Gut

Leading article

Endoscopic intervention in bleeding peptic ulcer

Endoscopic intervention can now be regarded as first line treatment for patients who present with major peptic ulcer haemorrhage. Randomised controlled trials have shown that a range of endoscopic treatments will stop active bleeding and reduce the risk of rebleeding. Surgery is now reserved for patients in whom endoscopic treatment fails. The best outcome depends upon close cooperation between the endoscopist and surgeon; skilled interventional endoscopists work closely with their surgical colleagues and each knows the limitations of the other.

Endoscopic therapy for bleeding ulcer improves the outcome only of high risk patients. This group comprises patients with major peptic ulcer bleeding and endoscopic stigmata of bleeding.^{1–4} The factors which predispose to further haemorrhage include shock at presentation, anaemia, and the need for blood transfusion.^{8 12–14} Other adverse clinical characteristics include advancing age, comorbid diseases, coagulopathy, and bleeding in patients admitted for an unrelated condition.^{8 12–14} Large ulcers¹³ and those located on the posterior inferior duodenal bulb or high lesser curve of the stomach¹⁵ are also associated with increased risk of rebleeding.

Endoscopic stigmata are the most useful predictor of outcome but interpretation of the endoscopic appearances is often difficult because the ulcer may be obscured by a blood clot or awkwardly positioned. Most endoscopists clean the ulcer base to define the bleeding site, although this may precipitate rebleeding. Patients with an active, spurting haemorrhage have the worst prognosis; the combination of active bleeding and shock is associated with continued bleeding or rebleeding in 80% of cases. Endoscopic identification of a non-bleeding vessel varies between 6% and 48%^{3 5}; identification of rebleeding from a visible vessel ranges even more widely, from 0% to 81%.^{6 7} This variation is probably due to differences in endoscopic interpretation, definition of rebleeding, and to the timing of endoscopy. Some studies have related the colour of the visible vessel to outcome, but the findings are inconsistent,^{6 9 10} probably because endoscopic interpretation tends to be subjective.¹¹ The endoscopic doppler can identify the position of the feeding artery and may predict the group of patients likely to rebleed.^{16–18} Rebleeding is rare in the absence of a doppler signal from the ulcer base.

Patients without endoscopic stigmata and those with

only minor stigmata (irrespective of other clinical risk factors) will almost invariably recover with conservative support and should not be treated endoscopically.

Endoscopic techniques

THERMAL

Lasers

Photocoagulation of bleeding ulcers was first attempted using argon lasers.^{20 21} The results were generally disappointing – partly because of the study design (many relatively low risk patients were included) but principally because the depth and intensity of tissue damage caused by the argon laser is often insufficient to induce arterial thrombosis. Animal studies subsequently showed that the ND-Yag laser would be a more appropriate thermal agent.²² Obliterative coagulation is probably the most important mechanism of laser haemostasis, although oedema surrounding the vessel may be an additional factor. Most early controlled trials showed a significant treatment benefit with ND-Yag lasers.^{23–26} Rebleeding, transfusion requirements, operation rates, and mortality were reduced. Krejs *et al.*²⁷ published a study which failed to show benefit for Nd-Yag laser treatment in a large number of randomised patients, although the most severe cases were not included and it is likely that many procedures were performed by relatively inexperienced operators.

Laser therapy for bleeding has proved safe, with low perforation rates. Bleeding is often precipitated by the treatment itself but it either stops spontaneously or can be arrested by further photocoagulation. A meta-analysis of controlled trials showed a significant reduction in the need for urgent surgery (common odds ratio (OR) 0.58 (95% confidence interval (CI) 0.38, 0.69)) and reduced mortality (common OR 0.49 (95% CI 0.30, 0.81)).²⁸ Criticisms of the laser include high capital and running costs and the difficulty of applying therapy without touching the mucosa with the laser fibre tip. Even in expert hands, 19% of patients in one study did not receive planned laser therapy because of technical difficulties.²³ For these reasons, and because the alternatives are at least as effective, enthusiasm for ulcer photocoagulation has waned.

Electrocoagulation

Electrocoagulation devices cause arterial thrombosis by passing an electric current through the bleeding area. Monopolar units apply a ball-tipped probe, and the electrical circuit is completed through a plate attached to the patient. The technique has the drawbacks of tissue adherence, unpredictable tissue damage, and the need to frequently clean the tip. An electrical conducting fluid can be used to transmit the current mucosa (liquid monopolar coagulation), and this largely overcomes the problem of tissue adherence and improves the performance of the system. Three controlled trials have shown that active bleeding can be stopped and rebleeding rates reduced by monopolar electrocoagulation^{29–31} but because of the unpredictable tissue injury associated with it, the device has largely been superseded by other contact methods.

Bipolar coagulation works by completing an electrical circuit between probes applied to the mucosa. The multipolar electrocoagulation pulse, known as BICAP, has three pairs of electrodes on its side and tip; electrocoagulation can be performed if any pair of electrodes are in tissue contact, and this allows tangential treatment. The amount of energy applied to the area and the degree of tissue damage is much more predictable than with monopolar units. Although early clinical trials with the BICAP were disappointing,^{32–33} two subsequent prospective randomised controlled studies from the same author showed that the device was effective. One small clinical study showed a significant haemostatic effect in actively bleeding patients,³⁴ and the other showed reduction of rebleeding in patients with non-bleeding visible vessels.³⁵ Both studies showed a reduced need for emergency surgery, a shorter stay in hospital, and reductions in transfusion requirements and hospital costs. Bleeding can be precipitated by treatment in almost a third of cases but this usually stops with repeated applications. A particular advantage of contact probes is the ability to stop bleeding by tamponade and the best results of BICAP are associated with forceful application of the larger (3.2 mm) probe, low watt setting, and prolonged periods of coagulation.³⁶

Heater probe

The heater probe transmits predetermined amounts of energy to the mucosa through a Teflon coated tip. Several early uncontrolled studies showed that the heater probe was both safe and effective.^{37–38} Subsequent randomised, controlled trials in high risk patients confirmed that treatment reduced rebleeding rates and the need for emergency surgery.^{39–40} Optimum therapy is best administered using the 3.2 mm probe, firm tamponade, a setting of 25–30 Joules and repeated applications before the probe position is changed. The heater probe is attractive because it is relatively cheap and portable. The facility to apply forceful tamponade, its capacity to apply energy tangentially, and a powerful water jet which cleans and irrigates the area are particular advantages.

INJECTION THERAPY

Endoscopic injection of agents into a bleeding ulcer is cheap and relatively easy. Haemostasis can be accomplished using a range of solutions, but the mechanism by which this occurs is not entirely clear. Many regimens include dilute adrenaline which causes vasoconstriction⁴¹ but may also act by enhancing platelet aggregation⁴² and by tamponade since a relatively large volume is used. In animal models, adrenaline rarely causes arterial thrombosis^{43–44} yet in clinical trials, injections seems to prevent rebleeding. Injection of sclerosants results in tissue

necrosis, ulceration, and thrombosis^{43–45–52} but does not cause vasoconstriction or spasm, yet some studies show benefit in active bleeding. Mechanisms of action for injection methods may be clarified if an appropriate model for peptic ulcer bleeding can be developed, yet this seems difficult to achieve. Examination of resection specimens from patients requiring surgery for ulcer haemorrhage is of little value because it is difficult to distinguish between the histological effects of chronic ulceration (which include endarteritis) and those of the injection.

Many endoscopists inject dilute adrenaline, either alone^{46–47} or in combination with sclerosants^{48–51} around and sometimes into the bleeding point. Other investigators have used sclerosants such as polidocanol⁵² and absolute alcohol^{53–54} without adrenaline. The rationale for a combined approach is that adrenaline causes vasoconstriction and stops active bleeding and the sclerosant leads to a vigorous inflammatory response causing endarteritis, arterial thrombosis, and prevention of rebleeding. Whether this actually happens in humans is unknown.

Although several groups have shown that the prognosis of bleeding peptic ulcer is improved by injection treatment, the most convincing data relate to reduction in rebleeding rates and the need for emergency surgery rather than mortality. The ideal regimen is unclear. We and the Hong Kong group believe that adrenaline is as good as any other agent or combination of agents.^{55–56} Other investigators consider that adrenaline should be followed by a sclerosant agent such as polidocanol,⁵⁷ and that absolute alcohol is at least as effective as any other treatment.^{58–59} Finally, Lin *et al*⁶⁰ reported that normal saline, 3% NaCl, 50% glucose/water and pure alcohol, were all comparable.

Unfortunately the inclusion criteria and the end points differ between trials and it is difficult to determine which regimen is best. All regimens seem effective and safe. Complications are unusual and perforation is rare. Sclerosants can, however, cause ulcer extension, perforation, and stomach necrosis,^{61–63} and because we believe that they confer no additional benefit to injection with adrenaline alone, our policy is to avoid them.⁵⁵

Approximately 8–10% of ulcers are inaccessible to injection treatment. Repeat injection is safe and most endoscopists now tend to reinject if there is evidence of rebleeding. The Hong Kong group routinely perform repeat endoscopy in all patients 24 hours after the initial injection and retreat the 10–20% of patients who continue to bleed.^{46–64} A recent randomised trial examined the value of 'second look' endoscopy. The trend towards a better outcome in the group who had repeat endoscopy did not reach statistical significance.⁶⁵ Our own policy is only to repeat endoscopy electively in patients in whom therapy has been suboptimal.

Comparison of endoscopic haemostatic treatment regimens

Trials comparing the various endoscopic therapies^{25–40–57–64–66–71} suggest that the BICAP, heater probe, and injection therapy are all as safe and effective as each other. The approach of adrenaline injection followed by a thermal method is logical, although clinical trials do not convincingly show that this is better than a single modality.^{57–73–74}

Other novel approaches

Endoscopic haemostasis can be achieved with metal clips,⁷⁵ clamps,⁷⁶ rubber band ligation,⁷⁶ and sewing.⁷⁷ These mechanical methods may be technically difficult, however, and none are yet established in clinical practice.

Failures of endoscopic therapy and when to operate?

We cannot predict which patients will fail endoscopic therapy. Our own data suggest that patients who present with anaemia, shock on admission, and active arterial bleeding from a posterior duodenal ulcer are at highest risk of failing endoscopic therapy (injection or heater probe).⁷⁸ This is perhaps not surprising since this group of patients had the worst prognosis without endoscopic treatment. It has been reported that patients who bleed from large posterior duodenal ulcers^{79 80} and those with comorbid disease⁷⁹ have the highest rate of failing endoscopic injection therapy.

To date there is no study comparing surgical and endoscopic control of bleeding. Most endoscopic studies consider that the need for surgery represents treatment failure. Alternatively, it can be argued that endoscopic control of bleeding facilitates safe, early elective surgery. A successful outcome may depend upon a combination of endoscopic and surgical approaches. Like so much in gastroenterology, good management is a team approach.

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- Foster DN, Miloszewski KJA, Losowsky MS. Stigmata of recent haemorrhage in diagnosis and prognosis of upper gastrointestinal bleeding. *BMJ* 1978; i: 1173-77.
- Griffiths WJ, Neumann DA, Welsh JD. The visible vessel as an indicator of uncontrolled or recurrent gastrointestinal haemorrhage. *N Engl J Med* 1979; 300: 1411-13.
- Storey DW, Bown SG, Swain CP, Salmon PR, Kirkham JS, Northfield TC. Endoscopic prediction of recurrent bleeding in peptic ulcers. *N Engl J Med* 1981; 305: 915-16.
- Wara P. Endoscopic prediction of major rebleeding - a prospective study of stigmata of haemorrhage in bleeding ulcer. *Gastroenterology* 1985; 88: 1029-14.
- N.I.H. Consensus Conference. Therapeutic endoscopy and bleeding ulcers. *JAMA* 1989; 262: 1369-72.
- Silverstein FE, Gilbert DA, Tedesco FJ. The national ASGE survey on upper gastrointestinal bleeding. II. Clinical prognostic factors. *Gastrointest Endosc* 1981; 27: 80-93.
- Branicki FJ, Coleman SY, Fok PJ. Bleeding peptic ulcer: a prospective evaluation of risk factors for rebleeding and mortality. *World J Surg* 1990; 14: 262-70.
- Peterson WL. Clinical risk factors. *Gastrointest Endosc* 1990; 36: S14-15.
- Swain CP, Salmon PR, Northfield TC. Does ulcer position influence presentation or prognosis of upper gastrointestinal bleeding? *Gut* 1986; 27: A632.
- Bornman PC, Theodorou NA, Shuttleworth RD, Essel HP, Marks IN. Importance of hypovolumic shock and endoscopic signs in predicting recurrent haemorrhage from peptic ulceration: a prospective evaluation. *BMJ* 1985; 291: 245-47.
- Chang-Chien C, Wu C, Chen P, Lin DY, Chu CM, Fang KM, et al. Different implications of stigmata of recent haemorrhage in gastric and duodenal ulcers. *Dig Dis Sci* 1988; 33: 400-4.
- Papp JP. Endoscopic electrocoagulation in the management of upper gastrointestinal bleeding. *Surg Clin North Am* 1982; 62: 797-805.
- Lin HJ, Perng CL, Lee SD. The predictive factors of rebleeding in peptic ulcer with non bleeding visible vessel: a prospective observation, with emphasis on the size and colour of the vessel. *Gastroenterology* 1992; 102: A113.
- Freeman ML, Cass OW, Peine CJ, Onstad GR. The non-bleeding visible vessel versus the sentinel clot: natural history and risk of rebleeding. *Gastrointest Endosc* 1993; 39: 359-66.
- Laine L, Freeman M, Cohen H. Interobserver agreement for stigmata of recent haemorrhage: a prospective evaluation in 202 endoscopists. *Gastrointest Endosc* 1993; 39: A281.
- Beckly DE, Casebow MP. Prediction of rebleeding from peptic ulcer: experience with an endoscopic doppler device. *Gut* 1986; 27: 96-9.
- Kohler B, Riemann JF. The endoscopic doppler: its value in evaluating gastroduodenal ulcers after haemorrhage and as an instrument of control of endoscopic injection therapy. *Scand J Gastroenterol* 1991; 26: 471-76.
- Fullarton GM, Murray WR. Prediction of rebleeding in peptic ulcers by visual stigmata and endoscopic doppler ultrasound criteria. *Endoscopy* 1990; 22: 68-71.
- Swain CP. Pathophysiology of bleeding lesions. *Gastrointest Endosc* 1990; 36: S21-22.
- Vallon AG, Cotton PB, Laurence BH, Armengol-Miro JR, Saloro-Uses JC. Randomised trial of endoscopic Argon laser photocoagulation in bleeding peptic ulcers. *Gut* 1981; 22: 228-33.
- Swain CP, Bown SG, Storey DW, Kirkham JS, Salmon PR, Northfield TC. Controlled trial of Argon laser photocoagulation in bleeding peptic ulcer. *Lancet* 1981; ii: 1313-16.
- Dixon JA, Berenson MM, McCloskey KW. Neodimium-YAG laser treatment of experimental canine gastric bleeding. Acute and chronic studies of photocoagulation, penetration and perforation. *Gastroenterology* 1979; 77: 641-51.
- Swain CP, Bown SG, Salmon PR, Kirkham JS, Northfield TC. Controlled trial of Nd-Yag laser photocoagulation for bleeding peptic ulcer. *Lancet* 1986; i: 1113-16.
- Rutgeerts P, Vantrappen G, Broeckart L. Controlled trial of YAG laser treatment of upper digestive haemorrhage. *Gastroenterology* 1982; 83: 410-16.
- Macleod IA, Mills PR, Mackenzie JE, Joffe SN, Russell RI, Carter DC. Neodidium yttrium aluminium garnet laser photocoagulation for major haemorrhage from peptic ulcers and single vessels. A single blind controlled trial. *BMJ* 1983; 286: 345-48.
- Mathewson K, Swain CP, Bland M, Kirkham JS, Bown SG, Northfield TC. Randomised comparison of Nd-Yag laser, heater probe and no endoscopic therapy for bleeding peptic ulcer. *Gastroenterology* 1990; 98: 1239-44.
- Krejs GJ, Little KH, Westergaard H, Hamilton JK, Spady DK, Polter DE. Laser photocoagulation for the treatment of acute peptic-ulcer bleeding. *N Engl J Med* 1987; 316: 1618-21.
- Cook DJ, Guyatt GH, Salena BJ, Laine LA. Endoscopic therapy for acute noncariceal upper gastrointestinal haemorrhage: A meta analysis. *Gastroenterology* 1992; 102: 139-148.
- Freitas D, Donato A, Monteiro JG. Controlled trial of liquid monopolar electrocoagulation in bleeding peptic ulcers. *Am J Gastroenterol* 1985; 80: 853-57.
- Moreto M, Zaballa M, Ibanez S, Setien F, Figa M. Efficacy of monopolar electrocoagulation in the treatment of bleeding gastric ulcer: a controlled trial. *Endoscopy* 1987; 19: 54-56.
- Papp JP. Endoscopic electrocoagulation in the management of upper gastrointestinal tract bleeding. *Surg Clin North Am* 1982; 62: 797-806.
- Kernohan RM, Anderson JR, McKelvey STD, Kennedy TL. A controlled trial of bipolar electrocoagulation in patients with upper gastrointestinal bleeding. *Br J Surg* 1984; 71: 889-91.
- Goudie BM, Mitchell KG, Birnie GG, Mackay C. Controlled trial of endoscopic bipolar electrocoagulation in the treatment of bleeding peptic ulcer. *Gut* 1984; 25: A1185.
- Laine LA. Multipolar electrocoagulation of active upper gastrointestinal tract haemorrhage. A prospective controlled trial. *N Engl J Med* 1987; 316: 1613-17.
- Laine LA. Multipolar electrocoagulation in the treatment of ulcers with non-bleeding visible vessels; a prospective controlled trial. *Ann Intern Med* 1989; 110: 510-14.
- Laine LA. Determination of the optimum technique for bipolar electrocoagulation treatment. *Gastroenterology* 1991; 100: 107-12.
- Storey DW. Endoscopic control of peptic ulcer haemorrhage using the heater probe. *Gut* 1983; 24: A967-68.
- Shorvon PJ, Leung JW, Cotton PB. Preliminary experience with the heater probe at endoscopy in acute upper gastrointestinal bleeding. *Gastrointest Endosc* 1985; 31: 364-6.
- Fullarton GM, Birnie GG, Macdonald A, Murray WR. Controlled trial of heater probe treatment in bleeding peptic ulcers. *Br J Surg* 1989; 76: 514-44.
- Jensen DM, Machicada GA, Kovacs TOG. Controlled, randomised study of heater probe and BICAP for haemostasis of severe ulcer bleeding. *Gastroenterology* 1988; 94: A208.
- Chung SCS, Leung FW, Leung JWC. Is vasoconstriction the mechanism of haemostasis in bleeding ulcers injected with epinephrine? A study using reflectance spectrophotometry. *Gastrointest Endosc* 1988; 34: 174-75.
- O'Brien JR. Some effects of adrenaline and anti-adrenaline compounds on platelets in vitro and vivo. *Nature* 1963; 200: 763-64.
- Rutgeerts P, Geboes K, Vantrappen G. Experimental studies of injection therapy for severe non-variceal bleeding in dogs. *Gastroenterology* 1989; 97: 610-21.
- Randall GM, Jensen DM, Hirabayashi K, Machicada GA. Controlled study of different sclerosing agents for coagulation of canine gut arteries. *Gastroenterology* 1989; 96: 1274-81.
- Rajgopal C, Lessels A, Palmer KR. Mechanism of action of injection therapy for bleeding peptic ulcer. *Br J Surg* 1992; 79: 782-84.
- Chung SCS, Leung JWC, Steel RJ, Croft TJ, Li AKC. Endoscopic injection of adrenaline for actively bleeding ulcers: a randomised trial. *BMJ* 1988; 299: 1631-33.
- Steele RJ, Logie JR, Munro A, Nichols DM. Endoscopic haemostasis in non-variceal upper gastrointestinal haemorrhage using adrenaline injection. *J R Coll Surg Edin*. 1989; 34: 133-36.
- Panes J, Vivier J, Forne M, Garcia-Olivares E, Marco C, Garan J. Controlled trial of endoscopic sclerosis in bleeding peptic ulcer. *Lancet* 1987; ii: 1292-94.
- Balanzo J, Sainz S, Such J. Endoscopic haemostasis by local injection of epinephrine and polidocanol in bleeding ulcer: a prospective randomised trial. *Endoscopy* 1988; 20: 289-91.
- Rajgopal C, Palmer KR. Endoscopic injection sclerosis: effective therapy for bleeding peptic ulcer. *Gut* 1991; 32: 727-29.
- Oxner RBG, Simmonds NJ, Gertner DJ, Nightingale JMD, Burnham WR. Controlled trial of endoscopic injection treatment for bleeding from peptic ulcers with visible vessels. *Lancet* 1992; 339: 966-68.
- Wordehoff D, Gros H. Endoscopic haemostasis by injection therapy in high risk patients. *Endoscopy* 1982; 14: 196-99.
- Sugawa C, Fugita Y, Ikeda T, Walt AJ. Endoscopic haemostasis of bleeding of the upper gastrointestinal tract by local injection of ninety-eight percent dehydrated ethanol. *Surg Gynecol Obstet* 1986; 162: 159-63.
- Pascu O, Draghici A, Acalovchi I. The effect of endoscopic haemostasis with alcohol on the mortality of nonvariceal upper gastrointestinal haemorrhage: a randomised prospective study. *Endoscopy* 1989; 21: 53-55.
- Choudari CP, Palmer KR. Endoscopic injection therapy for bleeding peptic ulcer: a comparison of adrenaline alone with adrenaline plus ethanolamine oleate. *Gut* 1994; 35: 608-10.
- Chung SCS, Leung JWC, Leong HT, Lo KK, Li AKC. Adding a sclerosant to endoscopic epinephrine injection in actively bleeding ulcers: a randomised trial. *Gastrointest Endosc* 1993; 39: 611-15.
- Rutgeerts P, Vantrappen G, Broekaert L, Coremans C, Janssens J, Hiele M. Comparison of endoscopic polidocanol injection and YAG laser therapy for bleeding peptic ulcers. *Lancet* 1989; i: 1164-67.
- Chiozzini G, Bortoluzzi F, Pallini P, Betetto G, Costantini R, Costa F et al. Controlled trial of absolute ethanol vs epinephrine as injection agent in gastroduodenal bleeding. *Gastroenterology* 1989; 96: A86.

- 59 Rutgeerts P, Gevers AM, Hiele M. Injection therapy for prevention of rebleeding from peptic ulcers with protruding vessel: which method is best? *Gastroenterology* 1990; **98**: A115.
- 60 Lin HJ, Perng CL, Lee FY. Endoscopic injection for the arrest of peptic ulcer haemorrhage: final results of a prospective, randomised comparative trial. *Gastrointest Endosc* 1993; **39**: 15–19.
- 61 Levy J, Khakoo S, Barton R, Vicary R. Fatal injection sclerotherapy of a bleeding peptic ulcer. *Lancet* 1991; **37**: 504.
- 62 Loperfids S, Patelli G, La Torre L. Extensive necrosis of gastric mucosa following injection therapy of bleeding peptic ulcer. *Endoscopy* 1990; **22**: 285–86.
- 63 Chester JF, Hurley PR. Gastric necrosis: a complication of endoscopic sclerosis for bleeding peptic ulcer. *Endoscopy* 1990; **22**: 287.
- 64 Chung SCS, Leung JWC, Sung JY, Lo KK, Li AKC. Injection of heater probe for bleeding ulcer. *Gastroenterology* 1991; **100**: 33–37.
- 65 Villanueva C, Balanzo J, Torras X, Soriano G, Sainz S, Vilardell F. Value of second-look endoscopy after injection therapy for bleeding peptic ulcer: a prospective and randomised trial. *Gastrointest Endosc* 1994; **40**: 34–39.
- 66 Waring JP, Sanowski RA, Sawyer RL, Woods CA, Foutch PG. A randomised comparison of multipolar electrocoagulation and injection sclerosis for the treatment of bleeding peptic ulcer. *Gastrointest Endosc* 1991; **37**: 295–98.
- 67 Lin HJ, Lee FY, Kang WM, Tsai YT, Lee SD, Lee CH. Heat probe thermocoagulation and pure alcohol injection in massive peptic ulcer haemorrhage: a prospective, randomised controlled trial. *Gut* 1990; **31**: 753–57.
- 68 Choudari CP, Rajgopal C, Palmer KR. Comparison of endoscopic injection therapy versus the heater probe in major peptic ulcer haemorrhage. *Gut* 1992; **33**: 1159–61.
- 69 Laine LA. Multipolar electrocoagulation vs injection therapy in the treatment of bleeding peptic ulcers: a prospective, randomised trial. *Gastroenterology* 1990; **99**: 1303–06.
- 70 Lin HJ, Tsai YT, Lee SD. A prospective randomised trial of heat probe thermocoagulation versus pure alcohol injection in nonvariceal peptic ulcer haemorrhage. *Am J Gastroenterol* 1988; **83**: 283–86.
- 71 Hui WM, Ng MMT, Lok ASF, Lai CL, Lau YN, Lam SKA. A randomised comparative study of laser photocoagulation, heater probe, and bipolar electrocoagulation in the treatment of actively bleeding ulcers. *Gastrointest Endosc* 1991; **37**: 299–304.
- 72 Chung SCS, Sung JY, Lai CW, Ng EKW, Chan KL, Yung MY. Epinephrine injection alone or epinephrine injection plus heat probe treatment for bleeding ulcers. *Gastrointest Endosc* 1994; **40**: A271.
- 73 Jensen DM, Kovacs T, Randall G, Smith J, Freeman M, Jutabha R. Prospective study of thermal coagulation (gold probe-GP) vs combination injection and thermal (Inj&Gp) treatment of high risk patients with severe ulcer of mallory weiss (MW) bleeding. *Gastrointest Endosc* 1994; **40**: A42.
- 74 Binmoeller KF, Thonke F, Soehendra N. Endoscopic hemoclip treatment for gastrointestinal bleeding. *Endoscopy* 1993; **25**: 167–70.
- 75 Swain CP, Mills TN, Northfield TC. Experimental studies of new mechanical methods of endoscopic haemostasis; stitching, banding, clamping and ulcer removal. *Gut* 1985; **26**: A1151.
- 76 Hepworth CC, Kadirkamanathan SS, Swain CP, Gong F. Comparison of endoscopic mechanical and injection methods of hemostasis on mesenteric vessels. *Gut* 1994; **35** (suppl 2): A T157.
- 77 Choudari CP, Palmer KR. Failures of endoscopic therapy for bleeding peptic ulcer; an analysis of risk factors. *Gut* 1994; **35** (suppl 2): A T150.
- 78 Villanueva C, Balanzo J, Espinos JC. Prediction of therapeutic failure in patients with bleeding peptic ulcer treated with endoscopic injection. *Dig Dis Sci* 1993; **38**: 2062–70.
- 79 Brullet E, Campo R, Bedos G, Barcons S, Gubern JM, Bordas JM, *et al*. Site and size of bleeding peptic ulcer. Is there any relation to the efficacy of haemostatic therapy? *Endoscopy* 1991; **23**: 73–75.