ARTÍCULO ORIGINAL

Efficacy of routine second-look endoscopy after endoscopic hemostasis in patients with acute peptic ulcer bleeding: systematic review and meta-analysis

Eficacia de la endoscopia control de rutina después de la hemostasia endoscópica en pacientes con hemorragia por úlcera péptica aguda: revisión sistemática y meta-análisis

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ABSTRACT

Objective: To evaluate the efficacy of scheduled second-look endoscopy in patients with acute peptic ulcer bleeding (PUB). **Materials and methods:** We systematically search in four databases for randomized controlled trials (RCTs) that evaluated the usefulness of scheduled second-look endoscopy vs. single endoscopy in patients with PUB. Our primary outcome was rebleeding. Secondary outcomes were surgery, mortality, and the number of units of blood transfused (NUBT). All meta-analyses were performed using a random-effects model. Pooled risk ratio (RR) and mean difference (MD), with their 95% confidence intervals (CIs) were calculated for categorical and continuous outcomes, respectively. The risk of bias was assessed using the Cochrane RoB 2.0 tool, and the quality of evidence (QoE) was rated with the GRADE approach. **Results:** Eight full-text RCTs and two RCT abstracts were included (n=1513). We did not find differences in rebleeding (RR, 0.78; 95% CI, 0.53-1.14, moderate QoE), surgery (RR, 0.58; 95% CI, 0.29-1.15, moderate QoE), mortality (RR, 0.89; 95% CI, 0.46-1.71, moderate QoE) or NUBT (MD, -0.01 units; 95% CI, -0.3 to 0.28, low QoE) between second-look and single endoscopy. Sensitivity analyses had similar results to the main analyses. **Conclusions:** Routine second-look endoscopy was not more efficacious than single endoscopy in patients with PUB.
Keywords: Endoscopy; Gastrointestinal hemorrhage; Meta-analysis (source: MeSH NLM).

RESUMEN

Objetivo: Evaluar la eficacia de la endoscopia de revisión programada en pacientes con hemorragia por úlcera péptica aguda (UPA). **Materiales y métodos:** Buscamos de forma sistemática en cuatro bases de datos ensayos controlados aleatorios (ECA) que evaluaran la utilidad de la endoscopia de control programada versus la endoscopia única en pacientes con UPA. Nuestro outcome primario fue el resangrado. Los outcomes secundarios fueron la necesidad de cirugía, la mortalidad y el número de unidades de sangre transfundidas (NUST). Todos los meta-análisis se realizaron mediante un modelo de efectos aleatorios. Se calcularon el riesgo relativo (RR) combinado y la diferencia de medias (DM), con sus intervalos de confianza (IC) del 95% para los resultados categóricos y continuos, respectivamente. El riesgo de sesgo se evaluó mediante la herramienta Cochrane RoB 2.0 y la calidad de la evidencia (QoE) se calificó con el enfoque GRADE. **Resultados:** Se incluyeron ocho ECA de texto completo y dos resúmenes de ECA (n = 1513). No encontramos diferencias en resangrado (RR, 0,78; IC 95%, 0,53-1,14, QoE moderada), cirugía (RR, 0,58; IC 95%, 0,29-1,15, QoE moderada), mortalidad (RR, 0,89; 95% IC, 0,46-1,71, QoE moderada) o NUST (DM, -0,01 unidades; IC del 95%, -0,3 a 0,28, QoE baja) entre la segunda revisión y la endoscopia única. Los análisis de sensibilidad tuvieron resultados similares a los análisis principales. **Conclusiones:** La endoscopia de control de rutina no fue más eficaz que la endoscopia única en pacientes con UPA.
Palabras clave: Endoscopía; Hemorragia gastrointestinal; Meta-análisis (fuente: DeCS Bireme).

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INTRODUCTION

Peptic ulcers are the main cause of upper gastrointestinal bleeding, accounting for almost half of the cases [1]. Endoscopic treatment is the therapy of choice in patients with high-risk bleeding peptic ulcers [2,3]. However, even though the endoscopic approach is effective in achieving initial hemostasis, rebleeding can occur in up to 18% of cases [4].

A scheduled second-look endoscopy in cases of bleeding from peptic ulcer has been proposed to reduce the risk of rebleeding and mortality [5]. Nevertheless, the available evidence has not been able to demonstrate the benefit of its application in daily practice [6]. For this reason, guidelines currently do not recommend the routine performance of a second-look endoscopy but they point out that the necessity of a new endoscopy should be reserved for patients at high risk of rebleeding [2].

New studies on this subject have been published recently, which is why a new updated review is needed. Therefore, we performed this systematic review and meta-analysis of randomized controlled trials (RCTs) to assess the utility of second-look endoscopy in patients with peptic ulcer bleeding (PUB) after initial successful hemostasia.

MATERIALS AND METHODS

This review was reported according to the 2020 PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) statement [7] and was registered on the PROSPERO database (CRD42022363862).

Search strategy

We searched the following four electronic databases: PubMed, Embase, Scopus, and Web of Science; from inception to September 11, 2022. We used the following keywords: "Endoscopy" AND "Gastrointestinal Hemorrhage" AND "Second-Look Surgery". There were no restrictions on language or publication date. Additionally, we conducted a hand-searching of reference lists of all included studies and relevant reviews to identify further studies.

Eligibility criteria

We included RCTs that evaluated the utility of second-look endoscopy in patients with PUB after initial successful hemostasia. Case reports, case series, observational studies, reviews, and editorials were excluded.

Study selection

Articles were downloaded from electronic search to EndNote X8 software. After removing duplicate records, selected studies were uploaded to Rayyan QCRI (https://rayyan.qcri.org/). Two authors screened the studies according to the inclusion and exclusion criteria (HBG and JA). Disagreements were resolved by a third researcher (CDA).

Outcomes

The primary outcome was rebleeding rate. Secondary outcomes were surgery and mortality rates, and the number of units of blood transfused (NUBT). We used study-reported definitions for all outcomes.

Data extraction

Two researchers (HBG and JA) extracted data independently on a previously designed Microsoft Excel® spreadsheet. The following data were extracted: author name, year and country of publication, sample size, type of treatment on the first endoscopy, characteristics of ulcer, and previously described outcomes.

Risk of bias assessment

Assessment of risk of bias will be done using the Cochrane RoB 2.0 tool for RCTs [8]. The RoB 2.0 tool assesses the following five domains: randomization process, deviations from intended interventions, missing outcome data, measurement of the outcome, and selection of the reported result. Overall, each domain and RCT was classified as follows: low risk of bias, some concerns, and high risk of bias, which followed a predetermined algorithm. Two authors (HBG and JA) independently evaluated the risk of bias and any disagreement was resolved by consensus.

GRADE certainty of the evidence

Quality of evidence will be described per outcome using the Grading of Recommendations Assessment, Development, and Evaluation (GRADE) methodology [9]. The GRADE methodology evaluates the following domains per outcome: risk of bias, inconsistency, indirectness, imprecision, and publication bias. The Summary of Findings table of primary and secondary outcomes was elaborated using the GRADEpro software.

Statistical analysis

All meta-analyses were conducted using the inverse variance method and the random effects model. The Paule-Mandel method was used to calculate the between-study variance tau^2. The effects of second-look endoscopy vs. single endoscopy on outcomes were expressed as mean difference (MD) with 95% confidence intervals (95% CIs) for continuous outcomes and as relative risk (RR) with 95% CIs for dichotomous outcomes. Statistical heterogeneity was evaluated using the Chi^2 test (threshold $p < 0.10$) and I^2 statistic, with values of >60% corresponding to substantial heterogeneity. Publication bias were tested with funnel plots and Egger's test if 10 or more studies were available. Sensitivity analyses were performed excluding conference abstracts and RCTs that considered monotherapy on index endoscopy (only epinephrine injection for treatment of PUB) and RCTs that used ranitidine instead of proton pump inhibitor (PPI). All analyses will be performed using R 3.6.3 (www.r-project.org).

RESULTS

Study selection

We found 1739 articles. After the removal of 659 duplicates, 1080 studies underwent title/abstract and

Table 1. Characteristics of included RCTs.

Author, yearref	Type of article	Inclusion criteria	Arm	Number of patients	Male, n	Age, mean (SD)	Time to first EGD	Type of treatment on first EGD	Time to second EGD	Other intervention in both groups	Active bleeding at initial endoscopy, n	Location of ulcer	Recurrent bleeding, n	Need for surgery, n	Mortality, n	Unit of blood transfused, mean (SD)	Size of ulcer, cm (SD)	length of stay (mean SD)	Follow up period
Villanueva, 1994	Full text	I-IIa	Second-look EGD	52	39	62.4 ± 16.4	<4 hours	Epinephrine injection	18-24 hours after 1st EGD	IV ranitidine	17	Gastric: 15 Stomal: 1 Pyloric: 2 Duodenal: 34	11	4	1	1.7 ± 1.9	N.A.	9.3 ± 8.6	Until discharge
			Single EGD	52	33	66.5 ± 13.5					23	Gastric: 12 Stomal: 4 Pyloric: 3 Duodenal: 33	15	8	2	2.5 ± 2.5	N.A.	11.8 ± 10.8	Until discharge
Saeed, 1996	Full text	Ia-IIb with high risk Baylor bleeding score	Second-look EGD	19	N.A.	55.5 ± 34.0	<24 hours	Heater probe ± epinephrine injection	At 24 hours	IV ranitidine	13	Esophageal: 2 Gastric: 6 Duodenal: 11	0	0	1	0	N.A.	N.A.	Until discharge
			Single EGD	21	N.A.	71.3 ± 28.1					14	Esophageal: 0 Gastric: 12 Duodenal: 9	5	0	2	0.9 ± 0.4	N.A.	N.A.	Until discharge
Messmann, 1998	Full text	I-IIb	Second-look EGD	52	29	63.1 ± 6.2	<4 hours	Epiniphrenie injection ± fibrin glue injection	16-24 hours	IV omeprazole twice daily for 48 hours and then oral once daily	25	Gastric: 22 Duodenal: 30	11	3	3	3.5	1.3 ± 0.4	14	4 weeks
			Single EGD	53	34	60.9 ± 5.9					21	Gastric: 24 Duodenal: 29	9	2	2	3.1	1.1 ± 0.3	12	
Chiu, 2003	Full text	I-IIb	Second-look EGD	52	70	68.7 ± 13.9	<24 hours	Epinephrine injection + heater probe	16-24 hours after first EGD	IV omeprazole twice daily for 72 hours	100	Gastric: 44 Duodenal: 56	5	1	2	1.9 ± 1.7	1.0 ± 0.5	8.4 ± 16.3	30 days
			Single EGD	52	62	67.5 ± 12.6					94	Gastric: 40 Duodenal: 54	13	6	2	2.1 ± 2.3	0.9 ± 0.5	8.4 ± 16.3	
Chiu, 2016	Full text	I-IIb	Second-look EGD	152	114	67.4	<24 hours	Epinephrine injection + heater probe or hemoclips	16-24 hours after first EGD	First first group: IV omeprazol twice daily for 72 hours. Second group: IV omeprazol 8 mg/h foro 72 hours	65	Gastric: 0 Duodenal: 91 Anastomic: 6	12	3	3	1.9 ± 2.4	1.0 ± 0.6	14 ± 35.6	30 days
			Single EGD	153	117	67.1					70	Gastric: 60 Duodenal: 87 Anastomic: 5	10	6	8	2.2 ± 2.7	1.2 ± 0.8	10.3 ± 24.4	
Belei, 2017	Full text	I-IIb (between 2 and 18 yo)	Second-look EGD	63	24	9.7 ± 1.5	<24 hours	Epinephrine injection + hemoclips	12-24 hours after first EGD	First group: esomeprazole 0.5mg/kg twice dialy for 72 hours. Second group: 1 mg/kg IV bolus followed by 0.1 mg/kg/h continuous infusion for 72 hours (for children >40 kg or age <12 yo, the standard dose was used)	26	Gastric: 15 Duodenal: 48	4	2	N.A.	N.A.	0.8 ± 0.6	N.A.	30 days
			Single EGD	64	23	10.5 ± 1.2					26	Gastric: 13 Duodenal: 51	3	1	N.A.	N.A.	1.0 ± 0.5	N.A.	
Park, 2018	Full text	I-IIb	Second-look EGD	158	124	58.4 ± 16.6	<24 hours	Epinephrine or fibrin glue injection + hemoclips or thermal coagulation	24-36 hours after first EGD	IV pantoprazol or esomperazol twice daily	66	Gastric: 92 Duodenal: 66	16	0	2	2.4 ± 1.7	N.A.	17.3 ± 42.2	30 days
			Single EGD	161	120	58.7 ± 18.3					65	Gastric: 101 Duodenal: 60	9	1	2	2.2 ± 1.6	N.A.	18 ± 45.9	
Pittayanon, 2022	Full text	I-IIb (at high risk of recurrent bleeding)	Second-look EGD	75	55	71.3 ± 12.0	N.A.	Hemoclips or thermal coagulation ± Epinephrine injection	The next morning	IV PPI twice daily for 72 hours	70	Angular incisura: 15 Lesser curve: 6 Posterior duodenal bulb: 16 Other sites: 38	9	0	6	9 ± 23.7	20.5 ± 35.6	19.5 ± 47.4	30 days
			Single EGD	76	57	73.0 ± 14.0					75	Angular incisura: 8 Lesser curve: 7 Posterior duodenal bulb: 23 Other sites: 38	14	0	3	6.3 ± 15.6	18 ± 28.1	28.8 ± 73.5	
Lin, 1996	Abstract	Bleedind ulcers	Second-look EGD	60	N.A.	N.A.	<48 hours	Epinephrine injection	N.A.	Ranitidine	N.A.	N.A.	4	N.A.	N.A.	N.A.	N.A.	N.A.	N.A.
			Single EGD	55	N.A.	N.A.					N.A.	N.A.	12	N.A.	N.A.	N.A.	N.A.	N.A.	
Lee, 2005	Abstract	I-IIb	Second-look EGD	70	N.A.	N.A.	N.A.	Epinephrine injection + hemoclips	N.A.	N.A.	N.A.	N.A.	7	N.A.	N.A.	N.A.	N.A.	N.A.	30 days
			Single EGD	73	N.A.	N.A.					N.A.	N.A.	12	N.A.	N.A.	N.A.	N.A.	N.A.	

Identification of studies via databases and registers
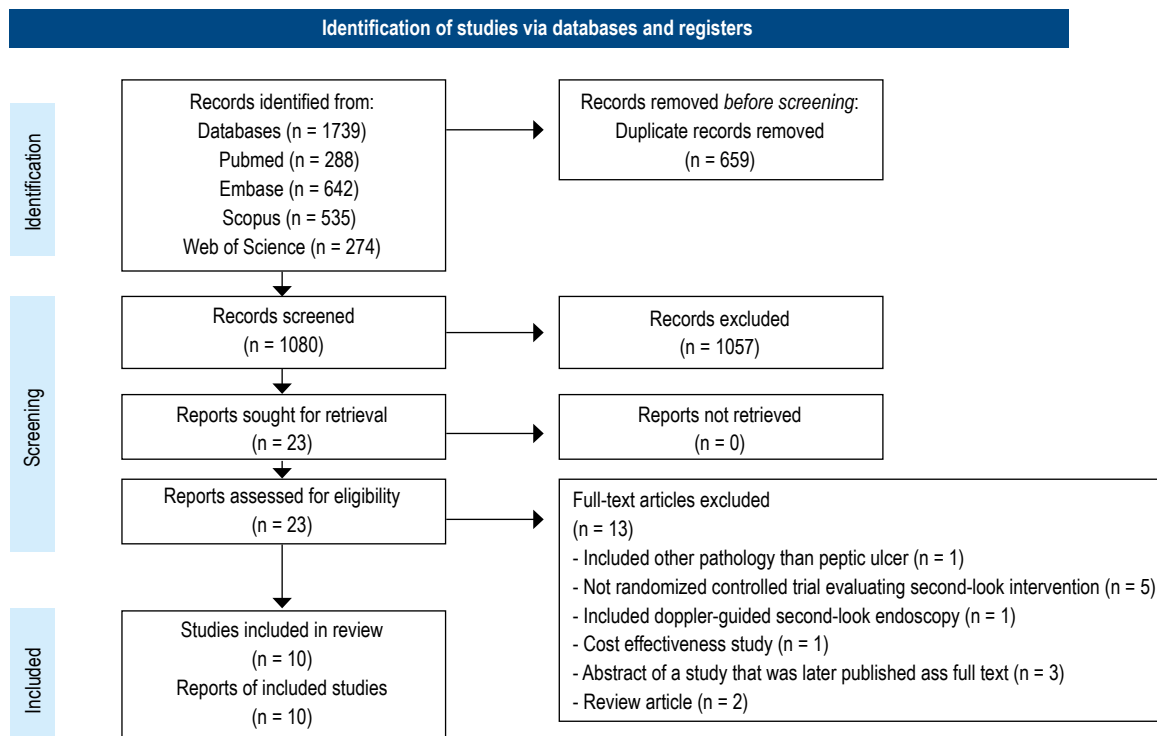

Figure 1. Flow diagram of study selection.

full-text screening. After the screening of studies by title/abstract, 1059 articles were excluded. After the full-text assessment of 23 articles, 13 articles were excluded. Finally, we included 10 studies [10-19] for analysis (Figure 1).

Study characteristics

The main characteristics of the 10 studies [10-19] are summarized in Table 1. The sample size varied from 40 to 305 participants. The mean age ranged from 9.7 to 73 years and 74% of patients were men. Two studies included only a single initial endoscopic treatment (epinephrine injection) [10,18]. Most of the studies performed the second-look endoscopy within the first 24-36 hours. The types of treatment used to achieve initial hemostasis were epinephrine injection, heater probe, fibrine glue injection, and hemoclips. Three studies included the use of ranitidine [10,11,18] instead of PPI. One study did not describe the type of acid-suppressing medicine used [19]. The follow-up time ranged from the discharge of the patient to 4 weeks after the index bleed.

Risk of Bias Assessment

All RCTs were evaluated as of low risk of bias for all domains. There was no evidence of publication bias.

Effect of second-look endoscopy on the primary outcome

Ten studies reported data on rebleeding (n=1513) [10-19]. Second-look endoscopy did not significantly reduce rate of rebleeding (RR 0.78; 95% CI, 0.53-1.14), with moderate heterogeneity (I^2=40%) (Figure 2).
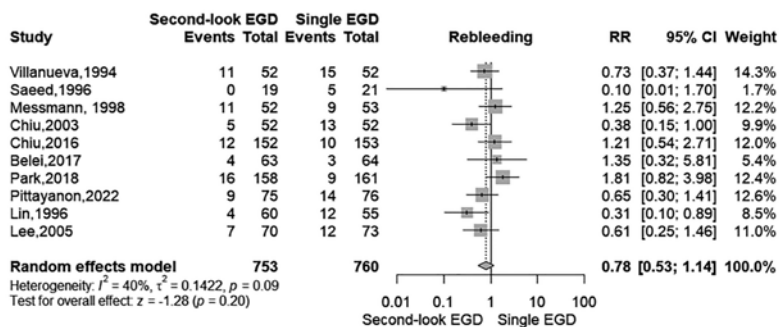
EGD: endoscopy; RR: relative risk; CI: confidence interval.

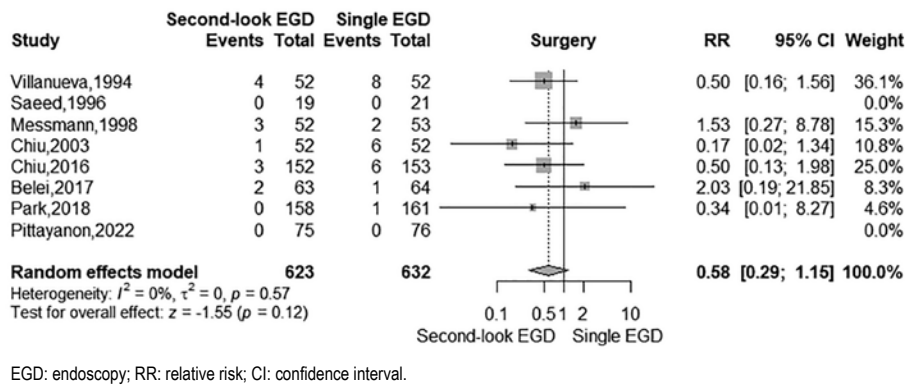**Figure 2.** Effect of second-look vs single EGD on rebleeding.

Figure 3. Effect of second-look vs. single EGD on surgery rates in full-text RCTs.

When conference abstracts were excluded [18,19], the effect on rebleeding remained not significant (RR 0.90; 95% CI, 0.60-1.34), with no substantial heterogeneity (I^2=36%). The results were similar when including studies that only applied combination therapy for the treatment of bleeding ulcers (RR 0.88; 95% CI, 0.57-1.35; I^2=38%) [11-17,19] and when including only studies that used PPI instead of ranitidine (RR 0.99; 95% CI, 0.63-1.55; I^2=36%) [12-17].

Effect of second-look endoscopy on secondary outcomes

Eight studies reported data on the effect of second-look endoscopy on surgery (n = 1255) [10-17]. Second-look endoscopy did not significantly reduce the rate of surgery (RR 0.58; 95% CI, 0.29-1.15), with no substantial heterogeneity (I^2=0%) (Figure 3). Seven studies reported data on the effect of second-look endoscopy on mortality (n=1128) [10-14,16,17]. Second-look endoscopy did not significantly reduce the rate of mortality (RR 0.89; 95% CI, 0.46-1.71), with no substantial heterogeneity (I^2=0%) (Figure 4). Effects on surgery and mortality were the same

when including studies that only applied combination therapy and when including only studies that used PPI.

Six studies reported data on the effect of second-look endoscopy on the number of units of blood transfused (n=977) [10-14,16]. Second-look endoscopy did not significantly reduce the number of units of blood transfused (MD -0.01 units; 95% CI, -0.3-0.28), with moderate heterogeneity (I^2=53%). Effect was the same when including only studies that used PPI.

GRADE summary of findings

Rebleeding, surgery, and mortality had a moderate certainty of the evidence. Only the number of units of blood transfused was judged as low certainty of the evidence (Table 2).

DISCUSSION

Our systematic review and meta-analysis, with 1513 patients from eight full-text RCTs and two RCT abstracts,
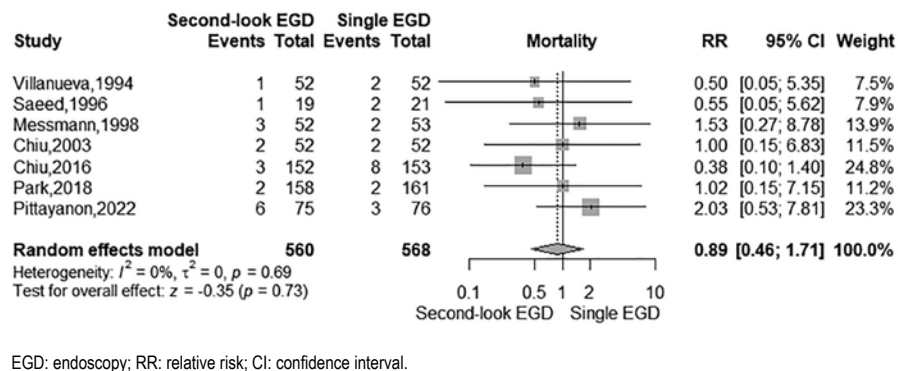

Figure 4. Effect of second-look vs. single EGD on mortality rates in full-text RCTs.

Table 2. Summary of findings of quality of evidence of primary and secondary outcomes.

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	№ of participants (studies)	Certainty of the evidence (GRADE)
	Risk with Single EGD	Risk with Second-look EGD			
Rebleeding follow-up: 30 days	13 per 100	10 per 100 (7 to 15)	RR 0.78 (0.53 to 1.14)	1513 (10 RCTs)	⊕⊕⊕◯ Moderatea
Surgery follow-up: 30 days	4 per 100	2 per 100 (1 to 4)	RR 0.58 (0.29 to 1.15)	1255 (8 RCTs)	⊕⊕⊕◯ Moderatea
Mortality follow-up: 30 days	4 per 100	3 per 100 (2 to 6)	RR 0.89 (0.46 to 1.71)	1128 (7 RCTs)	⊕⊕⊕◯ Moderatea
Number of units of blood transfused follow-up: 30 days	The mean number of units of blood transfused was 0 Units of blood	MD 0.01 Units of blood fewer (0.3 fewer to 0.28 more)	-	977 (6 RCTs)	⊕⊕◯◯ Lowa,b

EGD, endoscopy; RR, relative risk; CI, confidence interval; MD, mean difference.
Explanations:
a. Wide 95% CI
b. Moderate heterogeneity (I2 = 53%), p = 0.07

examined the effect of a scheduled second-look endoscopy in patients after initial successful hemostasia of bleeding ulcers. A scheduled second-look endoscopy did not significantly reduce the risk of rebleeding, surgery, mortality, and NUBT.

The performance of a scheduled second-look endoscopy after initial hemostasis of an ulcer bleeding is defined as the programmed repetition of a new endoscopy within 24 hours following the index endoscopy [2]. Originally this strategy was proposed for selected patients considered to be at high risk of recurrent bleeding to reduce the risk of rebleeding and mortality [5]. However, although some studies initially suggested the benefit of this approach [18,19], recent studies have failed to demonstrate economic or clinical benefit [6,20].

In a previous meta-analysis that included eight RCTs, Ouali *et al.* demonstrated the effectiveness of second-look endoscopy to prevent rebleeding (OR 0.55; 95% CI, 0.37-0.81) in the absence of high-dose PPI and in selected patients who were at high risk [21]. Ouali et al. also identified that of the three studies that reported a reduction in the risk of rebleeding, one lacked sufficient information to analyze it [18] and the other two included patients at extreme risk of rebleeding or very ill patients [11,13]; and when they performed the analysis removing these last two studies, no benefit was found. Moreover, these last two studies did not use the currently recommended high-dose PPI treatment [11,13].

H2 receptor antagonist as ranitidine is not recommended in the management of upper gastrointestinal bleeding after successful endoscopy and in former reviews, the superiority of the use of PPI was demonstrated [22,23]. In our study, three RCTs used ranitidine instead of PPI [10,11,18], but when we removed them from the analysis, there was also no benefit of performing a second-look endoscopy (RR 0.99; 95% CI, 0.63-1.55; I²=36%).

In vitro data suggests that an intragastric pH above 6 is required for promoting clot formation [24,25], and currently, the use of high-dose PPI therapy is recommended intermittently or continuously for three days after the index endoscopy [2,3]. In our review, two studies included a group of patients that received bolus plus continuous infusion of PPI in addition to a group that received the dose intermittently [14,15]. It could be speculated that patients that received infusion doses may have better prognosis than patients who do not, however, in a previous meta-analysis by Sachar et al. was found that these two kinds of administration of PPI are comparable [26].

International consensus indicates that a second endoscopy should be performed in selected cases guided by clinical judgment. A recent guideline from the American College of Gastroenterology did not include in their recommendations the performance of a new endoscopy on a scheduled basis after initial hemostasis [3]. The European Society of Gastrointestinal Endoscopy (ESGE) did not recommend a second routine endoscopy either but points out that it can be used in patients with a high risk of recurrent bleeding [2].

We must direct our approach to identify which patients can be considered ideal for a second-look endoscopy. Park *et al.* in a multivariate analysis identified three independent risk factors of rebleeding that may determine the need for a second-look endoscopy: unsatisfactory initial endoscopic hemostasis measured by expert endoscopists, use of nonsteroidal anti-inflammatory drugs, and larger amounts of transfused blood (≥4 units of red blood cells) [16]. Kim *et al.* included patients with a high risk of rebleeding defined as a Forrest classification above IIb and after a multivariate analysis found that the use of non-steroidal anti-inflammatory agents and larger transfusion volume (≥5 units of red blood cells) were risk factors for rebleeding [27].

In a recent RCT, Pittayanon *et al.* applied a tool to identify patients at increased risk of rebleeding for inclusion in the study and found a smaller number of patients with rebleeding in the group that underwent a second endoscopy, but without significant differences (9/75 [12.0%] vs. 14/76 [18.4%], p=0.281) [17]. They also found no differences between the rate of surgeries, NUBT, or mortality. It is important to highlight that in this study the NUBT was greater than that reported in other previous studies [median (range); 2 (0-32) vs 2 (0-21), p=0.853]. However, despite being higher than usual, there was no significant difference in NUBT between the group with a second-look endoscopy and the control group.

In addition, the ESGE recommends performing a second-look endoscopy in cases of patients with ulcers with active bleeding in the initial endoscopy, in case of incomplete examinations due to poor visualization, and in cases where the source of bleeding was not determined [2].

Should endoscopists perform routine second-look endoscopy in all patients or patients with a high-risk of rebleeding? Currently, the evidence has not shown a greater benefit in terms of rebleeding or mortality. However, we believe that this strategy can be applied in some selected patients according to the clinical criteria of the endoscopist. For example, in cases with suboptimal treatments or unsatisfactory initial endoscopic hemostasis. In addition, studies should continue to be carried out to identify who are the patients who can benefit from this approach.

It is also important to recognize that we currently have multiple endoscopic tools that allow us to achieve adequate hemostasis in cases of rebleeding such as over-the-scope-clips or hemostatic powders [28,29]. The availability of these devices has changed the management of PUB, letting us to reduce the number of surgical interventions in cases of refractory bleeding. However, the decision to use one of these tools should be based on a careful assessment of the patient's condition, the expertise and resources available.

To our knowledge, this is the most updated systematic review assessing the usefulness of the performance of a second-look endoscopy after index endoscopic We found that a scheduled second-look endoscopy did not significantly reduce the risk of rebleeding, surgery, mortality, and NUBT. However, our study has some limitations. First, we included two RCTs that were only available as abstracts [18,19], but when we performed the analysis without the data from these studies, the results were similar. Second, the definitions of rebleeding vary between studies. However, it is understood that patients who experience rebleeding will require additional intervention to control gastrointestinal bleeding. Third, the endoscopic therapy to achieve initial hemostasis was not the same in all the studies, which may increase the heterogeneity of the results. Fourth, three studies included the use of ranitidine as adjuvant therapy and a fourth study did not state what type of intravenous treatment

the patients included received. Finally, some studies used different scores to identify patients at higher risk of rebleeding who may benefit from second-look endoscopy.

In conclusion, our study shows that routine second-look endoscopy was not more efficacious than single endoscopy in patients with PUB. However, performing a routine second-look endoscopy can be reserved for selected cases according to the clinical criteria of the endoscopist.

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