REVISTA ESPAÑOLA DE
ENFERMEDADES DIGESTIVAS
The Spanish Journal of Gastroenterology

Title:
Vonoprazan vs. lansoprazole for the treatment of endoscopic submucosal dissection induced gastric ulcer: a systematic review and meta-analysis

Authors:
Tiaotiao Miao, Yao Zhang, Lin Bai, Xiangqian Yang , Xinli Wen

DOI: 10.17235/reed.2022.8863/2022
Link: PubMed (Epub ahead of print)

Please cite this article as:
Miao Tiaotiao, Zhang Yao, Bai Lin, Yang Xiangqian, Wen Xinli. Vonoprazan vs. lansoprazole for the treatment of endoscopic submucosal dissection induced gastric ulcer: a systematic review and meta-analysis. Rev Esp Enferm Dig 2022. doi: 10.17235/reed.2022.8863/2022.

REVISTA ESPAÑOLA DE
ENFERMEDADES DIGESTIVAS
The Spanish Journal of Gastroenterology

Vonoprazan *vs.* lansoprazole for the treatment of endoscopic submucosal dissection induced gastric ulcer: a systematic review and meta-analysis

Tiaotiao Miao[1] * Yao zhang[2] Lin Bai[1] Xiangqian Yang[1] Xinli Wen[2] *

[1] Shaanxi University of Chinese Medicine, Xian Yang, Shaanxi, 712046, China.

[2]Shaanxi Hospital of Traditional Chinese Medicine, Xi 'an, Shaanxi, 710000, China.

* The first two authors contributed equally for this work.

Corresponding author: Xinli Wen

E-mail address: wxli696@126.com. Tel: 15591821695

Abstract

Background: Vonoprazan is a potassium competitive acid blocker (P-CAB) approved in Japan in 2014 to treat endoscopic submucosal dissection (ESD)-induced ulcer and bleeding or perforation. Therefore, this meta-analysis is aimed to determine that whether Vonoprazan is more effective than lansoprazole in the treatment of ESD-induced ulcers which include ulcer healing , shrinking rate and so on. **Methods:** Randomized controlled trials (RCT) and retrospective studies were collected from the PubMed (Medline), Embase, Web of science, and Cochrane Library databases. Meanwhile, studies were selected according to predetermined qualification criteria and data were extracted by two researchers. We evaluated the quality of the methods for published papers using the modified Jadad scale. **Results:** There were five studies included in this meta-analysis, the ulcer healing rate effect was not significantly higher in the intervention groups than in the control groups at 4 weeks, [OR：1.07 (0.51, 2.22), 95% CI, I^2=2%, Z=0.18, *P*=0.86]. There was no significant difference in the ulcer shrinkage rate at 4 weeks [MD：0.20 (-1.51, 1.92), 95% CI, I^2=0%, *P*=0.82] and 8 weeks [MD: -0.09 (-0.30, 0.12), 95% CI, I^2=0%, *P*=0.39]. **Conclusion:** There were no significant difference between Vonoprazan and lansoprazole in the ulcers induced by treatment at 4 weeks and 8 weeks after treatment with ESD.

Keywords: Gastric ulcer. Meta-analysis. Vonoprazan. Lansoprazole. ESD. Systematic review.

1. Introduction

Endoscopic submucosal dissection (ESD) which developed in Japan in the 1990s, is an advanced procedure and has been widely accepted as a novel minimally invasive endoscopic surgical procedure for epithelial gastric adenoma and early gastric cancer (EGC) [1-2]. [1-2]. This technology has now been widely used such as China, South Korea and the other western countries. In Japan, ESD is better than conventional endoscopic resection (EMR). The main advantage of ESD is the technical of overall resection of superficial tumors in the digestive tract and preserving the stomach[3-4], effectively improving the quality of life [5]. Meanwhile, compared with EMR, ESD can effectively reduce the tumor recurrence rate[6]. However, several studies reported that ESD induces artificial ulcers, a commonly recognized complication and the other complications[7], such as delayed bleeding and perforation[3]. Based on the high prevalence of high-risk complications, it is generally recommended to treat with proton pump inhibitors (PPIs) after ESD[8], because the inhibition of gastric acid can promote the healing of ESD ulcers.

Vonoprazan (TAK-438) is a novel gastric acid inhibitor and active potassium competitive blocker (P-CAB) in Japan, treated acid-related therapeutic disease in 2015[9]. It could inhibit gastric H+ /K+ -ATPase activity, and was approved for clinical use in Japan in December 2014. Differing from the proton pump inhibitors (PPIs), P-CABs inhibit the proton pump enzyme in a reversible and potassium-competitive manner[10]. Furthermore, the absorption rate of P-CABs is unaffected by food and can be taken on independently of meal time [11-12]. Vonoprazan has been reported to inhibit gastric acid with faster, stronger, and more persistent than traditional PPIs in many diseases[13-14], such as gastroesophageal reflux disease, gastroduodenal ulcer, and Helicobacter pylori eradication. Though proton pump inhibitors are often used in the treatment of major treatments related to acid diseases, their efficacy still has certain limitations, such as instability in acid inhibition, relatively slow clinical effect, and unreliable effect of acid inhibition within 24 hours.

Several studies have been reported to contrast the safety and efficacy of Vonoprazan and lansoprazole (proton pump inhibitors) for treating ESD-induced artificial ulcers, 4 weeks of [15-16] and 8 weeks of [17-18], but the results remain controversial. Thus, it remains inconclusive whether Vonoprazan is more effective than lansoprazole in promoting ulcer effectiveness. we performed this systematic review and meta-analysis with the primary objective of assessing the comparison of the efficacy of Vonoprazan and lansoprazole on ESD-induced artificial ulcers.

2.Methods and analysis

2.1 Data source and retrieval strategy

We used the PubMed (Medline), Embase, Web of science, and Cochrane Library databases to retrieve the literature, and the search strategy used the following keywords: “gastric ulcer”, “Stomach Ulcers”, “Ulcer, Stomach” and “Vonoprazan”, “TAK 438” and “lansoprazole”, “Ogastro”, “AG 1749”. The cutoff date for the literature search was December 1, 2021. The results were limited to human studies, but animal studies excluded. There is not language restricted.

2.2. Eligibility criteria

Eligible studies were selected using the following inclusion and exclusion criteria:

2.2.1. Research design: We included a randomized controlled trial (RCT) studies. Abstract articles, case reports, review articles, preclinical studies, and other non-relevant studies were excluded.

2.2.2. Participants: The meta-analysis included only Rct and retrospective studies of patients with ulcer induction at age 18 years.

2.2.3. Interventions: This meta-analysis included only RCTS of vonoprazan treatment.

2.2.4. Comparators: This meta-analysis included only RCTs of lansoprazole

treatment.

2.2.5. Outcomes: This meta-analysis included RCTs that measured the ulcer healing rate, ulcer shrinking rate, and we excluded studies that did not include one of these 2 results.

2.3. Selection of the studies and extraction of the data

Two reviewers used the same eligibility assessment form to assess the RCTs. The conflicting assessments were discussed with a third investigator until the reviewers reached a consensus. Data was extracted by one reviewer and verifified by another. In addition to the outcomes, we extracted as the following information:

(1) authors and publication year,

(2) interventions (doses of vonoprazan and lansoprazole),

(3) participants' baseline characteristics,

(4) follow-up period duration,

(5) study design.

2.4. Quality assessment

The meta-analysis used a modified Jadad scale to assess the methodological quality of the study[19]. The modified Jadad scale for assessment standards was developed by Greenhalgh[20] and Oremus[21]. There are six items in the modified version of the Jadad scale, the six items are (i) randomization ("yes" scored 2 points, "no" scored 0); (ii) blinding ("yes" scored 2, "no" scored 0); (iii) description of withdrawals and dropouts ("yes" scored 1 point, "no" scored 0 points); (iv) inclusion/exc1usion criteria ("yes" scored 1 point, "no" scored 0 points); (v) adverse effects ("yes" scored 1, "no" scored 0); (vi) statistical analysis ("yes" scored 1, "no" scored 0)[21] .Scale scores range from 0 to 8 points, with higher scores indicating better quality. 1–3 signified low-quality while 4–8 signified high-quality[21].

2.5. Statistical analysis

This meta-analysis was used version RevMan version 5.4. Unlcer healing rate,

shrinkage rate, delayed bleeding, and perforation are expressed as an odds ratio of 95% CIs. The I^2 statistic describes the variation between trials rather than the sampling error, which is used to assess heterogeneity. I^2 values were 25%, 50%, and 75%, respectively, indicating the low, medium, and high heterogeneity, respectively. Statistical significance for all analyses was set as $P < 0.05$.

2.6. Ethical issues

This meta-analysis was an examination of literature only, and there was no direct contact with patients. Therefore, our study did not require ethics committee approval.

3. Results

3.1. Study selection

In the first search, 98 articles were retrieved, all determined through the literature database, 21 records were deleted through screening for duplicate literature, 77 records were retained on the title summary screen, excluding the following studies: 34 unrelated studies, 8 conference abstracts, 1 retrospective study, 1 non-human experiments, 14 reviews and other studies, 9 reports and letters, 2 unrelated outcome indicators, 2 unrelated interventions and 2 original data were missing. Four studies with sufficient data were finally selected to be included in this meta-analysis: four RCTs. The specific retrieval flow chart is shown in Fig. 1.

3.2. Study characteristics

The studies summarized the basic characteristics of the four studies, studies ranging from 2015 to 2020, and which were published from 2016 to 2021. Since vonoprazan was only available in Japan, all four studies were conducted in Japan. A total of 539 patients were included, which 274 received vonoprazan-based treatment and 265 were receiving lansoprazole-based treatment.

These studies included four RCTs (Table 1). Interventions included 20 mg/day Vonoprazan, the control study included 30 mg/day lansoprazole. All participants were adults (> 18 years) and had experienced an ESD. The number of patients

extracted for the meta-analysis showed ulcer healing or shrinkage rates, such as mean or standard deviation.

3.3. Classification of study quality

In these four included articles, one had a quality score of 7, three had a quality score of 5 in the modified Jadad scale, published in 2016, 2018, 2021, four RCTs (three studies were randomized through tag or permutation blocks and one study only mentioned randomization). Therefore, all included studies were of high quality literature (Table 2).

3.4. Synthesis of results from individual studies

3.4.1. Ulcer healing post-ESD at 4 weeks: A total of 2 studies[22-23], including 194 participants, reported ulcer healing and / or ESD induced artificial ulcer contraction ratio after Vonoprazan and Lansoprazole treatment, 99 participants intervention group (Vonoprazan) with 95 participants control group (Lansoprazole) with follow-up of 4 weeks, as depicted in the ulcer healing forest plot (Fig. 2), [OR：1.07 (0.51, 2.22), 95% CI, I^2=2%, Z=0.18, P=0.86], the healing rate effect was not significantly higher in the intervention groups than in the control groups, and the heterogeneity between the studies was small.

3.4.2. Shrinkage ration post-ESD at 4 weeks: In three studies[22-24], 390 participants were included in the meta-analysis of ESD-induced ulcer contraction rate, 200 in the intervention group (Vonoprazan 20mg) and 190 in the control group (Lansoprazole 30mg). Follow-up time was 4 weeks, as depicted in the shrinkage rate forest plot (Fig. 3), [MD：0.20 (-1.51, 1.92), 95% CI, I^2=0%, Z=0.23, P=0.82]. The ulcer shrinkage rate had no significantly difference with the control group, and less heterogeneity between studies.

3.4.2. Shrinkage ration post-ESD at 8 weeks: In two studies[22,24], 364 participants were included in the meta-analysis of ESD-induced ulcer shrinkage rate, 186 in the intervention group (Vonoprazan 20mg) and 178 in the control group (Lansoprazole

30mg).Follow-up time was 8 weeks. As depicted in the shrinkage rate forest plot (Fig. 4), [MD: -0.09 (-0.30, 0.12), 95% CI, I^2=*0%,* Z=0.85, *P=0.39*]. There is no significant difference existing in the ulcer shrinkage rate, and less heterogeneity between studies.

3.4.3 Delayed bleeding: Four studies included 539 participants[22-25], and the investigator had delayed bleeding complications in patients treated with Vonoprazan and lansoprazole. A total of 274 participants (Vonoprazan 20mg) were included in the intervention group, and 265 participants (Lansoprazole 30mg) were included in the control group. As depicted in the delayed bleeding forest plot (Fig. 5), [RR: 0.61 (0.23, 1.59), 95% CI, I^2=*0%,* Z=1.01, *P=0.31*]. There was no significant difference in delayed bleeding rate between the intervention group and the control group with no significant heterogeneity.

3.4.4 Ulcer perforation: Three studies included 513 participants[22,24-25], complications of perforation in patients treated with Vonoprazan and lansoprazole, 260 participants (Vonoprazan 20mg) in the intervention group, 253 participants (lansoprazole 30mg), As depicted in the perforation forest plot (Fig. 6), [OR: 1.19 (0.34, 4.19), 95% CI, I^2=*0%,* Z=0.27, *P=0.79*]. There was no significant difference in perforation rate between the intervention group and the control group with no significant heterogeneity between studies.

4. Discussion

Due to the potential complications of ESD, it is essential to promote the healing of artificial ulcers induced after ESD and reduce the risk of these complications. However, it is unclear that vonoprazan is more effective in treating gastric acid inhibition and superior to lansoprazole in promoting ulcer healing and delayed bleeding. In this systematic review and meta-analysis, which draws on the databases retrieved, we conclude that, the ulcer healing rate effect at 4 weeks after ESD was not significantly higher in Vonoprazan than in lansoprazole group[22-23]. The ulcer shrinkage rate with no significant differences existed in the vonoprazan and

lansoprazole groups at 4 weeks after ESD [22-24]. There was also no significant difference in shrinkage rate at 8 weeks after ESD[22,24]. In terms of delayed bleeding, the rate of delayed bleeding was not significantly higher in the Vonoprazan group compared with the lansoprazole group[22-25] . In terms of ulcer perforation, the perforation was not significantly higher in the Vonoprazan group than in the lansoprazole group[22,24-25]. Therefore, in terms of ulcer healing, considering multiple factors, such as the location of the ulcer, tumor size, Helicobacter pylori infection etc. Eri Uchida et al. found that ulcer healing after ESD was associated with the location of ulcers[26]. Yashiro Yoshizawa et al. found that ulcer healing after ESD was mainly related to the size of the tumor, while no time of H. pylori eradication, resected size, or CYP2C19 genotypes[27].

Dozens of studies reported that ESD has many advantages, such as comprehensive resection of superficial tumors of digestive tract, retention of stomach, effective reduction of tumor recurrence rate, and small trauma[3]. ESD is a new minimally invasive surgery without changing the structure of digestive tract. At present, conventional treatment for ESD-induced complications is mainly proton pump inhibitors, including omeprazole, lansoprazole, esomeprazole and rabeprazole. However, proton pump inhibitors (PPIs) act slowly and are not ideal at night due to cytochrome P450 polymorphism and are unstable under acidic conditions[28] .

In order to overcome these limitations of proton pump inhibitors and better meet clinical needs, a new potassium-competitive acid blocker Vonoprazan (P-CAB) was developed in Japan in 2015, which may highlight certain comparative advantages. Firstly, Vonoprazan is weak base and will undergo instantaneous protonation when it is in an acidic environment, it is relatively stable in acidic environments[29]. Secondly, vonoprazan can reach peak plasma levels when taken orally[30], therefore, it can block H+/K+ ATPase and is not affected by gastric secretion activities. The acid inhibition effect does not require the activation of proton pump, and it is faster and more stable in terms of effect[31]. Finally, because Vonoprazan has a slower dissociation rate than proton pump inhibitors, it can inhibit gastric acid secretion for a long time, especially at night, and has a certain long-term effect[28-29]. Several studies have questioned the safety and efficacy of Vonoprazan, although ESD

is higher than EMR complications, a systematic review results showed that the incidence of complications in ESD is 1%[32]. While some studies show that the safety of ESD is considered sufficient [33] , because most complications can generally be treated under endoscopy, the impact on clinical efficacy is greatly reduced. In China, Japan and the other Asian countries, ESD is regarded as the standard treatment mode for early gastric cancer and adenocarcinoma. Therefore, this meta-analysis mainly compared the efficacy of Vonoprazan and lansoprazole in ESD-induced artificial ulcer healing.

This systematic review and meta-analysis still have some limitations. First, this meta-analysis retrieval database is limited, there are some limitations to the number of literatures retrieved. The number of included literatures was small, there are also some differences in the specific treatment of the patients involved and may be some variability in the results of this meta-analysis. Next, literature is all obtained from Japan, due to the patient's constitution, living environment and other factors affected, the generality of its findings may be subject to some limitations. This treatment plan in China also needs to carefully formulate a reliable treatment plan according to the specific situation of patients. Finally, Inclusion in this meta-analysis was RCT and retrospective study.

5. Outlook

Based on this meta-analysis we can look at vonoprazan some wider clinical thought, because it is not affected by CYP2C19 gene polymorphisms, leading to differences between individuals is low, so there may be more in the aspect of clinical application in the field of application, for example: a product may not affect the activity of clopidogrel, does not affect its anti-platelet effect, for prevention of cardiovascular stress ulcer. Secondly, the combination of Vonoprazan and antibiotics in the treatment of helicobacter pylori ulcer infection respiratory tract infection and other anti-inflammatory antibacterial aspects may have a certain clinical effect in the future clinical application through experimental studies, Vonoprazan is likely to have a certain application in the cardiovascular field. Finally, in extensive clinical trials, the combination of drugs may be effective.

conflicts of interest

There is no conflicts of interest.

References:

[1] Ono H, Yao K, Fujishiro M, et al. Guidelines for endoscopic submucosal dissection and endoscopic mucosal resection for early gastric cancer. *Dig Endosc*. 2016;28(1):3-15.

[2]Tate DJ, Klein A, Sidhu M, et al. Endoscopic submucosal dissection for suspected early gastric cancer: absolute versus expanded criteria in a large Western cohort (with video). *Gastrointest Endosc*. 2019;90(3):467-479.e4.2

[3]Gotoda T, Yamamoto H, Soetikno RM. Endoscopic submucosal dissection of early gastric cancer. *J Gastroenterol*. 2006;41(10):929-942.

[4]Bhatt A, Abe S, Kumaravel A, et al. Indications and Techniques for Endoscopic Submucosal Dissection. *Am J Gastroenterol*. 2015;110(6):784-791.

[5]Nishizawa T, Yahagi N. Long-Term Outcomes of Using Endoscopic Submucosal Dissection to Treat Early Gastric Cancer. *Gut Liver*. 2018;12(2):119-124.

[6]Tanabe S, Ishido K, Higuchi K, et al. Long-term outcomes of endoscopic submucosal dissection for early gastric cancer: a retrospective comparison with conventional endoscopic resection in a single center. *Gastric Cancer*. 2014;17(1):130-136.

[7]Wang KK, Prasad G, Tian J. Endoscopic mucosal resection and endoscopic submucosal dissection in esophageal and gastric cancers. *Curr Opin Gastroenterol*. 2010;26(5):453-458.

[8]Yang Z, Wu Q, Liu Z, et al. Proton pump inhibitors versus histamine-2-receptor antagonists for the management of iatrogenic gastric ulcer after endoscopic mucosal resection or endoscopic submucosal dissection: a meta-analysis of randomized trials. *Digestion*. 2011;84(4):315-320.

[9]Garnock-Jones KP. Vonoprazan: first global approval. Drugs. 2015;75(4):439-443.

[10]Kondo M, Kawamoto M, Hasuoka A, et al. High-throughput screening of potassium-competitive acid blockers. *J Biomol Screen*. 2012;17(2):177-182.

[11]Graham DY, Dore MP. Update on the Use of Vonoprazan: A Competitive Acid Blocker. *Gastroenterology*. 2018;154(3):462-466.

[12]Martinucci I, Blandizzi C, Bodini G, et al. Vonoprazan fumarate for the management of acid-related diseases. *Expert Opin Pharmacother*. 2017;18(11):1145-1152.

[13]Hori Y, Matsukawa J, Takeuchi T, et al. A study comparing the antisecretory effect of TAK-438, a novel potassium-competitive acid blocker, with lansoprazole in animals. *J Pharmacol Exp Ther*. 2011;337(3):797-804.

[14]Jenkins H, Sakurai Y, Nishimura A, et al. Randomised clinical trial: safety, tolerability, pharmacokinetics and pharmacodynamics of repeated doses of TAK-438 (vonoprazan), a novel potassium-competitive acid blocker, in healthy male subjects. *Aliment Pharmacol Ther*. 2015;41(7):636-648.

[15]Ichida T, Ueyama S, Eto T, et al. Randomized Controlled Trial Comparing the Effects of Vonoprazan Plus Rebamipide and Esomeprazole Plus Rebamipide on Gastric Ulcer Healing Induced by Endoscopic Submucosal Dissection. *Intern Med*. 2019;58(2):159-166.

[16]Komori H, Ueyama H, Nagahara A, et al. A prospective randomized trial of a potassium competitive acid blocker vs proton pump inhibitors on the effect of ulcer healing after endoscopic submucosal dissection of gastric neoplasia. *J Int Med Res*. 2019;47(4):1441-1452.

[17]Hamada K, Uedo N, Tonai Y, et al. Efficacy of vonoprazan in prevention of bleeding from endoscopic submucosal dissection-induced gastric ulcers: a prospective randomized phase II study. *J Gastroenterol*. 2019;54(2):122-130.

[18]Tsuchiya I, Kato Y, Tanida E, et al. Effect of vonoprazan on the treatment of artificial gastric ulcers after endoscopic submucosal dissection: Prospective randomized controlled trial. *Dig Endosc*. 2017;29(5):576-583.

[19]Olivo SA, Macedo LG, Gadotti IC, et al. Scales to assess the quality of randomized controlled trials: a systematic review. *Phys Ther*. 2008;88(2):156-175.

[20] Greenhalgh T. Assessing the methodological quality of published papers. *BMJ*. 1997;315(7103):305-308.

[21].Oremus M, Wolfson C, Perrault A, et al. Interrater reliability of the modified

Jadad quality scale for systematic reviews of Alzheimer's disease drug trials. *Dement Geriatr Cogn Disord*. 2001;12(3):232-236.

[22]Kawai D, Takenaka R, Ishiguro M, et al. Vonoprazan versus lansoprazole in the treatment of artificial gastric ulcers after endoscopic submucossal dissection: a randomized, open-label trial. *BMC Gastroenterol*. 2021;21(1):236. Published 2021 May 22.

[23]Takahashi K, Sato Y, Kohisa J, et al. Vonoprazan 20 mg vs lansoprazole 30 mg for endoscopic submucosal dissection-induced gastric ulcers. World J Gastrointest Endosc. 2016;8(19):716-722.

[24]Ban H, Inatomi O, Murata M, et al. Vonoprazan vs lansoprazole for the treatment of artificial gastric ulcer after endoscopic submucosal dissection: a prospective randomized comparative study. *J Clin Biochem Nutr*. 2021;68(3):259-263.

[25]Hirai A, Takeuchi T, Takahashi Y, et al. Comparison of the Effects of Vonoprazan and Lansoprazole for Treating Endoscopic Submucosal Dissection-Induced Artificial Ulcers. *Dig Dis Sci*. 2018;63(4):974-981.

[26]Uchida E, Kato S, Tsuchiya I, et al. Percent reduction of the ulcer size at 4 weeks is a predictor of the complete healing of endoscopic submucosal dissection-induced gastric ulcers. Arab J Gastroenterol. 2020;21(3):183-188.

[27]Yoshizawa Y, Sugimoto M, Sato Y, et al. Factors associated with healing of artificial ulcer after endoscopic submucosal dissection with reference to Helicobacter pylori infection, CYP2C19 genotype, and tumor location: Multicenter randomized trial. Dig Endosc. 2016;28(2):162-172.

[28]Oshima T, Miwa H. Potent Potassium-competitive Acid Blockers: A New Era for the Treatment of Acid-related Diseases. J Neurogastroenterol Motil. 2018;24(3):334-344.

[29]Marabotto E, Ziola S, Savarino V, et al. Vonoprazan Fumarate for the Treatment of Gastric Ulcers: A Short Review on Emerging Data. Clin Exp Gastroenterol. 2020;13:99-104. Published 2020 Apr 15.

[30]Inatomi N, Matsukawa J, Sakurai Y, et al. Potassium-competitive acid blockers: Advanced therapeutic option for acid-related diseases. Pharmacol Ther. 2016;168:12-22.

[31]Martinucci I, Blandizzi C, Bodini G, et al. Vonoprazan fumarate for the management of acid-related diseases. Expert Opin Pharmacother. 2017;18(11):1145-1152.

[32]Repici A, Hassan C, De Paula Pessoa D, et al. Efficacy and safety of endoscopic submucosal dissection for colorectal neoplasia: a systematic review. *Endoscopy*. 2012;44(2):137-150.

[33]Ma MX, Bourke MJ. Complications of endoscopic polypectomy, endoscopic mucosal resection and endoscopic submucosal dissection in the colon. Best Pract Res Clin Gastroenterol. 2016;30(5):749-767.

REVISTA ESPAÑOLA DE ENFERMEDADES DIGESTIVAS
The Spanish Journal of Gastroenterology

study	Country	N	Study period	Experimental Intervention		T	Age(years)	M/F
				T	C			
Ai Hirai 2018	Japan	149	2015.4-2017.5	Vonoprazan 20 mg/day	Lansoprazole 30 mg/day	8w	V：73.16 [7.48] L：69.93 [11.0]	V:62/12 L:55/20
Daisuke Kawai 2021	Japan	168	2015.4-2017.12	Vonoprazan 20 mg/day	Lansoprazole 30 mg/day	8w	V:73 (47–89) L: 73 (33–90)	V:63/22 L:58/25
Hiromitsu Ban 2020	Japan	196	2015.9-2018.8	Vonoprazan 20 mg/day	Lansoprazole 30 mg/day	8w	V: 71.5 ± 8.8 L: 71.2 ± 8.6	V:76/25 L:69/26
Kazuya Takahashi 2016	Japan	26	2015.8-2016.3	Vonoprazan 20 mg/day	Lansoprazole 30 mg/day	4w	V: 71.9 ± 7.9 L: 74.8 ± 8.3	V: 12/2 L: 10/2

Table 2. Level of evidence and Jadad quality score

study	modified Jadad scale						
	Randomization (2)	Blinding (2)	Withdrawals and dropouts (1)	Inclusion/ Exclusion criteria (1)	adverseeffects (1)	statisticalanalysis (1)	Total
Ai Hirai 2018	1	2	1	1	1	1	7
Daisuke Kawai 2021	2	0	1	1	0	1	5
Hiromitsu Ban 2020	2	0	1	1	0	1	5
Kazuya Takahashi 2016	2	0	1	1	0	1	5

REVISTA ESPAÑOLA DE
ENFERMEDADES DIGESTIVAS
The Spanish Journal of Gastroenterology

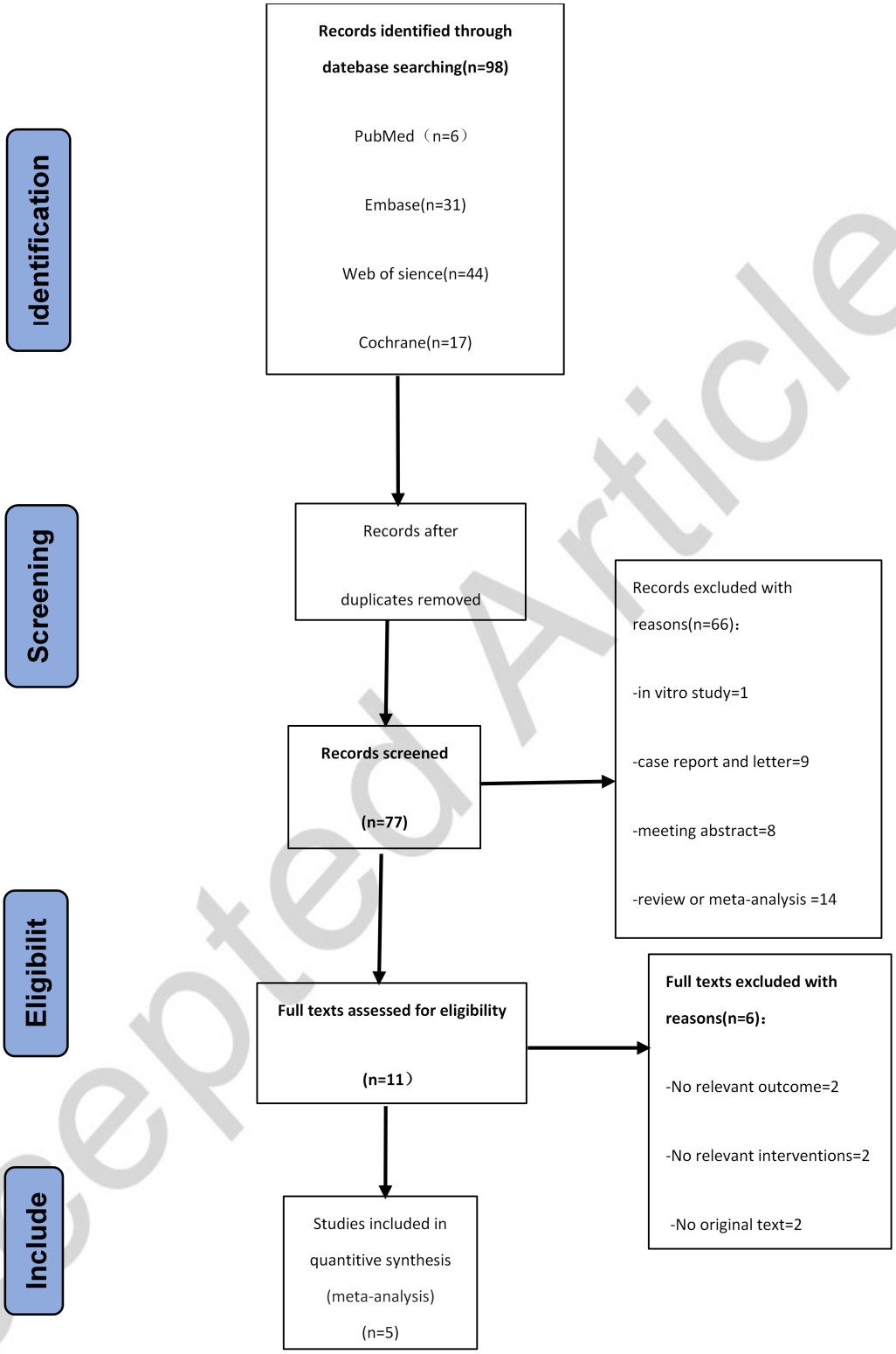


Figure1. Flow chart of the literature search

REVISTA ESPAÑOLA DE
ENFERMEDADES DIGESTIVAS
The Spanish Journal of Gastroenterology

Figure 2

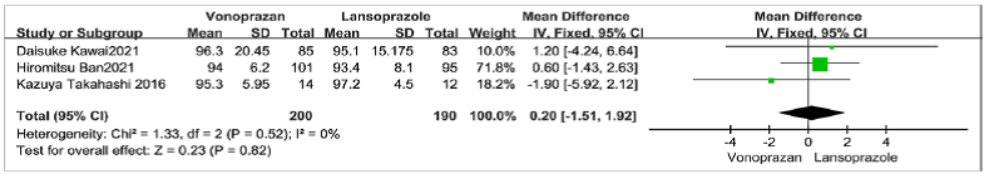


Figure 3

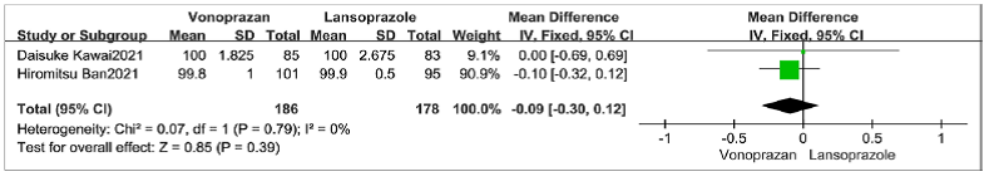


Figure 4

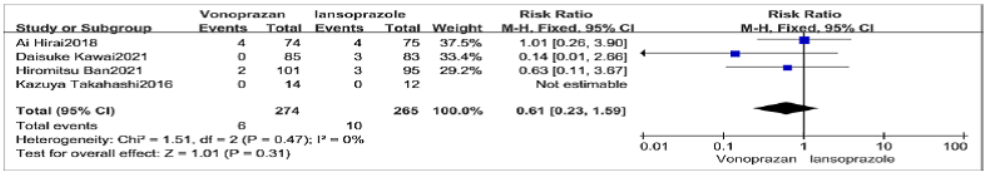
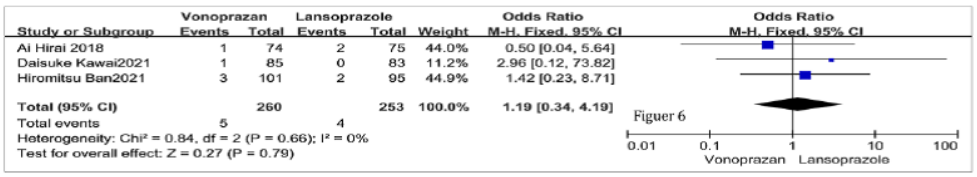


Figure 5



Figuer 6

Figure 6

REVISTA ESPAÑOLA DE
ENFERMEDADES DIGESTIVAS
The Spanish Journal of Gastroenterology