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Asia-Pacific working group consensus on non-variceal upper gastrointestinal bleeding: an update 2018

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Received 14 February 2018
Revised 28 March 2018
Accepted 29 March 2018

ABSTRACT

Non-variceal upper gastrointestinal bleeding remains an important emergency condition, leading to significant morbidity and mortality. As endoscopic therapy is the 'gold standard' of management, treatment of these patients can be considered in three stages: pre-endoscopic treatment, endoscopic haemostasis and post-endoscopic management. Since publication of the Asia-Pacific consensus on non-variceal upper gastrointestinal bleeding (NVUGIB) 7 years ago, there have been significant advancements in the clinical management of patients in all three stages. These include pre-endoscopy risk stratification scores, blood and platelet transfusion, use of proton pump inhibitors; during endoscopy new haemostasis techniques (haemostatic powder spray and over-the-scope clips); and post-endoscopy management by second-look endoscopy and medication strategies. Emerging techniques, including capsule endoscopy and Doppler endoscopic probe in assessing adequacy of endoscopic therapy, and the pre-emptive use of angiographic embolisation, are attracting new attention. An emerging problem is the increasing use of dual antiplatelet agents and direct oral anticoagulants in patients with cardiac and cerebrovascular diseases. Guidelines on the discontinuation and then resumption of these agents in patients presenting with NVUGIB are very much needed. The Asia-Pacific Working Group examined recent evidence and recommends practical management guidelines in this updated consensus statement.

BACKGROUND

Important advances in the management of non-variceal upper gastrointestinal bleeding (NVUGIB) have been made. The concept of pre-endoscopic treatment has changed. New devices in endoscopic haemostasis have been introduced. The increasing use of antiplatelets and anticoagulants has complicated the picture. Endoscopic interventions, such as mucosectomy and endoscopic submucosal dissection, have become standard care. These procedures are associated with marked risks of bleeding. For these reasons, the Asia-Pacific Working Group felt that it was necessary to update their consensus recommendations for the management of NVUGIB.

Similar to the previous Asia-Pacific consensus statements published in 2011,[1] this update aims to produce management guidelines for clinicians practising in community or referral hospitals. The Asia-Pacific Working Group decided that there was no need to repeat guideline statements previously recommended unless there was a change of view, but only to highlight recommendations based on new evidence reported in the past 5–10 years. Therefore, the 2011 consensus recommendations that are not dealt with in this update are considered to be still valid for the management of NVUGIB. The working group continued to use the same modified Delphi process as before[1] but chose to divide the updated consensus into three sections: (1) pre-endoscopic management, (2) endoscopic management and (3) post-endoscopic management of NVUGIB.

METHODS

The Asia-Pacific Working Group of upper gastrointestinal bleeding comprises key opinion leaders in the region/countries of Asia and Australasia—namely, Australia, China, Hong Kong, India, Japan, Korea, Malaysia, Philippines, Singapore and Taiwan. We also invited international experts from Europe and North America to share new scientific data and discuss the consensus statements. The group met during the Asia-Pacific Digestive Week 2017 in Hong Kong.

Literature search include Medline, EMBASE, the Cochrane Central Register of Controlled Trials and ISI Web of Knowledge with manual searches of bibliographies of key articles and abstracts of major gastroenterology conferences held in the past 5 years, 2012–2017 (Asian Pacific Digestive Week (APDW), Digestive Disease Week (DDW), United European Gastroenterology Week (UEGW)). Key words used included gastrointestinal bleeding, peptic ulcer disease and Asia.

The working group members from the 10 countries and regions mentioned above were selected from the scientific committee of the APDW 2017 for their expertise in areas of NVUGIB, evidence-based medicine and continuing medical education. The preparation committee in this working group comprised JJYS, PCYC, FKLC and JYWL, who drafted the initial statements based on the literature.

A modified Delphi process was used, and these drafted statements were sent to all group members for voting before the meeting, together with evidence-based reviews and other pertinent

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To cite: Sung JJY, Chiu PCY, Chan FKL, *et al*. *Gut* Epub ahead of print: [*please include* Day Month Year]. doi:10.1136/gutjnl-2018-316276

literature. Each statement was assessed on a five-point Likert scale: (1) accept completely, (2) accept with some reservation, (3) accept with major reservation, (4) reject with reservation, (5) reject completely. Results and comments were collated by emails. A statement was accepted when supported by ≥80% of the working group (ie, proportion of the working group voting on the 5-point scale for 1 or 2). Statements that did not reach consensus support during the first-round voting were modified. These modified statements were discussed during the meeting in Hong Kong, followed by a second round of voting with electronic keypads. Participants voted anonymously on statements after discussion and provided comments on the wording of the statements, which were progressively finalised through two separate iterations. If this again failed to reach consensus, the statement was rejected.

Each statement was then assessed for level of evidence by the following criteria: (a) high level of evidence; further research is very unlikely to change our confidence in the estimate of effect, (b) moderate level of evidence; further research is likely to have an important impact on our confidence in the estimate of effect and may change the recommendation and (c) low level of evidence; further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate.

The conference was supported by an unrestrictive grant from the GI Research Fund of the Institute of Digestive Disease of the Chinese University of Hong Kong. Industry support was not provided to avoid potential influence on the process of consensus development. Mandatory written disclosure of financial conflicts of interest within 24 months before the meeting was obtained from all voting participants.

In this updated consensus meeting, it was decided that the statements should focus on guiding clinical management of NVUGIB rather than on clarifying clinical concepts. There should be minimal overlap or repetition between this updated statement and the previous Asia-Pacific consensus on non-variceal upper gastrointestinal bleeding[1] unless new evidence had arisen that might change the recommendation. The panel also decided to report the statements that had not reached consensus as these are also considered useful in providing guidelines for the clinical management of such patients. Therefore, the first part of this report consists of consensus statements categorised under (1) pre-endoscopic management, (2) endoscopic management, (3) post-endoscopic management. The second part consists of statements that were rejected after deliberations and debate among panel members. These latter statements point towards new management concepts or strategies, but they are not accepted as recommendations because of insufficient evidence in the existing literature.

CONSENSUS STATEMENTS

Pre-endoscopic management

Statement 1: The Glasgow Blatchford Score (GBS) should be used in predicting clinical outcome of all patients presenting with upper gastrointestinal bleeding *(Accept—agreement: 94.5%, level of evidence: high)*

The most widely validated scoring methods for prediction of recurrent bleeding and mortality are the Rockall (RS), GBS and AIMS65. Many studies in the past 5 years have compared the performance of various scoring systems as a risk stratification tool.

The largest study is a multicentre prospective cohort that recruited over 3000 patients with UGIB from six hospitals in Europe, North America, Asia and Oceania. It compared the pre-endoscopy (admission RS, AIMS65 and GBS) and post-endoscopy scores (full RS, and Progetto Nazionale Emorragia Digestiva (PNED)) for their ability to predict clinical outcome. GBS was found to be the best of these scoring systems for predicting the need for intervention and mortality.[2] GBS also out-performed admission RS and AIMS65 in predicting the need for endoscopic treatment. GBS ≥7 is the best score to predict the requirement for endoscopic treatment.

Among these four scoring systems, GBS most accurately predicts the need for hospital admission and mortality. In Korea, a study recruiting 523 patients with NVUGIB concluded that GBS predicted the requirement of blood transfusion with highest accuracy.[3] It was comparable to the full RS and AIMS65 for predicting 30-day mortality and endoscopic intervention. A multicentre cohort study from Korea comparing GBS and RS confirmed that GBS was useful in predicting the need for hospital-based intervention, and RS was useful for predicting outcome.[4]

A smaller-scale study from Europe comparing GBS, AIMS65 and RS in 309 patients presenting with UGIB reported that GBS was the best for predicting the need for transfusion, identical to AIMS65 in predicting endoscopic intervention, and comparable to AIMS65 and RS in predicting inpatient mortality.[5]

In Denmark, 831 patients with UGIB were enrolled to compare the accuracy of GBS, the age-extended GBS, the Baylor Bleeding Score and the Cedars-Sinai Medical Centre Predictive Index using the outcome of (1) need for hospital-based intervention or 30-day mortality, (2) likelihood of rebleeding and (3) mortality.[6] GBS accurately identified patients most likely to need a hospital-based intervention, but none of these scores accurately predicted mortality or rebleeding.

Two studies from Australia were reported. From Victoria, a study comparing AIMS65, GBS and RS in 424 patients confirmed that the three scores were comparable in predicting a composite outcome of rebleeding and endoscopic/radiological intervention, and mortality.[7] GBS was the best for predicting blood transfusion. The AIMS65 score was better than both the GBS (area under the receiver operating characteristic curve (AUROC), 0.80 vs 0.76, P<0.027) and the pre-endoscopy RS (AUROC 0.74, P=0.001) and equivalent to the full RS (AUROC 0.78, P=0.18) in predicting inpatient mortality. The AIMS65 score was better than all other scores in predicting the need for intensive care unit (ICU) admission and length of hospital stay. In Adelaide, comparing just GBS and RS, investigators confirmed that GBS was superior in predicting blood transfusion and surgery, and was equivalent to RS in predicting the need for endoscopic therapy, rebleeding and death.[8]

A study from Thailand recruiting close to 1000 patients with UGIB compared GBS, full RS and pre-endoscopic RS and found that these scores were better in NVUGIB than variceal UGIB.[9] In Iran, 200 patients were recruited to compare the prediction value of GBS and full RS. GBS was more accurate than full RS for need for blood transfusion, rebleeding, ICU admission and endoscopic intervention. RS predicted 30-day mortality better than GBS in this study.[10]

A systematic review identified 16 studies evaluating pre-endoscopic risk scores (GBS, RS and AIMS65) on a composite outcome including recurrent bleeding, need for intervention and 30-day mortality.[11] The review concluded that GBS has the highest sensitivity and specificity to predict this outcome compared with the other scores. The results of these studies were very consistent. Most confirmed that GBS was the best score to predict which patients require a hospital-based intervention,

including blood transfusion, endoscopic therapy and surgery. There is still room for improvement for GBS in predicting recurrent bleeding and 30-day or long-term mortality. With the large amount of clinical data providing consistent results, The working group recommend that GBS is used for predicting clinical outcome of patients with NVUGIB. Patients with a score of 0–1 rarely need any clinical intervention, and can thus be safely discharged, with elective endoscopy at a later stage. In contrast, a high score (say 10–12) is associated with frequent need for intervention such as transfusion and therapeutic endoscopy. The level of evidence was graded as high.

Statement 2: Patients with a GBS of<1can be treated as an outpatient

(Accept-agreement: 94.5%, level of evidence: high)

Most of the studies are very consistent in showing that GBS is the best tool to predict which patients presenting with UGIB are likely to require a hospital-based intervention. This first pertains to blood transfusion and also to the need for endoscopic treatment and surgery. Several studies also point to setting the threshold of GBS <1–3 as an indicator for patients not requiring hospitalisation.[2 4–6 9–11]

The Upper Gastrointestinal Haemorrhage International Consortium has examined the subject of threshold of GBS in managing UGIB. In their study recruiting patients from four countries (Scotland, England, Denmark and New Zealand), they found that the GBS at a cut-off point of ≤1 and <2 identified low-risk patients with a higher level of specificity than setting the cut-off value of GBS at 0 (40–49% vs 22%).[12] The GBS at a cut-off value of <2 had the highest specificity to detect adverse outcomes but missed 3% of high-risk patients. Therefore, the authors suggested that a GBS cut-off point at <1 was most suitable as a guide for outpatient management.[12] Some argue that even the GBS has a relatively low specificity to predict adverse outcomes.[11] This comment is primarily based on a systematic review. The working group believe that by adopting a GBS cut-off point ≤1, most hospitals can reduce the majority of unnecessary hospital admissions without missing high-risk patients. It will naturally translate into a significant reduction in costs of managing UGIB. As we have pointed out in our previous consensus statement,[1] a low risk for recurrent bleeding is not the same as low risk for mortality. Patients whose bleeding is controlled might still die owing to non-bleeding related causes such as cardiac and pulmonary decompensation.[13] Therefore, the GBS score and its cut-off threshold cannot be interpreted as a score to predict mortality. The working group agreed that existing published data support this statement with a level of evidence graded as high.

Statement 3: Bloodtransfusion should be restricted in the management of upper gastrointestinal bleeding

(*Accept—agreement: 100%, level of evidence: moderate*)

It would seem uncontroversial to replace blood loss in UGIB by transfusion of red blood cell and plasma to restore and preserve tissue perfusion and blood pressure. The earliest study that suggested that blood transfusion might be harmful to patients with gastrointestinal haemorrhage was published over 30 years ago. A small group of patients with severe UGIB were randomised to receiving either a blood transfusion in cases of a haemoglobin <8 g/dL or shock, or transfusion of at least two units of blood regardless of haemoglobin level and haemodynamics.[14] Early blood transfusion appeared to lead to more recurrent bleeding in these patients, and the authors suggested that this was due to reversal of hypercoagulable response to haemorrhage thereby encouraging rebleeding and hence the need for surgery.

Almost three decades later, a study from Spain randomised 921 patients with severe acute UGIB to a restrictive blood transfusion strategy (transfuse only when haemoglobin level ≤7 g/dL) or a liberal transfusion strategy (transfuse only when haemoglobin ≤9 g/dL).[15] Significant differences were demonstrated in the overall survival, further bleeding and adverse events between the two groups in favour of restrictive transfusion. The major difference, however, was seen in the group of patients with cirrhosis and Child-Pugh class A or B diseases.

A more recent study from the UK (TRIGGER Study) took a cluster randomised feasibility trial approach in six hospitals. A slightly different definition of restrictive transfusion strategy (when haemoglobin ≤8 g/dL) versus liberal transfusion strategy (when haemoglobin ≤10 g/dL) was adopted.[16] Comparison of centres using different transfusion strategies showed that there was no significant difference in clinical outcome, including mortality, thromboembolic events, surgical or radiological intervention, therapeutic intervention, length of hospital stay and serious adverse events.

In Asia, a study from Korea randomised patients to receive restrictive transfusion (haemoglobin <8 g/dL) or liberal transfusion (target haemoglobin >10 g/dL),[17] and confirmed that restrictive transfusion was associated with less recurrent bleeding. Pooling these four studies together, a meta-analysis of randomised controlled trials concluded, admitting moderate heterogeneity of studies and over 90% of patients from two studies,[15 16] that restrictive blood transfusion conferred a lower mortality (relative risk 0.65, 95% CI 0.44 to 0.97) and lower rebleeding rate (relative rate 0.58, 95% CI 0.40 to 0.84).[18] There was, however, no difference in thromboembolic events associated with blood transfusion.

A retrospective nationwide survey of 5861 hospital admissions in Denmark showed that the number of units of red blood cells is a predictor of the need for repeated endoscopy, surgery and 30-day mortality.[19] In Canada, a retrospective cohort of 1677 patients with UGIB found that transfusion of red blood cells within 24 hours of presentation was significantly and independently associated with an increased risk of recurrent bleeding.[20] Another retrospective cohort from Australia, which included 2228 patients with NVUGIB, also reported that blood transfusion of more than four units is associated with increased risk of further bleeding, but not with higher mortality.[21]

It should be pointed out that the mechanisms explaining why transfusion may lead to recurrent bleeding in NVUGIB are not known. Based on existing published data, the Asia-Pacific Working Group recommended a restrictive transfusion strategy, without specifying whether the threshold should be 7 g/dL or 8 g/dL. Clinical discretion should be exercised when transfusion is given. In patients with active cardiovascular disease, the role of transfusion needs to be individualised based on assessment of blood loss and the cardiovascular status. In patients with massive active bleeding with dropping blood pressure, a more liberal transfusion strategy might be necessary. There is also an expectation that more data will allow a refinement of this recommendation. The level of evidence was agreed to be moderate.

Statement 4: Platelet transfusion has no benefit for patients with upper gastrointestinal bleeding taking antiplatelet agents

(Accept—agreement: 88.9%, level of evidence: low)

Antiplatelet agents, including aspirin and thienopyridines (eg, clopidogrel), are increasingly used in patients with various cardiovascular and cerebrovascular conditions as primary and secondary prevention. As aspirin and thienopyridines cause irreversible blockage of platelet function for the lifespan of the platelet, approximately 8–10 days, their effects are expected to last for days after discontinuation of this medication in patients with acute UGIB. It is common practice to transfuse platelets in patients with acute UGIB while receiving antiplatelet agents despite having normal platelet count.

A case–control study compared patients with UGIB with or without platelet transfusion irrespective of platelet counts. It showed that platelet transfusion did not reduce bleeding but probably increased the overall mortality.[22] The use of platelet transfusion was studied in another retrospective observational study comparing a group of patients with UGIB in the ICU for clinical outcome.[23] There was no demonstrable difference in total hospital stay, amount of blood transfusion and resulting haemoglobin levels between the platelet-transfused and non-transfused group. The platelet-transfused patients, however, were found to have had a shorter stay in the ICU. In view of the absence of any demonstrable improvement in clinical outcome, the working group did not recommend platelet transfusion in UGIB even if patients are taking antiplatelet agents. The working group considered the evidence for this recommendation weak and remarked that this statement applied only to patients with normal platelet counts.

Endoscopic management

Statement 5: Patients with haemodynamic shock and signs of upper gastrointestinal bleeding should be offered urgent endoscopy after resuscitation and stabilisation

(Accept—agreement: 100%, level of evidence: moderate)

The timing of endoscopy in patients with NVUGIB is a matter of debate. The previous Asia-Pacific Working Group consensus recommended 'endoscopic intervention within 24 hours of onset of bleeding in patients at high risk".[1] A systematic review concluded that endoscopy within 12 hours did not improve clinical outcome.[24] It has also been pointed out that in patients at very high risk who are haemodynamically unstable and in patients presenting with massive haematemesis, endoscopy should be performed as soon as they are stabilised with resuscitation.

Several studies examined the role of urgent endoscopy (within 12 hours) in the management of NVUGIB. In a retrospective cohort of 361 patients, it was found that patients who underwent urgent endoscopy had a greater than five-fold increased risk of adverse outcome (death, inpatient rebleeding, surgery or radiological intervention or repeated endoscopic therapy). In a subgroup analysis from this study, time to endoscopy was not significant as a predictor of worse outcome, hence less prognostic in the high-risk patients than in lower-risk patients.[25] A nationwide cohort study included 12 601 patients with peptic ulcer disease. It suggested that patients with haemodynamic instability or American Society of Anesthesiology score of 3–5 had reduced in-hospital mortality if receiving endoscopy within 6–24 hours after admission.[26] However, the exact timing within 24 hours is still not clear. A nationwide survey from the UK included 4478 patients. It showed that earlier endoscopy (<12 hours) was not associated with a lower mortality, or need for surgery, compared with endoscopy offered within 24 hours.[27]

Two studies from Asia also examined this question. In Singapore, a cohort study showed that in high-risk UGIB patients with a GBS>12, timing of endoscopy is the most important factor associated with all-cause in-hospital mortality.[28] The cut-off time of endoscopy that improved survival of such patients was within 13 hours from presentation. In contrast, a study from Hong Kong selected high-risk patients (GBS ≥12) for randomisation to urgent (within 6 hours of presentation) versus early (within 24 hours of presentation) endoscopy. This study did not confirm the benefit of very early endoscopy.[29] With endoscopy within 6 hours, patients had more active bleeding lesions requiring endoscopic haemostasis, but this conferred no benefit in prevention of recurrent bleeding, mortality, requirement of blood transfusion and duration of hospital stay. Urgent endoscopy within 6 hours of presentation for all NVUGIB seems unnecessary. The working group accepts that in some highly selected patients, such as those who present with haemodynamic shock or instability, an urgent endoscopy, say within 12 hours of admission, may benefit the patient after initial resuscitation and stabilisation. However, offering urgent endoscopy to all patients who present with NVUGIB is not considered necessary. The level of evidence is graded as moderate.

Statement 6: Endoscopic haemostatic powder spray (such as Hemospray) is useful as a stop-gap treatment in NVUGIB

(Accept—agreement: 83.3%, level of evidence: low)

The first human study of endoscopic haemostatic power spray in peptic ulcer disease was reported from Hong Kong.[30] In a small series of 20 patients with peptic ulcer bleeding, Hemospray stopped bleeding in 19 (95%) cases and recurrent bleeding occurred in 2 (10%). This initial success was echoed by a number of case series, in which the haemostatic spray was used either as a monotherapy, an adjunctive therapy or as a salvage therapy.[31–37] Most studies reported a relatively high success rate (80–95%), but also a relatively high recurrence rate of bleeding (range 10–40%). Endoscopic haemostatic powder is easy to use and associated with few adverse events. Haemostatic powder spray has also been used in patients receiving oral anticoagulants and showed similar success.[38] When endoscopy is repeated on the next day, most of the haemostatic power is washed away leaving a clean and non-bleeding lesion for definitive treatment. Unfortunately, so far there is no randomised controlled trial (RCT) comparing the efficacy of haemostatic spray with any other endoscopic modality. Only smaller series and retrospective cohort studies are available. A RCT is eagerly awaited to confirm the efficacy of this treatment.

The working group recommends endoscopic haemostatic power spray as a useful treatment for temporary control of bleeding in NVUGIB when definitive haemostasis cannot be achieved. This includes situations such as lack of endoscopic expertise or when despite attempts of endoscopic haemostasis, bleeding still continues. Patients with bleeding from upper gastrointestinal malignancy may also be benefit from haemostatic powder spray treatment. In view of the lack of RCTs and large-scale studies, the level of evidence was considered low.

Statement 7: Over-the-scope-clipping devices (such as Ovesco) are useful in treating lesions refractory to conventional endoscopic haemostatic therapy

(Accept—agreement: 94.4%, level of evidence: moderate)

In contrast to haemostatic powder spray, the over-the-scope-clip (OTSC), if successfully applied, appears to provide a firm and definite control of bleeding in NVUGIB.

Made from nitinol alloy, the OTSC fits to the tip of the endoscope and can be deployed by tightening the thread with the hand wheel using a mechanism similar to rubber band variceal ligators. After being released from the applicator, the shape-memory effect and elasticity of the alloy result in firm closure of the clip. Compared with conventional clips, the OTSC can take up much more tissue by grasping deeper layers of the gastrointestinal wall, and hence the device can be used to treat bleeding and bowel perforation.

Several case series reported promising results of successful haemostasis in the range of 70–100%.[39–42] Recurrent bleeding within 7 days occurred in 5–33%. This device, however, is technically slightly more demanding than other through-the-scope haemostatic treatments. Deployment of the OTSC requires accurate positioning and adequate retraction of tissue (either by suction or retractor) into the cap of the OTSC before the clip can be released properly. The retractor or anchor device is used in hard fibrotic ulcers, especially those located in difficult positions such as the high lesser curvature of the stomach. It punctures the base of the lesion and allows tissue to be pulled into the cap. At certain locations in the stomach (eg, proximal lesser curve of the stomach) and duodenum (junction of the first and second part of the duodenum), this can be technically challenging.

A multicentre randomised control trial comparing through-the-scope clips (TTSC) with OTSC has recently been reported,[43] In that study, 32 patients received TTSC and 33 received OTSC. Initial haemostasis was reported in 62.5% of those who received TTSC and 96.8% received OTSC (P=0.002). Recurrent bleeding within 7 days after treatment occurred at the same rate in both groups (33.3% vs 24.4%). The interim results of this study suggested that OTSC is a better haemostatic device than haemoclips in the treatment of peptic ulcer bleeding. In view of the promising interim results while waiting for a full report, the working group recommends the use of OTSC in treating lesions refractory to conventional endoscopic therapy, such as through-the-scope haemoclips, thermal device or endoscopic injection. There may be a role for OTSC in primary therapy, especially in peptic ulcer bleeding with large vessels. This device will add to the armamentarium for NVUGIB, with the level of evidence graded as moderate.

Statement 8: Endoscopic treatment of delayed bleeding after endoscopic mucosal resection or endoscopic submucosal dissection is similar to that for bleeding peptic ulcers

(Accept—agreement: 89%, level of evidence: moderate)

As endoscopic mucosectomy (EMS) and endoscopic submucosal dissection (ESD) are gaining popularity among tertiary centres worldwide, complications such as delayed bleeding require more guideline from experts. A meta-analysis which pooled data from over 70 studies (15 RCTs, three prospective trials, five prospective cohort studies, and 48 retrospective cohort and case–control studies) depicted clearly the risks associated with EMS and ESD.[44] Post-ESD bleeding occurred in 5.1% (95% CI 4.5% to 5.7%) of patients. Risk factors identified included male gender, cardiac disease, the use of antithrombotic agents, chronic liver or kidney disease, tumour size >2 cm or resected specimen size >3 cm, lesions on the lesser curve, flat or depressed lesion and invasive carcinoma. Procedure time was not a clear risk factor for post-ESD bleeding but the need for endoscopic haemostasis was a factor. Experienced practitioners of ESD stated that the management of post-ESD bleeding did not differ from that for peptic ulcer bleeding. Most post-ESD bleeding occurred within 24 hours after the procedure. Endoscopic devices used in peptic ulcer bleeding can also be used to treat post-ESD bleeding. Most post-ESD bleeds come from a focal bleeding point and are confined to mucosal and submucosal layers, without penetrating through the muscle layer. Hence, haemostasis in such circumstances is relatively easy. There is no agreement on whether proton pump inhibitors are better than histamine-2 receptor antagonists after ESD.[45 46] Second-look endoscopy has not been proved to be associated with less postprocedural bleeding,[47] Overall, the working group concluded that post-EMS and post-ESD bleeds can be managed like peptic ulcer bleeds. The level of evidence was graded as moderate.

Post-endoscopic management

Statement 9: As an adjunct to endoscopic treatment, high-dose oral proton pump inhibitors can be used to prevent rebleeding

(Accept—agreement: 88.9%, level of evidence: moderate)

The use of intravenous high-dose proton pump inhibitors (PPIs) has become standard practice in the management of upper gastrointestinal bleeding. At least three randomised trials, all from South Asia, showed that oral PPIs, given with or without endoscopic therapy, also reduce the risk of recurrent bleeding from peptic ulcer.[48–50] New evidence suggests that high-dose oral PPIs may have a similar effect to their action in preventing recurrent bleeding from peptic ulcers.

A study from Hong Kong recruited 118 high-risk patients with Forrest I or IIa/b peptic ulcer bleeding to receive either IV esomeprazole plus oral placebo or oral esomeprazole (40 mg every 12 hours) plus IV PPI placebo.[51] Recurrent bleeding within 30 days was reported in 7.7% in the IV esomeprazole group and 6.4% in the oral esomeprazole group. There was no difference in the requirement for blood transfusion, repeated endoscopic therapy and hospital stay between the two groups. It was noted that the study was stopped prematurely and was not designed as an equivalent trial. The trend suggests that the action of high-dose oral PPI peptic ulcer bleeding is comparable to that of IV PPI. In Taiwan, IV esomeprazole was compared with oral lansoprazole (30 mg four times a day for 3 days) in patients with peptic ulcer bleeding.[52] There was no difference in all the clinical outcome parameters, except that those who received oral PPI had a shorter hospital stay. In Korea, when IV omeprazole was compared with oral rabeprazole (20 mg twice daily), the recurrent bleeding rate, surgical intervention and mortality between the two groups were comparable.[53]

There is no properly powered RCT to confirm that high-dose oral PPI is as effective as IV PPI. The working group accepted that high-dose oral PPI can be used to prevent recurrent bleeding, but emphasised that it has to be used as an adjunct to endoscopic therapy. Only after endoscopic haemostasis is achieved, can high-dose oral PPI be recommended to prevent recurrent bleeding. The definition of high-dose oral PPI has been stated as at least 80 mg of esomeprazole (or

equivalent dosage of other PPIs). The high oral dose should be maintained for at least 3 days, which is the period of highest risk of recurrent bleeding. If the patient's condition remains stable, standard dose oral PPI can be resumed afterwards. All the reports were relatively small and underpowered, and thus the level of evidence was graded as moderate, in the hope that future studies might confirm this finding.

Statement 10: There is no special preference for a particular proton pump inhibitor when used concomitantly with clopidogrel

(Accept—agreement: 94%, level of evidence: moderate)

Concern about a potential interaction between PPIs and clopidogrel (a prodrug that requires CYP450 for metabolism) arose from a number of in vivo platelet aggregation studies.[54 55] Different PPIs may have unequal effects on clopidogrel metabolism, which further intensifies the debate about a potential interaction between PPIs and clopidogrel. It has been suggested that PPIs such as lansoprazole, pantoprazole and rabeprazole have less interaction with clopidogrel since they have fewer inhibitory effects on CYP2C19.[56–59] More data suggest that concomitant use of a PPI with clopidogrel increases the risk of major adverse cardiovascular events (MACE) in patients with high cardiovascular risk.

A retrospective cohort study from China, including about 6200 patients who received aspirin plus clopidogrel with a PPI, reported that PPI users had a 3% increase in MACE compared with non-users.[60] Another retrospective cohort from Italy reported an alarming 12% increase in MACE in patients receiving a PPI in conjunction with clopidogrel.[61]

PPIs interact with clopidogrel in patients with coronary, cerebrovascular and peripheral artery disease. This interaction was implicated in the Factores de Riesgo y ENfermedad Arterial (FRENA) Registry as leading to a doubling of the incidence of myocardial infarction and ischaemic stroke.[62] However, a number of studies showed otherwise. A Japanese study of patients with coronary stenting receiving dual antiplatelet agents showed no effect of PPIs on MACE or mortality.[63] The safety of prescribing a PPI with clopidogrel was also suggested in a case–control study enrolling 23 655 patients from the Netherlands.[64] Beside cardiovascular risk, the safety profile of using a PPI concomitantly with clopidogrel was also confirmed in group of 2765 patients who had strokes.[65]

Finally, the strongest support came from the only RCT, the Clopidogrel and the Optimisation of Gastrointestinal Events Trial (COGENT).[66] Patients receiving dual antiplatelet therapy (aspirin and clopidogrel) were randomised to receive omeprazole or placebo. Omeprazole significantly reduced rates of composite gastrointestinal events from 2.7% (without omeprazole) to 1.2% (with omeprazole). There was no significant excess of cardiovascular events in 3759 high-risk cardiovascular patients recruited in this study. Although the trial was terminated prematurely, the follow-up period was sufficient to demonstrate the rate of MACE related to the medication. These data from COGENT, the only large-scale RCT evaluating the effects of PPI on clinical endpoints in patients requiring dual antiplatelet therapy, provided reassurance about the safety of PPIs in high-risk cardiovascular subjects.[67] Therefore, the working group recommended the use of a PPI without preference for a particular type, in patients requiring gastrointestinal protection against dual antiplatelet therapy. The level of evidence was considered moderate as only one RCT has been carried out, with limitations.

Statement 11: Routine second-look endoscopy is not recommended for patients after gastric endoscopic submucosal dissection

(Accept—agreement: 88.9%, level of evidence: high)

Submucosal arterioles are often exposed after gastric ESD just above the level of muscularis propria. As mentioned above, the management of post-ESD haemorrhage is similar to that for bleeding peptic ulcers. However, the pathology is different as the artificial ulcers created by ESD have less fibrosis and hence it is easier to stop bleeding using either a thermal or mechanical device. In this situation, routine second-look endoscopy may not be necessary.

A single-centre randomised trial comparing routine second-look endoscopy with no second-look endoscopy after gastric ESD in 155 patients demonstrated no difference in recurrent bleeding and need for transfusion.[68] Two prospective randomised trials including larger (>35 mm) artificial ulcers after gastric ESD also showed no difference in outcome between those with and without second-look endoscopy.[69 70] Another large multicentre prospective randomised trial conducted in Japan, including 262 patients, further demonstrated that routine second-look endoscopy confers no protection against recurrent haemorrhage.[71] This result was confirmed by a meta-analysis including four randomised trials and four non-randomised trials. No difference in post-ESD bleeding rate was shown by the pooled data between those who did and did not receive second-look endoscopy.[47] The panel concurred with high agreement that based on current evidence, routine second-look endoscopy is not recommended for patients after gastric ESD, with a level of evidence graded as high.

Statement 12: Among patients with high cardiothrombotic risk receiving antiplatelet agents, these agents should be resumed as soon as haemostasis can be established

(Accept—agreement: 100%, level of evidence: high)

Patients with NVUGIB taking antiplatelet agents face a dilemma of discontinuing these drugs to facilitate controlling of haemorrhage or to continue taking these drugs to avoid thromboembolic complications. Using the UK primary care database, a study reported the cardiovascular and UGIB consequences of low-dose acetylsalicylic acid (ASA) in patients aged 50–84 years.[72] Based on this dataset, the attributable risks associated with ASA discontinuation for non-fatal myocardial infarction/coronary death and ischaemic stroke were 17 and 11 per 1000 people, respectively. On the other hand, the risk of UGIB with continued ASA was 1.6 per 1000 people. This amounts to eight extra cardiovascular events for a reduction of 0.4 UGIB events per year.

The only RCT examining this subject was reported by the Hong Kong group. It showed that immediate resumption of aspirin for high-risk cardiac patients was critical as it did not increase the risk of fatal haemorrhage but significantly improved the 30-day survival.[73] Subsequently, a retrospective analysis of 118 patients who received low-dose aspirin with 40% of cases discontinuing the drug for 2 years showed a sevenfold increase in risk for a cardiovascular event and cardiac death.[74] A study from Taiwan comparing 89 patients receiving esomeprazole alone versus 89 patients receiving

esomeprazole plus aspirin showed that the ulcer healing rate between the groups was almost identical. There is no evidence to suggest that aspirin would delay the healing of peptic ulcer when treated with a PPI.[75] It should be noted that these two studies used a relative low dose of aspirin (80–100 mg daily). Even at this dose, the cardioprotective effects of aspirin are retained and haemorrhagic complications are not detrimental. Similarly, although data are lacking on non-aspirin antiplatelet agents, the protective effects against thromboembolic events in cardiovascular and cerebrovascular diseases are considered more important than the increased risk of gastrointestinal bleeding.

No study has investigated the optimal timing for the resumption of antiplatelet agents, but one can consider resuming these agents on day 1 if endoscopy shows a clean-based ulcer. In patients who received endoscopic therapy for bleeding, antiplatelet agents can be resumed 72 hours after the treatment—that is, passing the period of highest risk for recurrent bleeding. The working group unanimously endorsed this recommendation of resuming antiplatelet agents early when UGIB is under control. The level of evidence of this statement was considered as high.

Statement 13: In patients receiving dual antiplatelet agents, at least one antiplatelet agent should be resumed in cases of upper gastrointestinal bleeding

(Accept—agreement: 94.4%, level of evidence: low)

The most commonly used antiplatelet agents are ASA (aspirin), a cyclo-oxygenase inhibitor and thienopyridines that bind to P2Y12 component of the adenosine diphosphate receptors. After stopping ASA, 7–9 days are required to regain full platelet function, whereas in the case of thienopyridines (such as clopidogrel or prasugrel), the minimum duration to restore platelet function is 5–7 days. Use of dual antiplatelet agents, often ASA plus a thienopyridine, may confer a threefold increase in the risk of UGIB over single-agent antithrombotic therapy.[76] There are no data guiding the management of these patients using dual antiplatelet therapy when they develop UGIB. We do not recommend withholding both antiplatelet drugs because the median time to coronary stent thrombosis can be as short as 7 days with both drugs withheld as compared with 122 days with only clopidogrel withheld.[77] Balancing the risk and benefit of discontinuation of antiplatelet agents, the ASGE recommends that cessation of all antiplatelet therapy after PCI should be avoided, and furthermore, when only one antiplatelet agent is used, aspirin should be continued as it is associated with a lower risk for causing recurrent bleeding. On the other hand, for patients with a high risk of thrombosis, such as those with drug-eluting coronary stents, clopidogrel should not be discontinued for more than 5 days.[78]

Cardiologists' opinion should be sought for the commencement of antiplatelet agents. In patients with low risk of recurrent bleeding from the gastrointestinal tract, antiplatelet agents should not be discontinued at all. The working group consider that this statement is primarily based on pharmacological characteristics of the antiplatelet agents. Clinical trials to test the safety of this strategy are eagerly awaited. The level of evidence was considered low.

Statement 14: Among direct oral anticoagulant (DOAC) or warfarin users with high cardiothrombotic risk who develop ulcer bleeding, DOAC or warfarin should be resumed as soon as haemostasis is established

(Accept—agreement: 83.3%, level of evidence: low)

Clinical evidence is lacking to support strategies for managing patients with NVUGIB and high cardiothrombotic risk who receive DOAC or warfarin. For such patients with atrial fibrillation and/or valvular heart diseases, management should depend on the balance between thrombotic risk and bleeding risk. In acute NVUGIB, DOAC or warfarin should be withheld to facilitate achievement of haemostasis.

If the patient is taking warfarin, four-factor prothrombin complex concentrate (PCC) and vitamin K or fresh frozen plasma can be given for life-threatening GI bleeding. Warfarin reversal should be used for life-threatening bleeding irrespective of the international normalised ratio (INR). Current evidence does not show any correlation between INR at presentation and outcomes of GI bleeding.[79] A combination of PCC and vitamin K is preferred for urgent reversal of warfarin. PCC has advantages over fresh-frozen plasma such as faster onset of action and minimal risk of fluid overload. Endoscopic therapy should not be delayed in patients with serious UGIB. Warfarin and DOAC treatment should be withheld in patients with ongoing NVUGIB.[80]

The Food and Drug Administration in October 2015 granted approval for idarucizumab, a potent monoclonal antibody against dabigatran, for use in patients with uncontrolled bleeding. In a multicentre study of 503 patients with uncontrolled bleeding who were about to undergo an urgent procedure, 5 g of idarucizumab reversed the anticoagulant effect of dabigatran within 4 hours in almost all patients.[81] However, its true benefit in NVUGIB is still unclear because of limited clinical data.

Once the bleeding is controlled, the decision to resume anticoagulants should be made by a multidisciplinary team with cardiologist, gastroenterologist, intensivist and, if feasible, with patient's participation. The CHA2DS2-VASC and HAS-BLED score are useful in assessing the need for continuing anticoagulation.[82–84] In patients with high cardiovascular risk, resumption of anticoagulants should not be delayed. A large prospective cohort study of patients with atrial fibrillation in Denmark showed that resumption of single anticoagulants was associated with lowest rate of all-cause mortality[85] Most data on vitamin K antagonists show that resuming the oral anticoagulant is associated with a lower mortality despite more frequent major bleeding.[86] A recent study suggested that dabigatran offers similar protection against thromboembolism with less rebleeding than warfarin after major bleeding.[87] The timing for resumption of warfarin should be assessed on a patient-by-patient basis. Since the time required for re-anticoagulation will be prolonged after warfarin reversal with vitamin K, we recommend early resumption of warfarin once haemostasis has been achieved, especially in patients with high thromboembolic risk. With DOAC, the effect should disappear in 1–2 days after stopping the drug. Therefore, once bleeding is under control, DOAC can be resumed earlier (within 1–2 days) bearing in mind that anticoagulation is achieved rapidly within hours and therefore might increase the risk of rebleeding. If early anticoagulation is indicated in patients with high thromboembolic risk, a bridge approach with heparin or enoxaparin is useful. The working group considered that this recommendation is based

primarily on expert opinion without data from RCTs, hence the level of evidence was graded as low.

Rejected statements

Statement 1: Video capsule endoscopy can be considered as a triage tool for patients who require early intervention

(Reject—agreement: 22.2%)

Modified: Capsule endoscopy can be considered as a triage tool for hospitalisation

(Reject—agreement: 39%)

The first attempt to use video capsule endoscopy (VCE) in assessment of patients with UGIB was conducted in a multicentre study in which patients received VCE, followed by nasogastric tube and then conventional endoscopy for evaluation of UGIB.[88] Blood was detected significantly more often by VCE than by nasogastric tube aspiration. There was no difference in identification of peptic or inflammatory lesions between VCE and conventional endoscopy.

In view of this initial encouraging result, a prospective RCTwas carried out. Seventy-one patients with UGIB were randomised to receive either the standard-of-care treatment in hospital or a VCE in the emergency room (ER). The need to admit to hospital was determined by the findings of VCE.[89] This study showed a reduction of hospital admission in the VCE group of >70% and with no serious adverse outcome. Comparison of the VCE results with GBS evaluation, showed also a significant reduction in hospital admission among the patients recruited to receive VCE in this RCT. Based on this result, the authors considered VCE in the ER a feasible triage tool to differentiate patients who do or do not require hospital admission.

Comparison of VCE and GBS and RS was conducted in another small-scale cohort study of 25 patients presenting with UGIB.[90] VCE accurately predicted high-risk endoscopic stigmata and compared favourably with GBS and RS for risk stratification. Training of ER physicians to interpret VCE images has also been found to be feasible in a survey study involving 126 emergency department physicians.[91] There are concerns about the costs of VCE used in such circumstances, but a cost-effectiveness analysis comparing VCE with other strategies for managing UGIB showed that VCE was cost-effective for patients at low and moderate risk presenting to the ER with UGIB.[92]

However, VCE may not be optimal in examination of the duodenum. In a risk stratification study of UGIB from Australia, authors found that because of low duodenal visualisation, there was poor concordance between VCE and conventional endoscopy in the findings of the bleeding source in patients with UGIB.[93]

Although the initial data look promising, the Asia-Pacific Working Group considered it premature at this stage to recommend the use of VCE as a risk stratification method for UGIB or as a triage tool to decide on hospital admission. There is so far only one small-scale RCT supporting the use of VCE as a patient triage tool. Besides inadequate duodenal visualisation, the possibility of missing lesions in the fundus of the stomach and other less accessible sites is a concern. The logistics of setting up VCE in the ER, and of training personnel to interpret the video bring further uncertainties. There were also concerns that VCE at the ER might delay endoscopy for those who require endoscopic intervention. The working group did not accept VCE as a triage tool and would like to await further clinical studies to prove its value.

Statement 2: Pre-endoscopy intravenous proton pump inhibitors are recommended in stable patients awaiting endoscopy

(Reject—agreement: 72.2%)

Modified: Intravenous proton pump inhibitors are recommended for patients with suspected gastrointestinal bleeding awaiting endoscopy

(Reject—agreement: 66%)

There are now at least six RCTs, comprising 2223 patients with UGIB being studied for the benefit of pre-endoscopy intravenous PPIs.[94–99] With PPIs, the stigmata of haemorrhage will be downgraded and hence endoscopic therapy less frequently needed, yet there is no reduction in recurrent bleeding, surgery and overall mortality between PPI and control treatment. The Cochrane review which pooled these six studies concluded that PPI treatment before endoscopy might reduce the proportion of patients requiring endoscopic therapy without affecting clinically significant outcomes.[100] It is possible that the overall costs of treatment and the need for experienced endoscopists could be reduced; however, the clinical impact is uncertain.

The working group noted that many physicians use intravenous PPIs for patients presenting in stable conditions with symptoms suggestive of UGIB, while waiting for endoscopy. These are commonly administered at the ER or at primary care clinics. This statement pertains to patients who are 'stable' or 'suspected' of UGIB waiting for endoscopy. The working group members voted to reject indiscriminate use of IV PPIs in such circumstances as there is no proven value. Indiscriminate use of IV PPIs will increase the cost of managing NVUGIB. This statement should be read differently from the previous Asia-Pacific Working Group consensus which stated that pre-endoscopy PPI is recommended where early endoscopy or endoscopic expertise is not available within 24 hours.[1] When endoscopy facilities or endoscopy expertise are not available within 24 hours, downgrading stigmata of recent haemorrhage and reducing the requirement for endoscopic intervention becomes much more justified.

Statement 3: Angiographic embolisation should be applied in patients with high-risk ulcers to prevent recurrent ulcer bleeding

(Reject—agreement: 38.9%)

When endoscopic haemostasis fails to control peptic ulcer bleeding, repeated endoscopy and surgery are considered viable options to control bleeding. There is little evidence to support the use of angiographic embolisation as an alternative to surgery after endoscopic treatment has failed except for two retrospective studies.[101 102] A Scandinavian study prospectively randomised 105 patients with peptic ulcer bleeding to arterial embolisation after endoscopic therapy or to standard treatment.[103] The authors used a composite endpoint which included transfusion requirement, development of rebleeding, need for haemostatic intervention and mortality as the primary endpoint. While there was a trend towards less rebleeding for those who received angiography, the study reported no difference in the outcome of those who received angiography versus standard treatment.

More recently a prospective randomised trial in Hong Kong tried to examine this by allocating patients with Forrest I/II peptic ulcer bleeding to pre-emptive angiographic embolisation

or standard-of-care management without embolisation.[104] In the intention-to-treat analysis, there was no demonstrable difference between the two groups in recurrent bleeding within 30 days, need for further endoscopic or surgical interventions, hospital stay, blood transfusion requirement and mortality. In the per protocol analysis of 90 patients who received angiographic embolisation compared with 113 patients who did not, there a trend favouring angiography, with a significant reduction in mortality. The size of ulcer (≥1.5 cm) is the best predictive parameter associated with benefit of angiography. However, this is a single study with a marginal benefit. The working group considered it premature to recommend angiography to prevent recurrent bleeding from peptic ulcer after endoscopic treatment. More evidence from future clinical trials is necessary.

Statement 4: A risk stratification score should be used to identify high-risk bleeding ulcers after endoscopic therapy for second-look endoscopy

(Reject—agreement: 55.6%)

Modified: A risk stratification score may be useful to identify high-risk bleeding ulcers after endoscopic therapy for second-look endoscopy

(Reject—agreement: 23%)

Recurrent bleeding occurs in 8–15% of patients with peptic ulcer bleeding and is associated with a two- to fivefold increase in mortality. The objective of routine second-look endoscopy, usually performed within 24 hours after index endoscopy, is to pre-emptively treat peptic ulcers with persistent stigmata of recent haemorrhage before they start bleeding again.

Second-look endoscopy was first investigated for its efficacy in prevention of peptic ulcer rebleeding by a few prospective randomised trials in the 1990s.[105–108] The results from these randomised trials were conflicting. Some showed that second-look endoscopy and repeated endoscopic haemostasis were effective in preventing recurrent haemorrhage[107 108] while others demonstrated no efficacy.[105 106] The reasons for these conflicting results included recruitment of patients with different levels of rebleeding risk, a non-standardised method of primary haemostasis and variation in the performance of second-look endoscopy. A meta-analysis based on eight prospective randomised trials concluded that second-look endoscopy reduced rebleeding in the absence of high-dose PPI especially in patients at very high risk.[109] Analysis of these pooled data also suggested that second-look endoscopy reduced the need for surgery but had no significant effect on mortality. However, after removing two trials that included patients with a high risk of rebleeding, no benefit from second-look endoscopy was found.[109 110] A recent randomised trial compared intravenous PPI infusion with second-look endoscopy in patients after receiving endosocopic haemostasis for peptic ulcer bleeding.[110] It demonstrated no difference in recurrent bleeding, need for surgery and mortality between the two treatment strategies. Furthermore, second-look endoscopy did not appear to be cost-effective when offered to all patients.

The question remains whether risk stratification with selection of high-risk patients may lead to a benefit from second-look endoscopy on the next day and with repeated treatment in case of persistent stigmata. The Baylor Bleeding Score attempted to select high-risk patients to receive second-look endoscopy versus controls and found a 24% difference in rate of recurrent bleeding.[111] A study including 699 patients from Korea showed that use of a non-steroidal anti-inflammatory drug, large transfusion volume and failure to perform second-look endoscopy were risk factors for recurrent bleeding after endoscopic therapy.[112] Another study from Taiwan which enrolled 316 patients receiving a high-dose PPI after endoscopic therapy attempted to formulate a predictive score using endoscopic monotherapy and serum albumin levels.[113] By this score, the receiver operating characteristic curve to predict need for second-look endoscopy appeared promising, but outcome data were lacking. To date, there is still a lack of evidence to suggest that any risk stratification method is effective in selecting patients at high risk who would benefit from second-look endoscopy and pre-emptive treatment.

The working group therefore rejected the statement that a risk stratification score may be useful to identify high-risk bleeding ulcers after endoscopic therapy for second-look endoscopy. Future studies should be conducted to verify the use of a risk stratification system.

Statement 5: A Doppler endoscopic probe should be used to guide endoscopic therapy in order to ensure adequate haemostasis

(Reject—agreement: 66%)

The use of a Doppler endoscopic probe is not new. Previous studies have shown that the technique requires skill and the results are often irreproducible. A study from the CURE group has recently reported that the Doppler endoscopic probe (DEP) can demonstrate major stigmata of peptic ulcer bleeding (spurting ulcer, blood clot and visible vessel) and had a significantly higher rate of detecting arterial blood flow than oozing ulcer and ulcer with flat pigmented spot.[69] The authors proposed that DEP can improve risk stratification in the management of peptic ulcer bleeding. This DEP is a FDA-approved disposable probe (Vascular Technology, Nashua, New Hampshire, USA) that can be inserted into the working channel of the gastroscope. Subsequently, the same group compared the standard endoscopic treatment (using a thermal or mechanical device with or without injection) with endoscopic treatment guided by DEP.[114] Endoscopic haemostasis was applied to peptic ulcers until DEP showed no Doppler signal of residual blood flow. The results showed that with DEP-guided therapy, recurrent bleeding can be reduced from 26.3% to 11.1%. However, because of the small number of patients with significant events, there was no difference demonstrated in requirement for surgery or angiography to salvage uncontrolled bleeding, and there was no reduction in mortality. Although a remarkable RCT, the working group concluded that it is too early to recommend DEP for the management of UGIB. This is based on the argument that only a single study from a renowned referral centre demonstrated the benefit of this skill-demanding technique. The working group opined that more data, from other centres recruiting more patients, are required to confirm the value of DEP.

CONCLUSION

Since the last Asia-Pacific consensus on NVUGIB published 7 years ago, significant advancement has been made in the clinical management of patients before endoscopy (risk stratification scores, blood and platelet transfusion, use of PPIs) and in the development of endoscopic haemostasis (haemostatic powder spray and over-the-scope clips). Emerging techniques, such as the use of capsule endoscopy for patient triage, a Doppler endoscopic probe for assessing adequacy of endoscopic therapy, and the pre-emptive use of angiographic embolisation, look promising but require further evaluation. The use of PPIs has been further clarified, showing that routine use of IV PPI is unnecessary but high-dose oral PPI after endoscopy may be beneficial. Experience in managing NVUGIB after EMR and ESD is accumulating. An emerging problem is the increasing use of

double antiplatelet agents and direct oral anticoagulants in patients with cardiac and cerebrovascular diseases, and clinical data to guide management are still minimal. Resumption of antiplatelet agents or anticoagulants is important but the timing and choice of drugs to be resumed require further clinical trials for guidance.

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Acknowledgements Moe Kyaw, John Wong, Jessica Ching and Thomas Lam.

Contributors Study design: JJYS; literature review: JJYS, PCYC, FKLC, JYWL, John Wong and Moe Kyaw; draft of the manuscript: JJYS; revision of the manuscript: all authors.

Funding This research received no specific grant from any funding agency in the public, commercial or not-for-profit sectors.

Competing interests None declared.

Patient consent Not required.

Provenance and peer review Not commissioned; externally peer reviewed.

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