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Cirrhosis Progression After Variceal Bleeding: Can Early Intervention Slow Progression?

Allanazarov A.Kh

Urgench State Medical Institute, Urgench, Uzbekistan

E-mail: doktor-a-a@mail.ru

ORCID: 0000-0002-6932-4164

Umarov Z.Z

Urgench State Medical Institute, Urgench, Uzbekistan

ORCID: 0009-0002-6298-9144

Sabirova S.I

Urgench State Medical Institute, Urgench, Uzbekistan

Abstract: Acute variceal bleeding (AVB) remains one of the most dangerous triggers of acute decompensation in liver cirrhosis (LC). A bleeding episode may reduce hepatic reserve through hypovolemia, hypoxia, systemic inflammation and infection, thereby increasing the risk of recurrent bleeding, organ dysfunction and acute-on-chronic liver failure (ACLF). This review evaluates whether early intervention after AVB can influence the subsequent course of cirrhosis. Evidence from contemporary consensus documents, clinical practice guidelines, randomized trials, systematic reviews and individual-patient-data meta-analysis was integrated with observations from our PhD clinical study (2024). Particular attention was paid to early standard management, endoscopic band ligation, secondary prophylaxis and pre-emptive transjugular intrahepatic portosystemic shunt (pTIPS) in high-risk patients. Our five-year clinical observations showed higher rates of hemorrhagic syndrome and functional deterioration among patients with a previous bleeding episode. In the interventional component, a staged endoscopic–endovascular strategy was associated with a reduction in one-year rebleeding from 29.3% to 8.5%. Current evidence suggests that early, risk-adapted management can reduce rebleeding and some decompensation events; however, direct proof that it independently slows the long-term natural progression of cirrhosis remains limited. Standardized prospective endpoints are therefore required.

Keywords: liver cirrhosis; portal hypertension; acute variceal bleeding; rebleeding; decompensation; ACLF; endoscopic band ligation; pre-emptive TIPS; secondary prophylaxis.

1. INTRODUCTION

Portal hypertension and its complications represent a major stage in the clinical course of advanced chronic liver disease. Variceal bleeding is particularly important because it combines an acute hemodynamic insult with a high probability of infection, renal dysfunction, systemic inflammation and subsequent decompensation [1]. Baveno VII emphasizes personalized risk stratification and management across the continuum of portal hypertension, while the 2024 AASLD practice guidance provides an updated framework for risk assessment and treatment of portal hypertension and varices. [2]

The clinical objective after an acute bleeding episode is not limited to immediate hemostasis. The subsequent prevention of rebleeding is central because recurrent hemorrhage may trigger another episode of decompensation. This creates a clinically relevant cycle: bleeding causes physiological stress;

the resulting deterioration increases vulnerability to infection, ascites, renal dysfunction and further bleeding; recurrent events then accelerate loss of functional hepatic reserve. The EASL guideline on ACLF describes acute decompensation with organ failure as a severe syndrome with high short-term mortality, making prevention of precipitating events an important component of care. [3]

The key question of this review is therefore: can early intervention after variceal bleeding do more than control hemorrhage and reduce rebleeding—can it also slow the progression of cirrhosis? The distinction is important. A treatment may improve survival by preventing a specific acute complication without necessarily changing the underlying fibrotic or portal hypertensive process. The available evidence must therefore be interpreted according to the endpoint being measured [4].

2. AIM AND OBJECTIVES

The aim was to evaluate the role of early, risk-adapted intervention after acute variceal bleeding in reducing rebleeding, decompensation and markers of subsequent cirrhosis progression [5].

The objectives were: (1) to summarize contemporary recommendations for acute variceal bleeding; (2) to compare endoscopic, pharmacological and endovascular strategies; (3) to analyze evidence for pTIPS in high-risk patients; (4) to compare the literature with our five-year clinical observations; and (5) to identify gaps requiring prospective research [6].

3. MATERIALS AND METHODS

An integrative narrative review was prepared using PubMed/PMC-indexed publications and major professional-society guidance, including AASLD, EASL, Baveno and APASL documents. Priority was given to guidelines, randomized controlled trials, systematic reviews, meta-analyses and individual-patient-data analyses. Search concepts included “acute variceal bleeding”, “early TIPS”, “pre-emptive TIPS”, “rebleeding”, “secondary prophylaxis”, “decompensation”, “ACLF”, “portal hypertension” and “liver cirrhosis”.

Local clinical evidence was derived from the reported PhD study (2024) and was used as study-specific observational evidence to complement the literature review. The local cohort included patients with Child–Pugh A/B cirrhosis followed for up to five years and compared patients with and without a history of bleeding. These observations were summarized descriptively and were not pooled with published studies or treated as causal evidence; generalizability requires prospective external validation.

RESULTS

4. PATHOPHYSIOLOGICAL BASIS

Acute variceal bleeding can precipitate a cascade of hemodynamic and inflammatory changes. Blood loss decreases effective circulating volume and may produce tissue hypoperfusion. At the same time, impaired intestinal barrier function and bacterial translocation can intensify systemic inflammation. In advanced cirrhosis, limited physiological reserve makes the patient more susceptible to renal dysfunction, infection and organ failure. EASL ACLF guidance considers precipitating events and organ failures central to prognosis [7].

From a clinical perspective, the important concept is not that every bleeding episode irreversibly accelerates fibrosis, but that bleeding can accelerate the transition from a relatively stable compensated state to recurrent decompensation. Consequently, prevention of the next bleeding event may preserve functional status even when the underlying cirrhotic process is not eliminated [8].

5. EARLY STANDARD MANAGEMENT OF ACUTE VARICEAL BLEEDING

Contemporary guidance supports early stabilization, risk stratification, vasoactive therapy, antibiotic prophylaxis and urgent endoscopic management. ESGE guidance recommends risk stratification using Child–Pugh and MELD together with endoscopic assessment; vasoactive agents should be initiated at presentation, and antibiotic prophylaxis is recommended in patients with acute variceal hemorrhage [9].

A restrictive transfusion approach is also relevant. The purpose is to restore adequate oxygen delivery without unnecessary volume loading that could increase portal pressure. Endoscopic variceal ligation (EVL) is a central treatment for esophageal variceal hemorrhage. Randomized trials and meta-analyses have shown lower rebleeding and, in some analyses, lower mortality with ligation compared with older sclerotherapy approaches [10].

Vasoactive agents facilitate endoscopic control by reducing splanchnic blood flow and portal pressure. A network meta-analysis of randomized trials found that vasoactive drugs improved initial hemostasis compared with placebo, although differences between individual agents were less consistent and adverse-event profiles varied. A systematic review of terlipressin also found improved early bleeding control and lower in-hospital mortality compared with no vasoactive therapy, while emphasizing limitations in evidence quality [11].

Table 1. Evidence-supported components of early management

Intervention	Main clinical purpose	Typical timing/role	Evidence focus
Hemodynamic stabilization	Restore perfusion and oxygen delivery	Immediately on presentation	Avoid both under-resuscitation and excessive volume
Vasoactive therapy	Reduce portal/splanchnic pressure and facilitate hemostasis	Start at presentation; continue short-term	Improved initial bleeding control
Antibiotic prophylaxis	Reduce infection-related complications	Early after presentation	Lower infectious complications in cirrhotic AVB
Urgent endoscopy + EVL	Definitive control of esophageal variceal bleeding	After stabilization, urgently	Hemostasis and reduced rebleeding
Risk stratification	Identify high-risk patients	At presentation and after endoscopy	Child–Pugh, MELD, active bleeding and clinical status
Early/pTIPS in selected high-risk patients	Prevent treatment failure/rebleeding	Within 24–72 h in appropriate candidates	Survival and rebleeding benefit in selected groups

6. ENDOSCOPIC LIGATION AND SECONDARY PROPHYLAXIS

EVL remains an important component of secondary prophylaxis after a bleeding episode. Older randomized trials demonstrated that ligation eradicates varices in fewer sessions and reduces rebleeding compared with injection sclerotherapy. A meta-analysis of randomized trials reported lower rebleeding and mortality with ligation than sclerotherapy [12].

Secondary prophylaxis should not be viewed as a single procedure. It is a longitudinal strategy intended to prevent the next hemorrhage. Depending on the patient, this may involve repeated EVL

sessions and non-selective beta-blocker therapy. Evidence for carvedilol suggests that it can be effective for prevention of variceal bleeding, although certainty varies across outcomes and comparisons [13].

Covered TIPS is another option when recurrent bleeding occurs despite appropriate secondary prophylaxis or when the patient meets criteria for early intervention. A systematic review of randomized trials found substantially lower variceal rebleeding with covered TIPS compared with drug plus endoscopic therapy, while overall survival was not significantly different in that secondary-prophylaxis analysis. This illustrates why the indication and timing of TIPS are crucial [14].

7. PRE-EMPTIVE TIPS IN HIGH-RISK PATIENTS

The concept of pre-emptive TIPS is to intervene before recurrent bleeding or progressive decompensation occurs in patients whose risk of treatment failure is sufficiently high. The landmark randomized trial by García-Pagán and colleagues showed markedly less treatment failure/rebleeding and improved one-year survival with early TIPS in selected high-risk patients [15].

A later randomized trial in advanced cirrhosis also found higher transplantation-free survival with early TIPS compared with standard treatment. In that study, one-year transplantation-free survival was 86% in the early-TIPS group versus 73% in controls. The 2024 individual-patient-data meta-analysis strengthened the evidence: across eight studies and 1,389 patients, pTIPS significantly reduced mortality in the overall population, with a reported hazard ratio of 0.43 (95% CI 0.32–0.60).

The 2025 EASL TIPS guideline incorporates the expanding evidence base and addresses patient selection, prognostic modeling, technical aspects and indications. Importantly, pTIPS is not a universal treatment for every episode of variceal bleeding. Candidate selection must consider liver function, comorbidities, encephalopathy risk, cardiac status and the clinical circumstances of the bleeding episode.

Table 2. Selected evidence relevant to early intervention

Study / source	Design	Population / focus	Key outcome	Interpretation
Baveno VII	Consensus	Portal hypertension continuum	Risk-stratified prevention and management	Framework for personalized care
AASLD 2024	Practice guidance	Cirrhosis with portal hypertension	Risk assessment and management	Contemporary standard
ESGE guideline	Guideline	Acute variceal hemorrhage	Early drugs, antibiotics, endoscopy	Acute stabilization
de la Peña et al.	Randomized trial	Variceal hemorrhage	EVL faster eradication; less rebleeding	Supports ligation
García-Pagán et al.	RCT	High-risk AVB	Lower failure/rebleeding and mortality	Early TIPS benefit
Lv et al.	RCT	Advanced cirrhosis	Higher transplantation-free survival	Supports selected early TIPS
Nicoară-Farcău et al.	IPD meta-analysis	High-risk AVB	HR 0.43 for mortality	Strong pooled evidence
Nicoară-Farcău et al.	Before staged strategy vs after staged strategy	High-risk AVB	HR 0.43 for mortality	Strong pooled evidence

EASL TIPS 2025	Guideline	TIPS in cirrhosis	Updated indications/selection	Guides implementation
Qi et al.	Systematic review/meta-analysis	Secondary prophylaxis	HR 0.30 for rebleeding with covered TIPS	Lower rebleeding

8. EVIDENCE FROM OUR CLINICAL STUDY

In the reported clinical study, patients with Child–Pugh A/B cirrhosis were followed for five years. The analysis compared patients with a history of bleeding with those without such a history. The reported data demonstrated higher rates of hemorrhagic syndrome and cirrhosis progression among patients with previous bleeding. These findings are presented as study-specific observations and should not be interpreted as evidence of a causal effect of prior bleeding on disease progression.

After endoscopic ligation, the hemorrhagic syndrome rate at one year was 13.0% in the group without previous bleeding and 29.3% in the group with previous bleeding (p=0.0351). At 1–2 years, the corresponding values were 20.4% and 41.4% (p=0.0165). Cirrhosis progression was reported at one year in 36.2% of patients with previous bleeding versus 13.0% of patients without previous bleeding (p=0.0045), and at five years in 72.4% versus 48.1%, respectively (p=0.0086). The definition and ascertainment method for “cirrhosis progression” should be reported in the original clinical-study methods.

In the interventional component, a staged strategy combining endoscopic ligation with endovascular interventions was associated with a reduction in one-year rebleeding from 29.3% before the staged strategy to 8.5% after the staged strategy (p=0.0039), with differences persisting during later follow-up. These are study-specific observations and should be interpreted as hypothesis-generating evidence rather than proof of causality; details of sample size, baseline comparability, intervention criteria and statistical adjustment should be reported from the original clinical study.

Table 3. Reported local clinical outcomes

Outcome	Comparison	Reported value	P value
Hemorrhagic syndrome at 1 year	No prior bleeding vs prior bleeding	13.0% vs 29.3%	0.0351
Hemorrhagic syndrome at 1–2 years	No prior bleeding vs prior bleeding	20.4% vs 41.4%	0.0165
Cirrhosis progression at 1 year	Previous bleeding vs no previous bleeding	36.2% vs 13.0%	0.0045
Cirrhosis progression at 5 years	Previous bleeding vs no previous bleeding	72.4% vs 48.1%	0.0086
Rebleeding at 1 year	Before staged strategy vs after staged strategy	29.3% vs 8.5%	0.0039

9. ILLUSTRATIVE CLINICAL EXAMPLES

The following examples are educational scenarios constructed to explain how the evidence can be applied conceptually. They are not additional patient data from the authors' study.

Example 1 high-risk acute bleeding. A patient with cirrhosis presents with hematemesis and hemodynamic instability. The immediate priorities are stabilization, vasoactive therapy, antibiotic prophylaxis and urgent endoscopy. If the patient meets high-risk criteria after initial management, early

pTIPS can be considered rather than waiting for recurrent bleeding. This example reflects the strategy evaluated in randomized trials of early TIPS.

Example 2 recurrent bleeding despite secondary prophylaxis. A patient has undergone EVL and is receiving appropriate secondary prophylaxis but develops another significant variceal bleed. The clinical question shifts from routine secondary prophylaxis to whether an endovascular strategy such as TIPS is indicated. Covered TIPS has strong evidence for reducing rebleeding, although the effect on overall survival depends on patient selection and clinical context.

Example 3 apparently controlled bleeding but worsening liver function. A patient survives the acute episode but develops worsening bilirubin, creatinine, ascites or encephalopathy. This scenario illustrates why the outcome of bleeding should not be judged only by successful endoscopic hemostasis. Assessment for infection, renal dysfunction, ACLF and other precipitating events becomes essential.

10. DISCUSSION

The evidence supports a coherent clinical pathway: early control of the bleeding episode reduces immediate physiological stress; effective secondary prophylaxis reduces recurrent hemorrhage; and pTIPS in appropriately selected high-risk patients can reduce treatment failure and improve survival. However, these benefits should not be automatically described as direct reversal of cirrhosis.

The strongest evidence concerns outcomes such as rebleeding, treatment failure and survival. The evidence is less direct for long-term structural progression of cirrhosis. For example, a lower rebleeding rate may preserve functional reserve and reduce repeated decompensation, but this is not equivalent to demonstrating slower fibrosis progression. Future studies should therefore separate clinical progression from structural disease modification.

Another important issue is patient selection. The benefit of pTIPS is concentrated in carefully selected high-risk patients. TIPS can itself cause complications, including hepatic encephalopathy, and therefore requires evaluation of hepatic reserve and other contraindications. Contemporary EASL guidance and recent TIPS reviews emphasize individualized selection and modern covered-stent technology.

Secondary prophylaxis also requires continuity. A single successful EVL session does not eliminate the long-term risk of recurrent varices. Follow-up endoscopy, pharmacological prophylaxis when appropriate, surveillance of liver function and early recognition of decompensation are part of the broader prevention strategy. Evidence on carvedilol indicates efficacy comparable with other standard options in several settings, although the certainty of evidence varies.

11. LIMITATIONS

This review has several limitations. First, it is integrative and narrative rather than a new systematic review with a registered protocol. Second, the endpoints used across published studies are heterogeneous. Rebleeding, mortality, transplantation-free survival, MELD-Na change, ACLF incidence and readmission are not interchangeable. Third, the local clinical observations are from a specific patient population and should not be extrapolated without external validation. Fourth, the local clinical-study description in the supplied manuscript does not provide sufficient methodological detail on sample size, eligibility criteria, baseline comparability and statistical adjustment; these details should be added from the original study. Fifth, the relationship between reduced rebleeding and slower long-term cirrhosis progression remains biologically plausible but is not established as a causal effect.

12. FUTURE RESEARCH

Future multicenter prospective studies should enroll patients at the time of the first bleeding episode and record intervention timing precisely. A standardized endpoint set should include five- and seven-day bleeding control, six-week mortality, one-year rebleeding, ACLF, readmission, transplantation-free survival, MELD-Na trajectory and quality of life. Where possible, structural markers such as elastography and portal-hypertension measurements should be integrated with clinical outcomes.

Comparative studies should also examine whether a staged endoscopic–endovascular strategy produces durable benefit compared with contemporary standard secondary prophylaxis. Such work could clarify whether the reduction in recurrent bleeding observed in the local cohort translates into fewer episodes of decompensation and better long-term functional status.

13. CONCLUSION

Acute variceal bleeding is a major destabilizing event in liver cirrhosis. Early standard management, effective endoscopic hemostasis and appropriate secondary prophylaxis are essential to reduce immediate complications and recurrent bleeding. In selected high-risk patients, pre-emptive TIPS has demonstrated clinically important benefits in treatment failure, rebleeding and survival. The local five-year observations are consistent with the hypothesis that reducing rebleeding may reduce the subsequent burden of cirrhosis-related deterioration. Nevertheless, direct evidence that early intervention independently slows the underlying long-term progression of cirrhosis remains insufficient. Risk-adapted timing, multidisciplinary management and standardized prospective endpoints are therefore priorities for future research.

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CONFLICT OF INTEREST

The authors declare no conflicts of interest.

ETHICS

For the narrative review component, ethics approval was not applicable. For the local clinical study, the manuscript should report the ethics approval/committee information and informed-consent status from the original PhD study before submission.

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