Erosive esophagitis associated with metabolic syndrome, impaired liver function, and dyslipidemia

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Abstract

AIM: To investigate whether erosive esophagitis is correlated with metabolic syndrome and its components, abnormal liver function, and lipoprotein profiles.

METHODS: We conducted a cross-sectional, case control study of subjects who underwent upper endoscopy during a health examination at the Health Management and Evaluation Center of a tertiary medical care facility located in Southern Taiwan. Metabolic syndrome components, body mass index (BMI), liver function, dyslipidemia, and cardiovascular risk factors, as defined by the ratio of total cholesterol to high-density lipoprotein cholesterol (HDL-C), and the ratio of low-density lipoprotein cholesterol to HDL-C were compared between individuals with and without erosive esophagitis. Risk factors for erosive esophagitis were evaluated by multivariate logistic regression.

RESULTS: Erosive esophagitis was diagnosed in 507 of 5015 subjects who were individually age and sex matched to 507 esophagitis-free control subjects. In patients with erosive esophagitis, BMI, waist circumference, blood pressure, fasting plasma glucose, triglyceride levels, aspartate aminotransferase, alanine aminotransferase, the ratio of total cholesterol to HDL-C, and the ratio of low-density lipoprotein cholesterol to HDL-C were significantly higher and HDL-C was significantly lower compared to patients without erosive esophagitis (all \( P < 0.05 \)). In a multivariate analysis, central obesity (OR = 1.38; 95%CI: 1.0-1.86), hypertension (OR = 1.35; 95%CI: 1.04-1.76), hypertriglyceridemia (OR = 1.34; 95%CI: 1.02-1.76), cardiovascular risk factors as defined by a ratio of total cholesterol to HDL-C > 5 (OR = 1.45; 95%CI: 1.06-1.97), and aspartate aminotransferase (OR = 1.59; 95%CI: 1.08-2.34) were significantly associated with erosive esophagitis.

CONCLUSION: Metabolic syndrome, impaired liver function, and a higher ratio of total cholesterol to HDL-C were associated with erosive esophagitis.

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Key words: Erosive esophagitis; Metabolic syndrome; Central obesity; Abnormal liver function; Dyslipidemia

Core tip: A cross-sectional, case control study of subjects who underwent upper endoscopy during a health examination was conducted. Metabolic syndrome components, body mass index, liver function, and dyslipidemia were compared between individuals with and without erosive esophagitis. Risk factors for erosive esophagitis were evaluated. Erosive esophagitis was diagnosed in 507 of 5015 subjects who were individually age- and sex-matched to 507 erosive esophagitis-free control
subjects. In addition to metabolic syndrome, we also found that abnormal liver function and predictors of future coronary heart disease were associated with erosive esophagitis.

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INTRODUCTION
The prevalence of erosive esophagitis in Asian countries has dramatically increased during the last two decades1-3. The prevalence of erosive esophagitis in the Taiwanese adult population is estimated to be 10%-15%4,5. Although the mechanism underlying this increase in prevalence remains to be determined, several risk factors of erosive esophagitis have been identified, including male sex, hiatal hernia, smoking, alcohol consumption, and obesity6-7. Metabolic syndrome is a complex disorder comprising central obesity, high blood pressure (BP), hyperglycemia, hypertriglyceridemia, and a low concentration of high-density lipoprotein cholesterol (HDL-C). In addition to being associated with cardiovascular disease and diabetes mellitus, metabolic syndrome and its component elements have also been associated with various gastrointestinal diseases and abnormal liver function8-10. The correlation between erosive esophagitis and body mass index (BMI) is controversial11-13, as is the association between erosive esophagitis and hypertriglyceridemia or hyperglycemia13,14. This study was undertaken to characterize the correlation between erosive esophagitis and metabolic syndrome and its components, abnormal liver function and abnormal lipoprotein profiles - that have been used to predict coronary heart disease.

MATERIALS AND METHODS
Subjects
This study was designed as a cross-sectional, case control study. From January 2008 to December 2008, 5981 subjects visited the Health Management and Evaluation Center of a tertiary medical care facility located in Southern Taiwan for routine health examinations. Our center offers a variety of healthcare tests and procedures, including upper gastrointestinal endoscopy. The majority of subjects underwent a self-paid physical check-up; others were employees coming for their regular medical check-up. Most of the subjects were free of symptoms and were not chronic alcohol drinkers. Of the 5031 subjects who underwent upper gastrointestinal endoscopy, 507 were diagnosed with erosive esophagitis. The severity of erosive esophagitis was graded from A-D according to the Los Angeles classification15. We matched each case subject, according to age and gender, with one control selected from the 4508 subjects with normal upper endoscopic findings. The study was approved by the institutional review board of the hospital in which the study was conducted.

Definition of metabolic syndrome and obesity
In this study, metabolic syndrome was defined according to the modified National Cholesterol Education Program Adult Treatment Panel III for Asian populations. The waist circumference cutoff measurement was altered according to the criteria of the Bureau of Health Promotion, Department of Health, because the absolute risk of diabetes and cardiovascular disease is greater in Asians with a lesser degree of obesity16,17. Metabolic syndrome was diagnosed when at least three of the following criteria were found: (1) waist circumference ≥ 90 cm for men and ≥ 80 cm for women; (2) systolic BP ≥ 130 mmHg, diastolic BP ≥ 85 mmHg, or current use of antihypertensive drugs; (3) triglyceride (TG) ≥ 150 mg/dL; (4) HDL-C < 40 mg/dL for men and < 50 mg/dL for women; and (5) fasting plasma glucose ≥ 110 mg/dL or current use of antihyperglycemic drugs. Subjects with a BMI ≥ 25 kg/m² were defined as obese according to the Steering Committee of the World Health Organization Regional Office for the Western Pacific18. Subjects with elevated serum alanine aminotransferase (ALT) (ALT > 40 U/L) or aspartate aminotransferase (AST) (AST > 37 U/L) levels were considered to have abnormal liver function. Cardiovascular risk, which is determined by a ratio of total cholesterol (TC)/HDL-C > 5 and correlates significantly with the risk for cardiovascular events19, was evaluated for its association with erosive esophagitis.

Statistical analysis
Statistical analysis were performed using SPSS (Statistical Package for the Social Sciences) 15 software (SPSS, Chicago, IL, United States). Continuous variables are expressed as the mean ± SD. Student’s t test was used to compare continuous variables. Univariate analysis was performed using a χ² test for categorical variables. For each variable, the OR and 95%CI were calculated. A two-tailed P value of < 0.05 was considered statistically significant. Multivariate analysis in the logistic regression model was conducted to examine the associations between erosive esophagitis and different risk factors.

RESULTS
Prevalence of erosive esophagitis
Of the 5031 subjects who underwent upper gastrointestinal endoscopy, 16 were excluded from the analysis because of prior gastric surgery, gastric cancer, or peptic ulcer. Erosive esophagitis was diagnosed in 507 of 5015 subjects. The mean age of subjects with erosive esophagitis was 51.2 ± 11.2 years, and 82.6% were male.
The presence of metabolic syndrome (≥ 3 metabolic criteria) was associated with a higher probability of erosive esophagitis than the presence of < 3 metabolic criteria (OR = 1.475; 95% CI: 1.149-1.895). The prevalence of metabolic syndrome was higher in subjects with erosive esophagitis than in those without (47.1% vs 37.7%, respectively; P < 0.005).

**DISCUSSION**

In this study, erosive esophagitis was identified in 10.1% of subjects who underwent routine health examinations. Central obesity, hypertension, hypertriglyceridemia, a high TC/HDL-C ratio (TC/HDL-C > 5), and AST > 37 U/L were significantly associated with erosive esophagitis. Previously, Chua et al.\(^5\) showed that an increase in BMI was related to an increase in erosive esophagitis, but Chung et al.\(^6\) did not find a significant association between BMI and erosive esophagitis. Our study showed that central obesity, but not BMI, was an independent risk factor for erosive esophagitis.

A possible reason for this finding is that BMI is not a good indicator of the percentage of body fat among Asian populations. Only the visceral component of abdominal fat increases the risk for erosive esophagitis because visceral adipose tissue is strongly associated with elevated serum levels of proinflammatory adipokines, which may play a role in the development of erosive esophagitis.\(^1,2,8\) In addition, central obesity may increase intra-abdominal pressure and decrease lower esophageal sphincter pressure, resulting in esophageal sphincter relaxation with acid reflux, which may lead to erosive esophagitis.\(^3,4\)

Studies have also shown that hypertriglyceridemia is associated with erosive esophagitis,\(^5,13-15\) but contrasting results have also been reported.\(^5\) The present study shows that hypertriglyceridemia is a potential risk factor for erosive esophagitis. Although the underlying mechanisms still need to be fully characterized, high dietary fat intake and delay in gastric emptying may increase the risk of erosive esophagitis.\(^2,4\)

The association of hyperglycemia and erosive esophagitis is controversial. Moki et al.\(^11\) demonstrated a positive relationship between erosive esophagitis and hyperglycemia. However, the majority of studies have found that hyperglycemia is not associated with erosive esophagitis.\(^13-15,25\) Our results also indicate that hyperglycemia is not associated with erosive esophagitis. Gastric emptying can be delayed by diabetic autonomic neuropathy, which may promote erosive esophagitis. However, most individuals in our study population were in generally good health, without diabetic autonomic neuropathy, which may explain our finding that hyperglycemia is not associated with erosive esophagitis. The association of hypertension and erosive esophagitis is also controversial. Gauld and colleagues\(^28\) suggested that erosive esophagitis was associated with hypertension, but Wu et al.\(^29\) failed to establish a significant relationship between hypertension and erosive esophagitis. Our study showed that hypertension...
Erosive esophagitis is becoming more prevalent in Asia, but the underlying mechanism remains unknown. Obesity has been associated with erosive esophagitis. However, the associations of metabolic syndrome, its components, and liver function with erosive esophagitis are controversial.

**Table 2** Logistic regression analysis of risk factors for erosive esophagitis

| Risk factor                  | OR (95%CI)   | P value | OR (95%CI)   | P value |
|------------------------------|--------------|---------|--------------|---------|
| Obesity                      | 1.72 (1.10-1.80) | < 0.05  | 1.38 (1.00-1.86) | < 0.05  |
| Central obesity              | 1.60 (1.20-2.14) | < 0.05  | 1.35 (1.04-1.76) | < 0.05  |
| Hypertension                 | 1.43 (1.11-1.86) | < 0.05  | 1.50 (1.15-1.95) | < 0.05  |
| Hyperglycemia                | 1.39 (1.07-1.80) | < 0.05  | 1.24 (0.91-1.67) | 0.192   |
| Hypertriglyceridemia         | 1.50 (1.15-1.95) | < 0.05  | 1.34 (1.02-1.76) | < 0.05  |
| Low HDL-C                    | 1.24 (0.91-1.67) | 0.192   | 1.67 (1.14-2.45) | < 0.05  |
| TC/HDL-C > 5                 | 1.57 (1.17-2.12) | < 0.05  | 1.59 (1.08-2.34) | < 0.05  |
| ALT > 40 (U/L)               | 1.40 (1.04-1.90) | < 0.05  | 1.963 (1.403-2.746) | < 0.05  |

1 Defined as body mass index ≥ 25 kg/m²; 2 Defined as waist circumference ≥ 90 cm for men and ≥ 80 cm for women. ALT: Alanine aminotransferase; AST: Aspartate aminotransferase; HDL-C: High-density lipoprotein cholesterol; TC: Total cholesterol.

**Table 3** Components of metabolic syndrome associated with erosive esophagitis (n (%))

| Metabolic factors | Erosive esophagitis (n = 507) | Matched normal control (n = 507) | OR (95%CI) | P value |
|-------------------|-------------------------------|----------------------------------|------------|---------|
| Number of criteria |                               |                                  |            |         |
| ≥ 1 criterion     | 473 (93.3)                     | 447 (88.2)                       | 1.867 (1.203-2.899) | 0.007   |
| ≥ 2 criteria      | 391 (77.1)                     | 335 (66.1)                       | 1.731 (1.312-2.283) | < 0.001 |
| ≥ 3 criteria      | 239 (47.1)                     | 191 (37.7)                       | 1.475 (1.149-1.895) | 0.003   |
| ≥ 4 criteria      | 112 (22.1)                     | 64 (12.6)                        | 1.963 (1.403-2.746) | < 0.001 |
| 5 criteria        | 28 (5.5)                       | 20 (3.9)                         | 1.423 (0.791-2.561) | 0.301   |

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**COMMENTS**

**Background**

Erosive esophagitis is becoming more prevalent in Asia, but the underlying mechanism remains unknown. Obesity has been associated with erosive esophagitis. However, the associations of metabolic syndrome, its components, and liver function with erosive esophagitis are controversial.

**Research frontiers**

Several previous studies have identified the risk factors of erosive esophagitis, including male sex, hiatal hernia, smoking, alcohol consumption, and obesity. This study further determined the associations between erosive esophagitis and metabolic syndrome, its components, and liver function.

**Innovations and breakthroughs**

The present study demonstrated that metabolic syndrome, impaired liver function, and dyslipidemia were associated with erosive esophagitis.

**Applications**

Individuals with metabolic syndrome and high cardiovascular risk, as defined by...
a higher ratio of total cholesterol to high-density lipoprotein cholesterol (HDL-C), are at higher risk for erosive esophagitis. This finding may suggest that treating metabolic disorders can prevent or reduce the risk of erosive esophagitis. However, further studies are needed to confirm this finding.

**Terminology**
Metabolic syndrome is a complex disorder comprising central obesity, high blood pressure, hyperglycemia, hypertriglyceridemia, and a low concentration of HDL-C. Cardiovascular risk, which is determined by a total cholesterol/HDL-C ratio > 5, correlates with the risk of cardiovascular events.

**Peer review**
Authors undertook to characterize the correlation between erosive esophagitis and metabolic syndrome and its components, abnormal liver function, and abnormal lipoprotein profiles. This case-controlled study is well organized and has enough potential for publication.

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