Prevalence of linked angina and gastroesophageal reflux disease in general practice

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Abstract

AIM: To evaluate the association between gastroesophageal reflux diseases (GERD) and coronary heart diseases.

METHODS: One thousand nine hundred and seventy consecutive patients who attended our hospital were enrolled. All of the patients who first attend our hospital were asked to respond to the F-scale questionnaire regardless of their chief complaints. All patients had a careful history taken, and resting echocardiography (ECG) was performed by physicians if the diagnostic necessity arose. Patients with ECG signs of coronary artery ischemia were defined as ST-segment depression based on the Minnesota code.

RESULTS: Among 712 patients (36%) with GERD, ECG was performed in 171 (24%), and ischemic changes were detected in eight (5%). Four (50%) of these patients with abnormal findings upon ECG had no chest symptoms such as chest pain, chest oppression, or palpitations. These patients (0.6%; 4/712) were thought to have non-GERD heartburn, which may be related to ischemic heart disease. Of 281 patients who underwent ECG and did not have GERD symptoms, 20 (7%) had abnormal findings upon ECG. In patients with GERD symptoms and ECG signs of coronary artery ischemia, the prevalence of linked angina was considered to be 0.4% (8/1970 patients).

CONCLUSION: The present study suggested that ischemic heart disease might be found although a patient was referred to the hospital with a complaint of GERD symptoms. Physicians have to be concerned about missing clinically important coronary artery disease while evaluating patients for GERD symptoms.

Key words: Linked angina; Epidemiology; General practice; Electrocardiography; Gastroesophageal reflux disease

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INTRODUCTION

Chest pain often precedes echocardiographic coronary angiography, electrocardiography (ECG), and scintigraphy for the diagnosis of angina. Many patients presenting to a hospital emergency room for chest pain turn out not to have coronary artery disease (CAD)\(^1\). According to data from a large university, 81%-86% of patients evaluated in an emergency room for acute chest pain did not have coronary ischemia\(^2\). It is well known that non-cardiac chest pain is closely related to gastroesophageal reflux diseases (GERD)\(^3\). Similarly, erosive esophagitis is not found in some patients with persistent GERD symptoms. Although GERD symptoms affect 10%-30% of the population in Western countries\(^4\), endoscopic esophagitis is less prevalent, and is reported to occur in up to 2% of individuals\(^5,6\). Only one-third of GERD patients have endoscopic positive findings, while others have no obvious mucosal breaks, even though GERD symptoms are present\(^7\). Chest pain of esophageal origin can be difficult to distinguish from that caused
by cardiac ischemia because the distal esophagus and the heart share a common afferent vagal supply, and GERD can cause episodes of non-cardiac chest pain that resemble ischemic cardiac pain\cite{10,11}. It is possible that GERD may be misclassified as angina pectoris and vice versa in clinical practice. The aim of this study was to evaluate the association between GERD and coronary heart disease and to clarify the presence of non-GERD heartburn.

**MATERIALS AND METHODS**

**Ethics**
The study was carried out in accordance with the Declaration of Helsinki, and approved by the ethical committee at Toho University.

**Patients**
Between October 2005 and May 2006, 1970 consecutive patients (934 men and 1036 women with a mean age of 43 years) who first attended the Outpatient Department of General Medicine and Emergency Care of Toho University Omori Hospital were enrolled. Informed consent was obtained from all the patients. None of the patients had a history of use of proton pump inhibitors, H2-receptor antagonists, antibiotics, steroids, or nonsteroidal anti-inflammatory drugs for a period of at least 2 mo before the investigation. Patients who had a previous history of partial gastrectomy were also excluded from the study.

**Questionnaire**
All of the patients who attended our hospital were asked to respond to the F-scale questionnaire regardless of their chief complaints. The questionnaire is a self-report instrument, written in a simple and easy-to-understand language, which contained 12 questions. As reported previously by Kusano et al\cite{12}, the following definitions were used to identify symptoms in the F-scale: (1) “Do you get heartburn?”; (2) “Is your stomach bloated?”; (3) “Does your stomach ever feel heavy after meals?”; (4) “Do you sometimes subconsciously rub your chest with your hand?”; (5) “Do you ever feel sick after meals?”; (6) “Do you get heartburn after meals?”; (7) “Do you have an unusual sensation in your throat?”; (8) “Do you feel full while eating meals?”; (9) “Do some things get stuck when you swallow?”; (10) “Do you get bitter liquid coming up into your throat?”; (11) “Do you belch a lot?”; and (12) “Do you get heartburn if you bend over?”.

Symptoms frequency was measured on the following scale: 0, never; 1, occasionally; 2, sometimes; 3, often; and 4, always. A score of more than 7 points, was considered positive for GERD.

**Electrocardiogram**
All patients had a careful history taken, and resting ECG was performed by physicians if diagnostic necessity arose. Patients with ECG signs of coronary artery ischemia were defined as having ST-segment depression based on the Minnesota code\cite{13}.

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**Table 1** Characteristics of study participants

| Cardiogram | Abnormal | Normal | \(P\) |
|------------|----------|--------|-------|
| No. of patients | 456 | 1514 | \(< 0.001\) |
| Age (yr) | 48.2 ± 17.6 (16-91) | 40.7 ± 15.7 (15-93) | \(< 0.001\) |
| Male/female | 231/225 | 703/811 | \(< 0.05\) |
| Hypertension | 49/407 | 84/1430 | \(< 0.001\) |
| Diabetes | 36/420 | 45/1469 | \(< 0.001\) |
| Hyperlipidemia | 79/377 | 146/1473 | \(< 0.001\) |
| Current smoker | 156/300 | 408/1026 | NS |

**Table 2** Relationship between GERD symptoms and ECG abnormalities

| Cardiogram | Abnormal | Normal |
|------------|----------|--------|
| GERD (+) | 8 | 166 |
| GERD (-) | 20 | 261 |

**Statistical analysis**
All values are expressed as means ± SD. Comparisons of groups were made using Student's \(t\) test or chi-square tests as appropriate. \(P < 0.05\) was considered statistically significant.

**RESULTS**
Overall, ECG was performed in 456 patients (23%, ECG group). The remaining 1514 patients were defined as controls. Patients in the ECG group were significantly older and the male to female ratio was significantly higher than in controls (Table 1). The prevalence of hypertension, diabetes mellitus, and hyperlipidemia was also significantly higher in the ECG group. There was no difference in the proportion of current smokers between the two groups.

Among 712 patients (36%) with GERD, ECG was performed in 171 patients (24%) and ischemic changes were detected in eight patients (5%). Four (50%) of these patients with abnormal findings upon ECG had no chest symptoms such as chest pain, chest oppression, or palpitations. These patients (0.6%; 4/712) were thought to have non-GERD heartburn, which may be related to ischemic heart disease. Of 281 patients who underwent ECG and did not have GERD symptoms, 20 (7%) had abnormal findings upon ECG (Table 2). No significant differences in the prevalence of ischemic changes were found between patients who underwent ECG and those who did not. As shown in Table 3, an exercise thallium test was performed in 12 GERD patients, of whom, one had ischemic coronary artery disease that was proven angiographically. In patients with GERD symptoms and ECG signs of coronary artery ischemia, the prevalence of linked angina, was considered to be 0.4% (8/1970 patients) (Figure 1). In contrast, patient with angina not related to GERD was found in 20 (1.0%).

**DISCUSSION**
Screening asymptomatic patients is an area of
considerable interest because silent CAD is an important cause of premature death; many of these patients have three-vessel CAD or left main coronary artery stenosis[14]. Little is known, however, about the effects of intervention on asymptomatic disease, and screening strategies for asymptomatic CAD have been difficult to justify. Of patients with a low pre-test probability of CAD, only about 20% with a positive exercise test will have angiographically verified CAD[15]. Little evidence exists currently to support doing resting ECGs[16] or exercise tests[17] in patients without clinical evidence of CAD or cardiovascular risk factors.

When coronary arteries appear normal upon angiography, particularly when there is no other cardiac disorder or objective evidence of ischemia, a diagnosis of non-cardiac chest pain is made. In that particular study[18], cardiac mortality was 0.09% and coronary event rate was 0.65% per year, but 81% of patients had chest pain after 9 years follow-up. The clinician often is faced with the problem of a patient with comparatively mild coronary disease but persistent severe symptoms despite anti-anginal drugs. This subset of patients presents a difficult clinical problem because both the patient and physician usually perceive the pain to be of cardiac origin. It is probable that many of these patients have coexisting coronary disease and a symptomatic esophageal disorder. Symptoms of chest pain are a major source of concern for patients and physicians alike because they can sometimes be the harbinger of acute life-threatening events. However, many patients who describe chest pain that sounds identical to the type associated with significant cardiac disease can actually be free of such disease. After appropriate evaluations, about 40% of patients admitted for potential acute coronary syndromes turn out not to have CAD[19,20]. A study at the Emergency Room Assessment of Sestamibi for Evaluating Chest Pain Trial (ERASE trial), and a second study at a large hospital center in Philadelphia, showed that 81%-86% of all patients presenting to the emergency department with chest pain did not have a final diagnosis of cardiac ischemia[3,21]. Thus, differentiation between cardiac- and esophageal-origin chest pain is especially difficult since both organs have overlapping sensory pathways: Th1-Th4 for the heart and C8-TH10 for the esophagus. Moreover, they have autonomic nerve reflex, the so-called vagal visceral reflex function between the heart and organs of the gastrointestinal tract[22].

Direct mechanical effects between the esophagus and the heart are thought to be compression of the left atrium by a huge hiatus hernia or extrinsic esophageal compression by cardiac enlargement. Other than these direct effects, a neural reflex, mediated by the vagus nerve, exists that allows changes in esophageal function to affect cardiac physiology[23]. Atrial tachycardia can be triggered by swallowing and belching, although the precise neural mechanism remains unclear[24]. Furthermore, bradycardia occurs in most people during balloon inflation within the esophagus and this may be blocked by atropine[25]. It has been suggested that esophageal dysfunction can itself trigger myocardial-ischemia-linked angina[26]. Smith et al[27] have coined the term “linked angina”, which implies that gastrointestinal factors bring on attacks of genuine angina in patients with established CAD. They have explained this on the basis of cardiovascular changes, although gastoesophageal acid reflux may equally explain the phenomenon. Instillation of acid into the esophagus has been shown to significantly reduce the exertional angina threshold at which angina occurs or can provoke angina with ischemic ECG changes[28]. A previous animal study has demonstrated the reduced coronary flow caused by distension of the stomach that does not occur after vagal section or after the administration of atropine. This suggests that reflex coronary vasoconstriction is initiated by vagal irritation in the gastrointestinal tract[29]. Mellow et al[30] have demonstrated that acid perfusion of the esophagus results in reduced coronary blood flow in patients with proven CAD. It should be emphasized that 67% of patients felt chest pain and two-thirds of them developed ischemic ST-segment changes upon ECG. Dobrzynski et al[31] have also reported that GERD patients have a larger total ischemic burden and higher incidence of ST depression. Thus, spontaneous GER may have a role to play in the causation of or provocation of cardiac chest pain. Linked angina can be defined as that induced by GER. However, most patients with asymptomatic angina or symptoms, that do not reach the threshold required to define disease, do not refer to a hospital. Therefore, the present study was designed in the Department of General Medicine to evaluate the association between GERD and coronary heart disease in the general population because general
practice registers offer the best means of sampling the general population[30]. We hypothesized that the prevalence of CAD in GERD patients who were referred for the first time to the gastroenterology outpatient clinic because of heartburn may be substantial.

The present study revealed a small number of patients with abnormal ECG findings but without chest symptoms such as chest pain, chest oppression, or palpitations. This suggests that the extra-esophageal condition causes GERD symptoms and that angina may be misclassified as GERD. Such patients are often treated with proton pump inhibitors and chest pain disappears, which suggests that CAD may be overlooked. The results may therefore have clinical relevance, as it has been reported in a previous population-based, nested case-control study that patients with GERD have an increased risk of angina pectoris in the year after GERD diagnosis[31]. Actually, the incidence of reflux esophagitis is increasing as the population grows older, which makes it likely that such disease may be present in patients with CAD[32]. Physicians have to be concerned about missing clinically important CAD while evaluating patients for GERD symptoms.

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