

Living FRIendly Summaries of the Body of Evidence using Epistemonikos (FRISBEE)

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Should prophylactic measures to prevent postpolypectomy bleeding after resection of large colorectal polyps be used?

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Abstract

Postpolypectomy bleeding after colonoscopy with resection of large colorectal polyps can cause significant morbidity (readmission for monitoring, transfusion, repeat endoscopy and therapy) and a significant cost to hospitals and insurers. Nevertheless prophylactic endoscopic measures could reduce risk of postpolypectomy bleeding. Searching in Epistemonikos database, which is maintained by screening 30 databases, we identified two systematic reviews including 10 randomized trials. We combined the evidence using meta-analysis and generated a summary of findings table following the GRADE approach. We concluded prophylactic endoscopic measures could be effective in reducing postpolypectomy bleeding after resection of large colorectal polyps.

Problem

Colorectal cancer is the third leading cause of cancer death in Western populations [1],[2]. Colonoscopy has become the most widely accepted method for colon cancer screening because it reduces mortality and the incidence of cancer by identification and removal of precancerous lesions [3],[4],[5],[6],[7],[8].

Bleeding is the most frequently observed complication after polypectomy that can occur early (during and within 24 hours of the procedure) or delayed (usually in the first few days until four weeks after colonoscopy). postpolypectomy bleeding can cause significant morbidity (readmission for monitoring, transfusion, repeat endoscopy and therapy) and a significant cost to hospitals and insurers.

The main predictor of postpolypectomy bleeding is the size of the polyp. For example, for polyps > 20 mm located in the right colon, postpolypectomy bleeding rates exceeding 10% have been reported [9],[10],[11],[12],[13],[14],[15],[16],[17].

Prophylactic measures like adrenaline injection, argon plasma coagulation or mechanical haemostasis (endoclips or endoloops) have been studied. These interventions could reduce risk of bleeding but have not been universally adopted for endoscopists, or recommended in guidelines [18],[19],[20],[21],[22],[23],[24].

Methods

We used Epistemonikos database, which is maintained by screening more than 30 databases, to identify systematic reviews and their included primary studies. With this information we generated a structured summary using a pre-established format, which includes key messages, a summary of the body of evidence (presented as an evidence matrix in Epistemonikos), meta-analysis of the total of studies, a summary of findings table following the GRADE approach and a table of other considerations for decision-making.

Key messages

- Prophylactic measures (adrenaline injection, argon plasma coagulation, endoclips, endoloops) reduce postpolypectomy bleeding risk and possibly reduce length of hospital stay without important adverse effects.
- The indication of prophylactic measures (adrenaline injection, argon plasma coagulation, endoclips, and endoloops) may be associated with a significant increase in the use of resources.

About the body of evidence for this question

What is the evidence. See evidence matrix in Epistemonikos later	We found two systematic reviews [25],[26], which include 10 randomized controlled trials [19],[20],[21],[22],[23],[24],[27],[28],[29],[30].
What types of patients were included	Patients undergoing colonoscopy with resection of colorectal polyps larger than 10 mm.
What types of interventions were included	Prophylactic endoscopic haemostatic measures (adrenaline injection, argon plasma coagulation, endoclips or endoloops).
What types of outcomes were measured	Early (within 24 hours of the procedure) or delayed bleeding (first few days until four weeks after colonoscopy). Presenting as haematochezia, >10% drop in haematocrit or decrease in the level of hemoglobin > 1 mg/d. Length of hospital stay Postpolypectomy syndrome (abdominal pain, fever, leukocytosis, increased C-Reactive Protein, or signs or symptoms of peritoneal irritation 4 to 24 hours after colonoscopic polypectomy with electrocoagulation in the absence of visualized perforation on abdominal computed tomography).

Summary of findings

Information on the effects of endoscopic prophylactic haemostatic measures for postpolypectomy bleeding is based on 13 randomized trials involving 4,899 patients.

Ten studies assessed at least one prophylactic measure versus no prophylaxis; five compared adrenaline versus no intervention or placebo (saline solution injection); one study compared detachable snare (endoloop) versus no intervention; another study compared endoloop or adrenaline versus no intervention; and three studies assessed clips versus no intervention. The remaining three studies compared different prophylactic measures (clips + endoloop versus adrenaline, endoloop + adrenaline versus adrenaline, and argon plasma coagulation versus adrenaline).

All studies reported total postpolypectomy bleeding (early + delayed), and seven studies also informed delayed bleeding. Three studies reported length of hospital stay but the information could only be extracted for two of them. One study also assessed postpolypectomy syndrome [19],[20],[21],[22],[23],[24],[27],[28],[29],[30],[31],[32].

The summary of findings is the following:

- Prophylactic measures (adrenaline injection, argon plasma coagulation, clips or endoloops) are effective in reducing the risk of total postpolypectomy bleeding (early + delayed) after resection of large colorectal polyps. The certainty of the evidence is high.
- Use of prophylactic measures (adrenaline injection, argon plasma coagulation, clips or endoloops) could be effective in reducing the length of hospital stay. The certainty of the evidence is low.
- The use of combined prophylactic mechanical measures (clips or endoloops) or argon plasma coagulation, plus adrenaline could be more effective than single adrenaline injection in reducing the risk of global postpolypectomy bleeding. The certainty of the evidence is low.
- The effect of prophylactic measures on postpolypectomy syndrome is not clear because the certainty of the evidence is very low.

- Prophylactic measures (adrenaline injection, argon plasma coagulation, clips or endoloops) are probably not associated with significant complications. The certainty of the evidence is moderate.

Measures to prevent post-polypectomy bleeding after resection of large colorectal polyps				
Patients	Adults undergoing colonoscopy with resection of colorectal polyps larger than 10 mm			
Intervention	Prophylactic endoscopic haemostatic measures			
Comparison	No prophylactic measures			
Outcomes	Absolute effect*		Relative effect (CI 95%)	Certainty of the evidence (GRADE)
	WITHOUT prophylaxis	WITH prophylaxis		
	Difference: patients per 1000			
Postpolypectomy bleeding **	70 per 1000	27 per 1000	RR 0.42 (0.28 to 0.62)	⊕⊕⊕⊕ ^{1,2} High
	Difference: 43 patients less per 1000 (Margin of error: 27 to 50 less)			
Delayed postpolypectomy bleeding #	25 per 1000	12 per 1000	RR 0.53 (0.27 to 1.03)	⊕⊕⊕○ ¹ Moderate
	Difference: 13 patients less per 1000 (Margin of error: 18 less to 1 more)			
Postpolypectomy syndrome	46 per 1000 ^	6 per 1000	RR 0.12 (0.06 to 0.95)	⊕○○○ ^{1,3,4} Very Low
	Difference: 40 patients less per 1000 (Margin of error: 2 to 43 less)			
Length of hospital stay	5 days	3.3 days	-	⊕⊕○○ ³ Low
	Difference: 1.7 days less (Margin of error: 1.5 to 1.9 days less)			
Adverse effects	Prophylactic measures were not associated with significant complications. ^^		-	⊕⊕⊕○ ³ Moderate

Margin of error = 95% confidence interval (CI).
RR: Risk ratio.
GRADE: evidence grades of the GRADE Working Group (see later in this article)

* The risks **WITHOUT prophylactic measures** are based on the risk of the control group in the included studies. The risk **WITH prophylactic measures** (and its margin of error) is calculated with the relative effect (and its margin of error).

We included patients with **early post-polypectomy bleeding (within 24 hours of the procedure) and **delayed** post-polypectomy bleeding (first few days until 4 weeks after colonoscopy). Presenting as haematochezia or a >10% drop in haematocrit or a decrease in the level of hemoglobin by more than 1 mg/d.

We included only patients with **delayed** post-polypectomy bleeding (usually in the first few days until 4 weeks after colonoscopy).

^The observed abdominal pain baseline risk in the only study that evaluated this outcome [32] was very high. This could be related to the observed lesion morphology (large [up to 40 mm] and flat), that required "piecemeal" endoscopic mucosal resections or endoscopic submucosal dissection (ESD).

^^A study [31] reported thermal damage of the colonic mucosa 3 (4.5%) and colonic perforation 1 (1.5%) but we judged the technique for placing the clips was inappropriate and decided to exclude these results.

¹ The certainty was downgraded by imprecision due to low number of events/patients not reaching optimal information size, and confidence intervals including possible benefits and harm
² The certainty was increased because the magnitude of the association
³ The certainty was downgraded because of risk of bias; absence of blinding by event allocators
⁴ The certainty was downgraded because indirectness (explanation ^)

About the certainty of the evidence (GRADE)*

⊕⊕⊕⊕

High: This research provides a very good indication of the likely effect. The likelihood that the effect will be substantially different† is low.

⊕⊕⊕○

Moderate: This research provides a good indication of the likely effect. The likelihood that the effect will be substantially different† is moderate

⊕⊕○○

Low: This research provides some indication of the likely effect. However, the likelihood that it will be substantially different† is high.

⊕○○○

Very low: This research does not provide a reliable indication of the likely effect. The likelihood that the effect will be substantially different† is very high.

*This concept is also called 'quality of the evidence' or 'confidence in effect estimates'.

† Substantially different = a large enough difference that it might affect a decision.

Other considerations for decision-making

To whom this evidence does and does not apply

- This evidence applies to adult patients undergoing colonoscopy and requiring resection of a colorectal polyp larger than 10 mm (regardless of colorectal lesion morphology or patient's bleeding risk).
- This evidence does not apply to patients presenting with colonic bleeding (active or recent) requiring a therapeutic intervention. Neither applies to patients with colorectal lesions smaller than 10 mm. It should be clarified that in most studies included in our analysis patients had lesions larger than 10 mm with the exception of two studies [28],[30], which also included patients with slightly smaller lesions. We decided to include these studies because their results are consistent and provide relevant information about the intervention.

About the outcomes included in this summary

- Major bleeding and need of surgery were not included in the summary of findings table because none of the published studies informed about these outcomes.
- Three studies reported length of hospital stay. These studies suggested a 1-2 days shorter length of hospital stay. However, they informed the results in a way it was only possible to combine two of them.
- Only one study reported 'abdominal pain/postpolypectomy syndrome' [32].
- All of the studies assessed the incidence of postpolypectomy bleeding and included events in the early and delayed period as the main outcome. The importance of this outcome can be defined as "not critical", since it is likely that most of these constituted minor bleeding events (only 6.8% required transfusion) and therefore of doubtful clinical significance.
- Eight of the studies included in the analysis informed about delayed postpolypectomy bleeding [20],[23],[24],[28],[30],[31],[32],[33]. We consider this outcome as more relevant than early bleeding, because delayed bleeding is thought to be related to scar detachment days after polypectomy, which exposes larger blood vessels with increased risk of major bleeding. Also, in this situation patients could delay medical consultation, which would result in a higher risk.
- Adverse effects associated with prophylactic haemostatic measures were only informed in one study [31] that reported thermal damage of the colonic mucosa in three patients (4.5%) and colonic perforation in one (1.5%). However, we assumed that all included studies evaluated the adverse effects of the intervention and did not found any. Exploring the reasons for this inconsistency we identified the technique for clips placement was inappropriate in the only

study finding adverse effects. In this context, we decided to exclude the results of this study [31] from the corresponding outcome analysis.

Balance between benefits and risks, and certainty of the evidence

- The use of any prophylactic measure reduces the risk of postpolypectomy bleeding and possibly the length of hospital stay, with a certainty of evidence moderate to high for bleeding risk and low for length of hospital stay. The risk of serious complications is probably low, so the balance is clearly in favor of using haemostatic measures.
 - The use of combined prophylactic mechanical measures (clips or endoloops), or argon plasma coagulation plus adrenaline, could be more effective than single adrenaline injection in reducing the risk of total postpolypectomy bleeding. The certainty of the evidence for this comparison is low (analysis not included in the summary of findings table).
-

What would patients and their doctors think about this intervention

- Given the prophylactic measures are not associated with significant complications nor discomfort, we assume that all patients would choose to receive the intervention if it were effective. A satisfaction survey was conducted in one of the studies included in this summary: satisfaction scores were significantly higher in patients who underwent clip placement than in patients who did not [32].
-

Resource considerations

- The intervention involves an increase in direct economic costs which might be relevant in deciding about the implementation of the intervention. According to a rough cost-benefit analysis conducted by the authors of one of the systematic reviews included [26], the routine use of prophylactic measures to prevent postpolypectomy bleeding could be cost effective in some health systems but not all.
 - Considering the above mentioned increase in use of resources, and considering some interventions might not be available in every health system, some endoscopists could choose not to routinely perform prophylactic measures to all patients undergoing resection of colorectal polyps larger than 10 mm and adopt a selective approach based on individual risk (e.g. larger lesions, localization in proximal colon, patients on antiplatelet or anticoagulant therapy).
-

Differences between this summary and other sources

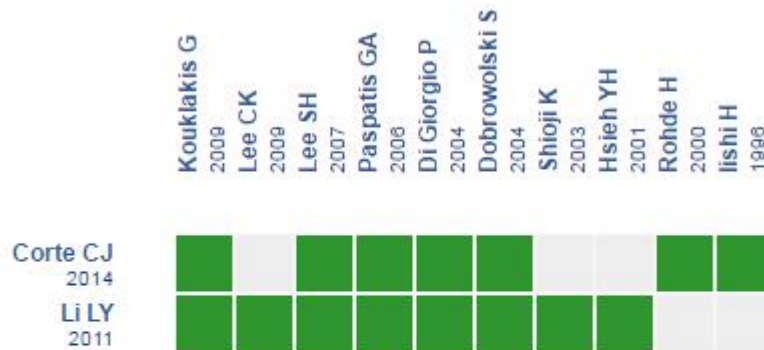
- The findings of the systematic reviews included in the analysis are consistent with each other and conclude that existing evidence suggests a beneficial effect of the intervention. The key messages of our summary are consistent with them.
 - All of the clinical practice guidelines agree on recommending the risk of postpolypectomy bleeding should be minimized. However, specific recommendations made in these guidelines do not favor routine use of prophylactic measures after resection of lesions larger than 10 mm, leaving the decision to the operator after considering degree of experience, and patient's preferences and bleeding risk [18],[34],[35],[36],[37],[38].
-

Could this evidence change in the future?

- The likelihood of future evidence changing the conclusions regarding the use of any prophylactic haemostatic measure is low because of the certainty of the evidence.
 - Ongoing randomized trials may contribute with new information about the efficacy of specific interventions such as the placement of prophylactic hemoclips [39],[40].
 - We identified three additional randomized trials not included in any review [31],[32],[33], so a new systematic review could provide relevant information.
-

How we conducted this summary

Using automated and collaborative means, we compiled all the relevant evidence for the question of interest and we present it as a matrix of evidence.



Starting from any systematic review, Epistemonikos builds a matrix based on existing connections in the database. The author of the matrix can select relevant information for a specific health question (typically in PICO format) in order to display the information set for the question. The rows represent systematic reviews that share at least one primary study, and columns display the studies. The boxes in green correspond to studies included in the respective reviews.

Follow the link to access the **interactive version**: [Prophylactic endoscopic treatments for colorectal postpolypectomy bleeding](#)

Notes

The upper portion of the matrix of evidence will display a warning of "new evidence" if new systematic reviews are published after the publication of this summary. Even though the project considers the periodical update of these summaries, users are invited to comment in *Medwave* or to contact the authors through email if they find new evidence and the summary should be updated earlier. After creating an account in Epistemonikos, users will be able to save the matrixes and to receive automated notifications any time new evidence potentially relevant for the question appears.

The details about the methods used to produce these summaries are described here <http://dx.doi.org/10.5867/medwave.2014.06.5997>.

Epistemonikos foundation is a non-for-profit organization aiming to bring information closer to health decision-makers with technology. Its main development is Epistemonikos database (www.epistemonikos.org).

These summaries follow a rigorous process of internal peer review.

Conflicts of interest

The authors do not have relevant interests to declare.

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