

PAPERS

A randomised controlled comparison of injection, thermal, and mechanical endoscopic methods of haemostasis on mesenteric vessels

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Abstract

Background and aims—A randomised controlled comparison of haemostatic efficacy of mechanical, injection, and thermal methods of haemostasis was undertaken using canine mesenteric vessels to test the hypothesis that mechanical methods of haemostasis are more effective in controlling haemorrhage than injection or thermal methods. The diameter of arteries in human bleeding ulcers measures up to 3.45 mm; mesenteric vessels up to 5 mm were therefore studied.

Methods—Mesenteric vessels were randomised to treatment with injection sclerotherapy (adrenaline and ethanolamine), bipolar diathermy, or mechanical methods (band, clips, sewing machine, endoloops). The vessels were severed and haemostasis recorded.

Results—Injection sclerotherapy and clips failed to stop bleeding from vessels of 1 mm (n=20) and 2 mm (n=20). Bipolar diathermy was effective on 8/10 vessels of 2 mm but failed on 3 mm vessels (n=5). Unstretched elastic bands succeeded on 13/15 vessels of 2 mm but on only 3/10 vessels of 3 mm. The sewing machine achieved haemostasis on 8/10 vessels of 4 mm but failed on 5 mm vessels (n=5); endoloops were effective on all 5 mm vessels (n=5).

Conclusions—Only mechanical methods were effective on vessels greater than 2 mm in diameter. Some mechanical methods (banding and clips) were less effective than expected and need modification. Thermal and (effective) mechanical methods were significantly ($p < 0.01$) more effective than injection sclerotherapy. The most effective mechanical methods were significantly more effective ($p < 0.01$) than thermal or injection on vessels greater than 2 mm.

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Although endoscopic therapy¹⁻³ with laser,⁴⁻⁹ thermal probe,^{8,10-15} or injection sclero-

therapy¹⁴⁻¹⁹ for bleeding peptic ulcers seems more effective than medical therapy alone, rebleeding is still common with reported rebleeding rates of 5%,¹⁹ 6%,^{11,12,20} 10%,^{4,20,21} 12%,²² 15%,²³⁻²⁵ 16%,^{16,26} 17%,²⁷ 18%,^{13,28} 20%,^{7,21} 22%,²⁹ 25%,³⁰ 30%,³¹ and 40%.^{14,15}

Examples from published randomised studies of endoscopic haemostatic methods show rebleeding rates of up to 75% (0%,^{11,21,25,32} 20%,⁴ 22%,³³ 31%,³⁰ 33%,²¹ 40%,²⁵ 46%,³¹ 55%,^{9,22,32} and 75%¹⁰) for spurting vessels and up to 27% (4%,²³ 6%,²⁵ 14%,^{4,33} 18%,²⁵ 20%,^{5,10,22} 23%,⁹ and 27%³⁰) for non-bleeding visible vessels. Vessels of external diameter of up to 3.45 mm are found in both the duodenum³⁴ and stomach^{34,35} in patients dying from bleeding peptic ulcer and experimental studies have shown that injection sclerotherapy is ineffective in animal models on vessels over 0.5 mm^{36,37} in external diameter, while thermal methods are only effective on vessels up to 2 mm³⁸⁻⁴³ in external diameter. Although direct extrapolation from animal data to human clinical studies may not be appropriate these data suggest that the most commonly used interventional endoscopic haemostatic methods may be ineffective in stopping bleeding from large vessels in ulcers.

At open surgery mechanical methods of haemostasis—sewing or clipping—are used on large vessels and thermal methods used only for small vessels. Surgeons use neither injection techniques nor diathermy, but thread^{44,45} to treat bleeding peptic ulcers at open surgery.

Endoscopic mechanical methods that have been used to achieve haemostasis clinically in patients with upper gastrointestinal haemorrhage include: haemoclip (in both variceal⁴⁶ and non-variceal^{47,48} haemorrhage); band ligation (in both variceal⁴⁹⁻⁵⁴ and non-variceal haemorrhage^{55,56}); and endoloop⁵⁷ (a detachable snare designed for achieving haemostasis following excision of polyps and troublesome bleeding from the stalk of the polyp, which has been reported to be of use in eradicating gastric varices⁵⁸ in a preliminary report of 10 patients). Other mechanical endoscopic methods that have been occasionally used clinically include: Escourou's screw,⁵⁹ used to stop bleeding in standard canine experimental ulcers and in two humans with gastric ulcers; and duodenal

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balloon tamponade,⁶⁰ endoscopically placed in three patients to stop bleeding from the first part of the duodenum. Endoscopic devices that have been used only in experimental animal studies include an endoscopic sewing machine,⁶¹ a stapling device,⁶² and an ulcer clamp,⁶³ all of which have been used to stop bleeding in standard canine experimental ulcers.

Mechanical endoscopic methods in present use clinically include band ligation, clips, and endoloops. These mechanical methods have not been evaluated in animal models to assess their efficacy on different vessel size, and no published studies exist comparing mechanical methods with injection or thermal methods in experimental models.

The following study was undertaken to test the hypothesis that mechanical methods in current use clinically, together with the sewing machine, might be more effective than injection sclerotherapy or thermal methods in achieving haemostasis on vessels of the sizes that are found in bleeding human peptic ulcers.

Materials and methods

Each of the mechanical methods to be used was initially applied to postmortem canine gastric mucosa on 20 occasions to gain familiarity with their use.

CANINE MODEL

Six adult beagles (14–17 kg, median 15 kg) were studied. Anaesthesia was induced with 10 mg/kg methohexitone sodium (Eli Lilly & Co. Ltd, Basingstoke, UK) followed by endotracheal intubation, and maintained with nitrous oxide (BOC, Surrey, UK), oxygen (BOC), and fluothane (ICI, Cheshire, UK). Normal saline, administered intravenously, replaced fluid loss.

A laparotomy was performed via an abdominal midline incision and small bowel mesenteric vessels were identified. By utilising smaller vessels close to the serosal edge of the bowel or larger ones close to the root of the mesentery the outside diameters of vessels measuring 1 mm to 5 mm inclusive were identified and measured using a metal ruler.

Because of the anatomical arterial arcade in the small bowel mesentery, bleeding can occur from both sides of the severed artery (this can also apply to the eroded vessel in a bleeding peptic ulcer). The haemostatic method was therefore applied both proximally and distally (1 cm apart) to a mesenteric vessel of measured external diameter, before the haemostatic efficacy was tested by severing the vessel in the middle. Any bleeding was recorded as a failure to achieve haemostasis. Active bleeding was observed from both cut ends of the severed vessel and spurting was seen when larger vessels were severed.

RANDOMISATION OF MECHANICAL OR INJECTION METHODS

For randomisation, a series of sealed envelopes was opened to show which haemostatic method was to be used. The operator was unaware of the treatment modality to be used

before selecting the mesenteric vessels. Vessels of diameter 1 mm to 5 mm (in 1 mm increments) were tested.

Each envelope included a haemostatic method to be used (in groups of five) on mesenteric vessels, beginning with vessels of 1 mm diameter. If haemostasis was achieved, the haemostatic method was applied to the next vessel of increasing diameter. If a method failed to achieve the expected haemostatic efficacy suggested by clinical studies, more experiments (in groups of five) were carried out to confirm the initial result.

When it was obvious that a haemostatic method was ineffective on a particular vessel size, no vessels with a larger diameter were tested. This was due to the fact that blood loss from these larger vessels would have been significant and resulted in the use of further animals. Further experiments were also performed on vessels, when it was found that by increasing the size of the vessel there was a notable loss of haemostatic efficacy.

INJECTION SCLEROTHERAPY

Adrenaline 1/10 000 (Martindale Pharmaceuticals, Romford, UK) was injected in three 2 ml aliquots (6 ml in total) around and into the vessel followed by 2 ml of ethanalamine oleate (5% wt/vol; Martindale Pharmaceuticals, Romford, UK). Injection was delivered using a 2.2 mm (outer diameter) varices injection needle (Wilson Cook TWIV/6F, Wilson Cook, Letchworth, UK).

THERMAL METHOD

Bipolar diathermy was applied using a 50 W generator and a 3.2 mm bipolar electrode (BICAP probe) at 5.5 settings, giving 10 two second pulses of coagulation (ACM, München, Germany) using firm pressure on the vessel during diathermy. This bipolar electrode cannot be passed through a conventional gastroscopy with a 2.8 mm diameter biopsy channel, but requires a gastroscopy with a larger 3.8 mm diameter biopsy channel.

MECHANICAL METHODS

A GIF-IT20 gastroscopy (Olympus) was used for the injection, band ligation, clips, endoloops, and diathermy. The sewing machine was mounted on a GIF-PQ20 (Olympus) gastroscopy.

Endoscopic band ligation

This was performed according to Van Stiegman *et al.*⁶⁴ Latex rubber bands (CR Bard Inc., Billerica, USA), in the form of preassembled "O" rings (bands placed on an inner plastic cylinder) administered via an endoscopic variceal ligator (CR Bard). The neoprene bands had a mean external diameter of 5.1 mm (range 5.0–5.3, n=5) and a mean internal diameter of 2.0 mm (range 1.9–2.1, n=5) when unloaded from the inner cylinder. These bands probably have a smaller diameter before they are placed on the O ring. Unstretched black latex haemorrhoidal bands (Downs, Sheffield, UK) had a mean external diameter of 4.5 mm (range 4.5–4.7, n=5) and a mean internal



Figure 1 Marker, haemostatic, and prototype clips (left to right).

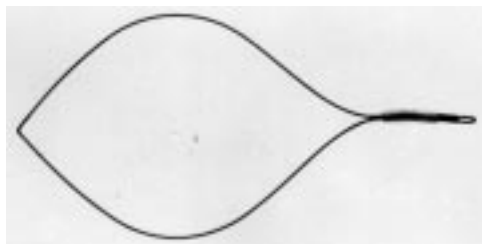


Figure 2 A nylon endoloop.

diameter of 1.4 mm (range 1.3–1.5, n=5). These were loaded onto the inner cylinder using a conical mounting device made by us.

Endoscopic clips

Three types of endoscopic clip (Olympus, Keymed, Southend-on-Sea, UK) were used: marker (MD 59), haemostatic (MD 850), and a prototype version of the newly released MH 858. The marker (MD 59) and the longer prototype had a 90 degree angulation at their tip (fig 1) while the MD 850 was at 135 degrees.

Table 1 Statistical significance of one haemostatic method versus another on 1–5 mm mesenteric vessels

	Mesenteric vessel diameter (mm)				
	1	2	3	4	5
Injection versus					
Marker clip	NS	NS	NS		
Haemostatic clip	NS	NS	NS		
Prototype clip	NS	NS	NS		
Elastic bands	<0.0001	<0.0001	NS		
Bipolar diathermy	<0.0001	<0.0001	NS		
Sewing machine	<0.0001	<0.0001	0.008		
Endoloop	<0.0001	<0.0001	0.008		
Clips					
Haemostatic v prototype	NS	NS	NS		
Marker v haemostatic	NS	NS	NS		
Marker v prototype	NS	NS	NS		
Unstretched bands versus					
Marker clip	0.0011	<0.0001	0.03		
Haemostatic clip	0.0003	0.0001	NS		
Prototype clip	0.008	0.0014	NS		
Bipolar diathermy	NS	NS	NS		
Endoloop	NS	NS	0.0256		
Bipolar diathermy versus					
Sewing machine	NS	NS	0.008		
Marker clip	<0.0001	0.0003	NS		
Haemostatic clip	<0.0001	0.0007	NS		
Prototype clip	0.0003	0.007	NS		
Endoloop	NS	NS			
Sewing machine versus					
Marker clip	0.0011	0.0004	<0.0001		
Haemostatic clip	0.0003	0.0003	<0.0003		
Prototype clip	0.008	0.008	0.008		
Elastic bands	NS	NS	0.026		
Endoloop	NS	NS	NS	NS	0.008
Endoloop versus					
Marker clip	0.0011	0.0004	<0.0001		
Haemostatic clip	0.0003	0.0003	0.0003		
Prototype clip	<0.0001	<0.0001	<0.0001		

The elastic bands shown are the unstretched bands as the prestretched ones failed to achieve haemostasis.

The prototype was 15 mm long whereas the other two types were 10 mm long. All were administered by means of the endoscopic clip fixing device^{65 66} (Olympus HX 3L) which can be passed through a 2.8 mm diameter biopsy channel of the gastroscope. The thickness of all the clips was the same and all were applied to postmortem gastric mucosa before commencing the study.

Endoscopic sewing machine

The endoscopic sewing machine⁶¹ had a suction cavity that was 7.1 mm wide and 8.7 mm long. The non-flexible part of the sewing machine which is attached to the distal tip of the gastroscope had a length of 33.1 mm and diameter of 9.0 mm. The mesenteric vessels were sucked into the suction cavity of the sewing machine; a nylon thread of 0.2 mm diameter was passed through the tissue around the vessel and the thread was tied with four half hitches.

Endoloops

Endoloops⁵⁷ (Olympus loops MH-477) are detachable snares, circular in shape and made from nylon with an external diameter of 0.46 mm (fig 2). They can be passed through a 2.8 mm or greater biopsy channel of an endoscope using the Olympus HX-20 delivery system. Tissue containing the mesenteric vessels was placed into the open loop and the loop was then closed and detached. The process was repeated along the vessel which was then severed.

STATISTICAL COMPARISONS

Fisher's exact test was used for statistical comparisons. A p value of less than 0.05 was regarded as significant.

Results

CONTROLS

All of the control vessels (n=5, for each diameter vessel studied) continued to bleed when incised until they were ligated after 30 seconds.

INJECTION SCLEROTHERAPY

Injection of adrenaline and ethanolamine failed to achieve haemostasis in any of the vessels tested (1 mm (n=20), 2 mm (n=20), and 3 mm (n=5)). There were no significant differences between injection sclerotherapy and the different types of clips; but both the elastic bands and bipolar diathermy were significantly superior (p<0.0001) than injection sclerotherapy on 1 mm and 2 mm vessels but there was no significant difference on 3 mm vessels. Both the sewing machine and the endoloop (table 1) were significantly superior to injection sclerotherapy when tested on 1 mm and 2 mm (p<0.0001) and 3 mm vessels (p<0.008).

BIPOLAR DIATHERMY

With bipolar diathermy, 1 mm vessels (n=10) were effectively electrocoagulated as were most 2 mm vessels (8/10). On the two occasions that the probe failed on the 2 mm vessels, haemostasis was achieved with a further 10 two second pulses. Bipolar diathermy was ineffective on 3

mm vessels (n=5) even after 20 two second pulses were given. Bipolar diathermy was significantly more effective than any of the clips (p<0.008), injection (p<0.0001), or pre-stretched bands (p<0.0001) on vessels of 1 mm and 2 mm diameter but of equal efficacy (p=1.0) to unstretched bands for vessels of 1 mm and 2 mm in external diameter. Both the snare and the sewing machine (table 1) were significantly more effective than bipolar diathermy on 3 mm vessels (p=0.008).

MECHANICAL METHODS

Elastic bands

Two types of elastic bands were tested. The prestretched bands (with a mean external diameter of 5.1 mm and internal diameter of 2.0 mm) commercially supplied on the "O" rings were tested and were unable to stop bleeding from vessels of any size on this model. When unstretched haemorrhoidal bands (mean external diameter of 4.5 mm and internal diameter of 1.4 mm) were tested they were successful in stopping bleeding on 1 mm (n=5) and 2 mm vessels (13/15) but failed on 3 mm vessels (7/10). There were no significant differences between the prestretched bands, clips, and injection sclerotherapy. The unstretched bands were significantly more effective than any of the clips (p<0.01), prestretched bands, or injection sclerotherapy (p<0.0001) on vessels up to 2 mm in diameter. These unstretched bands were as effective as bipolar diathermy in stopping bleeding in vessels up to 2 mm in diameter. The endoloop (table 1) was significantly more effective than unstretched bands only on 3 mm diameter vessels (p<0.0256).

Clips

Three different types of clip were tested: marker clip, haemostatic clip, and the new prototype clip. There was no significant difference in the performance of any of these despite one being termed a haemostatic and another a marker clip.

The marker clip (MD59) failed to stop bleeding on 1 mm vessels (17/20), on 2 mm vessels (18/20), and on 3 mm vessels (n=20). The haemostatic clips were unable to stop bleeding from 1 mm (n=10), 2 mm (n=10), and 3 mm vessels (n=10). The longer prototype clips were also unable to stop bleeding

from 1 mm (n=5), 2 mm (n=5), and 3 mm vessels (n=5). Only 15 prototype clips were available for study. There was no significant difference between any of the clips tested or between the clips and injection sclerotherapy. Clips were significantly less effective than unstretched bands (p<0.008) or bipolar diathermy (p<0.007) on vessels up to 2 mm in diameter and less effective than either the endoloop (p<0.001) or the sewing machine (p<0.008) on vessels up to 3 mm in diameter (table 1). Clips were not tested on vessels of 4 mm and 5 mm in diameter but as they were ineffective in stopping bleeding in vessels up to 3 mm in diameter it is reasonable to suppose that they would be ineffective in vessels above 3 mm in diameter.

Gentle pressure between thumb and forefinger when applied to the clip achieved complete haemostasis, suggesting that clip modification could improve their effectiveness. The shape of these clips made haemostasis unlikely as on closure of the clip there is a gap between the two blades of the clip (approximately 0.6 mm), with only the distal end of the clip in apposition.

Sewing machine

Complete haemostasis was achieved on vessels of 1 mm (n=5), 2 mm (n=5), 3 mm (n=5), and 4 mm (8/10) vessels using the endoscopic sewing machine. However it was unable to stop bleeding from 5 mm vessels (n=5) because the vessel was too large to be sucked into the cavity so that the needle and thread could not be passed completely round the vessel complex. The sewing machine was significantly more effective than injection sclerotherapy on 1–3 mm vessels (p<0.008), and was more effective than bipolar diathermy (p=0.008) and unstretched bands (p=0.026) on vessels of 3 mm diameter. The endoloop (table 1) was significantly more effective than the sewing machine on 5 mm vessels (p=0.008).

Endoloop

Complete haemostasis was achieved on all vessels tested: 1 mm (n=5), 2 mm (n=5), 3 mm (n=5), 4 mm (n=5), and 5 mm (n=5). Haemostasis was even achieved on a 12 mm external diameter splenic artery and vein. The endoloop was more effective than injection sclerotherapy (p<0.008), clips (p<0.0011), and prestretched bands on vessels up to 3 mm in diameter. There was no significant difference in efficacy between endoloops and either unstretched bands or bipolar diathermy on vessels up to 2 mm in diameter. The endoloop was however more effective than unstretched bands (p=0.0256) and bipolar diathermy (p=0.008) on vessels of 3 mm in diameter. It proved superior to the sewing machine only on vessels of 5 mm in diameter (p=0.0008). The endoloop was the only endoscopic method that was able to stop bleeding from vessels larger than 4 mm in diameter.

Table 2 Haemostatic efficacy of mechanical, thermal, and injection methods

Haemostatic method	Mesenteric vessel diameter (mm)				
	1	2	3	4	5
Control	0/5	0/5	0/5	0/5	0/5
Injection	0/20	0/20	0/5		
Clips					
Marker	3/20	2/20	0/20		
Haemostatic	0/10	0/10	0/10		
Prototype	0/5	0/5	0/5		
Elastic bands					
Preloaded	0/5	0/5	0/5		
Unstretched	5/5	13/15	3/10		
Bipolar diathermy	10/10	8/10	0/5		
Sewing machine	5/5	5/5	5/5	8/10	0/5
Endoloops	5/5	5/5	5/5	5/5	5/5

Results are expressed as the number of times successful haemostasis was achieved/total number of times that the procedure was tested. Bold figures indicate successful haemostasis; the remainder are failures.

OVERALL EFFICACY

In this study the most effective mechanical methods—endoloops and sewing machine—

were able to stop bleeding from vessels of 1–4 mm in diameter (table 2). Mechanical methods of haemostasis (endoloops or sewing machine) were significantly more effective in controlling haemorrhage from large vessels than injection or thermal methods.

Discussion

This randomised controlled study clearly shows that the best mechanical methods (sewing machine and endoloops) were more effective in stopping bleeding from vessels of 1–4 mm than either injection or thermal methods. Mechanical methods alone were able to provide secure haemostasis for all sizes of blood vessels found in human peptic ulcers.

Injection of adrenaline and ethanolamine was ineffective in this model and did not stop bleeding in vessels of 1–2 mm diameter. Most published studies in animal models suggest that injection methods can reduce blood flow but do not stop bleeding. Submucosally applied adrenaline has been shown in a rat model⁶⁷ to cause a reduction in local gastric blood flow. Adrenaline, absolute ethanol, or polidocanol showed a reduction in bleeding in standard canine ulcers with an external diameter less than 0.5 mm^{37, 68} but complete haemostasis was only achieved in 2/10 ulcers treated with adrenaline.⁶⁸

Absolute ethanol³⁶ was the most effective agent in causing arterial coagulation in canine serosal vessels of 0.5 mm diameter. Normal saline, hypertonic saline, adrenaline, and thrombin reduced the bleeding rate in serosal vessels of 1.6 mm to 2.1 mm but complete haemostasis ranged from 0% (normal saline) to 47% (adrenaline plus hypertonic saline).⁶⁹ Adrenaline and polidocanol were ineffective in canine mesenteric vessels greater than 0.5 mm in external diameter.³⁷

Injection is so ineffective in achieving complete haemostasis in animal studies that it is surprising it has done as well in clinical trials as the reports suggest. There is an apparently convincing body of evidence for clinical efficacy of injection sclerotherapy including retrospective studies,⁷⁰ randomised controlled studies,^{14–16, 22} and meta-analyses.^{1–3}

Bipolar diathermy has been shown to stop bleeding in canine ulcer models on vessels from 0.5 mm^{38, 40–43} and on isolated canine mesenteric vessels up to 2 mm^{38, 39} diameter. Several randomised controlled trials^{12, 13, 28} and meta-analyses^{1–3, 71} support the clinical efficacy of bipolar electrocoagulation in human peptic ulcer bleeding⁸ although there are some randomised clinical trials that have failed to show significant differences between bipolar electrocoagulation and injection sclerotherapy.^{12, 30}

Pre-stretched elastic bands in this study failed to achieve haemostasis on vessels of 1 mm or greater. Despite this there is a fair body of clinical evidence of efficacy for these unstretched bands in the treatment of bleeding varices^{49, 50, 52, 53} which includes meta-analysis⁵⁴ and reports of successful treatment of bleeding gastric ulcers⁵⁵ and angiodysplasia.⁵⁶ This is the first report to suggest that fatigue of the elastic

material may be one factor contributing to haemostatic failure with banding. When the bands were replaced with unstretched latex bands haemostasis was achieved in vessels up to 2 mm.

All the clips studied failed to secure haemostasis. This failure is due to two features intrinsic to the design of these clips: the shape of the clip and the limited force that the clip can exert at its distal end. On closure of the clip, only the distal end is in apposition and there is a gap between the two limbs of the clip of 0.6 mm resulting in very little pressure being exerted on a part of the bleeding vessel. This probably indicates that a different tip configuration to the clip is required to compress the lumen of the vessel. A small amount of finger pressure applied to the limbs of the clips following their application achieved haemostasis. More force is therefore required to compress the vessel than is able to be produced with present endoscopic methods. The haemoclips has been reported to be successful in uncontrolled studies of both variceal⁴⁶ and non-variceal^{47, 48} upper gastrointestinal bleeding, though a rebleed rate of around 11% still occurred. Provisional results from a randomised trial comparing clips and adrenaline with injection of adrenaline only showed a trend towards lower rebleeding for clips and injection in comparison with injection⁷² only.

Although the sewing machine seems promising in achieving haemostasis in vessels up to 4 mm its application in the clinical treatment of varices or bleeding ulcers is unproven. It has been used to underrun standard experimental bleeding ulcers.⁶¹ This method requires tissue to be sucked into the cavity of the sewing machine and once the thread has been passed requires the extracorporeal tying of four half hitches. The limitation on securing haemostasis on vessel size above 4 mm in diameter is due to the size of the suction cavity and by increasing the size of the suction cavity an increase in size of vessel haemostasis might be achieved. Possible drawbacks are that heavily scarred tissue occasionally found in peptic ulcers may not be able to be drawn into the cavity. Even if tissue could be drawn into the cavity, the force that is required to pass a needle deeply through scarred tissue and back out again to ligate—for instance, the gastroduodenal artery is greater than the force that can be applied at flexible endoscopy with present methods. Furthermore the tying of four half hitches⁷³ using an extracorporeal method means that, at present, six passes of the gastroscope are needed for each stitch thrown.

In this study endoloops were the only method that stopped bleeding from all sizes of vessels studied. Unfortunately it was difficult to deploy the endoloops in a manner that would be easy to achieve at flexible endoscopy in bleeding peptic ulcer. The mesenteric vessels had to be placed using forceps into the endoloop before closure. An improved method of endoscopic delivery is required, but if this could be achieved it might allow improved haemostasis if it could be applied. Preliminary work^{74, 75} suggests that the use of a suction end

cap and modification of the endoloop may allow easier application.

This animal model^{26, 40} was used as it allowed the limits of haemostatic efficacy to be assessed for each endoscopic method tested. The standard canine bleeding ulcer model that has been used by other groups,^{38, 41, 42, 68} which was initially developed by Protell *et al*⁶⁶ and modified by Dennis *et al*⁷⁷ was not used because the maximum diameter of vessels obtained has been estimated to be only 0.5 mm. It is known that human peptic ulcers can erode into vessels of diameters 0.1–3.45 mm (bleeding vessels from postoperative specimens of bleeding gastric ulcer range from 0.1 to 1.8 mm,³⁵ but in postmortem gastric and duodenal ulcers bleeding vessels range from 0.3 to 3.45 mm and from 0.1 to 3.45 mm respectively³⁴). This model therefore allows haemostatic methods to be applied to vessels which have been accurately measured and include the sizes of vessels that can be found in human bleeding peptic ulcers, especially those with large eroded arteries.

Although injection and thermal methods seem to offer efficacy in clinical studies the inability of these methods to arrest bleeding in this model suggests that these methods may be of limited clinical efficacy when used on large vessels as found in some cases of human peptic ulcer bleeding. Perhaps fortunately, most bleeding gastric ulcers in our pathological studies^{34, 35} bled from arteries that were smaller than 1 mm in diameter (mean diameter 0.9 mm) while a minority bled from larger vessels up to 3.45 mm. This might explain why the injection methods which uniformly failed to stop bleeding in this study seem to produce positive results in some randomised controlled trials. It is not very likely that minor methodological alterations in injection or thermal methods will much improve results.

Access is different when treating bleeding at flexible endoscopy or at laparotomy. In general the view is superior at flexible endoscopy but the ability to manipulate the bleeding rate is less; injection of adrenaline may help but it is harder at endoscopy to apply direct pressure to a bleeding vessel in order to control the bleeding while treatment is applied. Severe bleeding can limit access more at endoscopy than surgery. Deep duodenal ulcers and some high lesser curve ulcers can be difficult to access at flexible endoscopy.

The ability to apply treatment is also somewhat different at open surgery when compared with flexible endoscopy. At surgery, a strong force can be applied to compress a vessel or to get instruments to pass either side of a bleeding artery; at flexible endoscopy a maximum of 100–150 g force⁴⁰ can be applied however hard an accessory is pushed through a biopsy channel. It is probable that most methods that can be shown to work well at surgery may be sometimes more difficult to apply at flexible endoscopy. Coaptation (compression with subsequent welding of the endothelial surfaces of a blood vessel) of a bleeding vessel is sometimes possible using thermal probes but is not that reliable or easy to achieve during

flexible endoscopy. At surgery, access can be achieved from a variety of angles. At endoscopy, only one angle is generally feasible; this is usually acute and a 90 degree approach is only occasionally possible for some gastric ulcers.

The bleeding site seen in bleeding ulcers at flexible endoscopy differs from the mesenteric vessels that were studied in certain respects. Pathological studies show the tendency of the bleeding vessel to loop up to protrude or be eroded close to the floor of the ulcer. It is not possible to identify the orientation of the vessel in an ulcer at flexible endoscopy while the orientation of the mesenteric vessel is easy to see. It is probably more difficult at flexible endoscopy to flatten the vessel or to get mechanical, injection, or thermal methods to have an effect on the back wall of the bleeding vessel which is more inaccessible than at surgery. Peptic ulcers are exposed to acid and mesenteric vessels are not. The eroded artery in a bleeding peptic ulcer features acute and/or chronic inflammatory changes, including destruction of the outer wall over a variable length, fibrinoid necrosis, and a polymorphonuclear cell infiltrate which is not seen in the mesenteric vessels that were studied; this may make the application of mechanical, thermal, and injection methods more difficult. This pathology may also make recurrent bleeding after treatment more likely.

The presence of scar tissue with reduced compliance is a problem that applies to all mechanical methods. Methods that require suction to conform the ulcer into a shape that would allow the band, endoloop, or sewing machine methods to work in their current configuration are likely to work less well in heavily scarred ulcers. The clips are also less likely to work well in the presence of scarring. It can be technically difficult even at open surgery to pass a tie accurately round the bleeding vessel and even much stronger mechanical clips as used at open or laparoscopic surgery may not work well in the presence of scar tissue or a necrotic vessel.

We were surprised in this study to find that the most commonly used mechanical methods of haemostasis (clips and prestretched bands) were unable to achieve haemostasis even on 1 mm vessels. The force that can be exerted by the different mechanical methods is an important determinant of efficacy. The bands and clips failed to work because the force exerted on the bleeding vessel was insufficient or could not be maintained. Much more mechanical force can be exerted by a tied knot or a closed endoloop at flexible endoscopy. It is easier to exert more longitudinal force of pull type at flexible endoscopy than lateral force as exerted by bands and clips.

Despite these differences it remains true that the basic principles of surgical haemostasis should be applied to flexible endoscopic methods. This study shows that injection and to some extent thermal methods are relatively weak as haemostatic methods. Only mechanical methods were able to secure haemostasis from the larger vessels that might be encountered in bleeding peptic ulcers. Relatively little

engineering effort has gone into developing mechanical endoscopic methods for use with a flexible endoscope. If improvements are to be made in securing haemostasis and hence improving morbidity and mortality from bleeding peptic ulcer, it seems likely that mechanical methods will have to be developed for endoscopic use which are more effective on large vessels and are easier to use and deliver than at present.

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