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EDITORIAL

Optimizing care for gastric cancer with overt bleeding: Is systemic therapy a valid option?

Emad Qayed

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Abstract

Gastric cancer (GC) and gastroesophageal junction cancer (GEJC) represent a significant burden globally, with complications such as overt bleeding (OB) further exacerbating patient outcomes. A recent study by Yao *et al* evaluated the effectiveness and safety of systematic treatment in GC/GEJC patients presenting with OB. Using propensity score matching, the study balanced the comparison groups to investigate overall survival and treatment-related adverse events. The study's findings emphasize that systematic therapy can be safe and effective and contribute to the ongoing debate about the management of advanced GC/GEJC with OB, highlighting the complexities of treatment decisions in these high-risk patients.

Key Words: Gastric cancer; Overt bleeding; Systemic therapy; Endoscopic therapy; Hemostasis

Core Tip: This editorial discusses a recent study addressing the management of gastric cancer (GC) patients with advanced GC and overt bleeding, focusing on survival outcomes and the safety of systematic therapies. The study underscores the importance of tailored treatment strategies in this high-risk patient population, providing evidence that while systematic therapy can be safe even in the presence of bleeding prior to systemic therapy. Bleeding after systemic therapy was linked to lower overall survival.

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INTRODUCTION

Gastric cancer (GC) is the fifth most common malignancy worldwide and the third leading cause of cancer-related mortality. The prognosis for GC remains poor, particularly in advanced stages, where complications such as overt bleeding (OB) can significantly impact the course of treatment and patient survival. OB in GC patients is a clinical challenge due to the associated risks of rapid deterioration, reduced quality of life, and limited therapeutic options. Previous studies have explored various strategies to manage OB, including endoscopic interventions, palliative radiotherapy, and systemic chemotherapy. However, the optimal approach remains controversial, particularly regarding the timing and selection of therapies in patients with active bleeding[1,2].

THE BURDEN OF OB IN GC

OB is a frequent and severe complication in GC and gastroesophageal junction cancer (GEJC) patients, affecting approximately 10%-15% of these patients. The bleeding typically results from tumor invasion into blood vessels, leading to hemorrhage that can be life-threatening if not promptly managed[3,4]. The prognosis for patients with OB is generally worse than for those without bleeding, with studies reporting a median overall survival (mOS) as low as 3-6 months following the onset of bleeding[5,6].

ENDOSCOPIC MANAGEMENT OF BLEEDING IN PATIENTS WITH INOPERABLE GC

Endoscopic management has recently emerged as a possible hemostatic intervention for controlling tumor bleeding in patients with inoperable GC. Endoscopic techniques, including hemostasis using argon plasma coagulation (APC) and hemostatic spray therapy, have been developed to manage bleeding effectively and improve patients' quality of life[7]. Kim and Choi[8] highlighted the role of endoscopic management in such scenarios, emphasizing its effectiveness. Endoscopic hemostasis is particularly beneficial in cases where the bleeding source is accessible, and the tumor is localized. Techniques such as endoscopic clipping, injection therapy, and APC, and endoscopic hemostatic powder spray therapy have shown high success rates in achieving immediate hemostasis. These modalities have an overall endoscopic hemostasis success rate of 67%-100%. The success of endoscopic treatment is influenced by several factors, including the size and location of the tumor, the extent of bleeding, and the patient's overall health. Lesions larger than 2 cm or those located in challenging anatomical areas may be less amenable to endoscopic control, necessitating alternative or adjunctive therapies such as radiotherapy or systemic chemotherapy[7]. The integration of endoscopic management with other treatment modalities, such as palliative radiotherapy or systemic chemotherapy, has shown promise in improving outcomes for patients with inoperable GC. This multimodal approach allows for the stabilization of bleeding while addressing the underlying malignancy, thereby extending survival and enhancing the quality of life[8,9].

Despite the high success rates of endoscopic hemostasis, rebleeding rates remained a concern, ranging from 16%-80%. Consequently, the decision to initiate systemic therapy in patients with ongoing but relatively stable bleeding presents a significant clinical dilemma.

STUDY POPULATION

The study by Yao *et al*[10] included a cohort of 171 patients diagnosed with advanced or metastatic GC/GEJC treated at Peking University Third Hospital between January 2013 and December 2021. The study population consisted of patients who received systematic therapy, including chemotherapy, targeted therapy, or immune checkpoint inhibitors, as initial anticancer treatment. Among the included patients, 32 had OB before treatment (OBBT), while 61 did not. Propensity score matching was used to ensure balanced baseline characteristics between the two groups, allowing for a more accurate comparison of outcomes.

TREATMENT AND RESULTS

All patients received systematic anticancer therapy, with the majority receiving a chemotriplet or chemodoublet-based regimen. The study found no significant difference in the overall survival between patients with OBBT and those without OBBT, with a mOS of 15.2 months and 23.7 months, respectively. However, patients who developed OB after treatment (OBAT) had a significantly worse mOS of 11.4 months, compared to 23.7 months for those without OBAT. The incidence of grade 3-4 treatment-related adverse events was similar between the OBBT and non-OBBT groups, indicating that systematic therapy did not increase toxicity in patients with OB.

The study also identified several factors associated with an increased risk of OBAT, including a history of alcohol consumption, tumor location in the gastric body, and poor radiographic response to initial therapy. These findings underscore the importance of careful patient selection and monitoring during treatment to minimize the risk of bleeding-related complications.

IMPLICATIONS FOR CLINICAL PRACTICE

The study by Yao *et al*[10] has several important implications for clinical practice. First, the findings suggest that systematic therapy can be safely administered to patients with controlled OBBT, without significantly increasing the risk of adverse events. However, clinicians must remain vigilant for the development of OBAT, which is associated with significantly worse outcomes.

The role of endoscopic management in stabilizing patients before systematic therapy cannot be overstated. Endoscopic hemostasis should be considered a first-line intervention in patients presenting with OB, particularly when the bleeding source is accessible and amenable to endoscopic control[8]. By controlling bleeding early, clinicians can improve the safety and efficacy of subsequent systematic treatments, potentially extending survival and enhancing the quality of life for these high-risk patients. However, in patients with ongoing but manageable bleeding-such as stable vital signs with intermittent OB and a gradual decline in hemoglobin-systemic therapy should be considered. Withholding systemic therapy in these cases may not be justified.

FUTURE DIRECTIONS AND INNOVATIONS IN TREATMENT

Looking forward, future research should focus on the integration of novel therapeutic agents, such as immune checkpoint inhibitors and targeted therapies, with existing treatment modalities to improve outcomes for patients with GC and OB. The development of predictive biomarkers for bleeding risk could also help in the stratification of patients and the customization of treatment plans[11,12]. Future research should aim to clarify the optimal management strategies for patients with advanced inoperable GC who are being considered for systemic therapy. Key questions include determining the best treatment approach for controlling OB and identifying the appropriate clinical endpoints that should be achieved before initiating systemic therapy. Ideally, bleeding from inoperable GC should be reliably controlled prior to systemic therapy to reduce the risk of rebleeding, which, as the current study has shown, is associated with poorer overall survival.

Innovations in endoscopic technology, such as the use of advanced imaging techniques and more precise therapeutic tools, may further enhance the effectiveness of endoscopic management in inoperable GC. Exploring the combination of endoscopic hemostasis with other modalities, such as radiofrequency ablation or photodynamic therapy, could offer new avenues for controlling tumor bleeding while minimizing the risk of rebleeding[8,9]. Prospective multicenter studies with larger patient cohorts are needed to validate the findings of Yao *et al*[10] and to explore the long-term benefits of integrating endoscopic management with systematic therapy in this patient population.

CONCLUSION

The study by Yao *et al*[10] provides important insights into the management of GC/GEJC patients with OB, emphasizing that systematic therapy can be safe and effective even in patients with OB treatment. However, the development of OB during or after treatment is associated with significantly worse outcomes, underscoring the need for careful patient selection and close monitoring. Endoscopic management plays a crucial role in the multidisciplinary approach to treating inoperable GC with OB. By combining endoscopic techniques with systemic therapies, clinicians can offer a comprehensive treatment strategy that can potentially address both the immediate and long-term needs of these high-risk patients[8,9].

FOOTNOTES

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