaired left ventricular function (ejection fraction ≤ 50%), or with left main coronary artery stenosis were not enrolled. The studied patients were screened for gastro-oesophageal reflux disease by means of symptom analysis, upper gastrointestinal endoscopy and 24-h pH monitoring. Spastic oesophageal motility disorders (such as diffuse oesophageal spasm, and nutcracker oesophagus) were excluded by oesophageal manometry. All patients gave their informed consent prior to enrolment. The study protocol was approved by the Medical Ethics Committee of the University of Szeged.

2.1. Coronary angiography

The coronary angiography was carried out prior to this study in all the patients according to the standard Seldinger technique. Lesions were considered to be significant in case of at least 70% narrowing of the coronary artery lumen, causing typical chest pain and myocardial ischaemia confirmed by one of the following non-invasive tests: tredmill exercise electrocardiography, myocardial isotope perfusion test, stress echocardiography. When signs of suspected coronary spasm were detected ($n=7$), intracoronarial glyceriltrinitrate (200 μg) was administered to prove the presence of coronary spasm. Patients with a previous history of suspected coronary spasm, but having no signs of this at the time of coronarography ($n=3$), were submitted to a provocative test, involving the intracoronarial administration of increasing doses of ergonovine (5, 10, 25 and 50 μg) to evaluate the presence of provokable coronary artery spasm.

2.2. Coronary flow reserve (CFR) measurement

The coronary flow reserve was established by transoesophageal Doppler echocardiography (Toshiba Power Vision). A 5 MHz multiplane transducer was introduced into the oesophagus. Flow velocities were measured in the LAD according to our previously published protocol [24] originally described by Iliceto et al. [25]. Briefly, 0.56 mg/kg dipyridamole was administered intravenously in 4 min. The CFR was calculated as the ratio of the peak and the baseline diastolic flow velocities. In line with to our previous results, the CFR was accepted as normal if it exceeded 2.5 [24]. In patients with intact large coronary arteries at coronary angiography the decrease of CFR represents microvascular disease by definition.

2.3. Oesophageal symptom analysis

Patients were asked to fill a standardized questionnaire regarding their symptoms related to gastro-oesophageal reflux disease, such as heartburn, chest pain and gastro-oesophageal acid regurgitation.

2.4. Upper gastrointestinal endoscopy

The presence and the severity of oesophagitis were assessed by upper gastrointestinal endoscopy (Olympus Q130) on the basis of the Los Angeles classification [26]. The severity of oesophagitis was scored as: no erosions = 0, grade LA-A = 1, grade LA-B = 2, grade LA-C = 3, grade LA-D = 4.