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Editorial

Endoscopy in acute variceal bleeding: Not always the sooner, the better?

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Since the first consensus meeting on portal hypertension held in Baveno, Italy, in 1990, the statement that endoscopy should be performed as soon as possible in case of acute upper gastrointestinal bleeding in a cirrhotic patient was largely agreed upon by experts, despite limited evidence [1]. The overall severity of variceal bleeding in cirrhosis and the availability of effective endoscopic treatments argued in favour of early endoscopy according to the "the sooner, the better" strategy. Therefore, the consensus statement of Baveno VI that "endoscopy should be performed as soon as resuscitation is adequate, and preferably within 12 h of admission" appeared consistent, although some caution could appear in the ensuing comment that "endoscopic diagnosis during upper GI bleeding can be difficult when the view is obscured by blood" [2].

Although the death rate from acute variceal hemorrhage has been decreasing over the past two decades, probably because of improved general management (with prophylactic antibiotics) and more effective therapies as endoscopic variceal ligation and vasoactive drugs, variceal bleeding remains the worst clinical emergency in cirrhosis, associated with a 20% risk of death at 6 weeks. The latest guidelines state that the combination of pharmacological (vasoactive drugs and antibiotic prophylaxis) and endoscopic treatment is the most effective approach for patients bleeding from varices and still recommend that endoscopy should be performed within 12 h from hospital admission [2]. However, it must be acknowledged that only the first part of the statement is strongly evidence-based, whereas the level of evidence for the part regarding the timing of endoscopy is low, being founded on observational or retrospective studies [3–5].

Looking more in detail at the studies that, in the last decade, addressed the issue of endoscopy timing in variceal bleeding, we observe variable results.

In the study by Chen et al. [3], endoscopy performed within 12 h from admission was associated with lower 6 weeks re-bleeding (18.9% vs. 38.9%, p = .028) and mortality (27% vs. 52.8%, p = .031) rates only in patients presenting with hematemesis, whereas time to endoscopy was not relevant for mortality in patients without hematemesis as presenting symptom.

In the study by Wysocki et al. [4], if patients with acute variceal bleeding did not receive urgent endoscopy (defined as endoscopy within one day from admission) the mortality rate increased from 8.25% to 15.3%.

In the study by Hsu et al. [5], delayed endoscopy (> 15 h from admission) was an independent risk factor for in-hospital mortality (adjusted OR 3.67, 95% CI 1.27–10.39).

In contrast, in the study by Cheung et al. [6], performed in patients with hemodynamically stable variceal bleeding, there was no significant association of time to endoscopy with mortality (OR 1.0; 95% CI 0.92–1.08, p = .91).

Although all these studies identified a high MELD score as an important risk factor for re-bleeding and/or death within 6 weeks, none, until now, stratified the timing of endoscopy according to severity of liver disease.

In the present issue of Digestive and Liver Disease, Huh et al. address this subject [7]. The Authors retrospectively investigated the relationship between endoscopy timing and clinical outcome (a composite of 6-week re-bleeding and mortality) in 411 cirrhotic patients with acute variceal bleeding. All patients with suspected variceal bleeding received, at admission, terlipressin for 24–72 h and intravenous ceftriaxone at 1–2 g/24 h for 5–7 days, according to the guidelines [2]. Conversely, the decision on the timing of endoscopy depended on the discretion of the endoscopists on duty, the patient's will and hemodynamic status, at variance with current guidelines. As a result, 77% of patients underwent urgent endoscopy (within 12 h from admission) and the others had non-urgent endoscopy (more than 12 h from admission). Indeed, the median time to endoscopy differed greatly between the two groups (4.9 h vs. 32.7 h). Surprisingly, patients who received urgent endoscopy (≤12 h) had a higher unfavorable outcome than patients who received non-urgent endoscopy (> 12 h) (34.4% vs. 19.1%; P = .005), thus questioning the validity of the current recommendation that endoscopy should be preferably performed within 12 h from admission to the hospital. In the subgroup analysis, urgent endoscopy remained a significant predictor of unfavorable outcome in low-risk patients (identified as those with a MELD score

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≤17), while there was no significant difference in outcome in high-risk patients receiving urgent versus non-urgent endoscopy.

What are the possible drawbacks of this study? First, although most clinical features were comparable between patients receiving "urgent" versus "non-urgent" endoscopy, including CTP, MELD scores and hematemesis as presenting symptom, "urgent" patients had significantly faster baseline heart rates (98.4 vs. 88.7; P = .007), i.e. they were more hemodynamically unstable. Although a propensity score matching adjustment was done, not all potential confounders might have been accounted for. These are the recognized limits of a retrospective study.

Second, beside time to endoscopy, high MELD score, older age, infection and low systolic blood pressure, a further significant predictor of unfavorable outcome at multivariate analysis was "observation without endoscopic therapy", which scored the highest odds ratio, thus entailing that endoscopic treatment must be done in acute variceal bleeding also in "low-risk" patients. Therefore, both "urgent" endoscopy and observation without endoscopic therapy would be predictors of unfavorable outcome, which appears inconsistent.

The study by Huh et al. [7] questions the established paradigm of "urgent" endoscopy in variceal bleeding, as "low-risk" patients, identified as those with a MELD score ≤17, had a worse outcome and high-risk patients had no benefit. However, other recent data [8,9] support a different strategy, i.e. early TIPS (within 72 h, but ideally within 24 h), to decrease mortality in patients at high-risk of treatment failure after initial pharmacological and endoscopic therapy (identified as those in Child-Pugh class C <14 points or Child class B with active bleeding). In such a strategy, urgent endoscopy, as per current guidelines, is crucial for risk stratification.

In conclusion, the issue of the optimal timing of endoscopy in acute variceal bleeding remains controversial. Although the Authors of the study in the current issue of Digestive & Liver Disease seem reluctant to suggest a prospective, randomized study to assess the optimal timing of endoscopy in acute variceal bleeding, due to ethical issues, we need such a study. The results of their retrospective study suggest that urgent endoscopy might be more harmful than helpful, at least in patients with less severe liver disease, and might not affect the outcome of sicker patients. In everyday practice, we perceive that urgent endoscopy allows earlier identification of the bleeding source and control of bleeding, but also acknowledge that endoscopy-related complications may compromise these benefits, especially if unskilled personnel and assistants perform endoscopy, which may occur if early endoscopy is required at night. The question is substantial and ethical. Therefore, it requires a conclusive answer, based on prospectively collected data, possibly in the setting of a randomized controlled study.

Conflict of interest

None declared.

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