

Table 7. Meta-analyses of randomized trials comparing endoscopic thermal, injection, or clip therapy with no endoscopic therapy or another endoscopic therapy

Endoscopic therapy	Comparator therapy	No. of studies	Risk ratio (95% confidence interval)	
			Further bleeding	Mortality
Endoscopic therapy vs no endoscopic therapy				
Thermal contact with bipolar electrocoagulation or heater probe	No endoscopic therapy	15 (33)	0.44 (0.36–0.54)	0.58 (0.34–0.98)
Absolute ethanol injection	No endoscopic therapy	3 (33)	0.56 (0.38–0.83)	0.18 (0.05–0.68)
Epinephrine + polidocanol injection	No endoscopic therapy	6 (33)	0.60 (0.36–1.00) ^a	0.80 (0.40–1.61)
One endoscopic therapy vs another endoscopic therapy				
Thermal contact with bipolar electrocoagulation or heater probe	Absolute ethanol injection	5 (33)	0.69 (0.47–1.01)	1.60 (0.57–4.52)
Clips	Epinephrine injection	2 (64,65)	0.20 (0.07–0.56)	2.11 (0.60–7.44)
Clips	Thermal contact with bipolar electrocoagulation or heater probe	4 (33)	1.31 (0.36–4.75)	1.16 (0.38–3.52)
Epinephrine injection + second modality	Epinephrine injection	7 (33)	0.34 (0.23–0.50)	0.52 (0.23–1.16)
Argon plasma coagulation ± epinephrine	Epinephrine injection + second modality	3 (67–69)	0.82 (0.21–3.19) ^a	0.85 (0.30–2.33)
^a Heterogeneity ($I^2 > 50\%$).				

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RR = 0.34, 0.23–0.50 in meta-analysis of 7 RCTs (33) (Table 7). Thus, the panel recommends against the use of epinephrine alone. Epinephrine should always be used in combination with another hemostatic modality. Epinephrine is most commonly used in a 1:10,000 dilution, typically injected in 0.5- to 2.0-mL aliquots.

Epinephrine injection combined with other modalities. The panel also considered the question of whether modalities such as thermal contact devices or clips should always be used in combination with epinephrine injection. Endoscopists commonly use epinephrine in patients with active bleeding to reduce bleeding and improve visibility before application of the other modality or in patients with nonbleeding high-risk stigmata to prevent rebleeding during application of the other modality. Meta-analysis of 2 small RCTs comparing epinephrine before bipolar electrocoagulation vs bipolar electrocoagulation alone revealed lower further bleeding with combined therapy (RR = 0.35, 0.18–0.71) without a significant difference in mortality (RR = 0.49, 0.09–2.60) (33). Because rates of further bleeding (25%, 34%) were unusually high in the bipolar monotherapy arms and moderate-quality evidence indicates bipolar electrocoagulation or heater probe monotherapy reduces further bleeding and mortality, the panel did not believe this limited evidence allowed a suggestion that thermal contact devices should always be preceded by epinephrine injection. Meta-analysis of 2 small RCTs comparing clips plus epinephrine vs clips alone revealed no significant difference in further bleeding (RR = 1.10, 0.42–2.88) or mortality (RR = 0.63, 0.10–3.87) (64,78). However, in both studies, epinephrine was injected after clip placement. Some endoscopists use epinephrine after clip application rather than before to avoid local swelling with large volume injection that may make clip application more difficult or to treat residual bleeding after clip placement.

Hemostatic powder spray TC-325. We evaluated hemostatic powder spray, restricting our search to products commercially available in the United States at the time this document was

developed. TC-325 only adheres to actively bleeding lesions, so its use in nonbleeding lesions is likely ineffective (79). A delivery catheter with its tip 1–2 cm from the bleeding site is used to apply TC-325 in 1- to 2-second bursts until the bleeding site is covered and bleeding stops.

Two published RCTs were identified but not relied on because both included routine second-look endoscopies (80,81). We were aware of a large RCT from Lau et al. (82) at the time of our literature search (clinicaltrials.gov NCT02534571), and results of the full trial were subsequently published in 2020. This noninferiority RCT compared TC-325 with standard therapy (clipping or contact thermocoagulation ± previous epinephrine injection) in 224 patients with actively bleeding nonvariceal lesions, including 130 with ulcers. Their primary outcome, further bleeding at 30 days, occurred in 8/65 (12.3%) with TC-325 and 10/65 (15.4%) with standard therapy in patients with ulcers: difference = −3%, −15% to 9%.

Recent guidelines have suggested use of TC-325 as a temporizing measure that should be followed by use of a second definitive hemostatic modality (50,83). This is based on the fact that TC-325 powder sloughs off the mucosa and is eliminated from the GI tract within 24 hours after application (50,79,83) and further bleeding is common in observational studies of TC-325: e.g., 31% (95% CI 26%–37%) in a meta-analysis of 18 observational studies and 2 RCTs (84). By contrast, the results from Lau et al. suggest TC-325 may be effective as a single agent.

Given similar rates of further bleeding for TC-325 vs standard therapies and 95% CIs suggesting no more than a 9% higher rate of further bleeding with TC-325, the panel made a conditional recommendation for hemostatic powder spray TC-325 for actively bleeding ulcers. The panel believes that further research is necessary to confirm that TC-325 could be used as monotherapy, especially in patients with actively spurting bleeding which constituted only a small proportion