

Review of endoscopic thermal treatment of peptic ulcer hemorrhage

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ABSTRACT: Peptic ulcer hemorrhage is still an important cause of emergency surgery and death. The overall mortality is around 10% from gastrointestinal bleeding, and most of the preventable deaths occur in elderly patients with continued or recurrent bleeding from peptic ulcers. An effective nonsurgical method of hemostasis has long been recognized to be desirable. However it was only when the 'visible vessel' was recognized as the important risk factor for further bleeding that studies capable of testing new modalities adequately could be performed. Careful washing of the ulcer crater is essential for identification of these visible vessels. An effective endoscopic method was first demonstrated in 1981 in patients with visible vessels treated with argon laser. Many groups have now shown excellent efficacy of neodymium:yttrium-aluminum-garnet (NdYAG) laser in preventing further hemorrhage from ulcers with bleeding and nonbleeding visible vessels. Two controlled prospective studies have demonstrated efficacy of the heater probe, but one well designed study did not. Similar studies with both bipolar and monopolar electrocoagulation have shown significant reductions in rebleeding in patients with visible vessels treated using the chosen modality. More recent studies have achieved excellent results by pre-injection with adrenaline and one repeat endoscopic treatment for rebleeds. A few groups have now reported equally good results with injection alone. Long term follow-up of patients with peptic ulcer hemorrhage has confirmed prolonged hemostasis in groups treated with two thermal modalities and in controls. *Can J Gastroenterol* 1990;4(9):653-662

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L'électrocoagulation endoscopique des ulcères gastro-duodénaux hémorragiques: Une revue

RESUME: L'hémorragie provoquée par l'ulcère gastro-duodéal reste toujours une cause importante d'intervention chirurgicale d'urgence et de décès. La mortalité globale atteint près de 10% dans les hémorragies des voies gastrointestinales et la plupart des décès qu'il est possible d'éviter surviennent chez les patients âgés atteints d'hémorragies ulcéreuses persistantes ou récidivantes. On reconnaît depuis longtemps la valeur d'une méthode efficace et non chirurgicale d'hémostase. Néanmoins, c'est seulement depuis que l'on reconnaît le vaisseau

BLEEDING FROM PEPTIC ULCERS remains an important cause of hospital admission, emergency surgery and death. In the United Kingdom, upper gastrointestinal tract bleeding is responsible for 50 to 100 acute admissions per 100,000 population per year (1,2). Peptic ulcers account for 50 to 60% of these cases. The mortality from upper gastrointestinal tract hemorrhage has remained largely unchanged over the past 30 years at around 10% (1,3). This is despite improvements in resuscitation, intensive care, new surgical techniques and the introduction of fiberoptic endoscopy, probably due to the ever increasing proportion of elderly patients (3,4).

In a comprehensive analysis of 484 patients with gastrointestinal bleeding (3), it was found that of 55 (11.4%) who died, 22 (40%) were potentially avoidable deaths (either postoperative complications or persistent bleeding). The majority of patients who died had bleeding peptic ulcers, and all but one were 60 years of age or older. The study did not comment on the relative risk of rebleeding, but it has previously been documented that further peptic ulcer hemorrhage during hospital admission is associated with a 10- to 12-fold increase in mortality (5).

It was concluded that there were two possible ways of altering selection of patients for surgery in an attempt to

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visible comme facteur de risque important de resaignement que l'on effectue des études susceptibles de mesurer adéquatement les nouvelles modalités. Le lavage soigneux du cratère ulcéreux est essentiel au repérage de ces vaisseaux. Une méthode endoscopique efficace a été démontrée pour la première fois en 1981 et elle a entraîné la réduction significative des resaignements chez les patients dont les vaisseaux visibles avaient été traités au laser à l'argon. De nombreux groupes ont désormais prouvé l'efficacité du laser Neodymium Yttrium Aluminum Garnet (NdYAG) dans la prévention des hémorragies causées par les ulcères dont les vaisseaux visibles saignent ou non. Deux études prospectives contrôlées ont démontré l'efficacité de la thermosonde mais une étude bien conçue n'y est pas parvenue. Quelques études similaires sur l'électrocoagulation à la sonde bipolaire et monopolaire révèlent une réduction significative des resaignements chez les patients avec vaisseaux visibles traités de l'une ou l'autre manière. Lors d'études plus récentes, une préinjection d'adrénaline et la répétition d'un traitement endoscopique des resaignements ont donné d'excellents résultats. Quelques groupes rapportent maintenant des résultats tout aussi satisfaisants avec une seule injection. Le suivi à long terme des patients souffrant d'ulcères gastro-duodénaux hémorragiques confirme l'hémostase prolongée des groupes traités par deux modalités thermiques et chez les contrôles.

improve overall mortality rate. The first, which had been previously advocated (1), was to perform early surgery so that patients would be in better condition to withstand the operation. The second was to adopt a more conservative surgical approach in the elderly in the hope that some patients would stop bleeding spontaneously. It was also suggested that the most promising means of reducing mortality would be a non-surgical method of controlling bleeding so that emergency surgery could be avoided (3).

Groups advocating early surgery have reported excellent results (6,7) with overall mortality less than 4%, but to achieve this, operation rates of 30 to 60% were required. The only controlled comparison of early versus late surgery was performed in 1984 (8). In the elderly group, early surgical intervention significantly reduced mortality, but only in patients with bleeding gastric ulcers. The price for this improvement in mortality was a 62% operation rate in the early surgery group compared with 27% in the delayed surgery group. Since these trials, the prognostic accuracy of diagnostic endoscopy has improved.

It is now known that the detection of a 'visible vessel' at endoscopy constitutes a high risk of further bleeding. It is likely therefore that a policy of early surgery in combination with careful diagnostic endoscopy would result in fewer unnecessary operations. Such an

approach in this increasingly elderly group is still likely to result in significant morbidity and mortality. Fortunately, endoscopic techniques have progressed and can now provide the nonsurgical method advocated in 1979 (3). The majority of patients are now candidates for some kind of endoscopic therapy capable of terminating bleeding. Before considering trials of endoscopic hemostasis for peptic ulcer hemorrhage, it is important to consider identification of ulcers at high risk of rebleeding as it is only by including these in studies that hemostatic modalities can be adequately assessed.

ENDOSCOPIC PREDICTION OF FURTHER BLEEDING

Clinical indicators provide a guide to the likely outcome of a bleed in an individual. It has long been known that important negative prognostic factors on admission are: low blood pressure, gross anemia, old age and further bleeding (1). Endoscopic indicators have, however, proven more useful. Stigmata of recent hemorrhage in peptic ulcers that had bled were first identified and found to be associated with increased risk of further bleeding in 1978 (9). Three stigmata were described: fresh bleeding from the lesion; fresh or altered blood clot or black slough adherent to the lesion; and a vessel protruding from the base or margin of the ulcer.

In this early study 25 of 60 ulcers (42%) with stigmata of recent hemorrhage rebled compared with one of 29 (3%) without stigmata. In a prospective trial in 1981 (10) it was reported that when the ulcer crater was washed at endoscopy to clear overlying blood and secretions, visible vessels were found in 56 of 117 patients (48%) where full examination of the ulcer crater was possible. This is a higher proportion of patients than previously reported. In the absence of a spurting vessel or pulsating pseudoaneurysm, the visible vessel was defined more fully as "a red or blue spot, resistant to gentle washing, often associated with red clot and almost always unique in the ulcer crater."

The authors reported that the presence of a visible vessel implied a far higher risk of rebleeding (19 of 34 patients with untreated visible vessels, 56%) than the finding of other stigmata such as mild oozing from the ulcer crater, flat red/black spots or nonadherent clot (one of 13, 8%). The concept of major and minor stigmata of recent hemorrhage was born with this study. Further data obtained prospectively in two trials from the authors' unit (11,12) confirmed these findings. It was found that further bleeding occurred in 59% of patients with visible vessels (spurting or nonbleeding), but in only 5% of patients with minor stigmata. If nonbleeding visible vessels are considered alone, the chance of rebleeding is consistently around 50%, and further bleeding occurred in greater than 80% of patients with bleeding visible vessels.

Most series have confirmed the predictive value of the visible vessel (13-15). There are, however, two recent prospective studies in which the visible vessel did not emerge as a superior predictor of further hemorrhage (16,17). In the first, ulcers were not washed, and therefore many visible vessels must have been missed. In the second, although ulcers were washed, a proportion of ulcers remained covered with adherent clot and were therefore inadequately characterized. In two studies (16,18) the association of shock on admission with a visible vessel or an adherent clot at endoscopy was found

to be a better predictor of rebleeding than endoscopic signs alone.

NATURE OF THE VISIBLE VESSEL

In 1979 it was suggested that the visible vessel was an acutely eroded artery standing up in the floor of the ulcer (19). However a pathologic study of gastric ulcers with visible vessels which were subsequently resected (20) demonstrated that the artery only protruded above the ulcer crater in one in five cases. The visible vessel in the majority was in fact a thrombus extending from a rent in the side of the artery. The alternative terms 'sentinel clot' or 'pseudoaneurysm' are therefore more appropriate.

RESULTS OF TRIALS

There have been many anecdotal reports of successful laser and other thermal treatments of upper gastrointestinal tract hemorrhage; however, as the vast majority of these bleeds cease spontaneously, true assessment of efficacy can only come from looking at patients known to be at high risk of rebleeding in controlled and comparative studies. Studies of thermal methods to control peptic ulcer hemorrhage will now be considered. In all reports the incidence of rebleeding in ulcers without visible vessels has been low. Characterization of the ulcer crater following adequate washing is a common difference between studies which demonstrate benefit from the various techniques and similar studies which do not.

Argon laser: Two early studies (14,21) showed no significant difference in rebleeding rate, emergency surgery or mortality between ulcers treated with argon laser and control ulcers. In the first study there was a trend towards reduction in rebleeds in patients with spurting vessels, which did not reach significance. The authors of this study commented that their results required amplification in larger trials. In a two-centre trial (11), further hemorrhage occurred in significantly fewer patients with visible vessels treated with laser compared to the control group. This trial demonstrated for the first time a

TABLE 1
Results of argon laser trial (Swain et al 1981) (11)

	Laser				Control			
	Total	Rebled	Surgery	Died	Total	Rebled	Surgery	Died
Spurting	7	4	4	—	4	4 [†]	2 [†]	2*
Visible vessel	17	4	4	—	24	13 [‡]	12	5*
Oozing or other minor SRH	7	1	1	—	10	—	—	—

Visible vessels were nonbleeding. SRH Stigmata of recent hemorrhage. *Post rebleed; †One died before surgery; ‡One treated with laser after rebled out of trial. Rebleeding: Spurting and visible vessels combined $P<0.05$; visible vessels alone $P<0.05$. Other stigmata of recent hemorrhage: No significant difference. Mortality $P<0.02$

significant reduction in mortality with a nonsurgical method of treatment. Full results are described in Table 1.

In contrast to most preceding studies, patients were entered into this study only if laser therapy was thought to be technically possible at endoscopy. Thus treatment failures were truly due to inefficacy of laser treatment and not endoscopic technique. Such factors were identified in 5% of patients in this study. Most subsequent trials excluded these difficult cases.

NdYAG laser: This laser has greater power output and tissue penetration and superior hemostatic efficiency in animal studies than the argon laser (22). Laser output is focused onto the end of a 400 to 600 μm quartz fibre. This fibre is contained in a Teflon catheter 2.6 mm in diameter, which gives it mechanical strength and thus allows it to be passed down the working channel of an endoscope. It also allows a coaxial stream of gas to be passed to keep the metal tip of the fibre cool and clean – also to clear the target of blood and debris. This technique is noncontact. The tip of the fibre is positioned 5 to 10 mm from the target. Pulses are usually applied circumferentially around the visible vessel in 0.5 to 1 s shots using a power setting of 70 to 80 W.

Three early trials (23-25) showed no benefit of YAG laser. None of these studies, however, defined the precise nature of the bleeding point, and numbers were small. In addition, one study (23) was performed using a power of 50 W, which is suboptimal.

A later study (26) demonstrated initial hemostasis in patients with active nonspurting hemorrhage from treated peptic ulcers to be significantly better than controls. (Bleeding stopped in all

TABLE 2
Results for patients with visible vessels randomized to YAG laser or no treatment (McLeod et al 1983) (13)

	Total	Re-bleed	Emergency surgery	Died
Laser	8	1	1	—
Control	8	8	8	2

Rebleeding $P<0.02$. Emergency surgery $P<0.02$. Mortality no significant difference

38 patients in this group treated with laser, but in only 25 of 32 or 77% of controls.) Rebleeding occurred in two of 38 treated patients and five of 25 controls (not significant). Emergency surgery was required in four control patients and one patient treated with laser (not significant). A separate group of patients with peptic ulcers with stigmata of recent hemorrhage (visible vessel or fresh clot) were randomized to laser or no treatment: three of 14 rebled in the laser group and seven of 22 in the control; this again did not reach statistical significance. Unfortunately, the actively bleeding, nonspurting ulcers were not characterized further – these ulcers must constitute a heterogeneous group of both high and low risk lesions. A third group of patients with spurting arterial hemorrhage was treated with laser following a local ethical committee decision; 20 of 23 (87%) stopped bleeding with laser treatment, but the recurrence rate was high (11 of 20 or 55%). The operation rate in this group was 61%, which compares well with a rate of 95% for comparable historical controls.

A reduction in rebleeding in a small group of patients with visible vessels treated with YAG was first reported in 1983 (13). All patients had signs of major blood loss (shock or hemoglobin

TABLE 3
Results of NdYAG laser in peptic ulcers with stigmata of recent hemorrhage

	Laser (n=70)	Control (n=68)	
Further hemorrhage			
All ulcers with SRH	7/70 (10%)	27/68 (40%)	P<0.001
Spurting VV	2/10 (20%)	8/10 (80%)	P<0.002
Nonbleeding VV	4/28 (14%)	15/31 (48%)	P<0.001
Minor SRH	0/19 (0%)	1/14 (7%)	NS
Overlying clot	1/13 (8%)	3/13 (23%)	NS
Emergency surgery	7/70 (10%)	24/68 (35%)	P<0.005
Mortality	1/70 (1%)	8/68 (12%)	P<0.05

n Number of patients; SRH Stigmata of recent hemorrhage; VV Visible vessels; NS Not significant

TABLE 4
Results of pre-injection with adrenaline followed by YAG laser photocoagulation in patients with visible vessels (Rutgeerts *et al* 1984) (28)

	Spurting	Non-bleeding
Initial hemostasis	25/26	—
Final hemostasis	22/26	25/28
Emergency surgery	4/26	3/28
Mortality	4/26	1/28

less than 10 g/dL). From 657 unselected patients, 184 had peptic ulcers and 41 fulfilled inclusion criteria and had ulcers accessible to laser therapy. None of 25 patients with minor stigmata of recent hemorrhage (red or black spots) rebled. The results for patients with visible vessels are shown in Table 2.

Similar results were reported in another study (27) on patients with spurting and nonbleeding visible vessels. There was a trend towards reduction of rebleeding and the need for emergency surgery which was not statistically significant, but there was a significant reduction in mortality.

A detailed study from this unit produced convincing results (12). One hundred and thirty-eight patients with peptic ulcer hemorrhage who were found to have stigmata at endoscopy were randomized to receive YAG laser photocoagulation or conservative management. Their results are shown in Table 3. Patients with spurting hemorrhage or nonbleeding visible vessels treated with laser had significantly less chance of further hemorrhage than controls. Statistical significance was shown whether these groups were considered individually, together or as part

of the group showing stigmata of recent hemorrhage (Table 3). The incidence of rebleeding in ulcers demonstrating minor stigmata was very low. Ulcers with overlying clot demonstrated intermediate risk of rebleeding, presumably because this group included some patients with hidden visible vessels and some with minor stigmata. The need for emergency surgery and mortality were also significantly reduced in the laser group. The data on relative risk of rebleeding of the various stigmata previously discussed were derived from the combined results of this study and the argon laser study from the same group.

The protocol of this study was identical to the argon laser study. The hemostatic efficacy of the NdYAG laser can thus be compared directly with that of the argon laser. Such a comparison shows the NdYAG laser to be significantly better in the groups with all stigmata and with visible vessels alone.

A second study from the Belgian group (28) looked at the effect of pre-injection with 1:10,000 adrenaline prior to YAG laser treatment in patients with visible vessels (both spurting and nonbleeding) (Table 4). In 87% of the 54 patients studied, complete hemostasis was achieved. The results for bleeding visible vessels were particularly impressive: final hemostasis was achieved in 85% resulting in only 15% (four of 26) requiring emergency surgery. There was no control group in this study, but the figures compare very favorably with other published series. One might expect a rebleeding rate of around 50 to 60% in such cases overall – far higher than the 13% observed. The authors ascribed the apparent benefit of pre-injection with adrenaline to temporary hemostasis, which al-

lowed better visualization of the target. It is likely, however, that some benefit is also derived from vasoconstriction in the underlying artery and a consequent reduction in removal of heat from the area (the 'heat sink effect').

A further study from the Belgian group (29) and one from the present authors' unit (30), both discussed in more detail in the next section, have contributed to the weight of evidence confirming the efficacy of YAG laser in peptic ulcer hemorrhage.

One recent randomized controlled study (31) reported no benefit from YAG laser in bleeding peptic ulcers. Washing of clots at endoscopy was not performed, and thus the bleeding point was not adequately characterized in most patients. Only 29 visible vessels were detected in 174 patients included in the study (17%). This is very low in comparison with most series. The protocol excluded patients "too unstable to be moved to the laser facility." During the course of the study this amounted to 221 patients – more than the total number included. These patients were those with the most hemodynamically significant bleeds, and as such, they were likely to have visible vessels (perhaps explaining the low pick-up rate) and thus most likely to benefit from laser therapy. The very low mortality (1%) seen in this study surely reflects the exclusion of these high risk patients.

Heater probe: Experimental studies (32,33) comparing methods of electrocoagulation suggested the heater probe to be most promising in terms of efficacy and safety. The first of these studies found the heater probe and the bipolar electrode to cause full thickness damage significantly less frequently than the liquid or dry monopolar electrodes (20 versus 60%); thus, the risk of perforation was thought to be lower with these electrodes. The bipolar electrode, however, performed less well than the other three in hemostasis. The second study confirmed the heater probe and the bipolar electrode to be safest and found the two modalities to be equally efficacious.

The heater probe was developed in 1978 (34). It was designed to apply pres-

sure and heat simultaneously to a bleeding vessel. The probe comprises a hollow aluminum cylinder with an inner heater coil and an outer coating of non-stick Teflon. It also contains a separate thermocouple element in the tip to measure temperature. It can be heated to a maximum of 250°C, a temperature which is maintained until a preset amount of energy is delivered. There is also a proximal irrigation port to allow washing of the target even when the probe is applied forcibly to tissue. The technique employed is to apply the inactivated probe around the bleeding point with moderate pressure in order to tamponade bloodflow in the underlying vessel. The probe is then activated and a preset quantity of energy delivered (usually 30 J). This procedure is then repeated at multiple sites circumferentially around the bleeding point. This technique of vessel tamponade and thermal coagulation has been termed 'coaptive coagulation' and applies equally to all thermal methods apart from laser, for which the fibre tip is positioned 5 to 10 mm from the target.

Encouraging results were reported in a pilot study in 1983 (35) with an early heater probe. Patients already anesthetized for emergency operation were treated. Final hemostasis was achieved in 12 of 15 patients with gastric ulcers; only one of 15 required surgery. Experience with duodenal ulcers was not as impressive – only two of 10 avoided surgery. There were no deaths in the patients with gastric ulcers, but three died in the duodenal ulcer group. The exact nature of bleeding point was not discussed. A similar pilot study (36) also produced encouraging results – 12 of 16 patients proved treatable. (The others had large overlying clots or active hemorrhage.) Bleeding was arrested in all 12 patients treated, although one required a second application.

A retrospective study (37) of YAG laser and heater probe in patients with spurting and nonbleeding visible vessels showed a significant difference in final hemostasis in favour of the heater probe group: 19 of 20 (95%) of ulcers treated with heater probe and 24 of 35 (69%) of ulcers treated with YAG laser stopped bleeding ($P < 0.05$). Some

patients who rebled had second treatments, a protocol which has been used increasingly in subsequent studies. It is interesting to note the very high rate of induced bleeding (29%) in laser-treated patients. This did not occur in the heater probe group and may account for the apparent difference in final hemostasis. The difference in surgery and mortality in the two groups did not reach statistical significance. The authors concluded that heater probe was more effective than laser as well as being quicker and safer; however, the efficacy of heater probe has not been shown to be better than laser in any of the subsequent prospective studies.

The first prospective randomized comparison of the two modalities was performed in 1987 (30). Patients with peptic ulcers showing stigmata of recent hemorrhage (total 143) were randomized to receive YAG laser, heater probe or no endoscopic treatment. The rebleeding rate was significantly lower in the laser group (20%) than controls (42%). Rebleeding in the heater probe group (28%), however, was not significantly different from controls (although there was a strong trend towards reduced rebleeding). There was no statistical difference in deaths in the three groups. Combined analysis with results of a previous study from the same group (12) and with an identical protocol but no heater probe arm showed significantly fewer rebleeds and deaths in patients treated with laser rather than heater probe. Ulcers with both major and minor stigmata of recent hemorrhage were included in this study. A further analysis of subgroups may provide more information, although the authors did note that randomization was biased towards heater probe therapy.

Excellent results have subsequently been reported in an open prospective study (38). Fifty patients with visible vessels (28 with spurting hemorrhage) were treated with heater probe. The results are shown in Table 5. In all, 49 of 50 visible vessels (98%) were controlled with treatment, and only seven (14%) rebled within one week. Hemostasis was achieved in four of these

TABLE 5
Adapted results for peptic ulcers with visible vessels treated with heater probe (Lin et al 1988) (38)

	Spurting	Oozing and non-bleeding
Initial hemostasis	28/29	21/21
Final hemostasis	26/29	20/21
Emergency surgery		3/50
Mortality	1/29	0/21

patients with further heater probe treatment. The ultimate success rate was thus 46 of 50 patients (92%). The patient whose bleeding was not controlled by initial treatment had a deformed duodenal bulb, and the heater probe could not be applied to the bleeding source. This patient was the only fatality in the series. A total of three patients underwent surgery and survived.

A recent prospective randomized controlled trial from Scotland (39) has demonstrated efficacy of heater probe against controls. Patients with active bleeding were randomized to treatment or no treatment. No rebleeding occurred in 20 patients treated with heater probe, but five of 23 controls rebled ($P = 0.05$). Emergency surgery was performed in three of the control patients. Considering ulcers with visible vessels, seven of seven in the heater probe group did not rebleed but three of four controls rebled ($P < 0.04$).

Bipolar electrocoagulation: The bipolar probe consists of two or more (commonly three) pairs of bipolar electrodes allowing diathermy with tip angulation. It comes in various sizes, early probes being 2.3 mm in diameter and later ones 3.2 or 3.4 mm in diameter. There is a central irrigation channel. Early power sources delivered 25 W – the later units 50 W. The technique of vessel coagulation is identical to that employed with the heater probe. In experimental studies, the 3.2 mm probe has proven more efficient at coagulating bleeding mesenteric arteries than the 2.3 mm probe (40).

An early multicentre study (41) demonstrated clinical efficacy of the bipolar 2.3 mm probe. A total of 44 patients with various actively bleeding

TABLE 6
Patients with peptic ulcers treated with 2.3 mm bipolar probe or no treatment (O'Brien *et al* 1986) (44)

	Treated		Control	
	Total	Continued/rebleeding	Total	Continued/rebleeding
Adherent clot	18	4	39	5
Bleeding VV	40	6	21	13
Nonbleeding VV	43	7	43	16

Continued/rebleeding for all groups $P < 0.01$. VV Visible vessel

TABLE 7
A randomized comparison of 3.2 mm BICAP and YAG laser with pre-injection of adrenaline in patients with peptic ulcers with visible vessels (Rutgeerts *et al* 1987) (29)

	Laser (n=50)	Bipolar (n=50)
Initial hemostasis	45 (90%)	48 (96%)
Final hemostasis (one session)	36 (72%)	36 (72%)
Rebleeding after initial hemostasis	9/45 (20%)	12/48 (25%)
Second treatment successful	8/9 (89%)	7/11 (64%)
Final hemostasis (two sessions)	44 (88%)	43 (86%)
Emergency surgery	6 (12%)	3 (6%)
Perforations	1 (2%)	1 (2%)
Mortality	7 (14%)	7 (14%)

stomach and duodenal lesions were treated. Immediate hemostasis was achieved in 38 (86%), and only 11 patients subsequently rebled. No complications were encountered. This study paved the way for controlled trials.

Three controlled trials were conducted with the 2.3 mm probe. In the first (42), 46 patients with peptic ulcers which had bled were randomized. The ulcers were not characterized further, and no differences were shown between the 21 treated patients and controls. One treated patient suffered massive bleeding during the procedure. The second (43) found no difference between 21 treated and 24 control patients with stigmata of recent hemorrhage. Access with the probe, however, was inadequate in half of the patients treated. The third trial with this small probe did show a statistical reduction in rebleeding in patients treated with the 2.3 mm bipolar probe over controls (44). This trial was much larger than the previous two and included a detailed description of bleeding points (Table 6). Two hundred and four patients with stigmata of recent hemorrhage were randomized to bipolar treatment or control. Overall 17 of 101 (17%) treated patients continued to bleed or rebled within five days, versus

34 of 103 (34%) in the control group ($P < 0.01$). The differences were most marked in groups with visible vessels, although statistical analysis was not done on subgroups. There was no significant difference in surgery or mortality.

In an open study (45), 53 patients with various upper gastrointestinal tract lesions were treated with a larger (3.4 mm) bipolar electrocoagulator. Bleeding was stopped in 52 of 53 patients and rebleeding noted in only 15%. Three comparative studies have since been carried out with variable results. In the first (46), 41 patients with stigmata of recent hemorrhage were randomized to electrocoagulation or control; six of 20 treated and eight of 21 control patients suffered from rebleeding. There was no significant difference in any important parameter between the two groups. In another small study for active hemorrhage from various lesions (47), there was a significant reduction in the need for emergency surgery (14 over 57%, $P = 0.01$). The rebleeding rates were not discussed and there was no significant difference in mortality.

A detailed randomized comparison of YAG laser and 3.2 mm bipolar probe in patients with bleeding and non-

bleeding visible vessels was performed in 1987 (29). This study differed in two important respects from most previous trials. First, all ulcers were pretreated with an injection of 1:10,000 adrenaline. Also, a second treatment with the appropriate modality was attempted before patients were classified as treatment failures and treated surgically. The results of this trial demonstrated excellent hemostatic efficiency of both modalities (Table 7).

The bipolar probe appeared to be slightly better at controlling spurting hemorrhage (80 over 58%), although this difference was not statistically significant. The overall operative rate in this study (9%) is dramatically less than the rate expected (28%) if all rebleeds were subjected to surgery. As repeat endoscopic thermal treatment with the two modalities appeared safe, this practice represents a considerable advance.

Monopolar electrocoagulation: Monopolar electrocoagulation involves the passage of a high frequency current through an electrode which can be passed down an endoscope to tissue, through the body and to a ground plate in contact with the skin. It can be performed 'dry' or 'liquid' (through a layer of water), which helps reduce tissue adherence. The experimental data previously discussed confirmed the hemostatic efficacy of this technique, but the high incidence of full thickness damage (32) and undesirable erosion from electrical sparking (33) raised questions of safety, and relatively few clinical trials have been reported.

A small controlled study of dry monopolar coagulation in ulcers with nonbleeding visible vessels was reported in 1979 (48). Rebleeding occurred in only 7% of treated ulcers compared with 85% of controls. In a subsequent study by the same group 103 patients with actively bleeding peptic ulcers were treated with dry monopolar electrocoagulation (15). Initial hemostasis was achieved in 94% and the rebleeding rate was 12%. Another group (49) examined the efficacy of liquid monopolar electrocoagulation in 37 patients with gastric and stomal ulcers with visible vessels. Rebleeding was significantly less common in the treated

group (one of 16) than in controls (11 of 21). There was no difference in mortality. A similar study (50) in 31 patients with peptic ulcers with non-bleeding visible vessels produced similar results.

COMPLICATIONS OF ENDOSCOPIC THERMAL MODALITIES

Hemorrhage: The induction or aggravation of arterial hemorrhage from a visible vessel is the most commonly experienced complication of YAG laser therapy. This occurred in between 0 and 29% of patients from different series; however, the majority of these bleeds could be stopped with further therapy. Most series therefore report relatively few patients with important aggravated or induced hemorrhage. With argon laser, two patients with visible vessels suffered aggravated hemorrhage out of 22 treated; both had surgery and survived (11). With YAG laser four of 70 patients with visible vessels bled on treatment; all stopped with further laser shots, perhaps reflect-

ing the superior hemostatic ability of the YAG laser (12). With YAG laser plus adrenaline preinjection, six of 28 patients with nonbleeding visible vessels suffered aggravated bleeding with YAG laser, and five of 26 with bleeding visible vessels controlled with adrenaline injections rebled with the first laser shots; however, all of these patients stopped bleeding with further injections (28). Laser technique varied around the sentinel clot, not actually firing at it (12); this may account for the relatively low rate of induced bleeding in comparison with some studies. It seems likely that disruption of the sentinel clot and the underlying artery in the early phase of treatment before the feeding vessel has been coagulated is responsible for aggravation of bleeding in these cases. Precipitation of hemorrhage has not generally been found to be a problem with the other thermal methods; one trial (42) did however record an induced bleed with the bipolar probe.

Perforation: Two early studies (11,14)

with the argon laser reported only one possible perforation in more than 100 treated patients. The greater penetration of the infrared beam of the YAG laser in comparison with the argon laser led to concern regarding more frequent perforation. Experimental studies (22), however, established effective and safe guidelines for the use of the YAG laser in bleeding gastric ulcers. Clinical series have shown perforation to be very rare (less than 1%) when the laser is used according to guidelines. Most studies have reported very few perforations with other thermal methods (Table 8).

OTHER TREATMENT PROBLEMS

Some ulcers in all series are endoscopically inaccessible and thus not amenable to any thermal method, eg, duodenal ulcers with duodenal deformities or pyloric stenosis. Others are in difficult locations where correct targeting is not possible. These locations are the posterior/inferior duodenal bulb, the inferior post bulbar duodenum, the high gastric lesser curve and the post-

TABLE 8
Comparison of prospective randomized controlled trial results for thermal endoscopic hemostasis for bleeding peptic ulcers

	Modality	No. of patients randomized	Major bleed only	Active bleeding only	Active bleeding +SRH	Bleeding point defined	Benefit	Complications
Vallon (14)	Argon laser	136	-	-	+	+	No	? 1 perforation
Swain (11)	Argon laser	76	-	-	-	+	Yes FH+M	2 aggravated bleeding Both required surgery
Ihre (23)	YAG laser	25	+	+	-	-	No	1 perforation
Escourrou (24)	YAG laser	71	+	+	-	-	No	—
Rutgeerts (26)	YAG laser	129	-	-	+	+/-	No+	None
Macleod (13)	YAG laser	45	+	-	+	+	Yes S	—
Swain (12)	YAG laser	101	-	-	+	+	Yes FH, S, M	4 aggravated bleeding All stopped
Krejs (31)	YAG laser	174	-	-	+	-	No	4 aggravated bleeding, 2 required surgery, 1 perforation
Matthewson (30)	YAG HP	143	-	-	-	+	YAG Yes FH HP No	—
Fullerton (39)	HP	43	-	-	+	+	Yes FH	1 perforation
Groudie (42)	BICAP 2.3 mm	46	-	-	-	+	No	1 induced bleeding No perforations
Kernohan (43)	BICAP 2.3 mm	45	-	-	-	+	No	—
O'Brien (44)	BICAP 2.3 mm	204	-	-	-	+	Yes FH	—
Brearley (46)	BICAP 3.2 mm	44	-	-	-	+	No	1 perforation
Laine (47)	BICAP 3.2 mm	24	+	+	-	-	Yes S only	None
Moreto (49)	MP	37	-	-	-	+	Yes FH	None

FH Further hemorrhage; S Emergency surgery; M Mortality; + No benefit in terms of the above but there was significant initial control of bleeding. HP Heater probe; MP Monopolar; SRH Stigmata of recent hemorrhage

erior high gastric body. Duodenal ulcers are in general more difficult to treat than gastric ulcers. The proportion of ulcers that cannot be treated varies between 2 and 26% in different series.

Rebleeding following initially successful hemostasis by a thermal method occurs in 10 to 30% of ulcers demonstrating visible vessels. A study previously discussed (29) demonstrated that the majority of these rebleeds can be terminated by a further endoscopic treatment, and recent experience has confirmed this.

LATE OUTCOME OF PATIENTS TREATED FOR BLEEDING ULCERS

A recent study from the authors' unit (51) looked at long term follow-up of patients with peptic ulcer hemorrhage treated between 1984 and 1986 as part of a randomized controlled trial of endoscopic YAG laser and heater probe. Details on 93 of 131 patients were obtained for an average follow-up period of three years. A total of six patients suffered further peptic ulcer hemorrhage during this period: two of 25 bleeds occurred in the laser-treated group; three of 29 in the heater probe-treated group; and one of 17 in the control group who did not have surgery. No patients who had surgery rebled. This low rate of recurrent bleeding occurred despite a surprisingly high incidence of dyspeptic symptoms – 35% in patients treated with endoscopic thermal methods; 70% of these patients were taking H₂ receptor antagonists. It is concluded that endoscopic therapy for peptic ulcer hemorrhage followed by long term maintenance H₂ receptor antagonists provides long term hemostasis in almost all patients.

DISCUSSION

The discovery of the visible vessel as the important risk factor for further bleeding in peptic ulcer hemorrhage has allowed the identification of patients likely to benefit from endoscopic therapy. Most studies have been performed with the YAG laser and evidence for the efficacy of this modality is convincing. Direct comparison of argon and YAG lasers from studies with identical protocols from this unit confirmed the clinical impression that the YAG laser has superior hemostatic ability. There are less data for the other thermal modalities. Studies with heater probes have produced variable results. The authors' present study showed a trend towards reduced rebleeding in patients treated with heater probe over controls, but this was not significant, whereas there was a significant reduction in rebleeding in patients treated with YAG. It is likely that type 2 error (not enough patients) was responsible for the lack of significant difference between the heater probe and control groups. The clinical impression was that heater probe was effective but not as good as laser, at least in the authors' hands.

The other two prospective studies with the heater probe which characterized the bleeding point carefully both confirmed efficacy of this device. The results of one study (38) were particularly encouraging. The small number of trials conducted with bipolar and monopolar electrocoagulation have shown both of these modalities to be better than control, but few data are available on comparison with the YAG laser. The only comparative study (29) was well designed and gave excellent results for both YAG laser and bipolar; both groups were preinjected with

adrenaline. Subsequent studies (52,53) have shown that adrenaline injection alone is effective in reducing further bleeding from peptic ulcers, although the combination of adrenaline and a thermal method achieved better results. Two recent studies (53,54) also looked at a combination of injection with adrenaline and a sclerosant (Polidocanol, Methoxysclerol 1%, Germany). Results with this regimen in the second study were comparable with a combination of adrenaline and YAG laser. If these results are confirmed by other centres, excellent hemostasis is possible without a thermal modality and could therefore be used in nonspecialist centres with considerable benefit.

It is likely that all of the techniques described in this paper are effective at least to some extent. The evidence is most convincing for the NdYAG laser, but it is unlikely that any major difference between the modalities will emerge. The skill and perseverance of the endoscopist is almost certainly more important than the particular modality employed. Personal preference and experience may determine which method is most appropriate for each endoscopist. The authors' preference is for injection with adrenaline followed by NdYAG laser therapy. Of the last 21 patients in this hospital with peptic ulcer hemorrhage and visible vessels treated with this combination, only three suffered further bleeding. Permanent hemostasis was achieved in all three patients after repeat endoscopic therapy. These results are comparable with those achieved by the group who pioneered the combination of injection and a thermal modality (29), and it will clearly be difficult to improve on them.

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