Libyan international Medical University

Faculty of Basic Medical Science

Association between gastroesophageal reflux disease

and coronary heart disease

Submitted by : Khalil Khalifa El Gazzar **(**1492**)**, Second Year Medical Student.

Supervisor : Nawar montaser

Date of Submission : 4 / 5 / 2018

This Report Was submitted to fulfill the requirements for the 2y Medical Student.

Abstract:

In this report show the relation between gastroesophageal reflex disease (GERD) and coronary heart disease (CHD) and how affect on each other .

Introduction :

Gastroesophageal reflux disease (GERD) is the return of the stomach's contents back up into the esophagus which is digestive disorder that affects the lower esophageal sphincter (LES), the ring of muscle between the esophagus and stomach[1].Coronary heart disease (CHD) a disease of the coronary vessels causing stenosis and obstruction of coronary circulation that supply the heart [7].

Gastroesophageal reflux disease (GERD) is characterized by symptoms and complications such as esophagitis, esophageal stricture, Barrett esophagus, and esophageal adenocarcinoma, and is caused by the reflux of gastric contents.[1] Previous studies have reported the prevalence of GERD (as defined by experiencing heartburn or acid regurgitation at least once per week) was 14% to 24% in adults in Western countries, and 3% to 10.5% in Asian populations.[2,3] The manifestations of GERD include esophageal syndromes, such as erosive esophagitis and nonerosive reflux disease (NERD), and extra-esophageal syndromes such as reflux-associated cough, asthma, laryngitis, and dental erosion.[4]

The features of GERD-induced chest pain are similar to those of cardiac pain, and thus the 2 types of pain can be confused. In addition, GERD and coronary heart disease (CHD) can interact with each other to produce chest pain. Studies have shown that esophageal stimulation can cause cardiac pain by inducing cardiac dysrhythmia or coronary spasm to compromise coronary blood flow.[2,5,6] Studies have also shown that myocardial ischemia can worsen GERD by causing esophageal dysmotility or relaxation of the lower esophageal sphincter.[5,7,8]

A coexisting relationship between GERD and CHD has been widely accepted, though the mechanism underlying the relationship is complex. GERD and CHD share several components of metabolic disorders as common risk factors.[9] Previous studies have shown that male sex, obesity, diabetes, hypertension, smoking, and alcohol drinking are associated with GERD,[10–12] and that metabolic risk factors can influence the severity of symptoms or esophageal erosion in GERD patients.[13] Hyperlipidemia, hypertension, diabetes, alcoholism, and smoking are well-known risk factors for CHD.[14,15] However, the existence of an association between GERD and subsequent development of CHD remains under debate.[9]Moreover, it has been reported that proton pump inhibitors (PPIs) can reduce cardiac contractility and raise the risk of atherosclerosis by increasing the serum levels of homocysteine.[7,12]

We hypothesized that GERD might be related to an increased risk of the subsequent CHD development. In this nationwide population-based cohort study, we analyzed the data from the National Health Insurance Research Database (NHIRD) to evaluate the relationship between GERD and subsequent CHD development and to determine whether the risk of CHD increases after longer use of PPIs.

Discussion:

In this study, we aimed to determine the association between gastroesophageal reflux disease (GERD) and subsequent coronary heart disease (CHD) development, if any, and to evaluate whether longer use of proton pump inhibitors (PPIs) increases the risk of CHD.

Patients diagnosed with GERD between 2008 and 2013 were identified as the study cohort (n = 12,960). Patients without GERD were randomly selected from the general population, frequency-matched with the study group according to age, sex, and index year, and evaluated as the comparison cohort (n = 51,840). Both cohorts were followed up until the end of 2013 to determine the incidence of CHD. The risk of CHD was evaluated in both groups. The GERD patients had a greater probability of CHD than the cohort without GERD. The GERD cohort had a higher risk of CHD than the comparison cohort did after adjustment for age, sex, hypertension, diabetes, hyperlipidemia, alcohol-related illness, stroke, chronic obstructive pulmonary disease, asthma, biliary stone, anxiety, depression, chronic kidney disease, and cirrhosis.The risk

of CHD was greater for the patients treated with PPIs for more than 1 year than for those treated with PPIs for <1 year .

In population-based cohort study results indicate that GERD was associated with an increased risk of developing CHD, and that PPI use for more than 1 year might increase the risk of CHD.

Consistent with the results from previous studies, the study results show that GERD is more common in men than in women (50.8% vs 49.2%). We identified 12,960 GERD patients, diagnosed through endoscopy or 24-h pH monitoring, from a population of 1,000,000, indicating a prevalence of approximately 1.3%. In previous population-based studies on GERD in Chinese ethnic populations, the prevalence of GERD, diagnosed through direct interviews, was highly variable, with 0.8% identified in Singapore, 2.5% in Hong Kong, and 6.2% in South China.[3–11] The reason for higher incidence of GERD in men than in women has yet to be fully elucidated, though the relatively low parietal cell mass in women, relatively poor lower esophageal function in men, and higher body mass index or number of GERD-related comorbidities in men might contribute to the trend.[12,15] the study results indicate that the age-specific relative risk of CHD in the GERD cohort decreased with increasing age, but no difference was observed in the risk of CHD between patients age ≥65 years with and without GERD. It is possible that increased prevalence of other CHD-associated risk factors in patients age ≥ 65 years could have reduced the relative influence of GERD on CHD risk. Moreover, it has been reported that older patients tend to be insensitive to acid reflux and might become asymptomatic.[2]

The study results indicate that GERD patients have a greater number of comorbidities than do non-GERD patients, and indicate that GERD is associated with hypertension, diabetes, hyperlipidemia, alcohol-related illness, stroke, obesity, COPD, asthma, biliary stone, anxiety, depression, chronic kidney disease, and cirrhosis. According to our analyses, risk of CHD is increased in GERD patients who are older, male, or have hypertension, hyperlipidemia, or anxiety. In results indicate that GERD is associated with subsequent CHD development after adjustment for age, sex, hypertension, diabetes, hyperlipidemia, alcohol-related illness, stroke, COPD, asthma, biliary stones, anxiety, depression, chronic kidney disease, and cirrhosis. However, further investigation is required to determine whether GERD is a risk factor or epiphenomenon for CHD development.[9–11]

Previous studies have suggested that shared pathophysiological mechanisms might underlie the association between GERD and CHD. First, in linked angina, exposure of the esophageal mucosa to acid and reduced lower esophageal sphincter pressure might compromise myocardial perfusion resulting from coronary spasm and cause arrhythmia through sympathetic activation.[5,6,12–13] In addition, myocardial ischemia can induce esophageal dysmotility or relaxation of the lower esophageal sphincter.[5,7,8] Second, many visceral pain receptors are polymodal and sensitive to acid, mechanical distension, and changes in temperature. Cardiac and esophageal afferent sensory innervations entering the spinal cord can overlap, and thus stimulation of the esophagus or heart might be perceived and summed up over the dermatomes corresponding to either organ.[12,15] Third, the relationship between GERD and sleep disturbances is bidirectional and interactive,[14] and it is well established that sleep apnea increases the risk of a cardiovascular event. Finally, PPI use can reduce the cardioprotective effects of certain therapies by reducing the metabolism of antiplatelet agents to their active form.[4–9] PPIs might also reduce the contractility of myocardial tissue and increase homocysteine by impairing the absorption of vitamin B12.[6,10] Moreover, our results suggest that PPI use might have a detrimental effect on CHD, because the risk of CHD among the patients treated for more than 1 year was greater than that of patients treated for <1 year.

The increased prevalence of other CHD-associated risk factors in older patients might attenuate the effects of GERD on CHD risk with increasing age. The risk of developing CHD was consistently increased after we have controlled the confounding risk factors as possible as we could, even though the association might be caused by their shared risk factors. However, we still could not ascertain whether there is a causal relationship between GERD and CHD or whether the duration of PPI use imposes the deteriorating defect on CHD development in a dose–response effect. Johansson et al[9] reported that the incidence of CHD significantly differed between patients with and without GERD within 1 month of GERD diagnosis, and the authors suggested that the misinterpretation of prodromal ischemic symptoms as reflux symptoms could have caused this finding. Similarly, our results suggest that the risk of CHD is greatest in the first 2 years after GERD diagnosis rather than increasing incrementally with follow-up duration after GERD diagnosis.

The possible reasons for the discordance between the incidence of CHD and the total duration of GERD follow-up may include the delayed diagnosis of GERD for the patients with GERD symptoms, the early compromise of myocardial perfusion after GERD diagnosis, and misinterpretation because of overlapping sensory innervation of the esophagus and the heart. However, our results consistently indicate a close association between GERD and CHD, and suggest that GERD with PPI treatment for more than 1 year might increase the risk of CHD development.

Conclusion :

In conclusion, the results from the population-based cohort study indicate that GERD was associated with an increased risk of developing CHD, and PPI usage for more than 1 year might increase the risk of CHD.

Reference :

1. Vakil N, van Zanten SV, Kahrlas P, et al. The Montrel definition and classification of gastroesophageal reflux disease: a global evidence-based consensus. *Am J Gastroenterol* 2012; 101:1900–1920.

2. Dent J, El-Serag HB, Wallander MA, et al. Epidemiology of gastro-oesophageal reflux disease: a systemic review. *Gut* 2005; 54:710–717.

3. Jung HK. Epidemiology of gastroesophageal reflux disease in Asia: a systemic review. *J Neurogastroenterol Motil* 2015; 17:14–27.

4. Roman C, des Varannes SB, Muresan L, et al. Atrial fibrillation in patients with gastroesophageal reflux disease: a comprehensive review. *World J Gastroenterol* 2014; 20:9592–9599.

5. Chauhan A, Petch MC, Shofield PM. Effect of esophageal acid instillation on coronary artery blood flow. *Lancet* 1993; 341:1309–1310.

6. Manisty C, Hughes-Roberts Y, Kaddoura S. Cardiac manifestations and sequelae of gastrointestinal disorders. *Br J Cardiol* 2009; 16:175–180.

7. Liu Y, He S, Chen Y, et al. Acid reflux in patients with coronary artery disease and refractory chest pain. *Intern Med* 2013; 52:1165–1171.

8. Schofield PM, Whorwell PJ, Brooks NH, et al. Oesophageal function in patients with angina pectoris: a comparison of patients with normal coronary angiograms and patients with coronary artery disease. *Digestion* 1989; 42:70–78.

9. Johansson S, Wallander MA, Ruigómez A, et al. Is there any association between myocardial infarction, gastro-oesophageal reflux disease and acid-suppressing drugs? *Aliment Pharmacol Ther* 2003; 18:973–978.

10. Hampel H, Abraham NS, El-Serag HB. Meta-analysis: obesity and the risk for gastroesophageal reflux disease and its complications. *Ann Intern Med* 2005; 143:199–211.

11. Wu JC, Mui LM, Cheung CM, et al. Obesity is associated with increased transient lower oesophageal sphincter relaxation. *Gastroenterology* 2007; 132:883–889.

12. Moki F, Kusano M, Mizuide M, et al. Association between reflux oesophagitis and features of the metabolic syndrome in Japan. *Aliment Pharmacol Ther* 2012; 26:1069–1075.

13. Chung SJ, Kim D, Park MJ, et al. Metabolic syndrome and visceral obesity as risk factors for reflux oesophagitis: a cross-sectional case–control study of 7078 health check-up Koreans. *Gut* 2008; 57:1360–1365.

14. Chien KL, Hsu HC, Sung FC, et al. Metabolic syndrome as a risk factor for coronary artery disease and stroke: an 11-year prospective cohort in Taiwan community. *Atherosclerosis* 2007; 194:214–221.

15. Okwuosa TM, Klein O, Chan C, et al. 13-Year long-term associations between changes in traditional cardiovascular risk factors and changes in fibrogen levels: the coronary artery risk development in young adults (CARDIA) study. *Atherosclerosis* 2013; 22:214–219.