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**Article Appraisal**

**Article:   Timing of Endoscopy for Acute Upper Gastrointestinal Bleeding**

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**Background and Study Objective(s):**

Acute upper gastrointestinal bleeds (UGIB) have an estimated in-hospital mortality of 10%. Endoscopy allows for visualization of the source and hemostatic treatment. A gastroenterologist international consensus group recommends endoscopy within 24 hours for acute UGIB. Previous observational studies have shown that urgent endoscopy (within 2-12 hours after presentation) in an unselected patient population with acute UGIB did not decrease mortality. However, three of these RCTs were not designed to focus on patients at high risk for further bleeding or death and did not report any assessment of patient risk. Further studies have since been done that utilize the Glasgow-Blatchford score as a validated risk-assessment tool for predicting the need for endoscopic intervention and the risk of death. Two large cohort studies using this score yielded conflicting results. Cho et al. found that endoscopy performed within 6 hours was an independent predictor of lower mortality when compared with endoscopy between 6 and 24 hours in patients with a GB score > 7. However a study by Laursen et al. found that the lowest mortality was anywhere between 6 and 24 hours after admission. Therefore this study hypothesized that patients with acute GI bleeding who were predicted to be at high risk for future bleeding or death that underwent endoscopy within 6 hours would have improved outcomes compared to endoscopy performed within 6 to 24 hours after consultation.

**Study Design:**

The study is a prospective randomized controlled trial. A gastrointestinal bleeding team screened patients for eligibility and performed randomization in the ED or after admission to a medical ward. Patients with overt signs of acute UGIB (hematemesis, melena, or both) and a Glasgow-Blatchford score of 12 or higher were eligible for enrollment. The GB score was calculated on the basis of the lowest SBP and highest pulse rate recorded and the hemoglobin and urea levels on admission to the ED, or recent values obtained before GI consultation for inpatients. They excluded patients younger than 18, unable to provide consent, pregnant, or moribund from terminal illness. They also excluded patients in hypotensive shock or whose condition did not stabilize after initial resuscitation and required urgent intervention. Randomization occurred in a 1:1 ratio using a computer generated sequence that assigned a random number and treatment. Patients were assigned to undergo either urgent endoscopy within 6 hours after GI consultation (“urgent” endoscopy group) or early endoscopy the next morning and within 24 hours (“early” endoscopy group). Both groups received an IV high dose infusion of a PPI (80mg bolus then 8mg/hr infusion) on admission and at first sign of bleeding during hospital stay. Patients suspected of variceal bleeding received a vasoactive drug as well as IV antibiotics. At endoscopy bleeding was treated with thermocoagulation or hemoclips. Bleeding varices were treated with band ligation and injection of cyanoacrylate. The primary end point was death from any cause within 30 days after randomization. Secondary end points included receipt of endoscopic therapy at first endoscopy, further bleeding, duration of stay in hospital and ICU, receipt of further endoscopic therapy, emergency surgery or angiographic embolization, blood transfusions, and adverse events within 30 days after randomization. An analysis was performed on an intention-to-treat basis and used the log-rank test to compare time from randomization to the end points and a Cox proportional-hazards model to estimate the HR and 95% CI. A Shoenfeld residual test was used to verify the assumption of proportional hazards in the Cox analysis. Secondary end points were compared using a chi-square test for the difference in proportions and with the Student’s t-test and a Mann-Whitney U test for parametric and nonparametric data, respectively. All tests of significance were two-tailed and a P value of 0.025 or less was considered to indicate statistical significance.

**Results:**

A total of 4715 patients with acute UGIB underwent screening and 598 had a Glasgow-Blatchford score of 12 or higher and 516 were enrolled in the trial with 258 randomized to urgent and early endoscopy, respectively. All cause mortality at 30 days after randomization did not differ significantly between the two groups, with 23 deaths (8.9%) in the urgent endoscopy group and 17 (6.6%) in the early endoscopy group (HR, 1.35; 95% CI, 0.72 to 2.54; P = 0.34), with a difference in mortality between the groups of 2.3 percentage points (95% CI, -2.3 to 6.9). Further bleeding within 30 days occurred in 28 patients (10.9%) in the urgent-endoscopy group and 20 patients (7.8%) in the early-endoscopy group (HR, 1.46; 95% CI, 0.83 to 2.58). Endoscopic treatment was performed during first endoscopy in 155 (60.1%) patients in the urgent-endoscopy and in 125 (48.4%) in the early-endoscopy group. The duration of hospitalization did not differ between the urgent-endoscopy group and the early endoscopy group (median of 5 days in both groups), and the two groups were similar in the number of patients who were admitted to the ICU (4 and 3, respectively), the percentage of patients who received a transfusion (89.5% and 90.7%) and the mean number of units of packed red cells received by transfusion (2.4 units in both groups). Post-hoc analysis showed that the percentage of patients with further bleeding and the percentage of patients who died did not differ significantly according to the time of day of endoscopy (further bleeding, 10.7% [17 of 159] for endoscopy performed during office hours and 10.4% [10 of 96] for endoscopy performed after hours; death, 7.5% [12 of 159] and 10.4% [10 of 96], respectively). In the early-endoscopy group, 4 of 15 patients (26.7%) who underwent endoscopy within 6 hours after randomization and 3 of 44 (6.8%) of those who underwent endoscopy between 6 and 12 hours after randomization died within 30 days; among the 194 patients who underwent endoscopy more than 12 hours after randomization, 6 (3.1%) died.

**Validity of Results:**

This study addressed a focused clinical question with objective, clinically relevant outcomes. No competing interests or funding were identified, and the study contributors are clearly identified. As previously mentioned, the patients were randomized in a 1:1 ratio using a computer generated sequence that assigned a random number and treatment. One limitation of the external validity of this study may be attributed to the intention to treat analysis used. Approximately 8% of the patients randomized to the early group ended up getting emergent endoscopy due to deterioration, therefore the possibility exists that this allowance in the protocol led to bias in the treatment arm outcomes.

**Generalizability of Results:**

This study was conducted at a Hong Kong hospital with 24 hr access to a GI fellow and endoscopist, which is unlikely to be the case for many hospitals. In a province like British Columbia, where critically ill patients may need to be transferred from rural settings to tertiary care, the results of this study could have relevance in terms of resource allocation (air transport and crews) and timing of transport. These results cannot be applied to unstable or hypotensive patients as this population was not included in the study. Finally, the study had a low incidence of variceal bleeding, which could be higher in our patient population.

**The Bottom Line:**

This prospective randomized control trial comparing urgent versus early endoscopy showed no significant difference in mortality. Additionally, there were no significant differences in secondary outcomes between the two groups.