Letter to Editor
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Endothelin-1 and Gastrointestinal Bleeding: A Predictor for Clinical Outcomes

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To the Editor

I read the article prepared by Alparslan and Baykan, titled "Evaluation of Glasgow-Blatchford, Rockall Scores and Shock Index of Patients Admitted from the Emergency Department with A Diagnosis of Upper Gastrointestinal System Bleeding" distributed in the sixth volume and second issue of your journal with great interest (1). I congratulate the authors and the editorial board for the article investigating predictive ability for mortality by analyzing shock indices together with Glasgow Blatchford Scoring and Rockall Scoring, which are used in upper gastrointestinal bleeding.

Gastrointestinal bleeding has an important place in the management of surgical or medical critical patients in emergency department practice. Multidisciplinary management with emergency medicine specialist, gastroenterologist, general surgeon, interventional radiologist is the cornerstone of the management (2-4). Although significant progress has been made in stroke management and stroke teams have been established (5), local protocols are used in the management of gastrointestinal bleeding (4). Unfortunately, local protocols are usually shaped by transfusion outside of office hours. Therefore, parameters that will reveal the urgency of the patients and the necessity of endoscopic or radiological or surgical intervention are needed. Vital parameters and scoring systems have been frequently studied in this field. In gastrointestinal bleeding studies, unlike emergency medicine practice (mortality, morbidity), the outcome of the necessity of endoscopic intervention has been studied (6-9). In this article, we would like to talk about the gastrointestinal bleeding study of Endothelin-1 (ET-1), a previously known molecule (10).

ET-1 is a potent vasoconstrictive peptide primarily produced by endothelial cells lining blood vessels. It plays a crucial role in the regulation of vascular tone, blood pressure, and cardiovascular homeostasis. ET-1 is part of the endothelin peptide family, which includes ET-2 and ET-3, though ET-1 is the most biologically active and widely studied member (11).

The synthesis of ET-1 is stimulated by factors such as hypoxia, shear stress, and pro-inflammatory cytokines. It acts through two specific G-protein coupled receptors: endothelin receptor type A (ETA) and endothelin receptor type B (ETB). ETA receptors are mainly found on vascular smooth muscle cells and mediate vasoconstriction, while ETB receptors are located on endothelial cells, promoting vasodilation through nitric oxide and prostacyclin release (12,13).

Beyond vascular tone regulation, ET-1 is implicated in various pathophysiological processes, including hypertension, heart failure, pulmonary arterial hypertension (PAH), and atherosclerosis. Elevated ET-1 levels are often observed in these conditions and are associated with poor prognosis. ET-1 also has pro-inflammatory, proliferative, and fibrotic effects, contributing to vascular remodeling and organ damage over time (14).

Given its broad role in cardiovascular diseases, ET-1 and its receptors are therapeutic targets. Endothelin receptor antagonists, such as bosentan and ambrisentan, have been developed to treat PAH and other cardiovascular disorders, underscoring ET-1's significance in disease mechanisms and treatment strategies (15).

Current literature showed that elevated ET-1 plasma levels in cirrhosis contribute significantly to portal hypertension by regulating portal vein pressure and sinusoidal endothelial structure (16,17). Based on this data Wagih Shaltout et al. speculated that ET-1 can be a predictor of intervention on esophageal variceal bleeding (10). They investigated the role of ET-1 levels as a noninvasive predictor of early esophageal variceal rebleeding within 5 days following endoscopic variceal ligation (EVL). The study included 50 patients with liver cirrhosis and portal hypertension due to hepatitis C virus infection. The results revealed that elevated

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serum ET-1 levels were significant predictors of early rebleeding. Specifically, an ET-1 cutoff level of 65.29 was found to have 88.2% specificity, 87.5% sensitivity, and 88% accuracy in predicting rebleeding. They recommended that serum endothelin-1 levels provide a practical and reliable noninvasive method for predicting early variceal rebleeding, which is a serious complication. Moreover, ET-1 levels correlated with comorbidities, such as kidney dysfunction and the length of hospital stay, highlighting its clinical importance in managing patients after EVL.

As a conclusion ET-1 could be a predictor in gastrointestinal bleeding. Researchers should be encouraged to investigate the association of ET-1 with gastrointestinal bleeding.

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