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MANAGEMENT OF BLEEDING OF GASTRO DUODENAL ULCER

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INTRODUCTION

For management of bleeding gastro duodenal ulcer, endoscopy is primary treatment and has significantly reduced surgery rate. But in patients where bleeding is not controlled by endoscopy and interventional radiology, surgery is most important treatment **[1]**.

Peptic ulcer disease was one of the most common indication for gastric surgery but now infrequently requires operation, the development of potent antisecretory agents (H2 blockers and proton pump inhibitors) and the recognition **[2]** that treatment for H pylori infection can eliminate most ulcer recurrences, therefore the need of emergency surgery is decreasing **[3]**. But, complications related to peptic ulcer disease are same in numbers which includes bleeding, perforation, and gastric outlet obstruction. Surgical management remains important since surgery is the mainstay of emergency treatment of above mentioned life-threatening complications and for disease that is not responding to medical treatment.

The initial assessment and risk stratification,, proton pump inhibitor therapy, endoscopic therapy, timing of surgery, surgical procedure and prophylactic TAE will be discussed here.

Management of Patients With Ulcer Bleeding

INITIAL ASSESSMENT AND RISK STRATIFICATION

Initial assessments are to check for Hemodynamic status, hemodynamic status should be assessed immediately upon presentation and resuscitative measures should be taken immediately. Blood transfusions should target hemoglobin ≥7 g/dl, with higher hemoglobins targeted in patients with patients having hypotension, anemia or comorbidities such as coronary artery disease. Risk assessment should be performed to catogorise patients into higher and lower risk groups, this help in initial decisions such as timing of endoscopy **[4]**, time of discharge, and monitoring required. Discharge without inpatient endoscopy can be done in patients with urea nitrogen <18 mg/dl; hemoglobin ≥12.0-13.0 g/dl for men and women respectively, systolic blood pressure ≥110 mm Hg; pulse <100 beats/min; and absence of melena, syncope, cardiac failure, and liver disease, as they have *less* chance of requiring further intervention.

To assess risk we can use the pre-endoscopic Rockall score **[5]** and the Blatchford score. The pre-endoscopic Rockall score which ranges from 0–7 uses only clinical data on presentation, which is related to the severity of the blood loss that is systolic blood pressure and pulse rate and to the patient age and comorbidities. It can predict the risk of further blood loss and death in a population of patients hospitalized with UGIB **[6]**. The Blatchford score range from 0–23 and uses clinical data such as systolic blood pressure, pulse, melena, syncope, hepatic disease, and heart failure and laboratory data such as hemoglobin and blood urea nitrogen, these data is available after admission. It has been shown to predict the risk of intervention that is blood transfusion and endoscopic or surgical therapy and also death in a population of patients presenting to hospital with UGIB.

In general, risk assessment with scoring systems is not able to identify individual patients who will require intervention, with one exception. Patients with a Blatchford score of 0 that is urea nitrogen <18 mg/dl; hemoglobin ≥12.0-13.0 g/dl for men and women respectively, systolic blood pressure ≥110 mm Hg; pulse rate<100 beats/min; absence of melena, syncope, cardiac failure, and liver disease, which may occur in up to 20% of those presenting with UGIB, have <1% chance of requiring intervention **[6]**.

Proton pump inhibitor therapy

To decrease the rate of patients who are at higher risk of hemorrhage at endoscopy or who have received endoscopic therapy, pre-endoscopic intravenous proton pump inhibitor, 80 mg bolus followed by 8 mg/h infusion can be considered. However, PPIs do not improve complications e.g. recurrent bleeding, surgery, death

Intravenous PPI is recommended to reduce further bleeding, if endoscopy is delayed, or not performed **[7]**

ENDOSCOPIC THERAPY

Endoscopy can be considered as both diagnostic and therapeutic **[8]**. In bleeding patients, endoscopy requires higher skill and demands more technical support. Experienced endoscopist along with trained endoscopy nurse is required for management. Opinion of surgeon and radiologist as soon as possible should be taken, considering the clinical condition of the individual patient and expertise of local doctor is important and helps in selecting the optimum therapy for the patient **[9]**.

Complications such as bleeding, surgery and mortality rates in patients with ulcers with active bleeding or nonbleeding visible vessels, endoscopic therapy reduces risk factors significantly. However there is o clear study which tells us about treatment of adherent clot, but further bleeding occurs in 15–35% of patients with clots, suggesting that endoscopic management is useful in patient presenting with clots. Other effective methods are injection therapy, thermal contact methods and laser therapy. An injection therapy has advantages such as easy to use, portable, cheap and safe and is therefore commonly used in day to day practice. Addition of a sclerosant such as polidocanol **[10]** to epinephrine injection therapy is not proven benificial, sclerosant has a potential risk of perforation therefore not advised. Combination therapy is more preferred nowadays for some patients having spurting bleeding, combination therapy with epinephrine injection and thermal contact are proven to be useful. The endoscopic hemoclip is an alternative in some individual cases, but studies are to be performed before this method can be considered as standard therapy. Some studies have shown that platelet aggregation and blood coagulation become altered when the pH falls less than 7. The intragastric pH should therefore be 16 to achieve optimum coagulation. Therefore high-dose proton pump inhibitor should be administered intravenously i.e. 80-mg bolus injection, followed by 8 mg/h continuous infusion should be administered to achieve high gastric pH. A recent randomized trial has shown that high-dose iv omeprazole for

patients with peptic ulcer hemorrhage with high-risk complications such as active bleeding, nonbleeding visible vessel and adherent clot, reduced the rebleeding rate as compared to the placebo group with high significance. Surgery and mortality rate did not differ between the two groups. NSAIDs and H. pylori infection causes the majority of bleeding ulcers. H. pylori status should be checked and intake of NSAIDS should be discontinued as initial assessment in theses patients. Many surgeons prefer to take antral biopsy while doing emergency endoscopy surgery. However antimicrobial blanket therapy is important to patients, before leaving hospital to reduce recurrence. Taking antral biopsy and eradicating H.pylori infection is very important and should not be neglected.

In patients with recurrent peptic ulcer bleeding after initial endoscopic control, repeat endoscopic therapy reduced the need for surgery without increasing mortality as proven by recent randomized control trial. In the these patients with repeat endoscopic therapy there is significant decrease in complications as compared to the same group of patients with surgery. Repeat endoscopy is now the treatment of first choice. For group of patients with larger ulcers i.e. more than 12 cm and blood pressure <110 systolic, which indicates severe bleeding, surgery is a better choice than endoscopic therapy **[11]**.

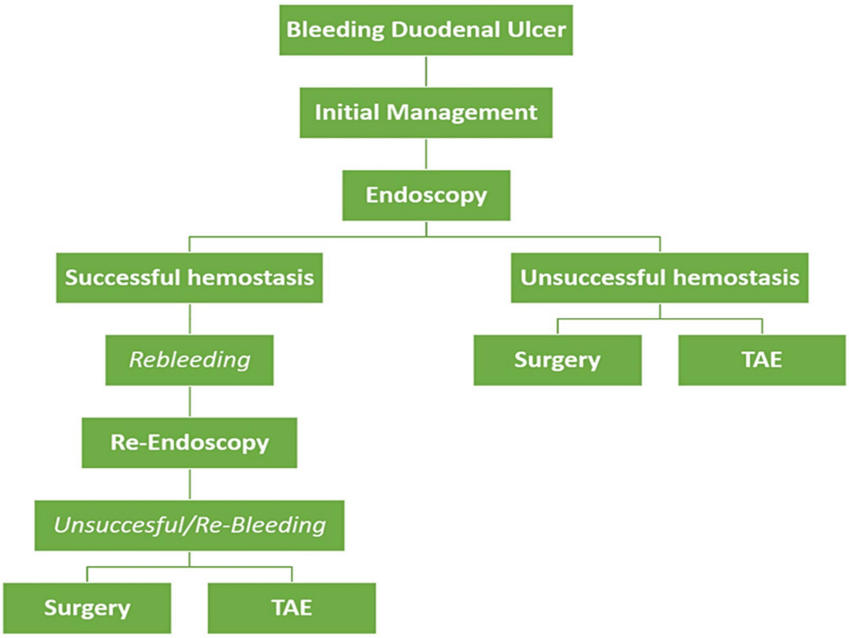

Fig 1: Schematic algorithm for the management of bleeding peptic ulcers [1]
Reference- Bleeding Duodenal Ulcer: Strategies in High-Risk Ulcers, Mille M.a · Engelhardt T.a · Stier A.a

Current Changes in Endoscopic Treatment

Mechanical therapy are nowadays considered as effective treatment options and are considered as a standard treatment in management of gastro duodenal ulcer. In most cases **- Through-The-Scope Clips** (TTSC) are used, their limitations are they cannot be used for large and fibrotic ulcers. There is difficulty in applications of clips here and difficulty in approximation, which causes insufficient hemostasis and therefore more chances of rebleeding. Therefore, **Over-The-Scope Clips** (OTSC) are more commonly used in the treatment of bleeding ulcer. OTSC can anchor much better in fibrotic ulcers because they have larger size, different design, and they have higher compression force. In recent RCT done for uses of OTSC in rebleeding, the study showed that use of OTSC has higher clinical success rate of 85% as compared to 45% using the standard therapy i.e. 94% TTSC and 6.5% gold probe. About 73% of bleeding ulcers in the OTSC group were located in the duodenum, explaining there importance in different anatomical locations as well. Multicentric FLETRock study has also shown that using OTSC in patients with a Rockall risk score ≥8 caused extreme reduction of rebleeding- and associated mortality as compared to the Rockall cohort. Efficiency and safety of OTSC were investigated in recent studies which includes 58 articles comprising 1,868 patients. This study showed a high success rate of 93.0% using OTSC in patients with hemorrhage as per a pooled proportion analysis. Also, a high clinical success rate of 87.5% was demonstrated using OTSC. These studies therefore suggest OTSC as a probable treatment of choice for patients with high-risk ulcers. Especially when rebleeding occurs, OTSC should be used in second endoscopic treatment **[12]**.

Timing of Surgery

Optimal timing for surgery is still a debatable topic and difficult to determine. Obvious indication for emergency surgery includes massive and life-threatening bleeding not controlled by endoscopic therapy. Three RCT has been performed to decide the timing of semi elective surgery. The first study performed included 142 patients. Patients with a visible vessel, the persistence of bleeding or the recurrence of bleeding were categories to 1) early aggressive or 2) delayed surgery. Surgeon decided the type of operation to be performed. All patients received i.v. cimetidine. For a subgroup of patients who are aged more than 60 was an early aggressive surgery which extremely

reduced in mortality. The second study included 69 patients. Patients with a Forrest I B, II B or II C ulcer were randomized to either 1) immediate surgery or 2) expectant management with surgery reserved only for rebleeders. Patients were treated with i.e. cimetidine. Mortality in patients with early surgery was 5 times higher than that in those exposed to expectant therapy. However, majority of patients included in this study had low risk of recurrent hemorrhage. Both studies after combining concluded that early surgery is not preferable but if rebleeding occurs patient should be immediately taken to surgery. This conclusion should be changed after taking into consideration of third trial, recently published, randomized trial by Lau et al, who showed that in patients with recurrent bleeding, endoscopic retreatment reduces the need for surgery and decreases the risk of death and has fewer complications. In conclusion, endoscopic treatment is the therapy of first choice in patients with active bleeding (Forrest I A and I B), a visible vessel (Forrest II A) or an adherent clot (Forrest II B) **[13]**.

Table 1: Forrest classification and the corresponding rebleeding risk without endoscopic therapy [1]

Forrest class	Endoscopic appearance	Rebleeding risk, %
Active hemorrhage		
Ia	Arterial, spurting	90
Ib	Oozing	50
Signs of recent hemorrhage		
IIa	Visible vessel	25–30
IIb	Adherent clot	10–20
IIc	Hematin-covered lesion	<10
Lesions without active bleeding		
III	Clean base ulcer	<5

Reference-- Bleeding Duodenal Ulcer: Strategies in High-Risk Ulcers, Mille M.a • Engelhardt T.a • Stier A.a

After treatment by endoscopy, for rebleeding again endoscopy should be reconsidered. Surgery is a better choice than endoscopic retreatment in Subgroup analysis for patients with larger ulcers (1- 2 cm) and hypotension. In patients with larger bleeding ulcers we can

perform semi elective surgery even before bleeding recurs. The complications of emergency salvage surgery might be avoided by semi elective surgery.

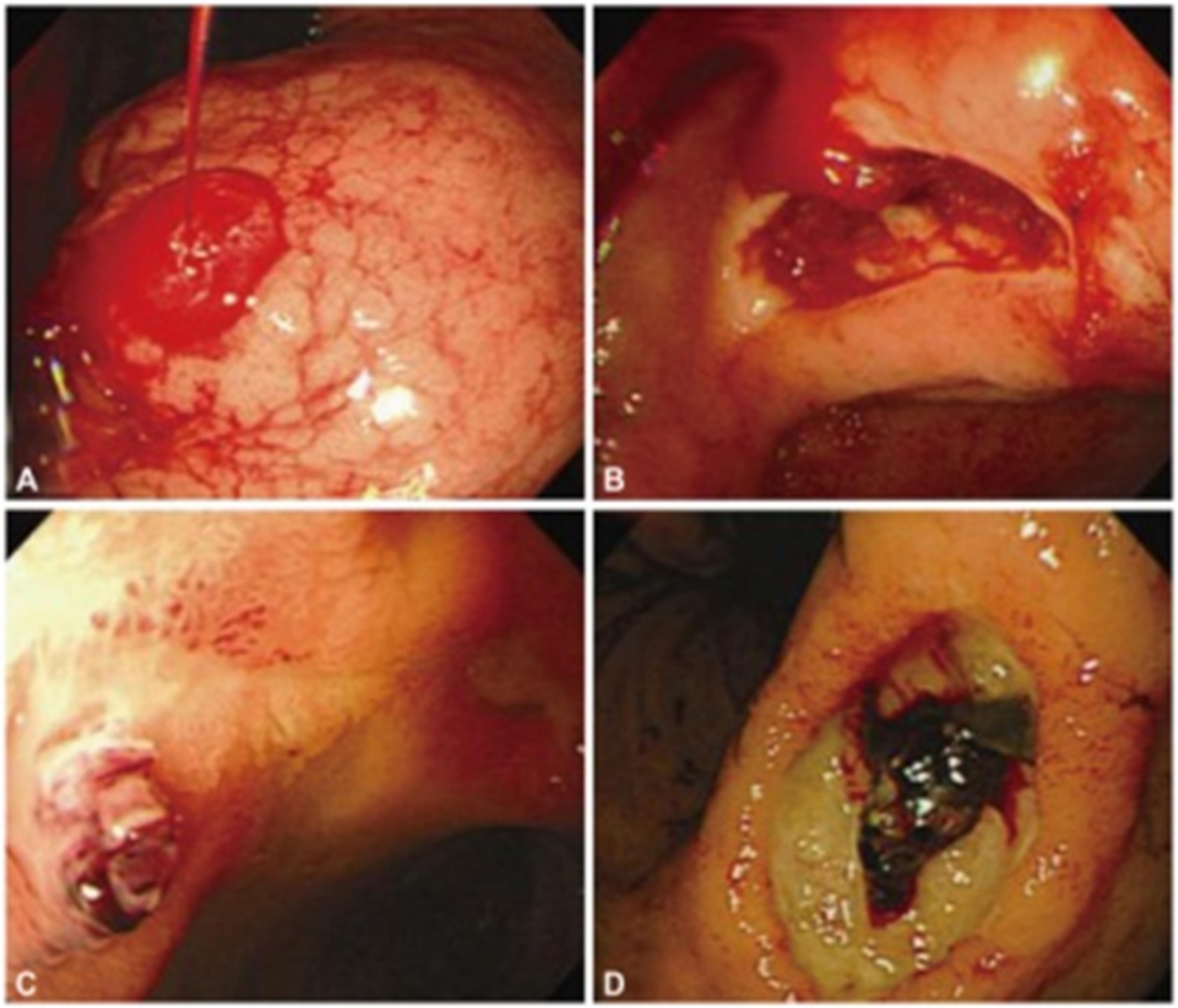

Fig 2: Bleeding status. (A) Active pumping. (B) Active oozing. (C) Vessel exposure. (D) Red or black clot. [16] Reference-Clinical Outcomes and Risk Factors of Rebleeding Following Endoscopic Therapy for Nonvariceal Upper Gastrointestinal Hemorrhage

SURGICAL PROCEDURES

The surgical procedures for a bleeding gastro duodenal ulcer are classified into 1) minimal approaches or 2) definitive approaches. Mainly the achievement of gastro duodenal ulcer hemostasis of bleeding is a minimal approach; however the addition of acid reduction procedures is classified as a definitive approach. The minimal approach includes under running of the ulcer, theses are also called simple intraluminal ligature or undersewing, plication or an

ulcerectomy, these may also include ligation of the blood vessel around the stomach or duodenum; the definitive approach include ligation of vessel for primary hemostasis along with either vagotomy and pyloroplasty or a partial or total gastrectomy as a gastric acid reduction surgery.

The topic of choice of surgery is still controversial and there is still difference in opinion for the same. Prospective RCT trial by. Poxon which compares minimal surgery i.e. simple intraluminal ligature or plication against definetive surgery i.e. ulcer excision along with either gastric acid reduction surgery or gastrectomy for primary hemostasis of bleeding gastro duodenal ulcer. There were no difference in the overall mortality rate, a high rate of fatal rebleeding in those randomly assigned to minimal surgery was observed. A RCT study comparing oversewing plus vagotomy done and drainage against gastrectomy for primary hemostasis of bleeding bulbar duodenal ulcer done by Millat This study showed that the more aggressive approach that is gastric resection resulted in a lower rebleeding rate i.e. 3% *vs* 17%, but studies did not show any difference in the overall mortality rate between above mentioned two groups. Above mentioned study shows that aggressive management can be taken under consideration for management of bleeding gastroduodenal ulcer. Nowadays the role of definitive surgical management has gone significantly down after discover and management of H. pylori infection, and there relation to peptic ulcer, *H. pylori* eradication, and the use of high-dose proton pump inhibitors the aim of emergency surgery nowadays is not to cure the disease but to stop the hemorrhage and rebleeding; therefore, definitive surgery is not practiced. As a result of the increasing use of PPI, the role for definitive management is controversial nowadays[14].

INTERVENTIONAL RADIOLOGY

Non operative options in patients where bleeding are not localized or controlled by endoscopy are angiography with transcatheter embolization. The technical success rate is very high which ranges from 90 to 100%; however, the clinical success rate is low and ranges from 50 to 8o %. A study showed no obvious difference between embolization and surgery in the incidence of rebleeding according to retrospective analysis and the need for additional surgery is 15% in embolization *vs* 3o% in surgery, and mortality rate is 25% in embolization *vs.* 21% in surgery, even though there were more comorbid patients in group of embolization. Other retrospective

study comparing between embolization and surgery showed that the mortality rate was significantly low in the embolization group i.e. 3% *vs* 14% in group of surgery. However there is need of controlled study comparing both embolization therapy with surgery a treatment of choice after failed endoscopic treatment, however the above data shows us that in comorbid patient or patient with increased age group, embolization can be considered more effective as it is minimal invasive. Embolization may not always be a permanent cure, but can be utilized to stabalise patient until definitive procedure is performed.

Patient not responding conservative, endoscopic or surgical management with upper or lower gastro duodenal bleed, embolization is known as a therapeutic option. Autologous blood clot was used as first embolization material on late 19's. Autologous blood is quickly lysed by the fibrinolytic system, this treatment was not durable and transcatheter intra-arterial infusion of vasopressin was introduced in replacement of blood clot as an alternative method. The effect of this treatment was also not that effective and had complications such as ischaemia. Using 3 to 5 Fr catheter systems, Catheter and guidewire technology are nowadays more reliable and has drastically changed the treatment modalities. New and safe material for embolization are also available nowadays. Microcoils, are nowadays preferred embolic agent as they produce permanent vessel occlusion and decrease the risk of bowel ischemia and infarction to very great extent. While handling duodenal circulation, precautions should be taken i.e. to occlude the vessel both proximal and distal to the site of bleeding this will avoid retrograde filling of the vessel. This shows that for many cases the gastro duodenal or pancreatic duodenal vessels have to be catheterized and emboli zed from both celiac axis approach and from a superior mesenteric approach. Embolization of duodenal ulcer hemorrhages have been studied. The series of studies have shown angiographic transcatheter embolization are more effective with bleeding control that achieves almost 50–90% of patients. 0 and 40% are rebleeding rates in these patient and there is also possibility of repeat embolization. Necrosis and ischemia of bowel or pancreases are almost 0-15% but almost nil according to literature

Coils have very promising results, but embolization is not widely excepted in the community of surgeons and gastroenterologists because of unfamiliarity

and fear of complications such as ischemia, also due to unavailability of equipment's and skilled interventional radiologist at many centers, and therefore there is need of study and RCT trials to know the understand the actual importance of semi invasive procedure.

Prophylactic TAE

TAE is more recent approach in patients having high risk for rebleeding after endoscopic procedure and hemostasis.

For now there is no studies performed for prophylactic TAE and thus there is less evidence in support of the above treatment. Also, suitable high-risk patients for prophylactic TAE, there selection and complications related to the procedure and group of patient to be selected is still controversial and has to be studied. Anyways, in gastro duodenal high-risk ulcers i.e posterior duodenal bulb with patient having risk profile and/or suboptimal endoscopic hemostasis, prophylactic TAE might be an essential therapy modality.

LONG-TERM PREVENTION OF RECURRENT BLEEDING ULCERS

Patients with H. pylori-associated bleeding ulcers should receive H. pylori therapy. After documentation of eradication, maintenance antisecretory therapy is not needed unless the patient also requires non-steroidal anti-inflammatory drugs (NSAIDs) or antithrombotics (Strong recommendation, high-quality evidence) **[15]**.

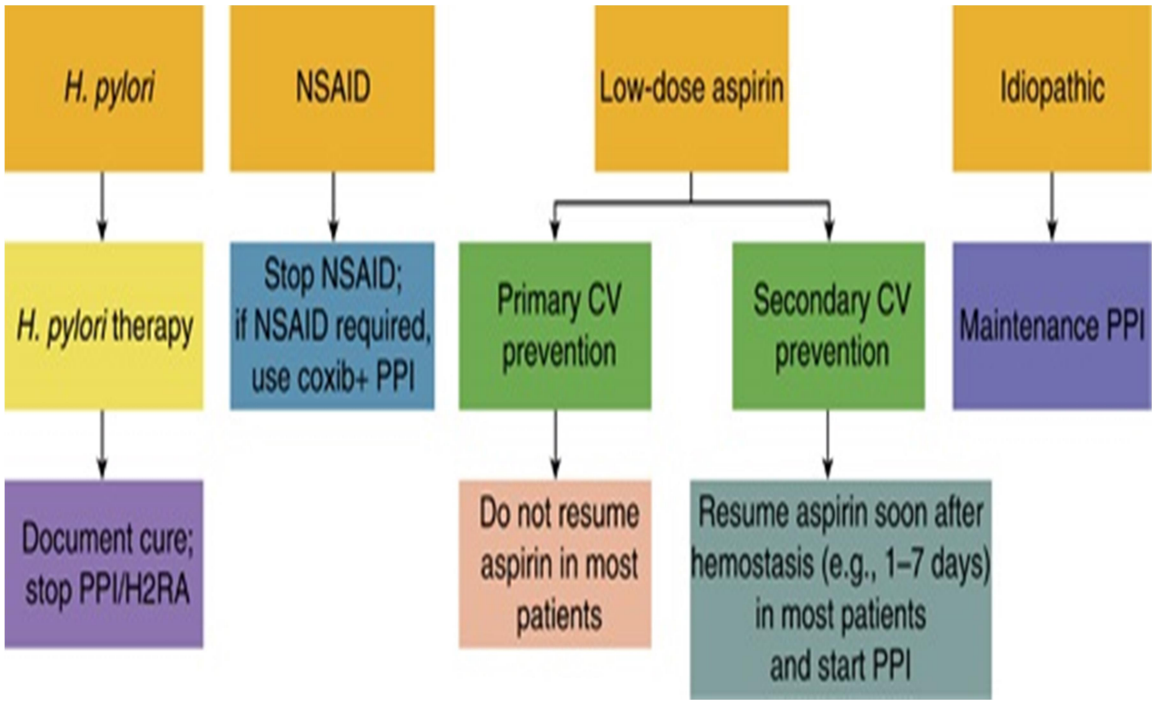

Fig 3: Recommended endoscopic and medical management based on stigmata of hemorrhage in ulcer base. IV, intravenous; PPI, proton pump inhibitor [14]
Reference-MANAGEMENT OF PATIENT WITH ULCER BLEEDING

CONCLUSION

Elective surgery for peptic ulcer disease has significantly reduced after understanding of H. pylori infection, its treatment and NSAID use causing peptic ulcer. But, complications related to peptic ulcer disease are same in numbers which includes bleeding, perforation, and gastric outlet obstruction. Surgical management remains important since surgery is the mainstay of emergency treatment of above mentioned life-threatening complications and for disease that is not responding to medical treatment.

However endoscopic therapy after rebleed and use of embolization and TEA in recent decades has changed the treatment modalities of peptic ulcer bleeding and there is need of further study, technical mastery and sitable equipments to carry out the procedure in many centres which may further improve the treatment of gastro duodenal bleeding management.

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