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ORIGINAL RESEARCH

# Essential Hypertension as an Independent Risk Factor for Erosive Esophagitis: Insights From a Single-Center Retrospective Cohort Analysis

Xiaoling Geng[1,2], Tao He[1,2], Lixia Wang[1], Zhifeng Zhang[1], Tianyu Zhao[3], Yuanjun Sun[4], Jiuyang Chang[4], Zhijun Duan[1,2]

[1]Department of Gastroenterology, First Affiliated Hospital of Dalian Medical University, Dalian, 116011, People's Republic of China; [2]Dalian Central Laboratory of Integrative Neuro-Gastrointestinal Dynamics and Metabolism Related Diseases Prevention and Treatment, Dalian, People's Republic of China; [3]Liver Disease Center of Integrated Traditional Chinese and Western Medicine, First Affiliated Hospital of Dalian Medical University, Dalian, 116011, People's Republic of China; [4]Department of Cardiology, First Affiliated Hospital of Dalian Medical University, Dalian, 116011, People's Republic of China

Correspondence: Zhijun Duan, Department of Gastroenterology, First Affiliated Hospital of Dalian Medical University, Dalian Central Laboratory of Integrative Neuro-Gastrointestinal Dynamics and Metabolism Related Diseases Prevention and Treatment, Dalian, 116011, People's Republic of China, Tel +86 83635963-3165, Email cathydoctor@sina.com; Jiuyang Chang, Department of Cardiology, First Affiliated Hospital of Dalian Medical University, Dalian, 116011, People's Republic of China, Tel +86 83635963, Email jiuyangchangcjy@126.com



**Objective:** This study aimed to investigate the association between essential hypertension and the incidence of erosive esophagitis (EE) using data from a single-center hospital cohort.

**Methods:** A total of 4844 patients who underwent gastroscopy at the First Affiliated Hospital of Dalian Medical University between June 2019 and December 2023 were included in this analysis. Participants were categorized into two groups: those with erosive esophagitis (EE) and those without, the latter comprising individuals who presented with neither reflux-related symptoms nor positive endoscopic findings. Logistic regression hazard models were used to assess the association between hypertension and EE. Correlation analyses were performed to evaluate the relationship between the severity of esophagitis and degree of hypertension.

**Results:** Among the participants, 2359 (52.41%) were classified in the EE group, while 2305 (47.59%) were in the non-EE group. Among the individuals with EE, 821 (32.3%) had a history of hypertension, compared to 640 (27.8%) in the non-EE group. This difference was statistically significant ($P < 0.05$). Furthermore, hypertension was associated with a significantly increased risk of EE (odds ratio [OR]: 1.243 [95% confidence interval [CI], 1.099–1.407], $P < 0.05$). After adjustments for potential confounders, hypertension was an independent risk factor for EE (OR: 1.213 [95% CI, 1.036–1.419]; $P < 0.05$). Additional independent risk factors for EE included high body mass index (OR = 1.034, [95% CI: 1.017–1.052; $P < 0.05$]), presence of hiatal hernia (OR = 5.722 [95% CI: 3.910–8.376; P < 0.05]), smoking history (OR: 1.249 [95% CI, 1.072–1.455]), and elevated albumin levels (OR = 1.046, 95% CI: 1.026–1.066; P < 0.05).

**Conclusion:** Essential hypertension was identified as an independent risk factor for erosive esophagitis, which suggests that individuals with essential hypertension may warrant closer monitoring for erosive esophagitis in clinical settings.

**Keywords:** erosive esophagitis, essential hypertension, gastroesophageal reflux disease, hiatal hernia, metabolic syndrome

## Introduction

Gastroesophageal reflux disease (GERD) is characterized by the reflux of gastric contents into the esophagus, oral cavity (including the pharynx), and/or lungs, resulting in various symptoms, end-organ effects, and potential complications. The most common symptoms of GERD include heartburn and acid reflux. GERD is primarily classified into erosive esophagitis, non-erosive reflux disease, and Barrett's esophagus. The global weekly prevalence of GERD symptoms is approximately 13%, with rates in Asian countries ranging from 5% to 10%, with recent data indicating increasing prevalence worldwide.[1,2]

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Essential Hypertension, a prevalent cardiovascular condition, is diagnosed by a systolic blood pressure (BP) of ≥ 140 mmHg and/or a diastolic BP of ≥ 90 mmHg, based on measurements taken in triplicate on separate days without antihypertensive medication excluded secondary factors like renal hypertension, renal vascular hypertension, endocrine and sleep apnea syndrome.. Individuals with a prior diagnosis of hypertension and ongoing medical treatment are also considered hypertensive.[3] Epidemiological data estimate that the global hypertensive population will reach 1.56 billion by 2025.[4] Some studies have suggested a potential link between gastroesophageal reflux disease (GERD), particularly erosive esophagitis, and essential hypertension. However, clinical research exploring this relationship remains limited. Therefore, this study conducted a retrospective analysis of patients who visited our hospital to investigate the potential association between erosive esophagitis and essential hypertension. Our research firstly suggested that essential hypertension was identified as an independent risk factor for erosive esophagitis, with additional risk factors including smoking, hiatal hernia, high BMI, and elevated albumin levels.

# Methods

## Participants

This single-center, retrospective study was conducted in the Department of Gastroenterology, the First Affiliated Hospital of Dalian Medical University, China. A total of 13,560 participants aged from 18–80 years old were enrolled randomly through a computer-generated random list between 30 June 2019 and 30 December 2023. Participants with a diagnosis of malignant tumors (N=903, peptic ulcer/patients on long-term proton pump inhibitors/ H2-receptor antagonists (N=3447), Achalasia or outflow tract obstruction (N=287), history of Gastrointestinal Surgery (N=989), pregnancy (N=11), secondary hypertension (N=369), incomplete medical records (N=2710) were excluded. Following these exclusions, 4844 participants were recruited in the final study cohort. Patients with EE were categorized into four groups based on the Los Angeles (LA) classification: LA-A (n = 1869), LA-B (n = 450), LA-C (n = 181), and LA-D (n = 39) (see Figure 1).

## Data Collection

Data were collected on general demographics and medical history, including sex, age, smoking and alcohol history, hypertension, fatty liver, and coronary heart disease. Blood pressure was recorded as the mean of three measurements. Smoking was defined as daily tobacco use, while alcohol consumption was defined as intake of more than 25 grams per day for men and more than 20 grams per day for women, sustained for a minimum of six consecutive months.

Blood samples were collected early in the morning after the subjects had fasted for at least ten hours on second day of hospitalized, including markers of liver function, (albumin (Alb), alanine aminotransferase (ALT), aspartate

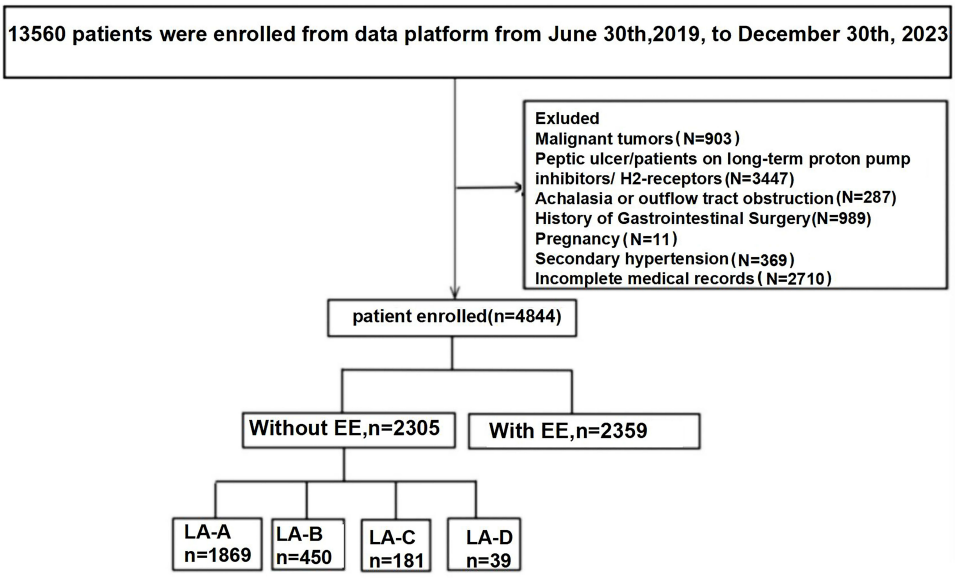


**Figure 1** Flow Chart of Participants Enrolled in the Study.

aminotransferase (AST), γ-glutamyl transpeptidase (GGT), alkaline phosphatase (ALP), total bilirubin (TB), direct bilirubin (DB), total bilirubin acids (TBA)), blood glucose (Glu), total cholesterol (TC), high-density lipoprotein cholesterol (HDL-C), low-density lipoprotein cholesterol (LDL-C), and uric acid (UA).

### Erosive Esophagitis (EE)

EE is characterized by the presence of esophageal mucosal lesions under the endoscopy, which are graded based on the Los Angeles (LA) Classification established during the World Congress of Gastroenterology.[5] The classification includes the following grades: LA-A: At least one mucosal break measuring ≤ 5 mm that does not extend between mucosal folds; LA-B: At least one mucosal break measuring > 5 mm that does not extend between mucosal folds; LA-C: At least one mucosal break that extends between mucosal folds but involves < 75% of the esophageal circumference; LA-D: At least one mucosal break that involves > 75% of the esophageal circumference. The non-erosive esophagitis group (non-EE) comprised individuals without reflux-like symptoms and with negative findings on endoscopy.

### Essential Hypertension

Essential hypertension is defined as a systolic blood pressure (SBP) ≥ 140 mmHg and/or diastolic blood pressure (DBP) ≥ 90 mmHg based on multiple measurements on different days. For this study, only patients with a history of hypertension of at least five years were included. Hypertension severity was categorized into four groups: normotensive (SBP < 140 mmHg and DBP < 90 mmHg), hypertensive group 1 (140 mmHg ≤ SBP ≤ 159 mmHg and/or 90 mmHg ≤ DBP ≤ 99 mmHg), hypertensive group 2 (160 mmHg ≤ SBP ≤ 179 mmHg and/or 100 mmHg ≤ DBP ≤ 109 mmHg), and hypertensive group 3 (SBP ≥ 180 mmHg and/or DBP ≥ 110 mmHg). These classifications align with the diagnostic criteria of the International Society of Hypertension (ISH) and the European Society of Hypertension (ESH).[6] Method for blood pressure measurement: the Omron desktop medical electronic blood pressure monitor (Omron HBP-9020 type) was adopted to measure blood pressure for the subject. The subject was measured three times, and the average value was taken when the subject was hospitalized first day.

## Statistical Analysis

Statistical analysis was performed using IBM SPSS 25.0 software (Armonk, NY, USA). Categorical data were described as absolute values (percentages). Continuous data following a normal distribution are expressed as mean ± standard deviation ($\bar{x}$ ± s), while non-normally distributed continuous data are presented as quartiles. Continuous variables were compared between the two groups using the Mann–Whitney *U*-test when the data does not conform to the normal distribution. Spearman correlation analysis was performed to evaluate relationship between the Severity of erosive esophagitis and hypertension grade. Univariate and multivariate logistic regression analyses were conducted to identify risk factors for EE, assess severity, with odds ratio (OR) and 95% confidence interval (CI) calculated for each variable. $P < 0.05$ was considered statistically significant.

# Results

## Baseline Characteristics of Study Participants

The baseline characteristics of study participants are presented in Table 1. Based on the inclusion and exclusion criteria, 2359 participants were classified into the EE group, while 2305 participants were included in the non-EE group. No significant differences in sex or age were observed between the two groups (all $P > 0.05$). The prevalence of essential hypertension was significantly higher in the EE group at 32.3% (821/2359) compared to 27.8% (640/2305) in the non-EE group. ($P < 0.05$). Among patients in the EE group, 73.6% (1869/2539) were classified as Los Angeles (LA) Grade A, 17.7% (450/2539) as LA Grade B, 7.1% (181/2539) as LA Grade C, and 1.5% (39/2539) as Grade D.

The mean systolic blood pressure was higher in the EE group (128.26 ± 15.53 mmHg) compared to the non-EE group (126.90 ± 27.5 mmHg). Furthermore, participants in the EE group demonstrated a higher prevalence of hypertension, smoking history, diabetes history, hiatal hernia, coronary heart disease, and fatty liver (all $P < 0.05$). Patients with EE had higher levels of ALT, AST, ALP, GGT, DB, GLU, CHOL, and LDL-C values compared to those without EE.

**Table 1** Baseline Characteristics of Study Participants

| Characteristics | EE (n=2359) | Non-EE (n=2305) | P |
|---|---|---|---|
| Gender (n, %) | | | 0.837 |
| Male | 1419 (55.9) | 1295 (56.2) | |
| Female | 1120 (44.1) | 1419 (55.9) | |
| Age (years) | 64.61±11.29 | 64.04±11.99 | 0.091 |
| BMI (kg/m$^2$) | 26.39±12.70 | 24.54±16.68 | 0.000 |
| Smoking (n, %) | 557 (21.9) | 439 (19) | 0.013 |
| Alcohol (n, %) | 417 (16.4) | 422 (18.3) | 0.084 |
| Hypertension (n, %) | 821 (32.3) | 640 (27.8) | 0.001 |
| Hiatal hernia (HH, n, %) | 975 (20.4) | 1155 (18.9) | 0.000 |
| Diabetes mellitus (n, %) | 341 (13.4) | 265 (115) | 0.045 |
| CAD | 149 (5.9) | 105 (4.6) | 0.041 |
| FLD | 361 (14.2) | 274 (11.9) | 0.016 |
| SBP (mmHg) | 128.26±15.53 | 126.90±27.50 | 0.037 |
| DBP (mmHg) | 79.40±9.8 | 78.97±10.40 | 0.143 |
| Glu (mmol/L) | 5.2191±1.27 | 5.09±1.15 | 0.000 |
| LDL-C (mmol/L) | 2.9 (2.42,3.26) | 2.72 (2.25,3.12) | 0.000 |
| HDL-C (mmol/L) | 1.26 (1.04,1.44) | 1.26 (1.06,1.46) | 0.901 |
| TC (mmol/L) | 5.01 (4.45,5.85) | 4.94 (4.23,5.7) | 0.000 |
| ALT (U/L) | 19 (13,27) | 17 (12,23) | 0.000 |
| AST (U/L) | 18 (15,22) | 18 (15,21) | 0.000 |
| GGT (U/L) | 20 (15,36) | 20 (15,33) | 0.000 |
| TB (pmol/L) | 12.1 (9.3,14.8) | 11.9 (9.2,14.7) | 0.625 |
| DB (pmol/L) | 3.7 (2.8~4.6) | 3.5 (2.6,4.4) | 0.000 |
| UA (μmol/L) | 309 (254,356) | 308 (253,349) | 0.244 |

**Abbreviations**: BMI, body mass index; SBP, systolic blood pressure; DBP, diastolic blood pressure; CAD, coronary artery disease; UA, uric acid; TBA, total bile acid; TB, total bilirubin; DB, direct bilirubin; AST, aspartate aminotransferase; ALT, alanine aminotransferase; GGT, γ-glutamyl transferase; ALP, alkaline phosphatase; ALB, albumin; LDL-C, low-density lipoprotein cholesterol; HDL-C, high-density lipoprotein cholesterol; GLU, glucose.

## Risk Factors for Erosive Esophagitis

Univariate logistic regression analysis indicated that a history of essential hypertension was significantly associated with an increased risk of EE (OR = 1.24395% CI: 1.099–1.407; $P < 0.05$). In addition, smoking (OR = 1.195, 95% CI: 1.038–1.374; $P < 0.05$), a high body mass index (BMI) (OR = 1.005, 95% CI: 1.000–1.011), hiatal hernia (OR = 5.711, 95% CI: 3.952–8.253; $P < 0.05$), fatty liver disease (OR = 1.229, 95% CI: 1.039–1.454; $P < 0.05$), diabetes (OR = 1.194, 95% CI: 1.006–1.418; $P < 0.05$), coronary artery disease (CAD) (OR = 1.306, 95% CI: 1.011–1.688; $P < 0.05$) were also found to potentially increase the risk of EE. Furthermore, higher levels of SBP (OR = 1.004, 95% CI: 1.000–1.007; $P < 0.05$), alkaline phosphatase (ALP) (OR = 1.002, 95% CI: 1.001–1.004; $P < 0.011$), glucose (GLU) (OR = 1.098, 95% CI: 1.045–1.153; $P < 0.002$), and albumin (ALB) levels (OR = 1.046, 95% CI: 1.029–1.064) were identified as additional risk factors for EE.

Multivariate binary logistic regression analysis was used to investigate independent risk factors for EE. The results indicated that a history of essential hypertension was an independent risk factor for EE (OR = 1.213, 95% CI: 1.036–1.419; $P < 0.05$) (see Table 2). Furthermore, smoking (OR = 1.249, 95% CI: 1.072–1.455; $P < 0.05$), high BMI (OR = 1.034, 95% CI: 1.017–1.052; $P < 0.05$), and hiatal hernia (OR = 5.722, 95% CI: 3.910–8.376; $P < 0.05$) were identified as factors that independently increased the risk of EE. In addition, higher ALB levels (OR = 1.046, 95% CI: 1.026– 1.066; ($P < 0.05$) were significantly associated with EE. The results of these analyses are presented in Table 3.

**Table 2** Risk Factors for Erosive Esophagitis (EE)

| Variables | B | Univariate Analysis | |
|---|---|---|---|
| | | OR (95% CI) | P |
| Hypertension | 0.218 | 1.243 (1.099–1.407) | 0.001 |
| BMI | 0.045 | 1.005 (1.000–1.011) | 0.045 |
| Smoking | 0.178 | 1.195 (1.038–1.374) | 0.013 |
| Alcohol | −0.131 | 0.877 (0.756–1.018) | 0.084 |
| Heart Rate | −0.003 | 0.997 (0.991–1.003) | 0.36 |
| SBP | 0.004 | 1.004 (1–1.007) | 0.033 |
| DBP | 0.004 | 1.004 (0.999–1.01) | 0.142 |
| Hiatus Hernia | 1.742 | 5.711 (3.952–8.253) | 0.000 |
| Fatty Liver Disease | 0.206 | 1.229 (1.039–1.454) | 0.016 |
| Diabetes Mellitus | 0.178 | 1.194 (1.006–1.418) | 0.042 |
| CAD | 0.267 | 1.306 (1.011–1.688) | 0.041 |
| UA | 0.001 | 1.001 (1–1.001) | 0.149 |
| TBA | −0.004 | 0.996 (0.99–1.001) | 0.126 |
| TB | −0.004 | 0.996 (0.99–1.002) | 0.211 |
| DB | −0.003 | 0.997 (0.989–1.005) | 0.456 |
| AST | −0.003 | 0.997 (0.994–1.001) | 0.106 |
| ALT | −0.001 | 0.999 (0.998–1.001) | 0.315 |
| GGT | 0.000 | 1.000 (0.999–1) | 0.392 |
| ALP | 0.002 | 1.002 (1.001–1.004) | 0.011 |
| ALB | 0.045 | 1.046 (1.029–1.064) | 0.000 |
| LDL-C | −0.005 | 0.995 (0.984–1.007) | 0.426 |
| HDL-C | −0.034 | 0.966 (0.933–1.001) | 0.058 |
| GLU | 0.093 | 1.098 (1.045–1.153) | 0.000 |

**Abbreviations**: BMI, body mass index; SBP, systolic blood pressure; DBP, diastolic blood pressure; CAD, coronary artery disease; UA, uric acid; TBA, total bile acid; TB, total bilirubin; DB, direct bilirubin; AST, aspartate aminotransferase; ALT, alanine aminotransferase; GGT, γ-glutamyl transferase; ALP, alkaline phosphatase; ALB, albumin; LDL-C, low-density lipoprotein cholesterol; HDL-C, high-density lipoprotein cholesterol; GLU, glucose.


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**Table 3** Independent Risk Factors for Erosive Esophagitis (EE)

| Variables | Beta | Univariate Analysis | |
|---|---|---|---|
| | | OR (95% CI) | P |
| Hypertension | 0.193 | 1.213 (1.036–1.419) | 0.016 |
| BMI | 0.034 | 1.034 (1.017–1.052) | 0.000 |
| Smoking | 0.222 | 1.249 (1.072–1.455) | 0.004 |
| SBP | −0.003 | 0.997 (0.993–1.002) | 0.214 |
| Hiatus Hernia | 1.744 | 5.722 (3.910–8.376) | 0.000 |
| Fatty Liver Disease | 0.050 | 1.051 (0.871–1.269) | 0.605 |
| Diabetes Mellitus | −0.006 | 0.959 (0.994–0.784) | 0.959 |
| CAD | 0.87 | 1.091 (0.817–1.456) | 0.556 |
| ALP | 0.001 | 1.001 (1.000–1.003) | 0.064 |
| ALB | 0.045 | 1.046 (1.026–1.066) | 0.000 |
| GLU | 0.039 | 1.039 (0.973–1.110) | 0.250 |

## Relationship Between the Severity of Erosive Esophagitis and Hypertension Grade

Among the study participants, a total of 821 patients were diagnosed with both EE and hypertension. The distribution of EE severity across different hypertension grades is detailed in Table 4. A significant correlation was observed between the severity of EE and the grade of hypertension ($P < 0.05$), as presented in Table 5 and illustrated in Figure 2.

## Blood Pressure by Severity of EE

The mean SBP was 126.9±27.5 mmHg in the non-EE group, 126.1±14.32 mmHg in the LA-A group, 133.2±13.2 mmHg in the LA-B group, 136.5±18.75 mmHg in the LA-C group, and 134.6±17.56 mmHg in the LA-D group. Statistically significant differences were observed between the non-EE group and the LA-B group, between the LA-A group and the LA-B group, and between the LA-A group and the LA-C group (all $P < 0.0001$).

**Table 4** Summary of Erosive Esophagitis (EE) Severity and Hypertension Grade

| | LA-A | LA-B | LA-C | LA-D |
|---|---|---|---|---|
| HBP1 | 97 | 37 | 18 | 6 |
| HBP2 | 129 | 109 | 29 | 8 |
| HBP3 | 195 | 106 | 78 | 9 |

**Table 5** Correlations Between Erosive Esophagitis (EE) Severity and Hypertension Grade

| | r | p | n |
|---|---|---|---|
| Grade of HBP | 0.072 | 0.04 | 821 |
| EE (LA classification) | | | |

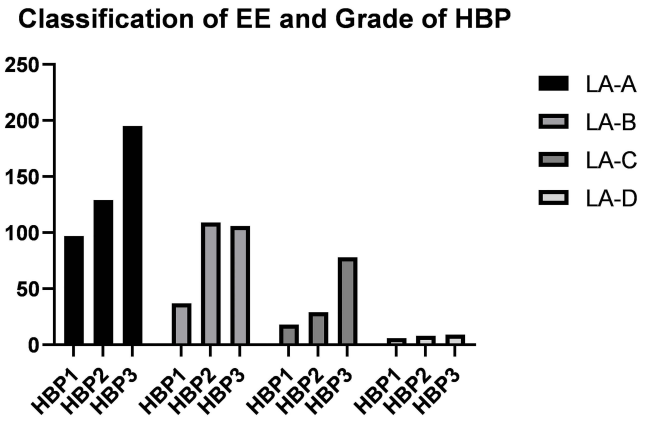


**Figure 2** Classification of Erosive Esophagitis (EE) and Hypertension Grade.

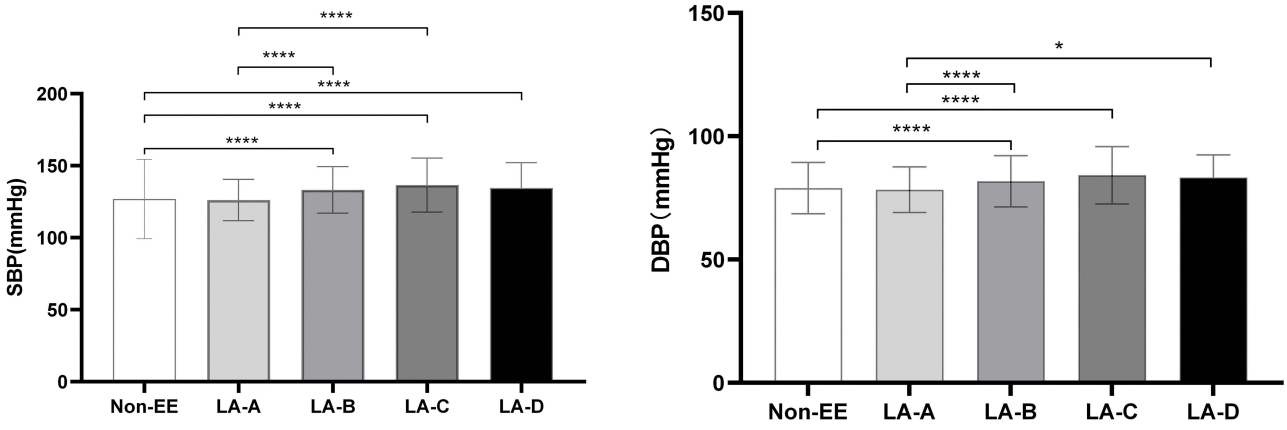


**Figure 3** Comparison of Systolic Blood Pressure (SBP) and Diastolic Blood Pressure (DBP) Among Patients with Different Severities of Erosive Esophagitis.
**Notes**: ****$P < 0.001$, *$P < 0.05$.
**Abbreviations**: EE, esophagitis; LA, Los Angeles Endoscopic Esophagitis Classification.

The mean DBP was 78.97 ± 10.40 mmHg in the non-EE group, 78.30 ± 9.24 mmHg in the LA-A group, 81.73 ± 10.44 mmHg in the LA-B group, 84.16 ± 11.68 mmHg in the LA-C group, and 83.23 ± 9.16 mmHg in the LA-D group. Significant differences were found between the LA-A group and the LA-D group, as well as between the LA-B group and the LA-C group (all $P < 0.05$) (see Figure 3).

## Discussion

The incidence of GERD has increased in recent years. There are many mechanisms underlying its pathogenesis. Recently, Zhao et al[7] explores the molecular mechanisms underlying EE and identifies potential therapeutic targets, which offered additional insights into the immune-related aspects of EE. The immune system is also indispensable in the development of vascular dysfunction and hypertension.[8] Our retrospective study demonstrated that patients diagnosed with EE exhibited a higher prevalence of hypertension compared to those without EE, with essential hypertension identified as an independent risk factor associated with greater EE severity. Similar findings were observed in a cohort study of Chinese retirees, where the final prevalence of GERD among individuals with hypertension reached 31.4% (137 out of 436), indicating a higher incidence of GERD among patients with hypertension.[9]

Another study involving 86 patients with essential hypertension, reported that 38 (44.2%) had reflux esophagitis.[10] This group experienced a total of 494 episodes of pathological reflux and 684 hypertensive episodes, with 102 (14.9%) of the hypertensive episodes coinciding with pathological acid reflux. Notably, patients with erosive esophagitis displayed


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significantly higher nocturnal blood pressure compared to those without reflux esophagitis. Acid suppression therapy resulted in significant reductions in both esophageal monitoring parameters and blood pressure parameters in patients with reflux esophagitis. This study demonstrated a significant association between hypertension and GERD, suggesting that acid suppression therapy not only restores normal esophageal pH but may also help maintain normotension.

Several potential pathophysiological mechanisms may explain the association between these two conditions. First, the vagus nerve affects esophageal peristalsis, the function of the lower esophageal sphincter, and gastric motor function.[11–13] The autonomic nervous system plays a crucial role in controlling blood pressure levels. Several experimental and clinical studies have confirmed that autonomic dysfunction is associated with the occurrence, development, and outcomes of hypertension.[14–16] Excessive activation of the sympathetic nervous system may elevate blood pressure through mechanisms such as cytokine imbalance, activation of the renin-angiotensin system, abnormal cardiopulmonary reflexes, and dysregulation of pressure receptors. Second, disturbances in gastrointestinal microbiota activate inflammatory pathways that contribute to esophageal mucosal injury. Such disturbances are associated with reduced lower esophageal sphincter resting pressure and delayed gastric emptying.[17] Intestinal microbiota may influence visceral neuromodulatory mechanisms along the "microbiota-brain-gut axis", potentially contributing to the development of visceral hypersensitivity.[18] In a recent bidirectional Mendelian randomization study, an association between GERD and the gut microbiome was confirmed. Class Mollicutes, Genus Anaerostipes, and Phylum Tenericutes emerged as potential GERD risk factors. In assessing reverse causation with GERD as the exposure and gut microbiota as the outcome, the findings indicate that GERD leads to dysbiosis in 13 distinct gut microbiota classes.[17] Furthermore, certain microbial taxa was confirmed as either protective or detrimental elements for esophageal cancer.[19]

Similarly, the abundance and diversity of gut microbes were significantly reduced in individuals with hypertension and animal models of hypertension compared to healthy controls. Intestinal microbiota can contribute to the development of hypertension through inflammatory factors, short-chain fatty acids (SCFAs), and lipopolysaccharides (LPS). Additionally, the direct infiltration of microbial components into vascular tissue may mediate inflammatory responses and dyslipidemia, which are relevant to atherosclerosis progression. The farnesoid X receptor (FXR) regulates the trimethylamine N-oxide (TMAO) convertase flavin monooxygenase 3 (FMO3), while sympathetic activation increases intestinal permeability, allowing SCFAs to mitigate inflammation driven by lipopolysaccharides (LPS).[20,21] Gomez-Arango studied 205 pregnant women and concluded that increased hypertension may be associated with alterations in gut microbiota composition and reduced butyric acid production during early pregnancy.[22] Additionally, lower nitric oxide (NO) elevated endothelin levels have been reported in patients with hypertension.[23,24] Abnormal NO levels may interfere with signaling pathways involved in the development of systemic and pulmonary hypertension.[25] Furthermore, NO plays a crucial role in regulating lower esophageal sphincter (LES) pressure, and a reduction in NO can lead to decreased LES pressure, thereby contributing to the development of esophageal reflux.[24]

Ingested food produces significant amounts of nitric oxide (NO) through entero-salivary gland recycling, leading to disturbances in the epithelial barrier, exacerbated inflammation, and accelerated transformation of the esophageal columnar epithelium.[26] The impact of NO on both esophageal function and blood pressure is substantial. In addition, patients with a history of hypertension frequently take medications such as calcium channel blockers (CCBs), β-blockers, and antiplatelet drugs. These medications can damage the esophageal mucosa, reduce the tension of the lower esophageal sphincter, contribute to the formation of the esophageal hiatus, and in some cases, lead to the development of a hiatal hernia, thereby exacerbating reflux.[27,28] This mechanism may play a significant role in the pathogenesis of gastroesophageal reflux disease. The present study identified hypertension as an independent risk factor for erosive esophagitis (EE), although systolic and diastolic blood pressure indices were not directly associated with EE. These findings suggest that the onset of erosive esophagitis may be associated with the use of antihypertensive medications.

In addition to hypertension, patients diagnosed with EE were more likely to have a history of hiatal hernia, smoking, diabetes mellitus, and fatty liver disease. Patients with EE typically exhibit elevated levels of Alanine aminotransferase (ALT), Aspartate aminotransferase (AST), Alkaline Phosphatase (ALP), Gamma-Glutamyl transferase (GGT), Direct bilirubin (DB), Glucose (GLU), Total Cholesterol (CHOL), and low density lipoprotein cholesterol (LDL-C levels).

Hiatal hernia is widely recognized as an independent risk factor for erosive esophagitis. The esophagogastric junction (EGJ) serves as the primary defense against esophageal reflux, and the presence of a hiatal hernia can compromise this

function by inducing structural abnormalities in the EGJ.[29] The anatomical morphology of the EGJ is a significant risk factor for EE and is associated with increased acid exposure time (AET) and reflux events.[30] In addition, patients with hiatal hernia have a higher risk of developing Barrett 's esophagus.[31]

Numerous studies have demonstrated that lifestyle factors, including smoking, play a crucial role in the development of GERD.[32,33] Smoking has been shown to reduce the pressure of the lower esophageal sphincter, which facilitates the reflux of gastric acid into the esophagus. Furthermore, smoking decreases saliva production in the mouth, which further impairs the esophagus's ability to neutralize and clear acid effectively. This diminished clearance prolongs exposure to harmful agents, thereby exacerbating esophageal mucosal injury. Studies have indicated that smoking cessation reduces the risk of GERD symptoms.[34]

A Japanese study identified a prevalence of erosive esophagitis at 7.5% and esophageal motility disorders at 45% among individuals with diabetes, rates notably higher than those observed in healthy controls.[35] These findings align with the baseline data presented in this study. Demeester scores were higher in the diabetic group, and parameters such as 24-hour pH impedance and high-resolution esophageal manometry (HREM) gastroscopy results were significantly greater compared to the healthy control group, which suggested that acid reflux is more prevalent among individuals with diabetes. Elevated blood glucose levels have been shown to impact esophageal sphincter function, esophageal motility, gastric emptying, and the transient relaxation of the lower esophageal sphincter.[36] Additionally, diabetic autonomic neuropathy, a complication involving nerve injury, can affect both motor and sensory functions of the esophagus, leading to delayed gastric emptying and decreased peristaltic activity.[37,38]

Metabolic syndrome (MetS) represents a group of interrelated metabolic disorders that affect multiple physiological systems. It encompasses various metabolic abnormalities, including dyslipidemia and hyperglycemia, and is clinically diagnosed based on five criteria: obesity, elevated blood pressure, elevated blood glucose, increased triglycerides, or decreased high-density lipoprotein (HDL) cholesterol levels.[39] The underlying mechanisms of MetS include insulin resistance and chronic inflammation. In this study, hypertension, hyperlipidemia, and elevated body mass index (BMI) were all found to be associated with an increased risk of erosive esophagitis. Loke et al[33] conducted a cross-sectional case-control study comparing individuals with and without chylous esophagitis, indicating a strong association between metabolic syndrome and chylous esophagitis.

Our study is first research which demonstrated that essential hypertension is an independent risk factor for erosive esophagitis. Other potential factors identified included smoking, the presence of a hiatal hernia, and a high body mass index. These factors may contribute to the development and severity of EE, underscoring the need for comprehensive management strategies that address both cardiovascular and gastrointestinal health in individuals at risk.

However, this study has several limitations. Firstly, the relatively low number of severe esophagitis (Grade C and D) may have influenced the stability of the findings, as severe esophagitis is less prevalent in China compared to other regions and countries. Additionally, several factors potentially affecting esophagitis, including sleep duration, exercise duration, dietary habits, and emotional evaluation, socioeconomic status, ethnicity, or geographic location were not included in this analysis. Future studies would benefit from a larger sample size and the inclusion of these additional variables to enhance the comprehensiveness and robustness of the findings.

## Conclusion

A history of essential hypertension is an independent risk factor for erosive esophagitis (EE). In addition to hypertension, other potential factors identified included smoking, the presence of a hiatal hernia, and a high body mass index.

## Abbreviations

EE, erosive esophagitis; BMI, Body Mass Index; SBP, systolic blood pressure; DBP, Diastolic Blood Pressure; CAD, Coronary artery disease; UA, Uric Acid; TBA, Total bile acid; TB, Total Bilirubin; DB, Direct bilirubin; AST, Aspartate aminotransferase; ALT, Alanine aminotransferase; GGT, Gamma-Glutamyl transferase; ALP, Alkaline Phosphatase; ALB, Albumin; LDL-C, low density lipoprotein cholesterol; HDL-C, High density lipoprotein cholesterol; GLU, Glucose; EGJ, esophagogastric junction.

## Data Sharing Statement

All data generated or analysed during this study are included in this article. Further enquiries can be directed to the corresponding author.

## Ethics Approval and Consent to Participate

The study was conducted in accordance with the Declaration of Helsinki (as was revised in 2013). The study was approved by Ethics Committee of the First Affiliated Hospital of Dalian Medical University (No.PJ-KS-KY-2023-33). For this retrospective study, individual consent was waived by Ethics Committee of the First Affiliated Hospital of Dalian Medical University.

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## Disclosure

The authors declare that they have no competing interests.

## References

1. Kroupa R, Konecny S, Dolina J. Current trends in the diagnosis and treatment of gastroesophageal reflux disease. *Vnitr Lek*. 2018;64(6):588–594. doi:10.36290/vnl.2018.081
2. Sandhu DS, Fass R. Current trends in the management of gastroesophageal reflux disease. *Gut Liver*. 2018;12(1):7–16. doi:10.5009/gnl16615
3. Zhou B, Perel P, Mensah GA, Ezzati M. Global epidemiology, health burden and effective interventions for elevated blood pressure and hypertension. *Nat Rev Cardiol*. 2021;18(11):785–802. doi:10.1038/s41569-021-00559-8
4. Kearney PM, Whelton M, Reynolds K, Muntner P, Whelton PK, He J. Global burden of hypertension: analysis of worldwide data. *Lancet*. 2005;365 (9455):217–223. doi:10.1016/S0140-6736(05)17741-1
5. Mari A, Na'amnih W, Ghantous L, Ahmad HS, Khoury T, Muhsen K. Quality of life and severity of symptoms among patients with various degrees of reflux esophagitis: a prospective study. *Sci Rep*. 2023;13(1):13970. doi:10.1038/s41598-023-41332-w
6. Nugroho P, Andrew H, Kohar K, Noor CA, Sutranto AL. Comparison between the world health organization (WHO) and international society of hypertension (ISH) guidelines for hypertension. *Ann Med*. 2022;54(1):837–845. doi:10.1080/07853890.2022.2044510
7. Zhao Y, Chen X, Huang Y, et al. Transcriptomic insights into hub genes, immune infiltration, and candidate drugs in erosive esophagitis. *J Inflamm Res*. 2024;17:7745–7760. doi:10.2147/JIR.S479032
8. Jung R, Wild J, Ringen J, Karbach S, Wenzel P. Innate immune mechanisms of arterial hypertension and autoimmune disease. *Am J Hypertens*. 2021;34(2):143–153. doi:10.1093/ajh/hpaa145
9. Chen T, Lu M, Wang X, et al. Prevalence and risk factors of gastroesophageal reflux symptoms in a Chinese retiree cohort. *BMC Gastroenterol*. 2012;12:161. doi:10.1186/1471-230X-12-161
10. Li ZT, Ji F, Han XW, Wang L, Yue YQ, Wang ZG. The role of gastroesophageal reflux in provoking high blood pressure episodes in patients with hypertension. *J Clin Gastroenterol*. 2018;52(8):685–690. doi:10.1097/MCG.0000000000000933
11. Cunningham KM, Horowitz M, Riddell PS, et al. Relations among autonomic nerve dysfunction, oesophageal motility, and gastric emptying in gastro-oesophageal reflux disease. *Gut*. 1991;32(12):1436–1440. doi:10.1136/gut.32.12.1436
12. Ding ZL, Xu XH, Wang ZF, Ke MY. Multi-channel electrogastrography and autonomic nervous system function in patients with non-erosive reflux disease and reflux esophagitis. *Zhonghua Yi Xue Za Zhi*. 2009;89(4):263–265.
13. Tornblom H, Simren M, Abrahamsson H. Gastrointestinal motility and neurogastroenterology. *Scand J Gastroenterol*. 2015;50(6):685–697. doi:10.3109/00365521.2015.1027265
14. Smith PA, Graham LN, Mackintosh AF, Stoker JB, Mary DA. Relationship between central sympathetic activity and stages of human hypertension. *Am J Hypertens*. 2004;17(3):217–222. doi:10.1016/j.amjhyper.2003.10.010
15. Mancia G, Grassi G. The autonomic nervous system and hypertension. *Circ Res*. 2014;114(11):1804–1814. doi:10.1161/CIRCRESAHA.114.302524
16. Valensi P. Autonomic nervous system activity changes in patients with hypertension and overweight: role and therapeutic implications. *Cardiovasc Diabetol*. 2021;20(1):170. doi:10.1186/s12933-021-01356-w
17. Rescigno M. Microbiota in reflux esophagitis and peptic ulcer disease. *Surg Infect*. 2023;24(3):245–249. doi:10.1089/sur.2023.021
18. Dinan TG, Cryan JF. Gut-brain axis in 2016: brain-gut-microbiota axis - mood, metabolism and behaviour. *Nat Rev Gastroenterol Hepatol*. 2017;14 (2):69–70. doi:10.1038/nrgastro.2016.200
19. Wang K, Wang S, Chen Y, et al. Causal relationship between gut microbiota and risk of gastroesophageal reflux disease: a genetic correlation and bidirectional Mendelian randomization study. *Front Immunol*. 2024;15:1327503. doi:10.3389/fimmu.2024.1327503
20. Verhaar BJH, Prodan A, Nieuwdorp M, Muller M. Gut microbiota in hypertension and atherosclerosis: a review. *Nutrients*. 2020;12(10):2982. doi:10.3390/nu12102982
21. Duttaroy AK. Role of gut microbiota and their metabolites on atherosclerosis, hypertension and human blood platelet function: a review. *Nutrients*. 2021;13(1):144.
22. Gomez-Arango LF, Barrett HL, McIntyre HD, et al. Increased systolic and diastolic blood pressure is associated with altered gut microbiota composition and butyrate production in early pregnancy. *Hypertension*. 2016;68(4):974–981. doi:10.1161/HYPERTENSIONAHA.116.07910

23. Korsager Larsen M, Matchkov VV. Hypertension and physical exercise: the role of oxidative stress. *Medicina*. 2016;52(1):19–27. doi:10.1016/j.medici.2016.01.005
24. Ma J, Li H. The role of gut microbiota in atherosclerosis and hypertension. *Front Pharmacol*. 2018;9:1082. doi:10.3389/fphar.2018.01082
25. Wu Y, Ding Y, Ramprasath T, Zou MH. Oxidative stress, GTPCH1, and endothelial nitric oxide synthase uncoupling in hypertension. *Antioxid Redox Signal*. 2021;34(9):750–764. doi:10.1089/ars.2020.8112
26. Iijima K, Shimosegawa T. Involvement of luminal nitric oxide in the pathogenesis of the gastroesophageal reflux disease spectrum. *J Gastroenterol Hepatol*. 2014;29(5):898–905. doi:10.1111/jgh.12548
27. Sugimoto M, Uotani T, Nishino M, et al. Antiplatelet drugs are a risk factor for esophageal mucosal injury. *Digestion*. 2013;87(4):281–289. doi:10.1159/000350438
28. Osadchuk AM, Davydkin IL, Gricenko TA, Osadchuk MA. Gastroesophageal reflux disease and esophagitis associated with the use of drugs: the modern state of the problem. *Ter Arkh*. 2019;91(8):135–140. doi:10.26442/00403660.2019.08.000228
29. Yu HX, Han CS, Xue JR, Han ZF, Xin H. Esophageal hiatal hernia: risk, diagnosis and management. *Expert Rev Gastroenterol Hepatol*. 2018;12(4):319–329. doi:10.1080/17474124.2018.1441711
30. Voulgaris T, Hoshino S, Yazaki E. Is there a direct relationship between hiatal hernia size, esophageal body hypomotility and symptomatic perception of gastroesophageal reflux episodes? *Ann Gastroenterol*. 2023;36(6):599–604. doi:10.20524/aog.2023.0830
31. Gordon C, Kang JY, Neild PJ, Maxwell JD. The role of the hiatus hernia in gastro-oesophageal reflux disease. *Aliment Pharmacol Ther*. 2004;20(7):719–732. doi:10.1111/j.1365-2036.2004.02149.x
32. Yuan S, Larsson SC. Adiposity, diabetes, lifestyle factors and risk of gastroesophageal reflux disease: a Mendelian randomization study. *Eur J Epidemiol*. 2022;37(7):747–754. doi:10.1007/s10654-022-00842-z
33. Loke SS, Yang KD, Chen KD, Chen JF. Erosive esophagitis associated with metabolic syndrome, impaired liver function, and dyslipidemia. *World J Gastroenterol*. 2013;19(35):5883–5888. doi:10.3748/wjg.v19.i35.5883
34. Ness-Jensen E, Lagergren J. Tobacco smoking, alcohol consumption and gastro-oesophageal reflux disease. *Best Pract Res Clin Gastroenterol*. 2017;31(5):501–508. doi:10.1016/j.bpg.2017.09.004
35. Fujiwara M, Miwa T, Kawai T, Odawara M. Gastroesophageal reflux disease in patients with diabetes: preliminary study. *J Gastroenterol Hepatol*. 2015;30 Suppl 1:31–35. doi:10.1111/jgh.12777
36. Monreal-Robles R, Remes-Troche JM. Diabetes and the esophagus. *Curr Treat Options Gastroenterol*. 2017;15(4):475–489. doi:10.1007/s11938-017-0153-z
37. Zhang S, Wen J, Du M, et al. Diabetes is an independent risk factor for delayed perforation after foreign bodies impacted in esophagus in adults. *United Eur Gastroenterol J*. 2018;6(8):1136–1143. doi:10.1177/2050640618784344
38. Pollis RM, Furlanetto D, Pagin E, Scaroni C, Barbot M, Voltan G. Ketosis-prone diabetes presenting with acute esophageal necrosis or "black esophagus": an intriguing new clinical association. *Endocr Metab Immune Disord Drug Targets*. 2023;23(12):1552–1556. doi:10.2174/1871530323666230621114503
39. Nomura M, Tashiro N, Watanabe T, et al. Association of symptoms of gastroesophageal reflux with metabolic syndrome parameters in patients with endocrine disease. *ISRN Gastroenterol*. 2014;2014:863206. doi:10.1155/2014/863206