

Beyond Watermelon Stomach: Risk Factors and Treatment of Recurrent Bleeding in Gastric Antral Vascular Ectasia (GAVE)

Abdulmajeed Albarrak 

Department of Medicine, College of Medicine, Qassim University, Qassim, Saudi Arabia

Correspondence: Abdulmajeed Albarrak, Department of Medicine, College of Medicine, Qassim University, Qassim, 11461, Saudi Arabia, Email braka@qu.edu.sa

Abstract: Gastric Antral Vascular Ectasia (GAVE) is a rare but clinically significant cause of chronic gastrointestinal bleeding and transfusion-dependent anemia, particularly in older women. Patients with comorbidities, such as cirrhosis, chronic kidney disease, or autoimmune disorders, are at risk of developing GAVE. Pharmacological therapies demonstrate limited efficacy in the management of GAVE. They are primarily utilized as a temporary measure, serving as a bridge to definitive therapy. Additionally, these agents may be considered for patients with contraindications to endoscopic or surgical interventions. Endoscopic therapy remains the first-line approach for GAVE. Among the available modalities, argon plasma coagulation (APC) and endoscopic band ligation (EBL) are most widely employed due to their proven effectiveness and safety profiles. However, both APC and EBL recurrence rates remain high, especially in diffuse or severe cases. Radiofrequency ablation (RFA) has emerged as a promising alternative, particularly for recurrent cases; however, long-term outcomes require further validation. Surgical interventions (eg, antrectomy) are reserved for refractory cases but carry higher risks.

Keywords: GAVE, recurrent bleeding, severity, endoscopic therapy, radiofrequency ablation, argon plasma coagulation, endoscopic band ligation

Introduction

Gastric antral vascular ectasia (GAVE), initially identified by Rider et al¹ and subsequently referred to as “watermelon stomach” by Jabbari et al² because of its distinctive endoscopic look, is responsible for about 4% of cases of non-variceal upper gastrointestinal bleeding cases.³

The syndrome is more common in elderly women than males, and it is accompanied with autoimmune disorders, chronic renal failure, and cirrhosis in 30–70% of cases. The female-to-male ratio is 2:1. In the majority of cases, patients will show signs of iron deficiency anemia due to hidden gastrointestinal bleeding. However, in rare circumstances, patients may experience acute hemorrhage along with hemodynamic instability.⁴

The pathophysiology of GAVE remains incompletely understood but may involve hormonal dysregulation (particularly of gastrin and prostaglandin E2) and mechanical stress on the antral mucosa.^{5,6} Histological confirmation of the diagnosis is required to identify ectatic veins in the lamina propria and submucosa, and endoscopic detection of distinctive vascular patterns, such as longitudinal stripes resembling watermelon stripes or diffuse honeycomb patterns, is also necessary.^{7–9}

This disease is often associated with systemic diseases, such as liver cirrhosis, chronic kidney failure, autoimmune conditions, diabetes mellitus, hypothyroidism, and cardiovascular diseases so this narrative review aimed to investigate the risk factors and treatment of recurrent bleeding in GAVE.¹⁰

Epidemiology and Clinical Presentation

In cirrhotic patients, 4–6% of non-variceal bleeding are caused by GAVE, and the yearly incidence of acute upper gastrointestinal hemorrhage (UGIH) is 40–150 instances per 100,000 people worldwide.^{11,12} With a mean diagnostic age of 73 years (range 53–89 years), the condition is overwhelmingly seen in females (71% of cases).¹³ Interestingly, when linked to liver illness, the average age of onset drops to 65 years, and men are more likely to experience it.¹⁴

Iron deficiency anemia is present in 89% of patients and serves as the most common clinical manifestation.¹³ Acute presentations may include hematemesis, melena, or hemodynamic instability (orthostatic hypotension, tachycardia, or rarely, hypovolemic shock).¹⁵ Abdominal pain or gastric outlet obstruction are exceptionally rare.¹⁵

Risk Factors for Disease Severity and Therapeutic Outcomes

There are three main factors that influence the course of stomach antral vascular ectasia: the appearance on endoscopy, the presence of systemic diseases, and the choice of treatment.^{16–18} Current evidence suggests that diffuse antral involvement, characterized by confluent vascular lesions rather than the classic striped pattern, portends worse clinical outcomes. A retrospective cohort study by Thomas et al¹⁵ demonstrated 2.3-fold higher rebleeding rates in diffuse versus striped variants (95% CI 1.4–3.8, $p=0.001$) during 24-month follow-up.¹⁵ This morphological distinction has been corroborated by histological studies showing greater submucosal vascular proliferation in diffuse presentations.¹⁹

Comorbid conditions exert substantial influence on disease behavior. Chronic renal failure, present in approximately 40% of refractory cases, appears to drive recurrence through ischemia-mediated neovascularization.^{13,20} The pathophysiological interplay between uremia and vascular endothelial growth factor overexpression may explain the 58% recurrence rate observed in this population following endoscopic therapy.²¹ While cirrhosis coexists in 30–70% of GAVE patients, contemporary data from Nagesh et al²² challenge previous assumptions by demonstrating comparable bleeding severity regardless of hepatic status (OR 1.2, 95% CI 0.8–1.8).

Pharmacological Management of GAVE

While endoscopic therapy remains first-line for GAVE, several systemic agents have been investigated with varying efficacy. These agents including hormonal therapies, anti-angiogenic agents, and anti-fibrinolytics.^{10,23} Octreotide, an analogue of somatostatin, decreases the risk of bleeding in GAVE by inhibiting the action of many vasoactive chemicals, including as gastrin, prostaglandin E2, vasoactive intestinal polypeptide, and serotonin.²⁴ Although it is more effective in portal hypertensive gastropathy, the use of octreotide reduces the blood-transfusion and iron supplementation to 50% in case reports.^{5,6,11–15,22,23,25,26} Octreotide was administered at a dose of 0.1 mg twice daily or 20 mg once a month.¹⁰

Thalidomide is an angiogenesis inhibitor, mainly vascular endothelial growth factor (VEGF). In a randomized controlled study, thalidomide prevented recurrent bleeding in 71% for all gastrointestinal vascular malformation, including patients with GAVE. The dose of thalidomide in previous studies ranged from 50 mg to 400 mg per day.¹⁰ Bevacizumab, a monoclonal antibody that competitively inhibits VEGF is considered as an option for gastrointestinal bleeding.²⁷ Bevacizumab dose is 5 or 7.5 mg/kg/2–3 weeks²⁸ In a case series, it showed that 9 out of 10 patients did not require further blood transfusion after bevacizumab treatment.²⁹ Potential adverse events included worsening of hypertension and epistaxis.²⁹ Prednisolone is reported to have an effective result with GAVE, though the evidence of its benefit is limited to case reports. Potential mechanisms include vasoconstriction, anti-angiogenesis, and enhanced capillary fragility, all of which might explain the impact. Long-term use would be limited, however, due to steroids well-established side effects.²³

Or In a 2020 case report, oral methylprednisolone was initiated at 16 mg daily for two weeks, then gradually tapered to 12 mg for two weeks, 8 mg for two weeks, and subsequently maintained at 6 mg daily for two months. This tapering strategy achieved sustained improvement in hemoglobin levels and effective control of bleeding, with clinical stability maintained throughout an 8-month follow-up period.³⁰

The plasminogen activator can be competitively inhibited by tranexamic acid. Tranexamic acid was found to be able to lower the rebleeding rate in early meta-analyses.^{23,31} One method for treating GAVE and controlling bleeding is to take 500–1000 mg of oral tranexamic acid three times a day.²³

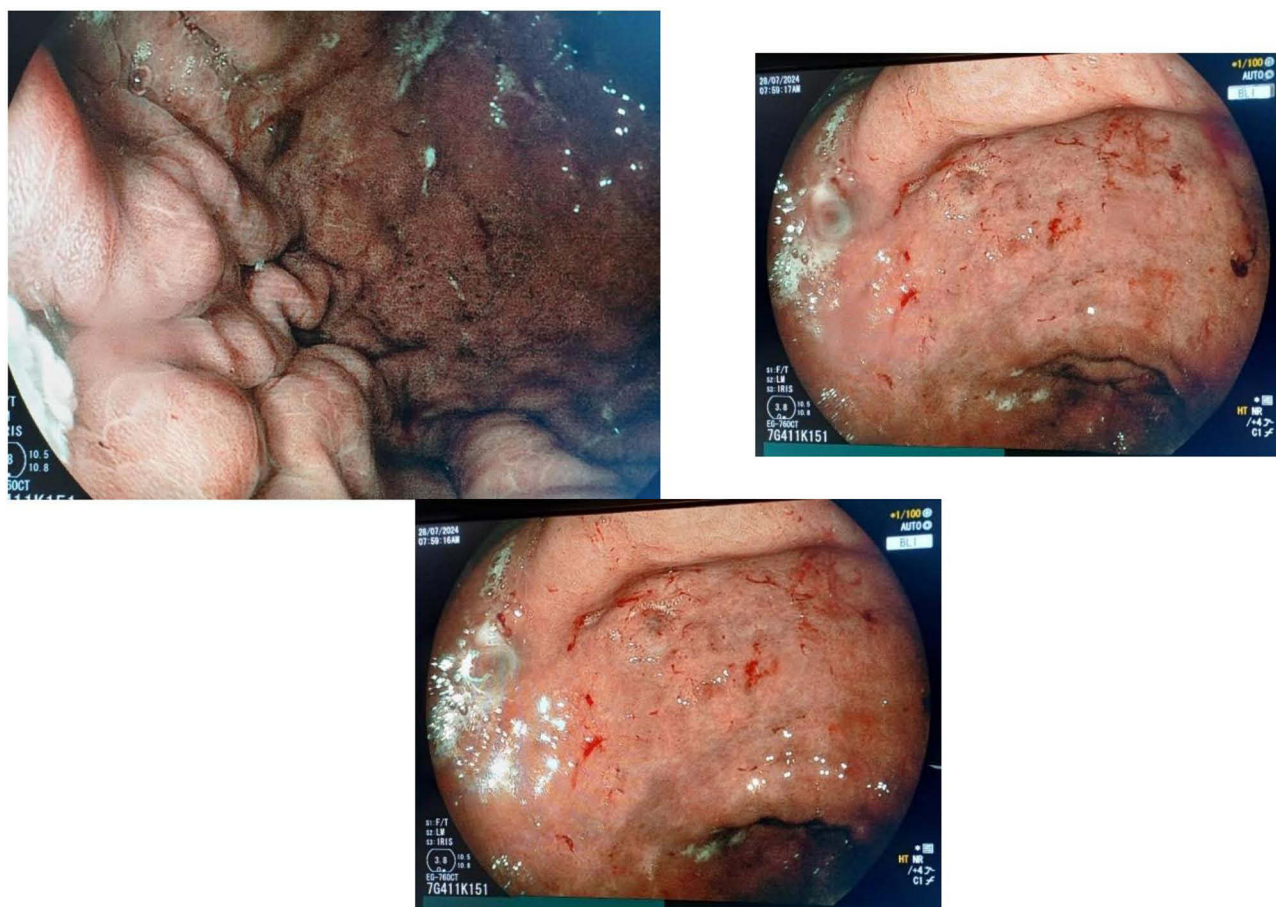


Figure 1 GAVE.

The estrogen–progesterone combination is reported to have an effect in reducing the need for transfusion for GI bleeding caused by gastrointestinal vascular malformation. In a small cross-over trial monitoring the patients for 6 months involving 10 patients, showing a significant reduction of the transfusion need in 7 of 9 patients.³² **Figure 1**

Endoscopic Therapeutic Approaches

Argon Plasma Coagulation: The Persistent Gold Standard

As the most extensively studied intervention, argon plasma coagulation maintains its first-line status through established safety profiles and technical accessibility. However, mounting evidence reveals significant limitations in durability. The inspiring work by Garg et al¹⁹ documented progressive efficacy decay, with rebleeding rates escalating from 35% at 6 months to 78.9% by 36 months post-treatment. This temporal pattern correlates with the modality's shallow (1–2mm) coagulation depth, often inadequate for complete submucosal vascular ablation.³³ Long-term outcomes remain particularly concerning, with only 25% of patients maintaining hemostasis at 46-month follow-up in prospective series.³⁴

Endoscopic Band Ligation: Depth versus Durability

The theoretical advantage of endoscopic band ligation lies in its capacity to engage deeper vascular plexuses. Initial clinical responses appear promising, with meta-analyses reporting 78–82% immediate hemostasis rates.¹³ Nevertheless, the procedure fails to address the fundamental neovascularization process, evidenced by 35–79% recurrence rates across studies.²¹ Emerging protocols combining APC with EBL show potential, particularly for circumferential lesions, with Eccles et al³⁵ reporting 42% reduction in reintervention requirements compared to monotherapy ($p=0.03$). **Figure 2**

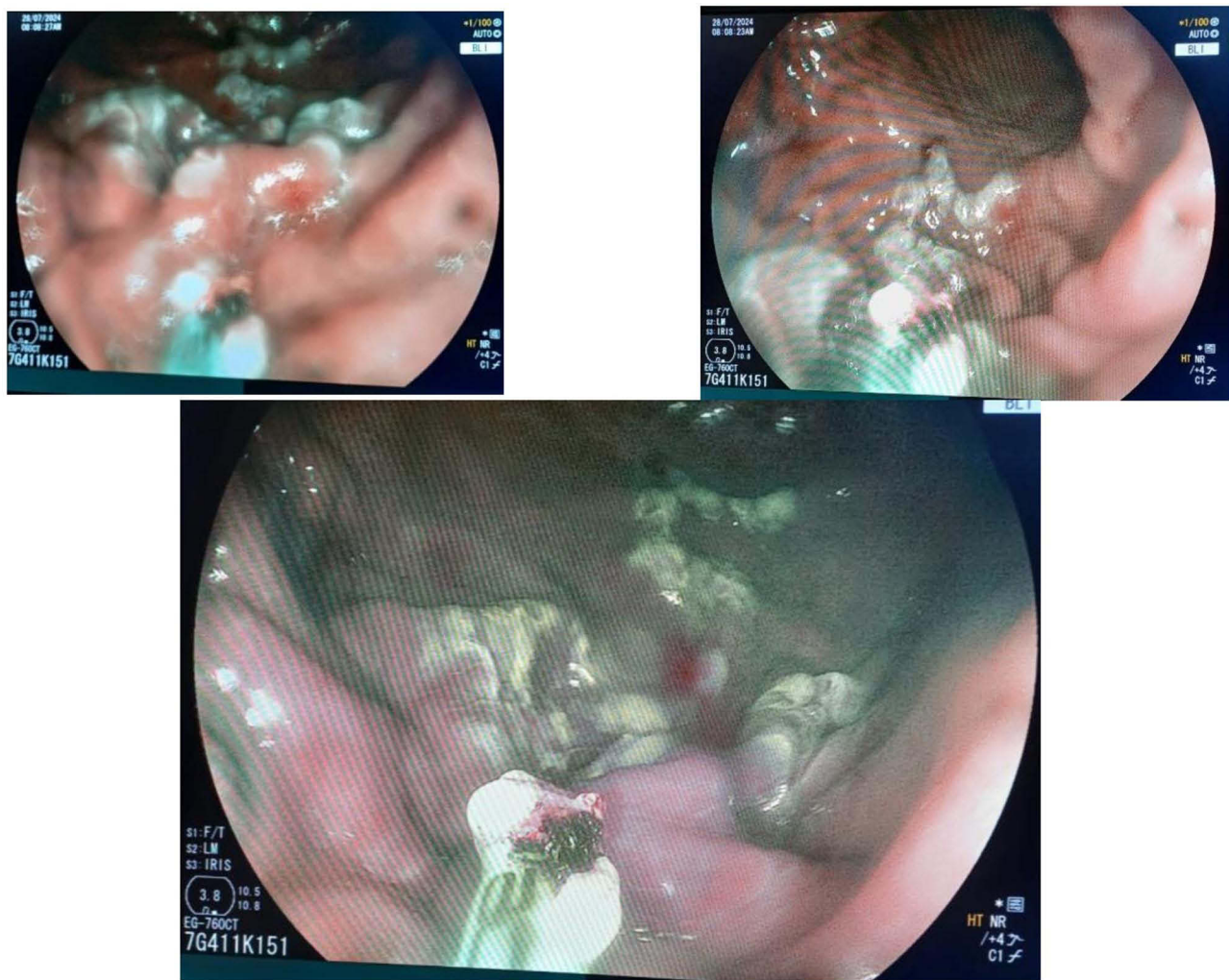


Figure 2 APC for GAVE.

Endoscope banded ligation typically begins at the pylorus and continues until the majority of lesions at the antrum have been addressed. The number of bands used to treat GAVE varies according to the extent of the lesions and the endoscopists' preferences. Submucosal capillary thrombosis follows EBL, which in turn causes ischemia necrosis of varying degrees, a superficial ulcer, and submucosal fibrosis.³⁶ [Figure 3](#)

Radiofrequency Ablation

The introduction of radiofrequency ablation has revolutionized management of refractory cases through controlled-depth (3–4mm) energy delivery. Prospective data from Magee et al³⁷ demonstrate superior performance metrics, including:

Initial technical success: 92% (vs 85% APC, $p=0.04$). 12-month rebleeding: 21–33% (vs 50–60% APC, $p=0.01$). Mean treatment sessions: 1.8 ± 0.7 (vs 3.2 ± 1.1 APC).

Notably, nodular subtypes exhibit particularly robust responses, with complete histological resolution in 68% of cases.²³ Modality nevertheless faces important constraints, including technical complexity and unresolved questions regarding optimal treatment intervals. Chronic renal failure continues to predict therapeutic failure, with recurrence rates persisting at 33% despite RFA application.³⁷ Current knowledge gaps emphasize the need for randomized controlled trials comparing RFA to conventional modalities with standardized outcome measures. [Table 1](#)

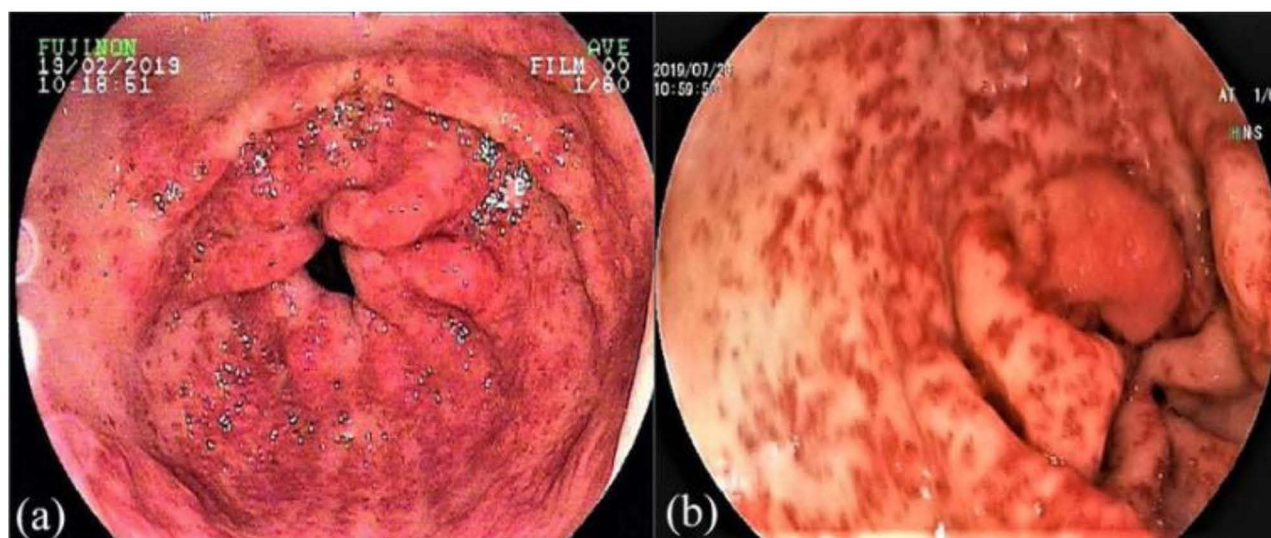


Figure 3 Endoscopic images of striped (a) and diffuse (b) GAVE.³⁶

Surgical Considerations in Refractory Cases

When endoscopic modalities prove unsuccessful, surgical intervention remains the definitive therapeutic option for gastric antral vascular ectasia (GAVE). Current consensus guidelines reserve antrectomy for specific clinical scenarios: patients demonstrating inadequate response to repeated endoscopic therapy (representing approximately 10–15% of cases), those requiring uninterrupted anticoagulation therapy, and individuals presenting with life-threatening hemodynamic instability.^{38,39}

The available outcome data, while limited by the rarity of surgical intervention, reveal several important considerations. Perioperative mortality rates range from 6.6–7.4% in contemporary series, with higher risk observed in patients with concurrent cirrhosis or portal hypertension.³⁸ Among survivors, postoperative complications occur in approximately 25% of cases, most commonly nutritional deficiencies (particularly vitamin B12, iron, and vitamin D) and dumping syndrome.⁴⁰ However, the therapeutic efficacy is substantial, with complete resolution of bleeding achieved in over 90% of cases, suggesting durable benefit for appropriately selected patients.^{38,39} Figures 4 and 5

There are no formal guidelines or consensus statements for GAVE management, and most recommendations are based on expert opinion or small studies.

Research Gaps

Most studies are retrospective, single-center, or case series. There is a need for randomized controlled trials comparing endoscopic modalities, defining optimal pharmacotherapy, and establishing criteria for surgery.

Table I Comparison of Endoscopic Therapies for GAVE

Therapy	Depth	Initial Success	Recurrence Rate	Advantages
APC	1–2mm	70–90%	35–80%	Widely available, low cost
EBL	3–4mm	75–85%	35–79%	Deeper vascular targeting
RFA	3–4mm	>70%	21–33%	Controlled depth, fewer sessions

Abbreviations: APC, Argon plasma coagulation; EBL, Endoscopic band ligation; RFA, Radiofrequency ablation.

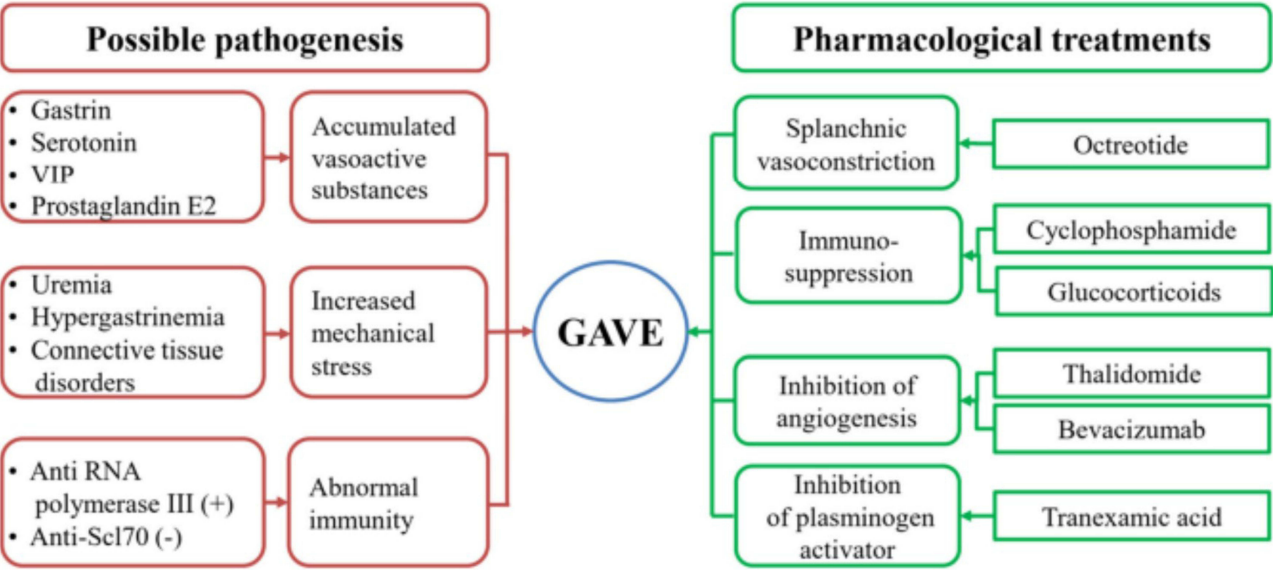


Figure 4 Potential pathogenesis of GAVE and its corresponding pharmacotherapy.²³

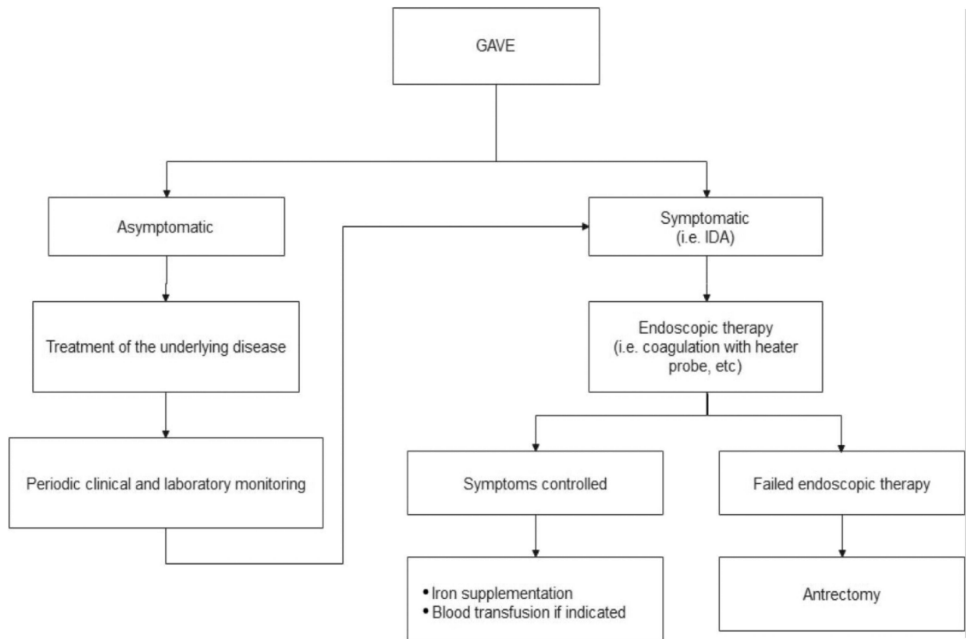


Figure 5 Management of GAVE.⁴¹

Conclusion

GAVE continues to present significant management challenges despite advances in endoscopic technology. Our synthesis of current evidence highlights several key insights. Radiofrequency ablation has emerged as a particularly promising modality, offering deeper tissue penetration (3–4mm) and superior outcomes for nodular subtypes compared to conventional argon plasma coagulation. Disease morphology remains a critical prognostic factor, with diffuse patterns and concurrent chronic renal failure portending poorer therapeutic responses across all treatment modalities. For complex cases, emerging data suggests potential benefits of combined endoscopic approaches, though optimal protocols require further standardization.

Several important knowledge gaps warrant attention in future research. Priority should be given to prospective, randomized trials directly comparing radiofrequency ablation with established techniques, employing standardized outcome measures and longer follow-up periods. The development of predictive biomarkers could revolutionize patient stratification, while investigation of novel anti-angiogenic agents may provide much-needed pharmacological options. For surgical candidates, minimally invasive techniques and enhanced perioperative protocols may help mitigate the considerable risks associated with intervention.

Abbreviations

APC, argon plasma coagulation; EBL, endoscopic band ligation; GAVE, gastric antral vascular ectasia; RFA, radiofrequency ablation; UGIH, upper gastrointestinal hemorrhage; VEGF, vascular endothelial growth factor.

Disclosure

The author(s) report no conflicts of interest in this work.

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