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# THE ROLE OF DIFFERENT FACTORS IN THE DEVELOPMENT OF COMPLICATIONS OF GASTRIC AND DUODENAL PEPTIC ULCER DISEASE

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**Abstract:** Peptic ulcer disease (PUD) of the stomach and duodenum remains an important clinical problem despite significant advances in the diagnosis and treatment of gastrointestinal diseases. The clinical significance of PUD is determined not only by its prevalence and recurrent course but also by the possibility of developing severe complications, including gastroduodenal bleeding, perforation, penetration, and pyloroduodenal stenosis [1,2]. These complications are associated with increased morbidity, prolonged hospitalization, the need for endoscopic or surgical treatment, and an increased risk of mortality.

The development of complications of PUD is multifactorial. The most important risk factors include Helicobacter pylori infection, the use of non-steroidal anti-inflammatory drugs (NSAIDs), acetylsalicylic acid, anticoagulants and antiplatelet agents, smoking, alcohol consumption, advanced age, severe comorbidities, previous ulcer disease and gastrointestinal bleeding, as well as the characteristics of the ulcer itself [3–6]. The interaction between several risk factors may substantially increase the probability of complications.

The highest risk of ulcer-related bleeding and perforation is observed in elderly patients, particularly those receiving NSAIDs, aspirin or antithrombotic therapy and those with cardiovascular or renal comorbidities [6,8]. Therefore, modern management of PUD requires not only treatment of the ulcerative defect but also comprehensive assessment of individual risk factors and preventive measures.

**Keywords**: peptic ulcer disease, gastric ulcer, duodenal ulcer, complications, gastrointestinal bleeding, perforation, penetration, stenosis, Helicobacter pylori, NSAIDs, risk factors.

## Introduction

Peptic ulcer disease is a chronic, multifactorial disorder characterized by the formation of a mucosal defect in the stomach or duodenum as a result of an imbalance between aggressive and protective factors. The major aggressive factors include gastric acid, pepsin, Helicobacter pylori infection, non-steroidal anti-inflammatory drugs, bile acids and impaired mucosal microcirculation. Protective mechanisms include the mucus-bicarbonate barrier, adequate mucosal blood flow, epithelial regeneration and prostaglandin-dependent cytoprotection [3,9].

Although the introduction of proton pump inhibitors and effective H. pylori eradication therapy has significantly improved the prognosis of patients with PUD, complicated forms of the disease remain clinically important. Gastrointestinal bleeding and perforation are the most dangerous complications, whereas penetration and pyloroduodenal stenosis may cause severe functional disturbances and often require surgical treatment [1,2].

The epidemiology of complicated PUD has changed considerably over recent decades. The decreasing prevalence of H. pylori infection in many populations has been accompanied by an increasing relative contribution of NSAIDs, aspirin and other antithrombotic drugs, particularly among elderly patients [8,9].

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The outcome of complicated PUD depends on the number and severity of risk factors, the patient's age, the presence of comorbidities, the characteristics of the ulcer, the severity of bleeding or peritonitis, and the timing of medical intervention [2,7].

Consequently, identification of factors associated with complications is essential for early risk stratification, prevention and individualized treatment.

**The Role of Helicobacter pylori Infection**

Helicobacter pylori infection is one of the major etiological factors of peptic ulcer disease. The bacterium colonizes the gastric mucosa and induces chronic inflammation, epithelial injury and disturbances of mucosal defense mechanisms [3,9].

The pathogenic effects of H. pylori are associated with several bacterial virulence factors, including urease, cytotoxins and components of the bacterial cell wall. These factors stimulate an inflammatory response and interfere with the integrity of the gastric mucosal barrier.

The relationship between H. pylori infection and complications of PUD is complex. Some studies have demonstrated a lower prevalence of H. pylori among patients with bleeding ulcers compared with patients with uncomplicated ulcer disease. This may be partly explained by the increasing role of NSAIDs and aspirin as causes of ulcer complications, particularly in elderly patients [8,9].

Nevertheless, eradication of H. pylori remains an important component of secondary prevention. Successful eradication reduces ulcer recurrence and decreases the risk of recurrent ulcer bleeding. Therefore, current clinical recommendations emphasize testing for H. pylori and eradication therapy in patients with peptic ulcer disease [4,7].

The effect of H. pylori may also depend on the coexistence of other risk factors. In patients receiving NSAIDs or aspirin, the presence of infection may further compromise mucosal integrity. However, the interaction between H. pylori and NSAIDs is not completely uniform across different patient populations, indicating the importance of individualized risk assessment [8,9].

**Non-Steroidal Anti-Inflammatory Drugs**

NSAIDs are among the most important medication-related risk factors for peptic ulcer formation and its complications. Their gastrointestinal toxicity is primarily associated with inhibition of cyclooxygenase and reduced prostaglandin synthesis. As a result, mucosal blood flow, mucus and bicarbonate secretion, and epithelial repair are impaired [5,10].

NSAIDs may cause both gastric and duodenal ulceration and increase the risk of bleeding and perforation. The magnitude of risk depends on the specific drug, dose, duration of treatment and individual patient characteristics [5].

The risk is particularly high in elderly patients and in those with a previous history of peptic ulcer disease or gastrointestinal bleeding. Concomitant administration of corticosteroids, anticoagulants or antiplatelet agents further increases the probability of gastrointestinal complications [6,10].

The prevention of NSAID-related complications requires appropriate assessment of gastrointestinal risk before treatment. In patients with an increased risk of ulcer complications, alternative analgesic strategies should be considered whenever possible. If NSAID therapy is necessary, the lowest effective dose and gastroprotective therapy with a proton pump inhibitor may be appropriate [5,7].

Thus, rational prescribing of NSAIDs is an important component of primary and secondary prevention of complicated PUD.

**Acetylsalicylic Acid and Antithrombotic Therapy**

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Low-dose acetylsalicylic acid is widely used for the prevention of cardiovascular and cerebrovascular events. However, even low doses can increase the risk of upper gastrointestinal bleeding because of both mucosal injury and inhibition of platelet aggregation [6,11].

The risk becomes substantially higher when aspirin is combined with NSAIDs, anticoagulants or other antiplatelet agents. A history of peptic ulcer disease or previous gastrointestinal bleeding further increases the risk [6].

Patients receiving long-term antithrombotic therapy therefore represent an important high-risk group. In such patients, the benefits of antiplatelet or anticoagulant therapy must be balanced against the gastrointestinal risk.

Eradication of H. pylori in infected patients and the use of proton pump inhibitors in individuals at high risk can reduce the probability of recurrent ulcer complications [7,11].

Therefore, prevention of aspirin-associated gastrointestinal bleeding requires an individualized approach that considers age, previous ulcer disease, concomitant medication and comorbid conditions.

**Age as a Risk Factor**

Advanced age is one of the strongest predictors of complicated peptic ulcer disease. Elderly patients have a higher incidence of ulcer bleeding, perforation and adverse clinical outcomes [2,8].

Several mechanisms may explain this increased risk. Aging is associated with reduced mucosal regenerative capacity, impaired microcirculation and a higher prevalence of chronic diseases. Elderly patients are also more likely to receive NSAIDs, aspirin, anticoagulants and other medications that increase the risk of gastrointestinal injury [6].

The clinical presentation of PUD in elderly individuals may be atypical or less pronounced. Consequently, diagnosis may be delayed until the patient develops a complication such as bleeding or perforation.

Advanced age is also associated with a poorer outcome after gastrointestinal bleeding. Elderly patients have reduced cardiovascular and physiological reserves and are therefore less able to tolerate acute blood loss [2,7].

For these reasons, age should be considered an important component of risk stratification in patients with PUD.

**Smoking**

Smoking is a well-established modifiable risk factor for peptic ulcer disease and recurrent ulceration. Nicotine and other components of tobacco smoke can impair mucosal blood flow, interfere with epithelial regeneration and reduce the effectiveness of mucosal protective mechanisms [3].

Smoking may delay ulcer healing and increase the probability of recurrence. It may also contribute to treatment failure and prolonged inflammatory activity.

The association between smoking and perforated peptic ulcer disease is of particular clinical importance. Case-control studies have identified smoking as an independent risk factor for perforation [12].

Smoking cessation should therefore be considered an essential component of comprehensive management of patients with PUD. It may improve ulcer healing and reduce the risk of recurrent disease and complications.

**Alcohol Consumption**

Alcohol may directly damage the gastric mucosa by increasing epithelial permeability and disrupting the mucosal barrier. Chronic or excessive alcohol consumption may therefore contribute to mucosal inflammation and ulcer development.

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The effect of alcohol is particularly important when combined with other risk factors. Concomitant use of alcohol, NSAIDs, aspirin or anticoagulants may increase the likelihood of gastrointestinal bleeding [6].

Although alcohol is not considered the sole cause of most peptic ulcers, reduction of alcohol consumption is recommended as part of a general strategy aimed at reducing gastrointestinal risk.

**Comorbidities and Polypharmacy**

Comorbid diseases have a major influence on the severity and outcome of complicated PUD. Cardiovascular disease, chronic kidney disease, diabetes mellitus and liver disease may increase both the probability of bleeding and the risk of adverse outcomes [2,6].

Cardiovascular disease is particularly important because many patients require long-term aspirin, antiplatelet or anticoagulant therapy. When these treatments are combined with an ulcerogenic condition, the risk of gastrointestinal bleeding may increase substantially [11].

Chronic kidney disease is another important risk factor. Patients with impaired renal function may have platelet dysfunction, anemia and a greater need for medications associated with gastrointestinal injury.

Polypharmacy represents an additional problem. The combination of NSAIDs with anticoagulants, antiplatelet agents or corticosteroids is associated with a substantially higher risk of upper gastrointestinal complications [6,10].

Therefore, medication review should be an integral part of the management of patients with PUD, particularly in elderly individuals.

**Characteristics of the Ulcer**

The characteristics of the ulcer itself have an important influence on the risk of complications. Ulcer size, depth, location and the presence of exposed vessels are relevant prognostic parameters [2,7].

Large ulcers, particularly those exceeding 1 cm in diameter, are associated with an increased risk of bleeding. Larger and deeper ulcers are more likely to involve larger blood vessels and may therefore result in severe hemorrhage.

The endoscopic appearance of the ulcer is particularly important in patients presenting with bleeding. Active bleeding, a visible vessel and an adherent clot are considered high-risk endoscopic findings and may require endoscopic hemostatic intervention [7].

Chronic ulcers in the pyloroduodenal region may lead to fibrosis and scarring. Progressive scarring can result in narrowing of the gastric outlet and development of pyloroduodenal stenosis, which may cause vomiting, weight loss, dehydration and electrolyte abnormalities.

**Risk Factors for Gastroduodenal Bleeding**

Gastroduodenal bleeding is one of the most common and clinically important complications of peptic ulcer disease. It occurs when an ulcer erodes a blood vessel within the gastric or duodenal wall [2].

The major risk factors include NSAID use, aspirin, anticoagulant therapy, previous ulcer bleeding, advanced age, severe comorbidities and large ulcer size [6–8].

Previous gastrointestinal bleeding is particularly important because it substantially increases the probability of recurrent bleeding. Patients with a history of ulcer bleeding should therefore be considered a high-risk population.

Endoscopic assessment is essential for determining the risk of continued or recurrent bleeding. The identification of high-risk endoscopic features allows clinicians to perform targeted hemostatic therapy and determine the need for intensive monitoring [7].

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Current international recommendations emphasize early endoscopy, risk stratification and appropriate endoscopic hemostasis in patients with high-risk ulcer bleeding [7].

**Perforation of Peptic Ulcers**

Perforation is one of the most severe complications of PUD. It occurs when the ulcer penetrates through the entire thickness of the gastric or duodenal wall, resulting in leakage of gastrointestinal contents into the peritoneal cavity and subsequent peritonitis.

Important risk factors for perforation include NSAID use, smoking, advanced age, previous ulcer disease and severe comorbid conditions [12].

The depth and chronicity of the ulcer are also important. Progressive tissue destruction may result in penetration through all layers of the gastrointestinal wall.

Delayed presentation is a major determinant of poor outcome. Prolonged peritonitis increases the risk of sepsis, organ dysfunction and mortality. Therefore, rapid diagnosis and urgent treatment are essential in suspected perforation [2].

Several studies have also identified low body mass index, anemia and smoking as factors associated with perforation [12]. These factors may reflect poor nutritional status, chronic disease or impaired tissue repair.

**Penetration and Pyloroduodenal Stenosis**

Penetration occurs when the ulcer extends beyond the wall of the stomach or duodenum into adjacent tissues or organs. The pancreas is among the most frequently involved adjacent structures in penetrating duodenal ulcers.

Penetrating ulcers are usually associated with chronic, longstanding disease and may present with persistent or atypical pain. In some patients, the pain pattern changes because of involvement of adjacent organs.

Pyloroduodenal stenosis is generally a consequence of repeated cycles of ulceration, inflammation and fibrosis. It is more common in patients with chronic ulcers located near the pylorus or proximal duodenum.

Clinical manifestations include postprandial fullness, nausea, vomiting, weight loss and metabolic disturbances. Severe obstruction may require endoscopic or surgical intervention.

Early recognition of these complications is important for preventing severe nutritional and metabolic consequences.

**Interaction Between Risk Factors**

Current evidence indicates that complications of PUD usually result from the interaction of several risk factors rather than from a single isolated factor. For example, an elderly patient with a previous history of ulcer disease who takes NSAIDs and aspirin has a considerably higher bleeding risk than a younger patient without these characteristics [6,8].

Similarly, the combination of smoking and NSAID exposure may further impair mucosal defense and healing. Cardiovascular comorbidities may increase the risk because of the need for long-term antithrombotic therapy.

Therefore, assessment of a single risk factor is insufficient for accurate prediction. A comprehensive risk profile should include age, H. pylori status, medication use, previous ulcer complications, comorbidities, smoking, alcohol consumption and ulcer characteristics [2,6].

Such an approach provides a more accurate estimation of individual risk and allows preventive treatment to be appropriately targeted.

**Prevention of Complications**

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Prevention of PUD complications requires a multifactorial strategy. One of the most important interventions is detection and eradication of H. pylori. Successful eradication promotes ulcer healing and substantially reduces the risk of recurrence [4,7].

Patients requiring NSAIDs or aspirin should undergo individualized gastrointestinal risk assessment. In patients with increased risk, proton pump inhibitor therapy may reduce the probability of ulcer formation and bleeding [5,7].

Avoidance of unnecessary NSAID use, smoking cessation, limitation of alcohol consumption and appropriate management of comorbid diseases are additional preventive measures.

Patients receiving anticoagulants or antiplatelet drugs require particularly careful monitoring. The indication for antithrombotic treatment should be reviewed, and gastroprotective therapy should be considered when gastrointestinal risk is high.

Early recognition of alarm symptoms and timely endoscopic examination are also essential for preventing severe complications.

**Conclusion**

Complications of gastric and duodenal peptic ulcer disease develop as a result of a complex interaction between infectious, pharmacological, behavioral, demographic and systemic factors. The most important risk factors include H. pylori infection, NSAID use, aspirin and antithrombotic therapy, smoking, advanced age, severe comorbidities and a history of ulcer complications [1–6].

Gastroduodenal bleeding is particularly associated with NSAIDs, aspirin, anticoagulants, previous gastrointestinal bleeding, advanced age and significant comorbidity. Perforation is associated with NSAID exposure, smoking, chronic ulceration and several patient-specific characteristics [8,10,12].

The prevention of complications should therefore be based on comprehensive individual risk assessment rather than on the identification of a single risk factor. Detection and eradication of H. pylori, rational use of NSAIDs and antithrombotic drugs, proton pump inhibitor prophylaxis in high-risk patients, smoking cessation and limitation of alcohol consumption are important components of preventive management [4,7].

Identification of patients at high risk of complications remains an important clinical objective. Future studies should focus on developing integrated prognostic models combining clinical, endoscopic, pharmacological, inflammatory and genetic markers. Such models may allow more accurate prediction of bleeding, perforation and other complications and contribute to personalized prevention and treatment of peptic ulcer disease.

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