

## Improving outcomes in patients with acute upper gastrointestinal bleeding

In the issue of the Journal, there are three articles on ‘acute upper gastrointestinal bleeding (AUGIB)’. Kola *et al.*<sup>[1]</sup> report a randomized controlled trial (RCT) that compared a restrictive to liberal transfusion strategy in patients with AUGIB. The threshold to transfusion was 7 g/dl and 8 g/dl respectively in either group. The primary outcome endpoint was mortality at day 45. In the restrictive and liberal group, 10 of 112 (8.9%) and 12 of 112 (10.7%) met primary endpoint (absolute difference 1.8%; 95%CI-6.27% to 9.93%), respectively, The RCT was of a non-inferiority design with a margin of 3.5%. The authors concluded that a restrictive transfusion would not be inferior to a liberal transfusion strategy. There is a methodological issue over the acceptance of non-inferiority. The authors<sup>[2]</sup> should nonetheless be commended for this RCT which adds to other RCTs in the literature. In the current trial, 48% of patients had cirrhosis. With a small difference between transfusion thresholds (7 vs. 8 g/dL), one would not be surprised to see no difference in outcomes. The mean packed cells transfused between groups was not significantly different (1.72 units and 1.96 units, respectively). The Spanish multicenter study by Villanueva *et al.*<sup>[3]</sup> enrolled 921 patients, 21% of them had variceal hemorrhage and 31% had cirrhosis. This landmark trial compared the transfusion threshold of 7 g/dl to 9 g/dl. It found a 4% difference in mortality at day 45 mostly observed in patients with Child-Pugh class A or B cirrhosis. The TRIGGER trial<sup>[4]</sup> conducted in the United Kingdom was a clustered RCT. Six hospitals were randomized to adopt either a restrictive or a liberal transfusion strategy (8 g/dl vs. 10 g/dl). A total of 936 patients were enrolled. Fewer patients in the restrictive transfusion group received blood transfusion (33 vs. 46%) and the mean unit of packed red cell transfusion was 1.2 and 1.9, respectively. The difference was not significantly different. Not surprisingly, in this trial, clinical outcomes following either strategy were similar. All of the above cited RCTs varied in their designs and patient demographics. The caveats are, however, in exsanguinating patients and in patients with cardiovascular co-morbidities, where with holding red cell transfusion can be hazardous. In a pilot RCT<sup>[5]</sup> that enrolled 110 patients with acute

coronary syndrome or angina undergoing percutaneous coronary intervention, 6 (10.9%) patients in the liberal group (transfusion when Hb <10 g/dl) met primary outcome (death, myocardial infarction or unscheduled revascularization) compared to 14 (25.5%) in the restrictive group (transfusion when Hb <8 g/dL).

A second study in this issue of the Journal is a retrospective study by Almadi *et al.*<sup>[6]</sup> conducted in a university hospital. In this cohort of 259 patients with a mean age of 57.1, 80.1% were bleeding from a non-variceal cause. The authors compared their study to a large United Kingdom audit of AUGIB in 2007.<sup>[7]</sup> There were more ulcer diseases (36 vs. 27%), a lower rebleeding rate (8.9 vs. 13%) and a lower crude mortality rate (4.4 vs. 10%). Interestingly, only 13.9% in this cohort compared to 43% in the UK audit received red cell transfusion. The authors suggested a link between a lower rate of transfusion and mortality. In this series, none of the patients required surgery for hemostasis.

The third study was a time trend analysis of the causes of upper gastrointestinal bleeding in 2075 patients over 13 years (2004–2016) from a single tertiary care public hospital in Saudi Arabia.<sup>[8]</sup> The causes of bleeding were quite consistent throughout these years with nonvariceal causes constituting to 80.5% of them. Gastro-duodenal ulcers (34.3%) were the dominant endoscopic diagnoses.

Authors to these studies ought to be complimented for their contribution to medical knowledge. With these studies, readers are allowed a glimpse of the ‘upper gastrointestinal bleeding’ landscape in the Kingdom, the epidemiology of the condition and how it has been managed. Through critical appraisal, authors can compare and contrast current practice with what is happening in the rest of the world.

Advancements in the management of patients with AUGIB have come in small increments. Endoscopic treatment represents a major advance and is the cornerstone to the management of AUGIB. Acid suppression and use of vasoactive drugs have reduced recurrent bleeding in non-variceal and variceal bleeding, respectively. Patients with severe variceal bleeding are increasingly salvaged using Trans-jugular intrahepatic portosystemic shunts. In

refractory non-variceal cases, angiographic treatment is now preferred over surgery. As evident from one of the studies, transfusion medicine is now an integral management component. The International Consensus Group in the management of nonvariceal upper gastrointestinal bleeding suggested several research areas with a view to further improve care of patients with AUGIB.<sup>[9]</sup> These include issues in critical care including the optimal fluid regimen, management of anti-thrombotics in the acute setting and in secondary prophylaxis, identification of those at risk of further bleeds and deaths, novel endoscopic treatments specifically over TC-325, a hemostatic powder, and over-the-scope clips, and efficacy to different regimens of acid suppression. We are excited to see research studies abound on the management of AUGIB. These studies will no doubt continue to lead to improvements in patient care.

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