

## Injecting Technique to Control Bleeding Esophageal and Gastric Varices

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### EXTRACT

Endoscopic controlling bleeding esophageal varices and gastric varices are totally different. Agents and techniques are not exactly the same. Gastric variceal obliteration requires a higher skill due to its awkward control of the scope. In addition, tissue glue to be used can cause scope damage if perform injection carelessly. Moreover, the most fearful complication from glue injection of gastric varices is systemic emboli. Therefore, endoscopist who would like to deal with this technique is mandatory required special training.

**Key words :** injecting, bleeding esophageal, gastric varices

*[Thai J Gastroenterol 2005; 6(2): 87-93]*

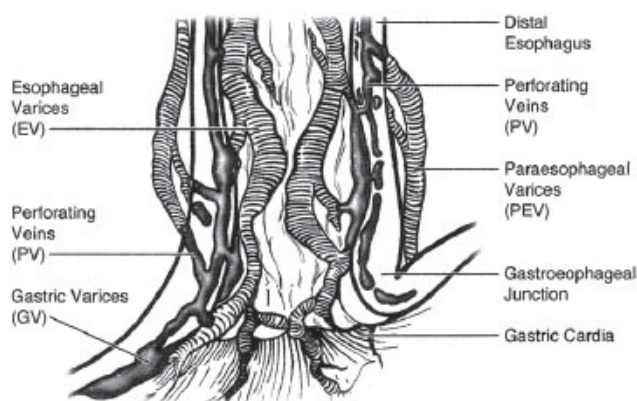
### INTRODUCTION

Bleedings esophageal and gastric varices account as majority causes of gastrointestinal hemorrhage related to portal hypertension. Pharmacologic agents such as vasopressin, terlipressin, somatostatin and octreotide are able to control part of these bleeding but not all. Over the last decade, endoscopic treatment has become a standard armamentarium for variceal obliteration. Generally, endoscopic injections of substance to obliterate esophageal and gastric varices are different in term of technique and agents. This review will explain detail on patient preparation, agents and technique to control these two types of varices. Technique for endoscopic variceal ligation will not be included.

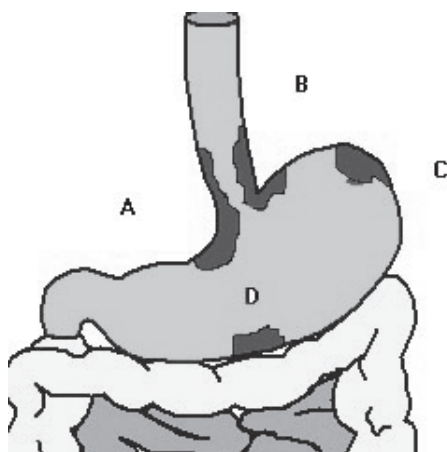
### Anatomy of Varices

**1. Esophageal varices (EV)** The visible esophageal varices during endoscopy usually represent group of deep submucosal veins. These veins connect to paraesophageal veins with perforating veins. The paraesophageal veins always feed the deep submucosal veins as back water system<sup>(1-3)</sup>. Therefore, technique to obliterate esophageal varices has to cover deep submucosal veins and perforators in order to disconnect this system from paraesophageal veins. Otherwise, incomplete obliteration would have been result into recurrent varices. (Figure 1)

**2. Gastric varices (GV)** There are many classifications of gastric varices. However, the most suitable classification is Sarin's<sup>(4)</sup>. This system is superior



**Figure 1** Anatomy of esophageal varices and perforating veins



**Figure 2** Classification of gastric varices

- A) GEV1 = Gastroesophageal varices at lesser curve
- B) GEV2 = Gastroesophageal varices at fundus
- C) IGV1 = Isolated gastric varices at fundus
- D) IGV2 = Isolated gastric varices at ectopic area

to others due to its simple criteria and ability to predict the chance of recurrent bleeding. (Figure 2)

2.1 Gastroesophageal varices (GEV). These are gastric varices that continue from esophageal varices. GEV locate near lesser curvature are classified as GEV1. In contrast, GEV that sit in greater curvature are defined as GEV2

2.2 Isolated gastric varices (IGV). These are gastric varices that have no continuity from esophageal varices. If they locate in gastric fundus then IGV1 is called. Gastric varices locate away from gastric fundus or ectopic gastric varices can be classified as IGV2. However, IGV2 is very rare and the prognosis is unpredictable compared to others GV<sup>(5)</sup>.

## Patient Preparation during Active Bleeding

For elective patient, there is no special preparation that different from other cases of routine esophagogastroduodenoscopy. However, patient with active bleeding has a higher chance of aspiration. Hence, elective endotracheal intubation may be required prior to endoscopy. If the risk of aspiration is increasing during endoscopy, the procedure may be put on hold while intubation is performed in between the procedure<sup>(6)</sup>.

Intravenous fluid replacement is the mainstay of therapy for patient with hypotension. Pack red blood cell is the best component for resuscitation. However, over transfusion may lead to recurrent variceal rupture. Therefore we recommend transfusing blood only to keep hematocrit not to be over 36%.

The perfect coagulation profiles are prothrombin time with international ratio (INR) less than 1.4 and platelet number above 50,000/dl. In the situation that the number is uncorrectable, endoscopy may be proceed with overhanging fresh frozen plasma and platelet transfusion continuously during the procedure.

In addition, broad spectrum antibiotics administration for these patients has been proofed to be effective not only for subsequent infection but also to reduce the risk of recurrent bleeding<sup>(7-9)</sup>. Antibiotics of choice can be either quinolones, third generation cephalosporins or derivative of ampicillins.

Somatostatin and analogue administration prior to endoscopy is very helpful to stop bleeding. Variceal obliteration in non-active bleeder is much easier than the active one. In addition, risk of complications and time to be used for endoscopy are also lower when dealing with non-active bleeder<sup>(10,11)</sup>.

## Sclerosing Agents for Variceal Obliteration

There are many agents to be used for esophageal varices obliteration. They usually cause inflammation and fibrosis around the varix tissue and subsequent obliteration will occur. Some of them introduce thrombotic effect inside the varix directly. All of them can be injected trough the accessory channel of the gastro-scope via sclerotherapy needles. The size of needle gauge can be varies from number 23 to 21.

1. **Sodium tetradecyl sulfate (STS)** is a synthetic anionic detergent with 1.5-2% concentration. It can be mixed with radio-contrast for visualization under fluoroscopy. The average volume for injection is around 2-4 ml. The efficacy to obliterate varices from this agent is about 85%<sup>(12-14)</sup>. Interestingly, lower con-

centration of STS may have a better variceal control<sup>(15)</sup>.

**2. Ethanolamine Oleate (EO)** is a synthetic derivative of fatty acid. It has very strong reaction to esophageal tissue by causing severe inflammation and then fibrosis forming will develop later. Therefore, paravariceal injection is not recommended due to a higher chance of deep ulcer formation<sup>(16,17)</sup>. The average dose for intravariceal injection is 1-3 ml of 5% EO.

**3. Polidocanol or ethoxyscleral** is another synthetic detergent. It is the most popular agent for sclerotherapy in Thailand. Generally, the standard concentration is 1% and 0.5-2 ml. can be injected per column of varices. Unfortunately, this agent appeared to have the lowest efficacy compared to others. Tatemichi M, *et al.* demonstrated that Polidocanol has a higher rebleeding rate compared to EO, 46% vs. 14 %<sup>(18)</sup>.

**4. Absolute alcohol** This agent is inexpensive and very effective. Its efficacy is comparable to STS. In addition, the number of sclerotherapy to complete variceal obliteration may be less<sup>(19)</sup>. Its use is very popular in Asia especially in India.

**5. Sodium morrhuate** is a mixture of sodium salt and cod oil. The recommended concentration is 5%. Each injection usually requires 1-2 of sodium morrhuate. It has been proofed to be equivalent to STS for bleeding control. The overall complication rate also seems to be similar<sup>(20)</sup>. The only disadvantage of this agent is the chance of developing severe reaction especially anaphylaxis.

**6. Cyanoacrylate glue or N-butyl-2-cyanoacrylate (Histoacryl™, B. Braun, Melsungen, Germany)** is a tissue adhesive. It controls hemostasis by immediate thrombin and clot formation. Due to its hyperviscosity and immediate hemostasis effect, the recommendation is to mix it with Lipiodol™ (Laboratoire Guerbet, Aulnay-Sous-Bois, France) in 1:1.6 ratio and injected as a bolus dose of 1-3.9 cc, depending on the size of varices. This agent has been more accepted to control gastric variceal bleeding. However, in the situation of failure to control esophageal bleeding despite standard therapy such as variceal ligation or sclerotherapy by many agents described above, Histoacryl can be used as a salvage therapy. Importantly, this agent initiates only thrombin formation but there is no inflammatory or fibrogenic effect<sup>(21)</sup>.

### Technique for Injection of Sclerosing Agents

Currently, there are two techniques available;

intravariceal and paravariceal injection. Intravariceal requires a higher dose of sclerosants but its advantage is more immediate hemostatic control<sup>(22)</sup>. Conversely; paravariceal injection uses a lower dose of sclerosants to introduce tissue inflammation and fibrosis formation. However, many studies have shown that intention for intravariceal injection turned out to be paravariceal injection in 1/3 of the procedures. (Figure 3)

**1. Intravariceal injection** After completing routine diagnostic endoscopy, the endoscopist put the tip of gastroscope close to the varices. The preferred location is within 5 cm distance from esophagogastric junction. Before pushing the sclero-needle to the injection site, moving the up-down wheel a little bit up to make a tangential view for injection is recommended. Once the needle is inside the varices, small amount of sclerosant (0.5-2 ml.) can be injected (Figure 4). The

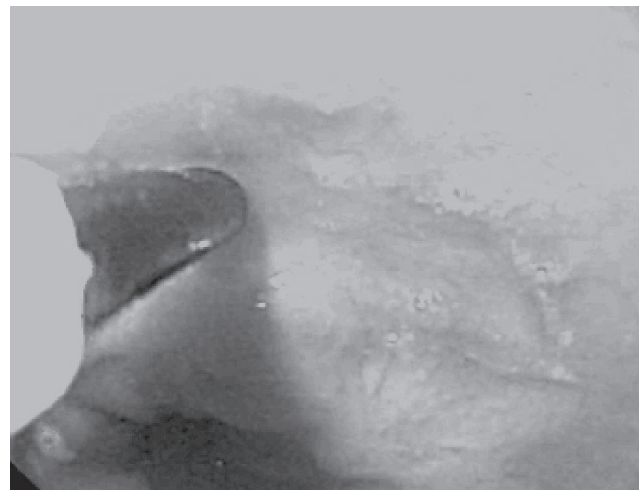


Figure 3 Paravariceal injection

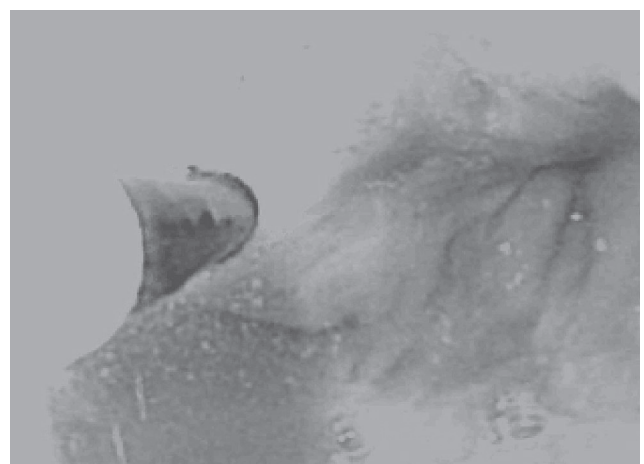
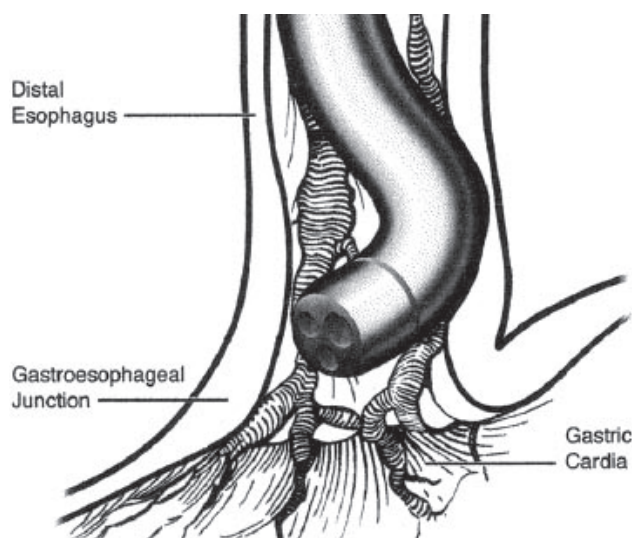


Figure 4 Intravariceal injection



**Figure 5** Scope tip to control immediate bleeding post injection

depth of the needle to be inside mucosa should be around 0.5-1 cm. If the bleb is detected, superficial injection may occur. After completion of each injection, the scope tip should be pushed against the wall of esophageal mucosa at the site of injection. This technique may reduce the chance of immediate bleeding and also has better control the possibility of sclerosants leakage (Figure 5). In case of continue bleeding, repeating the same technique in the same varix but at the higher level may help controlling bleeding

**2. Paravariceal injection** The main idea of this technique is to initiate fibrotic formation. Hence immediate hemostasis may not be effective due to poor thrombogenic effect. The average volume for sclerosant for each dose is lower than intravariceal technique. Bleb formation is a good indicator for successful injection (Figure 3). However, over injection with a large volume of sclerosant is prohibited due to higher chance of deep ulcer formation.

Followed up endoscopy for repeat injection can be performed at 1-3 weeks interval. Careful evaluation for residual large ulcer is mandatory. If significant ulcers still present, postponement of injection for another 2 weeks is recommended for better ulcer healing.

To date, there is no role of sclerotherapy for primary prophylaxis of variceal bleeding. A landmark study from VA hospital in US demonstrated significant higher complications and disability rate from sclerotherapy as primary prophylactic measure<sup>(23)</sup>.

## Complication from Endoscopic Sclerotherapy

The overall incidence of complications ranged from 10-50%, death from procedure is the most fearful complication ever occurred. Generally, there are local and systemic complications.

### Local Complications

**1. Immediate chest pain** from post injection related esophageal spasm. This complication is typically resolved spontaneously within 2-3 hours. Chest pain that last longer than 2 days may be resulted from ulcer. Typically, odynophagia is accompanied with this ulcer related pain. Another cause of chest pain is reflux esophagitis. This may be due to injection induced lower esophageal sphincter relaxation. Post injection ulcer and reflux esophagitis both can be relieved by proton pump inhibitors.

**2. Bleeding** is mainly secondary to post injection ulcer. Bleeding can be severe if there is significant size of varices underneath. Treatment can be either repeat sclerotherapy or attempting band ligation. If ulcer is the only problem oral administration with sucralfate with additional proton pump inhibitors may provide some benefit.

**3. Esophageal perforation** is very infrequent. Deep injection can cause perforation immediately. Secondly, deep ulcer may develop and subsequent full thickness perforation occurs later.

**4. Dysphagia** may be resulted from stricture formation or post injection related dysmotility. Recently studies demonstrated that distal esophagus decreased peristaltic activity after sclerotherapy<sup>(24,25)</sup>. Fortunately it resolved spontaneously with time. However, dysphagia persists longer than usual may require repeat esophagoscopy to exclude and treat for ulcer. The chance of stricture to develop range from 5 to 30%. Standard technique for esophageal dilation can be used but special concern for bleeding and perforation is recommended.

### Systemic Complications

**1. Low grade fever** The incidence is around 20-50%. It usually develops within 24-48 hours post injection. This may be related to sclerosant induced phlebitis or direct pyrogenic effect from sclerosant. High grade fever with chill last longer than 72 hours indicates bacterial infection such as, esophageal perforation, aspiration pneumonia, mediastinitis or primary bacteremia. One study has shown that bacter-



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emia can develop in 17 % of all sclerotherapy patients<sup>(26)</sup>. Therefore, prophylaxis with broad spectrum antibiotics covering gram negative bacteria may be needed.

**2. Brady arrhythmia and heart block** may develop especially post polidocanol injection. The risk will be higher with larger volume of injection.

**3. New development of gastric varices and portal hypertensive gastropathy** The chance of these complications to develop post sclerotherapy is uncertain. Some reports have shown that this may be related to recurrent bleeding<sup>(27,28)</sup>. Thus routine surveillance with endoscopy not only for recurrent esophageal varices but also for gastric varices and portal hypertensive gastropathy can be beneficial.

**4. Miscellaneous** Pulmonary emboli, bronchoesophageal fistula, chylothorax, pleural effusion, empyema are very rare but they have been reported earlier to be related to injection of sclerosants.

### Gastric Varices Treatment by Injection of Tissue Glue

Not all of GV require injection treatment. Majority of GV patients has GEV1 (75%) which act liked esophageal varices. Hence, these GVs can be obliterated by variceal ligation. Only some of those with large size GEV1 will demand injection treatment. Conversely, GEV2 and all IGVs obliteration will require injection therapy. Fortunately, GEV2 and IGV account as only 20% of all GV.

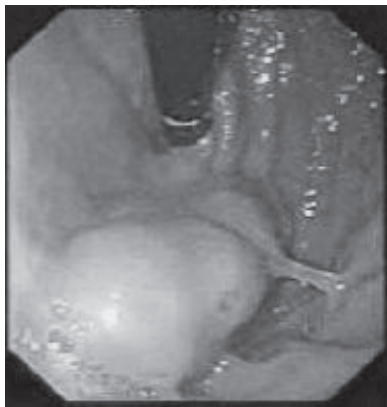
IGV2 contains as 4% of all GVs. Its special techniques for obliteration are varies and depend on location of varices<sup>(4)</sup>.

Currently, there are 3 types of polymerized agents for gastric variceal hemostasis available in the market but n-butyl-2-cyanoacrylate (Histoacryl; B-Braun, Melsungen, Germany) is the most popular among all three. Unfortunately, this agent is not available in United States. Therefore, of label use of 2-Octyl cyanoacrylate (Dermabond; Ethicon, Inc, Somerville, NJ) has been introduced for this purpose in US. The beauty of Dermabond is no need for mixing with other agent like Histoacryl. It can be injected directly into GV and thrombogenesis then gradually develops. In addition, the injector can be slowly removed without worry of scope channel clogging liked Histoacryl. The unpopular agent that is also available in US is Isobutyl-2-cyanoacrylate (Bucrylate; Ethicaon, Inc, Somerville, NJ). To date, there is no randomized control study to dem-

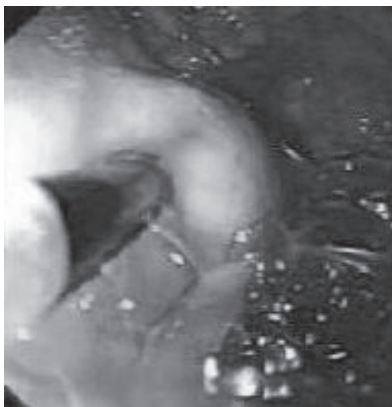
onstrate the benefit of one agent over others yet.

In Thailand, Histoacryl is the only available agent. Practically, this agent has a very high viscosity and it forms clot rapidly. To slow the process of clot formation and decrease the viscosity for standard injection, Lipiodol (labaratoric Guerbet, Aulnay Sous- Bois, France) or Ethiodol (Savage, Laboratories, Melville, NY) or olive oil is recommended to mix in a ratio of 1:1 or 1.3:1 with Histoacryl before injection. Generally, one unit of Histoacryl contains 0.8 ml. of active ingredient. There by, mixing the agent with Lipiodol or others into 1.3 -3.9 ml. is preferred. This is depended on the size of GV. The injector needle sizes are varies from number 23 to 21 but we recommend number 21 for individual who require more than one unit of injection. This is because of a high chance of needles clogging from very small needle. There is a concern of using large needle may cause a high rate of post injection immediate bleeding. In our experience we did not encounter the problem of bleeding immediately after injection like sclerotherapy.

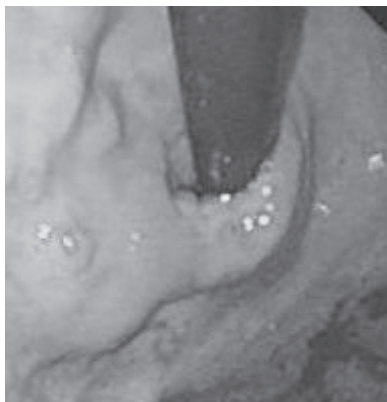
Unlike technique for esophageal varices sclerotherapy, GV injection has to be performed with gastro-scope in retroflexion. Hence paradoxical movement form routine scoping has to be adjusted. After the endoscopist is able to maintain the precise and stable position for injection, the assistant can mix the ingredient and apply all apparatus in to scope channel. At his moment, we recommend unplugging the suction tube for prevention of accidental suction of dripping glue while performing injection. The needle can be put into the varix with 0.5-1.0cm dept. Then the assistant can inject glue into varix slowly. This process usually takes less than 5 minutes. After the needle has been pull away form the varix, then normal saline can be flushed into the injector to maintain patency of injector before further injection. The tip of injection with needle inside can be use to poke the recently injected varix to check complete clot formation. If varix is not firm by endoscopist feeling, this usually means inadequate injection. Then repeating the same process can be performed again and again until all varices can be obliterated (Figure 6-8). Usually the average volume of each session of GV injecton is around 1.3 to 5.2 ml. The final step is to pull both scope and injector out from the patient all together without attempting removal of injector trough the scope. By pulling the injector trough the scope, there is a chance of introducing glue to form clog inside the scope channel. We recommend



**Figure 6** Gastric varices before injection



**Figure 7** Gastric varices during glue injection



**Figure 8** Site of post injection at 6 weeks after

cutting the injection near scope tip and this is followed by pulling the injectors retrogradely from the point that has been cut.

Repeat injection can be performed again in another 1-3 week and the average number of sessions required for GV obliteration is around 1-3<sup>(4,29,30)</sup>. In our experience, we rarely performed more than 3 sessions to complete the process<sup>(30)</sup>.

### Complications from GV Injection

1. Venous emboli in many areas of body such as pulmonary emboli, mesenteric emboli and arterial emboli in patient with right to left shunt. In our series, the risk of patient developing systemic emboli from glue injection is around 4%<sup>(30)</sup>. Many experts recommended not to inject a high volume of tissue glue to prevent development of this complication.

2. Fever and bacteremia. The risk for this complication to be developed may be higher than variceal ligation. However, we did not find any development of significant infection after elective GV injection. However, routine prophylactic administration of antibiotics in patient with recent or active bleeding is recommended. The rationale behind this is the same as esophageal varices bleeding treatment<sup>(8)</sup>.

3. The needle may be stuck into gastric varices after finishing injection. This is rarely occurred but it can happen in patient who has Histoacryl injection without mixing with Lipiodol. This may be due to premature glue injection induced clot formation before finishing injection. To solve this problem, we recommend pulling the scope out while the first injector is still inside the varix. After finishing injection with the second injector, both first and second injectors can be cut and all equipment can be removed.

### SUMMARY

Endoscopic controlling bleeding esophageal varices and gastric varices are totally different. Agents and techniques are not exactly the same. Gastric variceal obliteration requires a higher skill due to its awkward control of the scope. In addition, tissue glue to be used can cause scope damage if performed injection carelessly. Moreover, the most fearful complication from glue injection of gastric varices is systemic emboli. Therefore, endoscopist who would like to deal with this technique is mandatory required special training.

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