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Advancements in Upper Gastrointestinal Endoscopic Therapy: A Comprehensive Review

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Abstract:- This paper focuses on endoscopic therapeutic advances in gastrointestinal conditions. Over-The-Scope Clips (OTSC) are effective in non-variceal upper gastrointestinal bleeds (NVUGIB) and have promising results in large fibrotic ulcers. The Apollo endoscopic suturing system is effective for refractory peptic hemorrhage. Endoclip application +/- epinephrine is considered for large peptic ulcers. Persistent bleeding is controlled by Hemospray with a hemostatic endoscopic procedure. Stand-alone therapies like Endoclot and Polysaccharide hemostatic powder hold potential but require further research. Endoscopic ultrasound-guided cyanoacrylate and coil embolization are effective for gastric varices, while Endoscopic Band Ligation is preferred for esophageal varices. Endoscopic submucosal dissection can excise Barrett's lesions of any size but is challenging; hence, for multiband mucosectomy, an Endoscopic mucosal resection (EMR) is used. Argon plasma coagulation is effective for smaller lesions after EMR. Radiofrequency ablation (RFA) is preferred for Barrett's esophagus, and cryotherapy is used if RFA fails. When life expectancy is less than two months, Self-expanding metallic stent is preferred, and Endoscopic gastrojejunostomy is provided when it is more than three months. However, Brachytherapy is recommended for long-term relief. Laser modalities show promise for mid-esophageal tumors, while cryoablation compliments others for advanced conditions. In conclusion, many methods have a user-friendly interface and are easy to master. The problems with resource availability, funding, proper training, and the lack of larger studies still limit some of the above-described techniques.

Keywords:- *Endoscopy; Variceal ligation; Stenting; Cryoablation; Barrett's.*

I. INTRODUCTION

Gastrointestinal bleeding (GIB) remains a critical medical emergency in gastroenterology, with mortality rates ranging from 5% to 10% for peptic ulcer bleeding, 15% for variceal hemorrhage, and between 11% and 14% for various causes of gastrointestinal bleeding [1]. Another cause of concern in today's world is metaplasia and cancer of the gastrointestinal tract. GI cancers contribute 26.3% of the world's tumor prevalence and are responsible for 35.4% of deaths worldwide [2]. The mainstay of treatment for gastrointestinal bleeding, metaplasia of the esophagus, and palliative care for malignancy is endoscopy.

In the past two decades, therapeutic endoscopy has significantly advanced in treating variceal and non-variceal upper gastrointestinal bleeding. Advanced tools such as the over-the-scope clip system, Coagrasper, hemostatic sprays, and endoscopic suturing have been developed and expanded. Innovational endoscopic devices (over-the-scope clips, Coagrasper, hemostatic sprays, radiofrequency ablation, cryotherapy, endoscopic suturing devices, and endoscopic ultrasound-guided radiotherapy) are now primary methods or alternatives when conventional therapeutic instruments (epinephrine injection, argon plasma coagulation, heater probe, and placement of through-the-scope clips) fail [3].

Regarding gastrointestinal malignancy, the early stages of colorectal cancer are identified and treated endoscopically through procedures such as endoscopic mucosal resection and endoscopic submucosal dissection [4]. Earlier diagnosis and treatment of esophageal cancer due to advances in endoscopy have caused a significant shift in the outcome of esophageal cancer in the current world [5]. Endoscopic enteral stenting is also utilized in cases of malignant gastric obstructions, providing relief to the patient and improving their quality of life and outcome [6]. This comprehensive review focuses on the role of therapeutic endoscopy in managing upper gastrointestinal bleeding and its application in treating metaplasia and cancer. The study will include an in-depth analysis of the various endoscopic modalities used in UGIB. Additionally, emerging techniques like endoscopic submucosal dissection (ESD) and endoscopic mucosal

resection (EMR), which have revolutionized the management of metaplasia and early-stage gastrointestinal cancers, will be explored.

A comprehensive literature search on secondary data was conducted using PubMed, Google Scholar, Scopus, and Cochrane databases with focus on upper gastrointestinal bleeding and malignancy. In addition, we reviewed current guidelines from relevant societies and selected bibliographies from the articles included. The authors utilized advanced search strategies specific to each database. English-language peer-reviewed publications on the therapeutic aspect of endoscopy on humans were included here. The terms used were relevant keywords such as "therapeutic endoscopy," "variceal bleeding," "upper gastrointestinal disease," "gastroesophageal reflux disease," "Barrett's esophagus," "esophageal cancer," "gastric cancer," "peptic ulcer disease," "Advances," "endoscopy." Studies published from 2013 to March 2023 that evaluated the therapeutic aspect use of endoscopic in adults were included. After removing duplicate and irrelevant studies, two authors independently assessed each article for study eligibility. Using a standard form, information was extracted. If the paper's title, abstract, and keywords did not provide sufficient information, we reviewed the entire document, and the references of the included articles were also screened.

II. REVIEW

A. *Endoscopic Therapies for Upper GI Bleeding*

Endoscopic therapies have revolutionized the management of upper gastrointestinal bleeding (UGIB) by offering targeted and precise treatments. By reducing the reliance on invasive surgeries, endoscopic therapies improve outcomes and contribute to the evolution of UGIB management strategies.

- *Mechanical therapy*

Emerging novel endoscopic therapies, such as over-the-scope clips (OTSC), endoscopic suturing, coagulation grasper, and endoscopic ultrasound (EUS)-guided treatment, have played essential roles in achieving hemostasis for bleeding management. Hemostatic endoscopic procedures, such as injection agents, contact and non-contact thermal devices, and mechanical devices, can achieve endoscopic hemostasis in approximately 67-100% of cases. However, rebleeding may occur in 25-30% of treated individuals [7].

- *Over the scope clips*

It has been established that the over-the-scope clip system is safe and effective as a first line and in the rescue management of non-variceal gastrointestinal bleeding caused by large and fibrotic ulcers at anatomic locations that are difficult to treat with through-the-scope (TTS) clips or at risk of perforation [3]. The success rates range from 78%-100%, and the risk of rebleeding is <1% [8]. However, approximately 26% with coronary artery disease experienced rebleeding [9,10]. Implanting the clip is simple and requires no endoscopic expertise [11]. Even so, it is challenging to close chronic and severe fibrotic lesions, and the scope cannot be used in emergencies due to operational difficulties [3]. A novel technique, through-the-scope endoscopic suturing, played a crucial role in successfully treating a large refractory duodenal ulcer, as demonstrated in this case report, where the device oversewn the ulcer in a figure 8 pattern [12].

- *Endoscopic suturing*

The endoscopic suturing device guides a suture through the stomach lining or small intestine, facilitating the convergence of two areas involving the mucosa and deeper wall layers. In a recent multicenter series, the Apollo endoscopic suturing system successfully treated ten patients with refractory peptic hemorrhage, and no rebleeding was observed. The chronic blood loss from anastomosis and marginal ulcers has been reduced to a minimum by this device. Although studies have not mainly addressed hemostasis, endoscopic suturing after endoscopic mucosal excision and ESD is appealing. It is not expensive and has a relatively steep learning curve [13]. The OverStitch suturing device is used for the acute therapy of non-variceal upper gastrointestinal bleeds (NVUGIB). Due to certain device limitations, such as the requirement for a specialized double-channel endoscope, reduced visibility during active bleeding, and limited maneuverability, access to particular anatomical locations has limited its use in the acute setting. However, the device effectively controls anastomotic ulcer-related chronic blood loss and prevents delayed bleeding after EMR or ESD [14]. The endoscopic suturing device is particularly suitable for treating larger, deep, and fibrotic ulcers [15].

- *Endoscopic Band Ligation (EBL)*

Endoscopic band ligation has emerged as a valuable treatment modality for acute bleeds and secondary prevention of esophageal varices. In comparison to its predecessor, sclerotherapy, this technique provides a significantly lower mortality rate (OR=0.67 95%CI: 0.46-0.98), lower risk of rebleeding (RR=0.68, 95%CI:0.57-0.81), and adverse events (RR=0.28 95%CI: 0.13-0.58) [16–18]. However, it is pertinent to note that endoscopic band ligation is not a preferred option for gastric varices due to the thickness of the mucosa and the large size of the varices in the stomach, which can potentially result in failure and severe bleeding [16,19].

Band ligation is also utilized to treat nodular gastric antral vascular ectasia. Endoscopic Band ligation is superior to argon plasma coagulation (APC) and endoscopic thermal therapy in terms of the reduction of treatment sessions (mean of 2.98 sessions vs. 3.48 sessions) and needs for transfusion (mean of 2.5 units vs. 4.6 units), making it a promising and effective alternative modality [20]. However, more extensive research is required [3].

- *Endoscopic epinephrine injections*

Epinephrine injection is an extensively utilized approach due to its ease of administration and the minimal need for coordination between the endoscopist and assistant. Vergara et al found that diluted epinephrine injections (from 1:10000 to 1:20000) can facilitate primary hemostasis for active bleeding [21]. Epinephrine alone is less effective due to rebleeding risk of 14.2% within 30 days after injections [22]. To minimize rebleeding risk, it is recommended to follow epinephrine injection with a secondary method of mechanical or thermal therapy for definitive hemostasis [21,23]. On comparing clips with various doses of epinephrine, the

endoscopic success rates were 72.2%-90.6%. In peptic ulcer bleeds, if the Rockall score is high and the ulcer size is larger than 2 cm, endoclip application with or without epinephrine can be considered [24].

- *Endoscopic ultrasound-guided angiotherapy*

Endoscopic ultrasound-guided vascular interventions with the addition of Doppler and contrast-enhanced capabilities have further contributed to real-time visualization of blood flow in vessels of the gastrointestinal tract [25]. The current standard of treatment for gastric varices is glue therapy with cyanoacrylate [25]. Endoscopic ultrasound-guided cyanoacrylate glue injection when compared to direct endoscopic injection has low rates of rebleeding (8.8% vs 23.7%) and also requires less volume of cyanoacrylate [26]. Color Doppler also permits the identification of the source of bleeds and can verify the eradication of varices [25].

Furthermore, by allowing direct visualization of perforating vessels, precise obliteration of the varices is achieved with a lesser volume of cyanoacrylate glue. The theoretical risk of embolization related to the high volumes of cyanoacrylate glue is avoided by using endoscopic ultrasound guided technique [25,27]. Recently, a novel glue, histoacryl (n-butyl-2 cyanoacrylate) used through an endoscopic ultrasound-guided technique resulted in complete hemostasis of both acute and active bleeding in less than 24 hours [25,28]. Also, EUS-guided thrombin injection has been tried for treatment for gastric varices, with a recent study demonstrating encouraging outcomes (66% and 100% hemostasis in active and elective bleeding, respectively [25,29].

EUS guided-coil embolization is another treatment modality indicated in the treatment of gastric varices [25]. This technique has fewer adverse events, such as embolism, when compared to glue injection (9% vs. 57%; $p<0.01$) [30]. These coils are made of a light metal alloy and covered with synthetic fibers to induce clot formation and subsequent hemostasis to eradicate gastric varices [25]. In addition, fibers can serve as a scaffold for cyanoacrylate if injected during the same procedure, thereby preventing adverse effects such as embolization [25]. Regardless, retrospective data have demonstrated that the combination of glue injection and coil embolization coils is comparable with similar efficacy (94%) with no embolism events and less required glue volume [25,31]. In addition, recent meta analysis also showed that a combination of these techniques (EUS-guided CYA injection and EUS-guided coil embolization) has better technical and clinical success rates with lower adverse events compared to CYA alone (10% vs 21%; $p<0.001$) and coil embolization alone (10% vs 3%; $p=0.05$) [25,32].

Endoscopic ultrasound has been shown to be effective for variceal bleeding, but for non-variceal etiologies, little to no evidence exists. No studies have compared EUS therapy to other management modalities, such as endoscopic, surgical, and interventional radiology. Additional large-scale comparative studies are required. This may be due to the non-availability of endosonography with specialized training and the limited availability of endoscopic ultrasound in acute care settings [25].

- *Emergent thermal treatment options*

When used as monotherapy, thermal ablative methods have yielded a significantly comparable rate of successful endoscopic hemostasis. New thermal treatment options for non-variceal gastrointestinal bleeding include coagrasper, radiofrequency ablation, cryotherapy, and endoscopic laser coagulation [3].

- *Laser Coagulation and Coagulation Grasper*

Endoscopic argon plasma coagulation (APC) has been shown to be effective in treating upper gastrointestinal bleeds that are not variceal, but it is not routinely used. Nd: YAG laser has technical difficulties, which include the large size of the laser delivery unit and the need for unique electrical and water supplies. But Nd: YAG laser is the least cost-effective relative to other modalities utilizing a laser-based approach [3,25]. Monopolar hemostatic forceps (Coagulation grasper) have a shallow risk of perforation as it operates at a lower voltage than other thermal treatments, coagulates tissues without carbonization, and do not penetrate deeper tissue [3]. The forceps can treat multiple bleeding sites, for ulcers under challenging locations or those with a fibrotic base, and is cost-efficient [3,33]. They can be an effective alternative to other mechanical and thermal treatments [33]. Hemostasis using an over-the-scope clip should be considered in NVUGIB when conventional electrosurgical coagulation and hemostatic clips have failed [33].

- *Cryotherapy*

Cryotherapy uses compressed carbon dioxide or liquid nitrogen to freeze tissues and create surface necrosis. CryoBalloon ablation is practical and safe for patients with GAVE who do not respond to APC therapy [34,35]. Patel et al., using CryoBalloon ablation found that the vast majority achieved endoscopic response (87%) and transfusion independence (83%), and a mean hemoglobin rise of 2.55 g/dl at six months [35]. Recently, self-venting balloon-based cryotherapy has been established, offering advantages over spray cryotherapy. These advantages include enhanced vision through direct visualization using the balloon and the absence of gas leakage into the stomach [35]. However, a report demonstrated perforation due to cryotherapy-induced barotrauma, and further longitudinal studies showing long-term outcomes are needed [36].

- *Emerging Topical Treatment Options*

Hemostatic powders like Hemospray (TC-325), EndoClot, and Polysaccharide hemostatic powder are commonly used, administered through a delivery catheter inserted via an endoscope's working channel [37].

- *Hemospray (TC-325)*

Hemospray, an inorganic hemostatic powder before being introduced as an endoscopic hemostatic agent for use [38]. Hemospray provides non-contact administration, greater coverage, and potential benefits in promoting platelet aggregation, activating the clotting cascade, and stimulating tissue formation. Currently employed for rapid hemostasis or as rescue therapy following operations such as esophageal or duodenal endoscopic mucosal excision [37]. Hemospray demonstrates an immediate success rate of 88.5% and varying rebleed rates are reported from 16.2% to 38% [15,39].

Hemospray is user-friendly and has minimal risks but further studies are needed to establish its efficacy as a standalone treatment and long-term effectiveness [37]. Hemospray followed by hemostatic endoscopic procedure HEP is promising for persistent bleeding [23,37,40].

➢ *Endoclot*

EndoClot forms a gel matrix that sticks to the mucosa, creating a physical barrier and enhancing the local concentration of red blood cells, coagulation factors, and platelets. The mucosa does not absorb it but rather eliminates it through physical forces and enzymatic degradation [15]. Endoclot has been shown to have similar rates of immediate hemostasis and rebleeding compared to standard conventional HEPs (epinephrine, ethanol, and cyanoacrylate, contact thermal devices, non contact thermal devices, and mechanical devices) [7]. To further assess the effectiveness of endoclot as a rescue therapy, a study by Beg et al. involving 21 patients with gastrointestinal bleeding lesions found that immediate hemostasis was achieved in all patients. The rebleeding rate after 30 days was 4.8%, and the mortality rate was 19% [15].

➢ *Polysaccharide hemostatic powder (PHP)*

In a case control analysis, Polysaccharide hemostatic powder, and conventional therapy (injection therapy, hemoclips, or thermocoagulation) were compared for treating gastrointestinal bleeding. The study found no significant differences in immediate hemostasis and rebleeding rates between the Polysac PHP and conventional therapy groups after matching based on the type of lesion [41]. This indicates the feasibility and effectiveness of this technique in treating non-variceal UGIB and its potential as a promising hemostatic method [41]. However, studies focusing on complications and mortality are limited.

B. Endoscopic eradication therapy

Endoscopic eradication therapy is the standard of care for the management of early Barrett's neoplasia, by removing early dysplastic lesions, eradicating residual Barrett's esophagus, and maintaining surveillance [42,43]. This approach is more cost-effective and results in better survival outcomes with fewer adverse effects than esophagectomy [42]. Endoscopic therapy is indicated for intramucosal adenocarcinoma (T1), high grade dysplasia, and select cases of low grade dysplasia [42,43]. Despite successful endoscopic therapy, metaplasia recurrence rates remain high at 9.5%, emphasizing the need for continued surveillance [44].

➢ *Endoscopic Mucosal Resection*

Endoscopic mucosal resection (EMR) is widely recognized as the preferred endoscopic resection technique for Barrett's esophagus. EMR encompasses two techniques, namely Endoscopic Resection-Cap and Multiband mucosectomy [43]. Endoscopic resection-cap has been replaced by newer methods such as multiband mucosectomy due to expensive costs with long procedure timings and the risk of adverse events like perforations [43]. Multiband mucosectomy (MBM) is a modification of variceal band ligation with a polypectomy snare. The safety of this technique is high compared to the cap technique but with a very low risk of adverse complications. These complications include perforation of less than 1%, bleeding of 1-2%, and strictures of 3-4%. Other advantages of this technique include short procedure time and less cost [45]. Therefore, it is the most preferred technique for EMR in Barrett's esophagus [43].

➢ *Endoscopic Submucosal Dissection*

Despite the similar rates of adverse events like perforations, delayed bleeding, and strictures, studies have shown that there is no significant clinical benefit when comparing EMR with endoscopic submucosal dissection (ESD) [43,46]. ESD is only advantageous over EMR as it enables the en bloc resection of lesions of any size [45]. However, it is technically more challenging than EMR with a steep learning curve and longer procedural timings. ESD is typically indicated only for lesions that are bulky, scarred, larger than 15 mm or have a high suspicion of submucosal adenocarcinoma [43,45,47].

➢ *Ablation methods*

- Radiofrequency Ablation

Radiofrequency ablation (RFA) introduced in 2010 is the preferred ablative modality for Barrett's esophagus (BE) and Gastric Antral Vascular Ectasia (GAVE) [43,48]. Radiofrequency ablation (RFA) using a focused catheter (BarrxTM HALO90 and HALOULTRA) or the Barrx TTS RF was originally used to treat Barrett's esophagus and is now an emerging endoscopic treatment. A review of 72 patients with GAVE treated with RFA showed 74.3% achieved a clinical response, while nonfatal adverse effects have been reported in 4.2% [48]. The ability to deliver uniform ablation to a consistent depth of the esophageal wall is the primary reason for its widespread adoption in BE [45]. Complete eradication of intestinal metaplasia (CE-IM) in 94%, an annual recurrence rate of 2-4% for metaplasia, and 1-2% for dysplasia was observed [43]. However, this comes at a cost of 21% adverse events, which include 15% esophageal strictures and 4% bleeding [43]. Patients in the RFA group were more likely to achieve complete eradication of intestinal metaplasia when compared to cryoablation (OR 2.9, 95%CI=1.4–6.0, p=0.004) [49]. Also, RFA is very cost-effective compared to esophagectomy, mainly due to the discounting of future costs of healthcare [43,50].

- Argon Plasma Coagulation

Argon plasma coagulation (APC) is a technique that is widely accessible and cost-effective, allowing for the ablation of flat dysplastic or residual dysplastic BE following endoscopic resection [43]. Results from an RCT conducted over a period of 2 years have demonstrated that APC ablation after endoscopic resection achieved complete eradication of intestinal metaplasia (CE-IM) in 79% of patients and reduced the recurrence rate from 37% to 3% [43]. Despite its effectiveness, this technique is not the preferred method due to its heterogeneity and long procedural times, particularly in circumferential lesions. Consequently, APC is limited to the ablation of small residual dysplastic BE or lesions without access to radiofrequency ablation (RFA) [43]. However, a similar technique, hybrid APC, which involves a modification in the APC probe and the addition of an

integrated waterjet for submucosal saline injection, provides high power and more homogeneous ablation to improve outcomes [43]. Although hybrid APC is not superior in terms of efficacy when compared to APC, it has lower stricture rates and is therefore also recommended for the ablation of dysplastic or residual BE [43,45].

- Cryoablation

Cryoablation was introduced in 2010 and can be done with three different cryogenics- liquid nitrogen, carbon dioxide, and nitrous oxide [51]. Retrospective cohort evidence suggests that cryoablation is similarly effective to radiofrequency ablation (RFA) in eradicating dysplasia (CE-D) and metaplasia (CE-IM) of BE [43,52]. RFA is more cost effective compared to cryoablation due to fewer ablation sessions required for the same response [52]. But, a prospective cohort study revealed that patients in the RFA group had five times greater odds of experiencing pain compared to the cryoablation group, possibly due to the cryo analgesic effect [52,53]. Moreover, in a recent meta analysis in 2019, subgroup analysis with patients who failed RFA showed the rate of CE-IM with cryoablation (58.4%, 95% CI=47.2–68.8) lower than the rates achievable with RFA and the rate of CE-D in the same population (81.9%, 95%CI=72.5–88.6) was comparable to RFA. Additionally, subgroup analysis on treatment naive patients showed CE-IM rate with cryoablation was 53.7% compared to the literary data on RFA CE-IM rates of 78%. Hence, cryoablation cannot be recommended as a first-line treatment for BE, and should only be considered as salvage therapy in cases of RFA failure or intolerance [51,52].

C. Palliative for esophageal and gastric malignancies

➢ *Self-Expanding Metallic Stents (SEMS) vs Self-Expanding Plastic Stents (SEPS)*

Since their introduction in the 1990s, self-expanding metallic stents (SEMS) have demonstrated the ability to provide durable relief (for more than a month) from malignant obstruction, with low rates of adverse events and minimal cost. Later on, plastic stents were introduced during the early 2000s. Currently, there are cover versions of both plastic and metal stents [54,55]. Uncovered stents have a lower chance of migration but with high rates of tumor ingrowth in the stent, making stent removal very difficult. In contrast, fully covered stents have the advantage of being removable and have virtually no risk of tumor ingrowth and occlusion [54,56,57]. Esophageal stenting provides acute relief of malignant dysphagia with high success rates [54,56].

Retrospective studies comparing both SEMS and SEPS have unveiled similar rates of both survival and improvements in dysphagia [55]. However, SEPS has reported a high incidence of major adverse events (22% vs 9%; p=0.05) of which migration and esophageal fistula were higher [55]. Biodegradable stents were developed recently to prevent these complications such as migration and tumor ingrowth; however, their use has not been successful, mainly due to stent migration rate (8.8%) and tissue ingrowth (14.5%), with few cases even reporting TE fistula and stent collapse in the esophageal lumen [55,58]. For this reason, SEMS and SEPS have become the standard treatment for malignant esophageal strictures and fistulae [55]. SEMS, both fully and partially covered, is recommended for patients with esophageal obstruction caused by unresectable esophageal cancers [59], and the use of newer technology such as drug-eluting or radioactive stents is being developed to lower recurrence rates [56].

In gastric outlet obstruction (GOO) with life expectancy of less than 2 months and poor functional status, clinicians should consider the insertion of an enteral stent [59]. Self-expanding metal stent (SEMS) insertion is a highly effective treatment option for GOO, with high clinical success rates of 87% and low technical failure rates (3%) [56]. Additionally, stenting has been found to be safe and better tolerated by patients with minimal adverse events such as intestinal ulceration and bleeding (1%) [56]. In 2015, randomized trials found that covered stents with anti-migratory properties (WAVE stent) had significant long-term stent patency rates (WCS 68.6% vs. UCS 41.2%; p< 0.01) and comparable migration rates (WCS 9.5% vs. UCS 5.4%; p=0.4) compared to uncovered stents for the palliation of GOO in patients with inoperable gastric cancer [60]. Therefore, the newly developed WAVE stent presents a promising option for these patients [60]. The WCS group demonstrated superior clinical outcomes, which were largely driven by significantly lower stent migration and restenosis rates when compared to the UCS group [60].

➢ *Endoscopic Brachytherapy*

For the palliation of esophageal cancer, one technique that has been utilized for several years is brachytherapy, which involves the introduction of a radioactive source into the tumor via endoscopy [54,55]. This approach offers the advantage of targeting the tumor specifically, with minimal involvement of surrounding healthy tissues [54,55]. Although brachytherapy requires multiple treatments and carries the risk of complications such as esophagitis and stricture, it is generally well-tolerated. It has been shown to offer long-term relief and quality-of-life outcomes comparable to those of palliative stenting [54,55]. Esophageal stenting provides acute relief of malignant dysphagia with high success rates, but recurrence occurs in up to 50% of patients [54,56]. However, radiotherapy effectively provides long-term relief from dysphagia, even though the effects are gradual [56]. The complementary effects of these two therapies (immediate relief- stent insertion; long-term relief- brachytherapy) make the combination of palliative stenting and brachytherapy an appealing option [56]. When managing malignant esophageal obstruction who are not candidates for resection, clinicians should consider using SEMS insertion or brachytherapy either as a sole therapy or in combination [59].

➢ *Dilatation Techniques*

Esophageal dilation is primarily indicated for benign or malignant dysphagia, EUS tumor staging, placement of esophageal stents, and placement of PEG for feeding purposes [55]. In cases of malignant esophageal obstruction, dilation procedures are effective only for prompt relief of dysphagia symptoms and do not provide long term benefits [54,55]. Esophageal dilation is a procedure that utilizes upper endoscopy and can be accomplished using either a pneumatic balloon or wire-covered bougie [54]. Two primary types of

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bougies are currently in use, namely, mercury or tungsten-filled bougie (Maloney) and over-the-wire (OTW) polyvinyl bougies [55]. Through the telescope (TTS) balloons are introduced through the accessory channel of the endoscope [55]. Studies have reported that esophageal perforation is a major complication associated with endoscopic dilation, with Maloney dilators posing a higher risk compared to OTW bougies and TTS balloons (4% vs 0% vs 0% respectively) [55]. An overall perforation rate of 2.6% with dilation, more common in malignant strictures than benign strictures (6.4% vs 1.1%) is reported [55].

- *Ablation methods*

Photodynamic therapy has been historically used and limited due to its high cost and side effect profile of esophageal stricture and perforation [55]. There is a lack of studies comparing photodynamic therapy to other modalities used nowadays [55]. Nevertheless, this procedure has been found to be useful in patients with recurrent dysphagia following previous radiotherapy and surgery [55].

Laser therapy has demonstrated positive outcomes have been demonstrated in the palliation of dysphagia (70-80%), wherein bulky mid esophageal tumors exhibit better responses compared to those with small upper or lower esophageal tumors [54,55]. The use of laser therapy or photodynamic therapy is not advised due to a lack of evidence for effective outcomes [59]. Endoscopic injection of chemotherapeutic drugs, such as 5-fluorouracil and mitomycin C, combined with laser ablative therapy has shown to be effective, safe, and economical in esophageal cancer who refuse surgery or are inoperable due to accompanying serious diseases or older age [54].

Argon plasma coagulation helps in managing local disease and occluded stents, it does not provide durable relief of dysphagia, and studies have found that patients need multiple treatment sessions for adequate response [54,55].

Endoscopic cryoablation is a safe and well-tolerated therapy effective in achieving local control with no serious complications. However, the dysphagia relief was not long-lasting [54,61]. Nevertheless, it can be used as part of a multimodal approach with other ablative therapies to palliate dysphagia or obstruction in patients with advanced esophageal cancer [54].

- *EUS-Guided Gastroenterostomy*

Laparoscopic gastrojejunostomy (GJ) is considered for gastric outlet obstruction (GOO) patients with life expectancy of more than three months and good functional status [59]. EUS-guided gastroenterostomy (EUS-GE) was first introduced in 2012 and is considered as a potential alternative for the above patients depending on the proficiency of the endoscopist [56,57,59]. The method enables the creation of a fistulous tract between the stomach and the jejunum, similar to laparoscopic GJ. Direct visualization with a minimally invasive approach is carried out, thereby potentially reducing the incidence of associated adverse events [59].

Despite this, adverse events were still noted in 12% of patients, with the most common being stent misdeployment [59]. EUS-GE achieves comparable long-term outcomes to surgical gastroenterostomy, with reduced complications and faster recovery [59]. Moreover, EUS-GE and laparoscopic gastrojejunostomy (Lap-GJ) exhibit comparable success rates, but EUS-GE has lower rates of adverse events and symptom recurrence [59]. EUS-GE has better outcomes in terms of symptom recurrence (4% vs. 28.6%, p=0.015) and re-intervention (8.3% vs 32.0%, p=0.021) compared to enteral stenting [59]. In the near future with more experience, this will be a widely accepted standard of care with such promising evidence [59].

III. CONCLUSION

For esophageal varices, we recommend EBL for controlling bleeding. Endoscopic ultrasound guided methods (cyanoacrylate and coil embolization) are most effective in gastric varices. In NVUGIB, mechanical therapies are preferred. OTSC is optimal for large fibrotic ulcers at difficult to treat locations and is utilized when electrosurgical coagulation and hemostatic clips have failed. For refractory peptic hemorrhage, Apollo endoscopic suturing system shows promising results, and endoclip application with or without epinephrine is considered in peptic ulcer bleeds (size >2 cm).

Hemospray followed by a hemostatic endoscopic procedure is effective for persistent bleeding. Endoclot, PHP can be used as a stand alone therapy but application in larger sample size is required. ESD is preferred over EMR for treating BE. En bloc resection of lesions of any size can be achieved with ESD but it has a challenging technique. Due to this, Multiband mucosectomy, an EMR technique is utilized widely.

Argon Plasma Coagulation is effective only after EMR, as the usability is limited to smaller lesions. Off the ablation techniques, RFA is the preferred modality for BE. When RFA fails, cryotherapy is utilized, and it is not used as a first line therapy. When acute obstruction of the esophagus and gastric outlet occurs due to malignancy, SEMS is recommended as the first line for life expectancy of less than two months. SEMS has lower risk of migration and fistula formation. Endoscopic gastrojejunostomy is recommended for GOO with life expectancy of more than three months and good functional status.

Techniques that utilize lasers are used for bulky midesophageal tumors and cryoablation is used as part of multimodal approach with other ablative therapies to palliate dysphagia or obstruction in advanced esophageal cancer. When patients are willing to undergo multiple treatments to gain long term relief with a lower risk of recurrence brachytherapy is recommended.

In conclusion, many methods have user-friendly interfaces and are quick to master. The problems with resource availability, funding, proper training, and lack of larger studies still limit some of the above-described techniques.

Table 1: Endoscopic eradication therapy- Devices and Manufacturers

Instruments	**Manufacturer**	**Cost**	**FDA Approval**
Endoscopic Resection Devices [62,63]			
EMR kits (include cap, needle, and 25-mm crescent snare)	Olympus America Inc, Center Valley, PA, United States	$347	Yes
Duette Multi-Band Mucosectomy device	Cook Medical Inc, Winston-Salem, NC, United States	$315	Yes
Needle type Knife	Olympus, Tokyo, Japan	$60	Yes
Dual type Knife	Olympus, Tokyo, Japan	$80	Yes
IT Knife	Olympus, Tokyo, Japan	$100	Yes
Hook Knife	Olympus, Tokyo, Japan; MTW, Wesel, Germany	$70	Yes
Systems [64–66]			
Barrx Flex generator (includes Flex RFA foot switch: FlexFS-010A and Flex RFA output cable: FlexCC-020A)	Medtronic Inc, Sunnyvale, CA, United States	$135,000	Yes
Habib EUS-RFA	EMcision Ltd, London, United Kingdom	$1795	Yes
Modified low-pressure CO2 cryotherapy system(Polar Wand)	GI Supply, Camp Hill, PA, United States	NA	Yes
Low-pressure liquid nitrogen system (CryoSpray Ablation System)	CSA Medical, Inc, Lexington, MA, United States	NA	Yes
C2 CryoBalloon Focal Cryoablation System	Pentax Medical, Montvale, NJ, United States	NA	Yes
ERBE	Erbe USA, Marietta, GA, United States	NA	Yes
Electrosurgical generator	CONMED,Westborough, MA, United States	NA	Yes
Canady Technology	US Medical innovations, MD, United States	NA	Yes

Table 2: Palliative devices - Stents and Dilators

Instruments	**Manufacturer**	**FDA Approval**
Stents [67]		
Alimaxx-E	Alveolus Medical, Charlotte, NC, United States	Yes
Esophageal Z-stent	Cook Medical Inc, Winston-Salem, NC, United States	Yes
Evolution	Cook Medical Inc, Winston-Salem, NC, United States	Yes
Flamingo Wallstent	Boston Scientific, MA, United States.	Yes
Gianturco-Z	Cook Medical Inc, Winston-Salem, NC, United States	Yes
Niti-S	Taewoong Medical, Gyeonggi-do, South Korea	Yes
Polyflex	Boston Scientific, MA, United States.	Yes
SX-ELLA	Ella-CS, Hradec Králové, Czechia	Yes
Ultraflex	Boston Scientific, MA, United States.	Yes
Wallflex	Boston Scientific, MA, United States.	Yes
Applicators [68]		
Esophageal Bougie Applicator	Varian Medical Systems, Palo Alto, CA, United States	Yes
The Esophageal Applicator	Ancer Medical, Nashua, NH, United States; Ancer Medical, Hialeah, FL, United States	NA
Dilators [69]		
Mercury- or tungsten-filled bougies	Medovations, Inc., Germantown, WI, United States	Yes
Wire-guided polyvinyl dilators	Wilson–Cook, Winston-Salem, NC, United States.	Yes
TTS balloon dilators	Microvasive/Boston Scientific Corporation Watertown, MA, United States	Yes

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Table 3: Endoscopic therapies for upper GI bleeding- Devices and Manufacturers, References: [70]

Instruments	Manufacturer	FDA Approval
Mechanical Therapy		
Over the scope clip (OTSC)	Ovesco Endoscopy USA Inc, Caret, NC, United States	Yes
OverStitch	Apollo Endosurgery, Austin, TX, United States	Yes
Speedband Superview Super 7	Boston Scientific Corporation, Natick, MA, United States	Yes
EpiPen Auto-Injector EpiPen Jr Auto-Injector	Meridian Medical Technologies Inc, Columbia, MD, United States	Yes
Endoscopic guided ultrasound therapy		
VTI Endoscopic Doppler System	Vascular Technology Inc, Lowell, MA, United States	Yes
Endo-DOP system	DWL GmbH, Singen, Germany	NA
Thermal Treatments		
APC Probe FiAPC Probe	ERBE USA Inc, Marietta, GA, United States	Yes
Trufreeze	CSA Medical, Baltimore, MD, United States	Yes
Polar Wand	GI Supply, Camphill, PA, United States	Yes
Topical Treatments		
Hemospray Endoscopic Hemostat	Wilson Cook Medical Inc, Wilson-Salem, NC, United States	Yes
EndoClot	EndoClot Plus Inc, Santa Clara, CA, United States	Yes
PerClot Polysaccharide Hemostatic System	Artivion Inc, Kennesaw, GA, United States	Yes

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