PhD THESIS SUMMARY:

RISK STRATIFICATION AND CLINICAL OUTCOMES IN UPPER GASTROINTESTINAL BLEEDING IN PATIENTS WITH CIRRHOSIS: ENDPOINT-DEPENDENT PREDICTION AND ENDOSCOPIC HEMOSTASIS IN VARICEAL BLEEDING

PhD student: Ilie-Marius Ciorba, MD
PhD supervisor: Professor Simona Bățagă, MD, PhD

BACKGROUND AND OBJECTIVES

Upper gastrointestinal bleeding (UGIB) in patients with cirrhosis remains a high-risk emergency despite vasoactive therapy, antibiotic prophylaxis, and endoscopic hemostasis. Prognosis reflects the interaction between the severity of the bleeding episode and baseline hepatic reserve, while the usefulness of a risk score depends on the clinical outcome for which it is applied. The overall aim of this thesis was to evaluate risk stratification in cirrhosis-associated UGIB by comparing general bleeding scores with liver-specific severity scores; developing and internally validating the VBM-5 model for in-hospital mortality; assessing CLIF-C AD for six-week mortality and early rebleeding; and performing an adjusted comparative analysis of argon plasma coagulation (APC) versus endoscopic band ligation (EBL) in acute variceal bleeding.

MATERIALS AND METHODS

The thesis comprises retrospective, observational, single-center studies of consecutive admissions to a tertiary referral center in Târgu Mureș between January 1, 2024 and December 31, 2025. The cohort included 224 adults with cirrhosis and UGIB who underwent emergency upper endoscopy; for repeat presentations, only the first eligible episode was retained. AIMS65, Rockall, and Glasgow-Blatchford were evaluated together with MELD-Na, Child-Pugh, ALBI, PALBI, PTAR, APRI, and BAR. VBM-5 incorporated age, serum albumin, serum creatinine, INR, and the initial hemoglobin value. Outcomes were in-hospital mortality, intensive care unit (ICU) admission, six-week mortality, and five-day rebleeding. Predictive performance was assessed using AUROC, DeLong testing, calibration measures, and the Brier score. Internal validation used bootstrap optimism correction, and clinical utility was explored through decision-curve analysis. Multivariable logistic models and marginal standardization were used for the APC-EBL comparison, with confounding by indication explicitly addressed.

RESULTS

Mean age was 59.7 ± 11.4 years and 77.7% of patients were male. Alcohol-related cirrhosis was present in 77.2%, while variceal bleeding was confirmed in 212/224 patients (94.6%). In-hospital mortality was 23.7% (53/224), and 16.5% (37/224) were admitted to the ICU. In score validation, MELD-Na provided the strongest discrimination for in-hospital mortality (AUROC approximately 0.90), followed by the liver-centered indices PTAR and ALBI. AIMS65 and Child-Pugh also performed well, whereas Rockall and Glasgow-Blatchford were

less informative for this endpoint. MELD-Na showed near-ideal calibration and the lowest Brier score.

ENDPOINT-SPECIFIC PERFORMANCE

The continuous VBM-5 model retained discrimination of approximately 0.90 after optimism correction and outperformed AIMS65 (AUROC 0.829). Its point-based version preserved a clinically meaningful risk gradient and net benefit across plausible thresholds, but requires external validation before clinical use. Endpoint-specific analyses showed that hepatic disease severity dominated mortality prediction, whereas AIMS65 and Rockall better reflected observed ICU triage. Combining MELD-Na with AIMS65 increased the AUROC for mortality to 0.919, while the AIMS65 plus Rockall model achieved an AUROC of 0.963 for ICU admission; the latter estimate reflects local triage decisions rather than an objective requirement for organ support alone. By six weeks, 76/224 patients (33.9%) had died, including 23 deaths after discharge, and 33/224 (14.7%) had five-day rebleeding. CLIF-C AD strongly discriminated six-week mortality (AUROC 0.891; 95% CI 0.844-0.935), comparably to MELD-Na (0.866) and AIMS65 (0.886), with near-ideal bootstrap-corrected calibration (intercept -0.019; slope 0.986; Brier score 0.119). Baseline physiological scores did not adequately predict early rebleeding. A model adding endoscopic findings and the hemostatic modality achieved an optimism-corrected AUROC of 0.671, supporting the predominantly lesion- and procedure-level nature of this outcome.

ENDOSCOPIC HEMOSTASIS, ORIGINALITY AND CONCLUSIONS

In the comparative effectiveness analysis, 177 patients with variceal bleeding were treated with EBL (n=152) or APC (n=25). APC was selected for technically difficult scenarios and a more complex clinical profile. After adjustment for age and MELD-Na, the hemostatic modality was not strongly and independently associated with mortality, whereas MELD-Na remained the dominant prognostic determinant. These findings support EBL as first-line endoscopic therapy and APC as a pragmatic rescue or adjunctive option when banding is not feasible; they do not establish equivalence between the two techniques. The originality of the thesis lies in integrating liver- and bleeding-centered scores within the same cohort, evaluating discrimination together with calibration and optimism correction, proposing the VBM-5 model and establishing an explicit endpoint-dependent prognostic framework. The results support a two-step clinical approach: rapid triage based on acute physiological compromise, followed by mortality estimation using cirrhosis-specific tools. Post-bleed mortality and hemostatic failure should be treated as distinct predictive targets. The retrospective single-center design, limited APC subgroup, and influence of local ICU admission criteria require external multicenter validation before broad implementation.

Keywords: *cirrhosis; upper gastrointestinal bleeding; variceal bleeding; risk stratification; MELD-Na; CLIF-C AD; VBM-5; endoscopic hemostasis*