Is routine second-look endoscopy effective after endoscopic hemostasis in acute peptic ulcer bleeding? A meta-analysis

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CRD summary
The author concluded that without high-dose proton-pump inhibitor, routine second-look endoscopy appeared effective in patients with very high risk of peptic ulcer bleeding; the generalisability of these results to the patients with bleeding and high-risk stigmata was questionable without high-dose proton-pump inhibitor. The authors' conclusions reflect the evidence presented and seem reliable.

Authors' objectives
To evaluate the effectiveness of routine second-look endoscopy in peptic ulcer bleeding in patients with high-risk stigmata.

Searching
MEDLINE, EMBASE, The Cochrane Library, Cochrane Central Register of Controlled Trials (CENTRAL) and Web of Knowledge databases were searched from 1990 to 2011 for relevant studies published in French and English. Search terms were not reported. Relevant abstracts presented in major conferences were handsearched. Reference lists of the relevant articles were scanned.

Study selection
Randomised controlled trials (RCTs) that compared routine second-look endoscopy (with or without high-dose proton pump inhibitors) with alternate strategies (for example no second-look endoscopy) were eligible. Only patients with peptic ulcer bleeding who showed signs of high-risk stigmata seen at index endoscopy were included. The included studies had to achieve successful haemostasis at the index endoscopy and include re-bleeding as an outcome. Secondary outcomes were surgical intervention and mortality.

Included studies involved patients with bleeding gastric or duodenal ulcers that ranged from Forrest class Ia to IIb: Ia (spurting haemorrhage), Ib (oozing haemorrhage), IIA (visible vessel) and IIb (adherent clot). Two studies recruited high-risk groups of patients. Characteristics of the included studies were comparable to each other except for one study that included men only (other studies included both sexes). The index endoscopy was normally performed within four to 24 hours. Second-look endoscopy was defined as a pre-planned repeated endoscopy performed within 16 to 48 hours after the index endoscopy. Endoscopic treatment included epinephrine injection, thermal coagulation, clips or a combination of epinephrine injection along with thermal coagulation or clips. Most patients received a daily dose of proton-pump inhibitors or intravenous H2 receptor antagonists, where reported.

Two reviewers independently identified and evaluated the relevant studies. Any disagreements were resolved by a third reviewer.

Assessment of study quality
Study quality was assessed using a Jadad scale (5 points) for randomisation, blinding and withdrawals and a generic specific quality score (11 points) that assessed the methodological quality of content-specific components of the study. By combining these two, a maximum score of 16 points could be achieved.

Two reviewers independently assessed study quality. Any disagreements were resolved by involving a third reviewer.

Data extraction
Data were extracted to calculate odds ratios (OR), weighted mean differences (WMD) and their 95% confidence intervals (CI).

It appeared that more than one reviewer extracted the study data.
Methods of synthesis
Pooled odds ratios (OR), weighted mean differences and their 95% CIs were calculated using a fixed-effect model where there was no evidence of heterogeneity; otherwise a random-effects model (DerSimonian-Laird method) was used. Heterogeneity was assessed using $I^2$ statistic ($I^2$ of 25% was considered as low heterogeneity, 50% moderate and 75% high). Publication bias was assessed using Egger’s and Begg’s tests.

Sensitivity analysis was performed to explore heterogeneity by removing one study at a time. Subgroup analyses were also performed to assess the influence of re-bleeding definitions, endoscopic haemostasis methods, high-risk stigmata spectrum, proton-pump inhibitor use on re-bleeding and study quality score.

Results of the review
Eight RCTs were included in the review (938 patients, range 40 to 194). Study quality scores ranged from 4 to 14 (median 8.5). Most patients were monitored until discharge from hospital or up to a 30-day follow-up, where reported.

Routine second-look endoscopy significantly decreased re-bleeding compared with the control group (OR 0.55, 95% CI 0.37 to 0.81; $P=9%$; eight RCTs). Similar results were found when performing sensitivity analysis by removing one trial at a time. However, when removing two studies with high-risks patients, no significant benefit was found for routine second-look endoscopy.

The meta-analysis showed that second-look endoscopy significantly reduced the need for surgery in patients with peptic ulcer bleeding (OR 0.43, 95% CI 0.19 to 0.96; $P=3%$; five trials) but not mortality (five trials), length of hospital stay (one trial) and blood transfusion (five trials).

Subgroup analyses showed the benefit of second-look endoscopy with varying definitions of re-bleeding. However, no significant difference in re-bleeding was found between the two groups with varying endoscopic haemostasis method and proton-pump inhibitor therapies. Re-bleeding was significantly reduced by second-look endoscopy in studies with a lower quality score but not with a higher quality score (>8). There was no evidence of publication bias.

Authors’ conclusions
In the absence of a high-dose proton-pump inhibitor, especially in patients at very high risk (for example, active bleeding), routine second-look endoscopy appeared effective in these selected patients with peptic ulcer bleeding. The generalisability of these results to the era of high-dose proton-pump inhibitor and otherwise unselected patients with high-risk stigmata was unclear.

CRD commentary
The review addressed a clear question and was supported by appropriate inclusion criteria. Relevant sources were searched. Attempts to identify unpublished data minimised the chance of publication bias. Studies in languages other than English and French were not searched for so relevant studies may have been missed. Attempts were made to minimise reviewer bias and errors in the review process. Appropriate criteria were used to assess study quality but details of the quality assessment for each individual study were not reported.

Appropriate methods were used to pool the studies and investigate statistical heterogeneity. Subgroup and sensitivity analyses were performed. The authors acknowledged the significant clinical differences between trials and the small sample size of very high risk cohorts, which can confound outcomes and limit generalisability to present-day practice.

The authors’ conclusions reflect the evidence presented and seem reliable.

Implications of the review for practice and research
Practice: The authors stated that routine second-look endoscopy was not recommended in patients with bleeding and high-risk stigmata and this approach should be reserved for selected patients at particularly increased risk of bleeding (such as those with haemodynamic instability, active bleeding or large ulcers).

Research: The authors did not state any implications for research.

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