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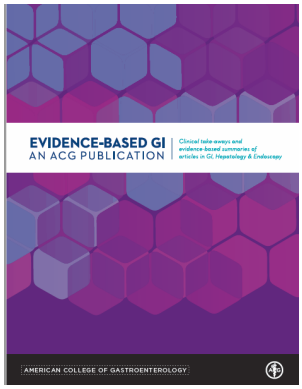

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Treating *Helicobacter pylori* Infection With Vonoprazan, A Potassium-Competitive Acid Blocker: A New Paradigm

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This summary reviews: Chey WD, Megraud F, Laine L, et al. Vonoprazan Triple and Dual Therapy for *Helicobacter* pylori Infection in the US and Europe: A Randomized Controlled Trial. Gastroenterology 2022 Jun 6;S0016-5085(22)00609-6. https://pubmed.ncbi.nlm.nih.gov/35679950

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STRUCTURED ABSTRACT

Question: Are vonoprazan triple (Voquezna TriplePak) and dual regimens (Voquezna DualPak) non-inferior to standard lansoprazole-based triple regimen (Prevpac) for treatment-naïve individuals with *Helicobacter pylori* infection?

Design: Phase III, multicenter, double-blind randomized controlled trial.

Setting: Patients from 103 sites in the US, United Kingdom, Bulgaria, the Czech Republic, Hungary, and Poland.

Patients: Included patients were: (a) ≥ 18 years old; (b) indication to test for *H. pylori*, including dyspepsia, recent diagnosis of non-bleeding peptic ulcer, history of peptic ulcer with no prior treatment

of *H. pylori*, or requirement for long-term NSAID use; (c) positive ^{13}C-urea breath test for *H. pylori* infection; and (d) no prior treatment for *H. pylori* infection. All eligible patients then underwent eophagogastroduodenoscopy with biopsy for culture and antimicrobial susceptibility testing as well as histology. All study patients had active *H. pylori* infection confirmed by culture or histology.

Interventions/Exposure: Eligible patients were randomized 1:1:1 to open-label vonoprazan dual therapy (vonoprazan 20 mg b.i.d. plus amoxicillin 1g t.i.d X 14 days) vs double-blind vonoprazan triple therapy (vonoprazan 20 mg b.i.d. plus amoxicillin 1 g b.i.d. plus clarithromycin 500 mg b.i.d. X 14 days) vs lansoprazole triple therapy (lansoprazole 30 mg b.i.d. plus amoxicillin 1 gm b.i.d. plus clarithromycin 500 mg b.i.d. X 14 days).

Outcome: The primary endpoint was *H. pylori* eradication based on negative ^{13}C-urea breath test obtained at least 4 weeks after last dose of study medication. Patients with persistent *H. pylori* infection underwent repeat eophagogastroduodenoscopy with repeat antimicrobial susceptibility testing. Per FDA guidance, the primary non-inferiority endpoint was assessed in the study patients with *H. pylori* strains that were not resistant to clarithromycin or amoxicillin. Pre-determined secondary endpoints assessed frequency of *H. pylori* eradication in all study patients and frequency of eradication in study patients with clarithromycin-resistant strains of *H. pylori*.

Data Analysis: Modified intention-to-treat analysis and per-protocol analysis (defined as patients who took $\geq$ 75% of study drug) was performed for the primary endpoint and both secondary endpoints. Analyses were conducted in a hierarchical order for each comparison: vonoprazan dual therapy vs lansoprazole triple therapy and vonoprazan triple therapy vs lansoprazole triple therapy for non-inferiority of *H. pylori* eradication among patients with strains that were susceptible to clarithromycin and amoxicillin. Again, this analysis was guided by the US Food and Drug Administration (FDA). Secondary endpoints were

then assessed using superiority analysis for clarithromycin-resistant strains and for all patients.

Funding: Phathom Pharmaceuticals, manufacturer of vonoprazan.

Results: From December 2019 through January 2021, 3,385 patients were screened for eligibility, 1,046 were randomized, and 992 were fully evaluated (mean age: 51-52 years old; 37% male; 90% White; 42% from US; 98% with dyspepsia as indication to test for *H. pylori*; 20% with clarithromycin-resistant strains; 1% with amoxicillin-resistant strains; 63% with metronidazole-resistant strains). For the primary endpoint requested by the FDA, vonoprazan dual therapy and vonoprazan triple therapy were non-inferior to lansoprazole triple therapy for eradication of *H. pylori* with no resistance to clarithromycin or amoxicillin (78.5% vs 84.7% vs 78.8%, respectively) (**Figure 1**). Vonoprazan dual therapy and vonoprazan triple therapy were superior to lansoprazole triple therapy for *H. pylori* eradication when evaluating all patients (77.2% vs 80.8% vs 68.5%, respectively, $P < 0.01$) and when evaluating patients with clarithromycin-resistant strains (69.6% vs 65.8% vs 31.9%, respectively, $P < 0.001$). (**Figure 1**)

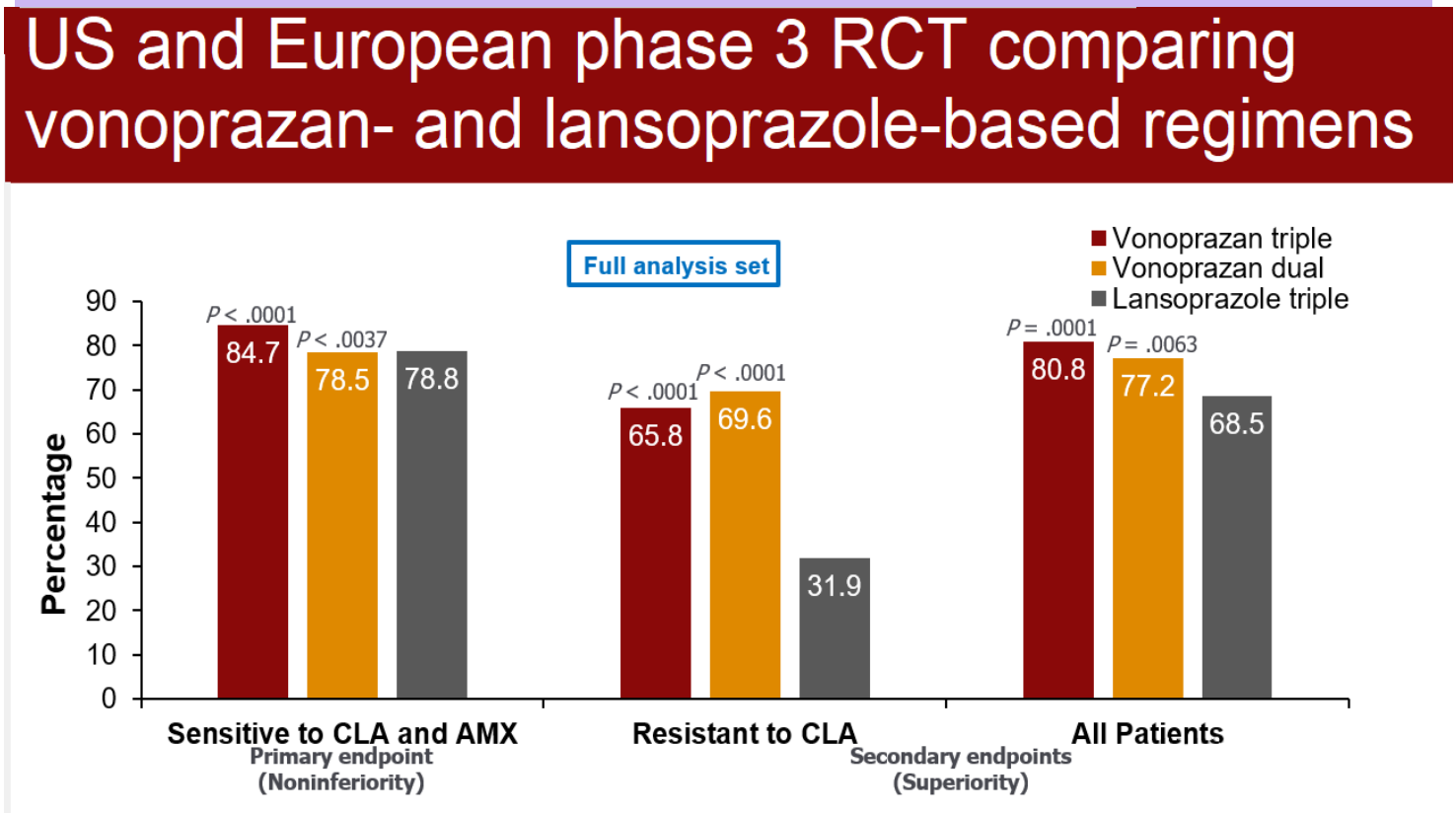

Figure 1: *Helicobacter pylori* eradication rates.
AMX, amoxicillin ; CLA, clarithromycin; RCT, randomized controlled trial.

COMMENTARY

Why Is This Important?

Quite simply, lansoprazole-based triple therapy with clarithromycin should not be used unless antimicrobial sensitivity testing has confirmed clarithromycin-sensitivity.[1] This is because lansoprazole-based triple therapy with clarithromycin and similar regimens only achieve 30% eradication rates in clarithromycin-resistant strains, and rates of clarithromycin resistance exceed 20% in most parts of the US. As seen in this study, this translates to successful eradication in only about 65%-70% of US patients with lansoprazole-based triple therapy with clarithromycin, which is far from optimal. Nevertheless, US database studies estimate that lansoprazole-based triple therapy with clarithromycin and similar regimens account for almost 50% of prescriptions.

Bismuth-based quadruple therapy and rifabutin-based triple therapy (Talicia) for 14 days are preferred regimens.[1,2] Unfortunately, compliance and pill burden make bismuth-based quadruple therapy regimens cumbersome and use of rifabutin-based therapy seems to have been limited by cost, limited formulary availability, co-pays, and lack of awareness. Therefore, the recent FDA approval[3] of vonoprazan-based dual therapy and vonoprazan-based triple therapy for *H. pylori* treatment are welcome.

Vonaprazan, a potassium-competitive acid blocker, produces earlier and more potent acid suppression than conventional proton pump inhibitors and this translates to more successful treatment of *H. pylori*. Specifically, enhanced gastric acid suppression optimizes the activity of amoxicillin and clarithromycin, which may be destabilized by lower pH. Also, active bacterial replication of *H. pylori* increases at higher gastric pH and this replication facilitates antibiotic eradication.

Key Study Findings

Vonoprazan dual therapy and vonoprazan triple therapy were superior to lansoprazole triple therapy for *H. pylori* eradication when evaluating all patients (77.2% vs 80.8% vs 68.5%, respectively, $P < 0.01$) and when evaluating patients with clarithromycin-resistant strains (69.6% vs 65.8% vs 31.9%, respectively, $P < 0.001$). (**Figure 1**)

Caution

Since only treatment-naïve *H. pylori* patients were enrolled, this study doesn't provide data about management of patients with refractory *H. pylori* infections. Otherwise, this is a very well-designed, Phase III RCT, which met all FDA requirements and led to FDA approval of vonoprazan-based dual therapy and triple therapy regimens.

My Practice

At my VA Medical Center, my current preferred therapy is bismuth -based quadruple therapy and I'm limited by my formulary to only using rifabutin-based triple therapy for salvage therapy in patients with refractory *H. pylori* infection.

Vonoprazan-based dual therapy with amoxicillin is ideal for good antibiotic stewardship.[4] If cost and availability concerns can be addressed at my VA Medical Center, then this will be my preferred first-line therapy.

It's also worth emphasizing the ACG Guideline recommendation that post-treatment testing should be performed routinely to ensure successful eradication.[2] I prefer to do this with stool antigens for *H. pylori* and have the specimen collected at least 4 weeks after completing antibiotics and 2 weeks after discontinuing acid suppression therapy.

For Future Research

Future studies should assess real-world efficacy of vonoprazan-based therapies in patients with refractory *H. pylori* infection. Additional studies should use next-generation sequencing[5] or other tools to better define rates of antibiotic-resistant strains in different geographic regions of the US.[5] Quality improvement research should also assess interventions to improve frequency of testing for eradication 4 weeks after patients complete treatment.

Conflict of Interest

Dr. Schoenfeld reports being an advisory board member and consultant for Phathom Pharmaceuticals.

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EVIDENCE-BASED GI
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ESOPHAGUS

In Case You Missed It: Peroral Endoscopic Myotomy (POEM) for Achalasia: At Least As Good As Laparoscopic Heller's Myotomy

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This summary reviews: Werner YB, Hakanson B, Martinek J, et al. Endoscopic or Surgical Myotomy in Patients with Idiopathic Achalasia. N Engl J Med 2019;381:2219-2229. https://pubmed.ncbi.nlm.nih.gov/31800987/

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STRUCTURED ABSTRACT

Question: Is peroral endoscopic myotomy (POEM) as effective as surgical laparoscopic Heller's myotomy (LHM) with Dor's fundoplication for patients with idiopathic achalasia?

Design: Prospective, multicenter, unblinded, randomized non-inferiority clinical trial.

Setting: Eight centers in 6 European countries.

Patients: Adult patients with symptomatic achalasia (subtypes I, II, and III) confirmed on manometry and with Eckardt score >3 who had not undergone any prior esophagogastric surgery. Patients who had undergone prior endoscopic interventions such as pneumatic dilation or botox were allowed.

Interventions/Exposure: Patients were randomly assigned in a 1:1 ratio to POEM or LHM with Dor's fundoplication, which were performed according to current standards by experienced endoscopists and surgeons

Outcome: The primary outcome was clinical success defined as Eckardt score ≤3 at 2-year follow-up. The Eckardt symptom score is a validated questionnaire that is calculated by grading 4 components: dysphagia, regurgitation, chest pain, and weight loss. Each component is graded on a 0-3 scale with higher scores indicating more severe symptoms. Secondary outcomes included symptoms (Gastrointestinal Quality of Life Index score and GERD), endoscopic findings of esophagitis, manometry, and abnormal acid exposure time on pH studies. Clinical data was collected as 3, 6, 12, and 24 months, and endoscopy, manometry, and esophageal pH studies were performed at 3 and 24 months

Data Analysis: Primary analysis was a modified intention-to-treat which included all patients randomized and the assigned intervention. Additional analyses included per-protocol population which was all patients in this modified intention-to-treat population who completed follow up.

Funding: European Clinical Research Infrastructure Network, Olympus Europa, and additional public foundations.

Results: Between December 7, 2012 and October 9, 2015, 221 study patients were enrolled and assigned to POEM (n=112) or LHM (n=109). At 2 years, clinical success, defined by Eckardt score < 3, was similar in POEM and LHM patients (83.0% vs 81.7%) and met predefined criteria for non-inferiority (difference = 1.4 percentage points, 95%CI -8.7 to 11.4, *P*=0.007 for noninferiority). Clinical success rates were similar between groups at 3, 6, 12, and 24 months (Figure 1). Eleven patients had persistent symptoms: 2 of 3 in the POEM group had reintervention and all 8 patients in the LHM had reintervention. Improvement in esophageal function as measured by the integrated relaxation pressure of the lower esophageal sphincter on manometry was similar between the 2 groups (difference -.075 mm Hg, 95% CI -2.26 to 0.76). Improvement in symptoms according to the Gastrointestinal Quality of Life Index scores was also similar between the 2 groups (difference 0.14 points, 95% CI -4.01 to 4.28).

Reflux esophagitis on endoscopy was higher in the POEM group

compared to LHM group, respectively, at 3 months (57% vs 20%, odds ratio [OR]= 5.74, 95% CI 2.99-11.00) and 24 months (44% vs 29%, OR = 2.00, 95% CI 1.03-2.85), although rates of LA Grade C/D erosive esophagitis were similar in both groups at 3 months (6% vs 3%) and 24 months (5% vs 6%). Proton-pump inhibitor (PPI) use was also more common in the POEM group vs LHM group at 24 months (52.8% vs 27.2%). Serious adverse events were numerically lower in POEM vs LHM groups (2.7% vs 7.3%) but this difference was not statistically significant.

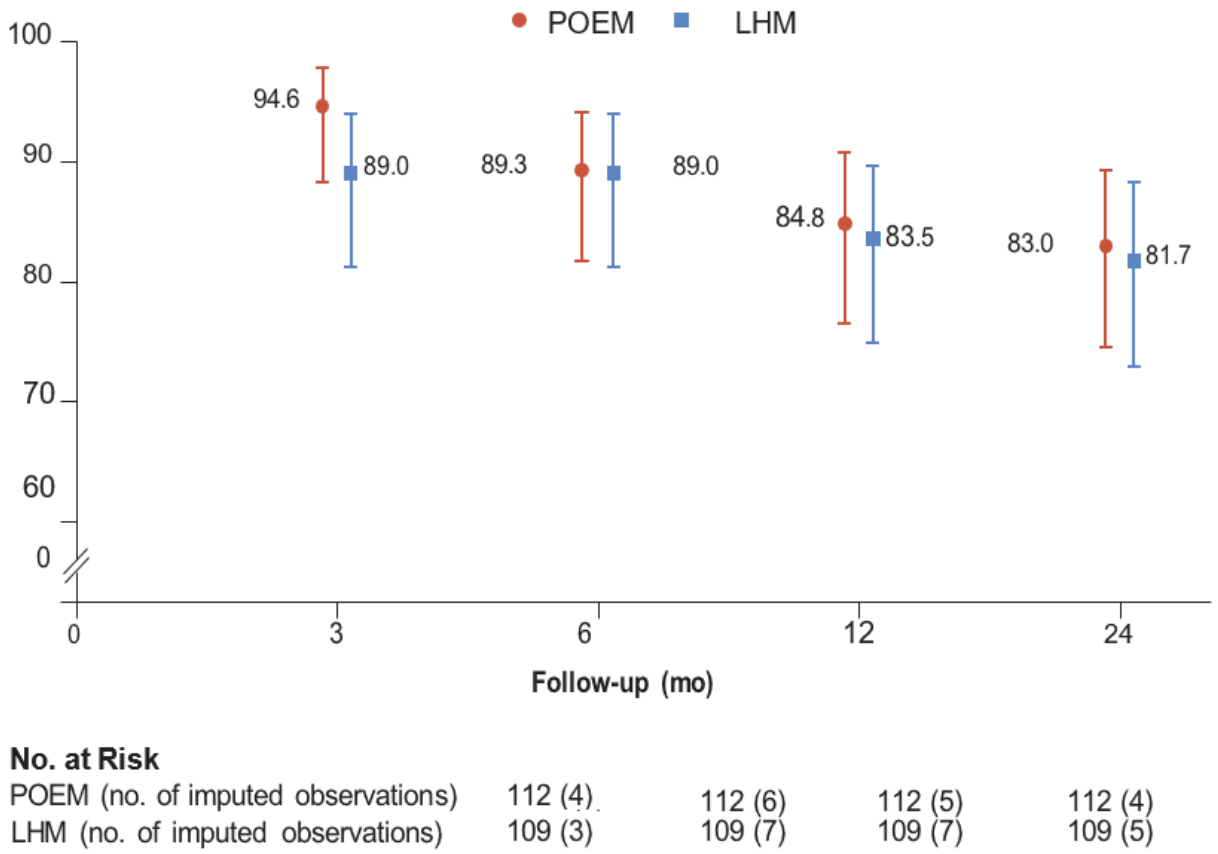

Figure 1: Percentage of Patients with Clinical Success

COMMENTARY

Why Is This Important?

Esophageal motility disorders are becoming more mainstream as our diagnostic modalities expand and our therapeutic armamentarium grows. Although the traditional approach to treating achalasia had always been LHM or pneumatic dilation, POEM has gained traction as a less invasive, safe, and effective option. A meta-analysis of 36 studies including

2,372 patients demonstrated high rates of clinical success (Eckardt score ≤3: 98%), with varying rates of symptomatic GERD (8.5%), erosive esophagitis on endoscopy (13%), and abnormal acid exposure (47%).[1]

This is the first randomized trial to directly compare POEM to LHM in patients with all subtypes of achalasia. Since this landmark article, multiple professional GI society guidelines have adopted POEM as a comparably effective first line therapy for patients with type I or type II achalasia and a preferred treatment option for those with type III achalasia.[2-4] Further evidence for this change in practice comes from a recent study in *JAMA Surgery* that used insurance claims data to highlight a 19 fold increase in POEM utilization from 2010 to 2017.[5]

Key Study Findings

In a head-to-head comparison, clinical success was similar between POEM and LHM for patients with achalasia. Secondary outcomes including improvement in manometry and quality of life scores were also similar. Serious adverse events occurred in 2.7% of patients who had POEM and 7.3% who had LHM. GERD is common after both interventions and initially higher in patients who undergo POEM compared to LHM, but at 24 months the rates of LA Grade C/D esophagitis are similar. Correspondingly, POEM patients were more likely to be using PPIs at 2-year follow-up (52.8% vs 27.2%). This is not surprising since LHM patients also get an anti-reflux measure, the Dor fundoplication, in this study.

Caution

Endoscopists in this study underwent formal POEM training and supervision, emphasizing that POEM is a highly technical procedure that requires specialized training. This study did not address the optimal therapy for patients who have had prior esophageal or stomach surgery or prior surgical therapy for achalasia.

My Practice

The combination of medical and surgical history, anatomy, and patient preference are critical factors in choosing the optimal therapy for achalasia. For type I ("classic" with minimal contractility in the esophageal body) and type II (with intermittent periods of panesophageal pressurization) achalasia, POEM and LHM are both effective options and I always offer patients a surgical consultation, but find that they prefer the endoscopic, less invasive approach. POEM is the first line therapy for type III achalasia (spastic with premature or spastic distal esophageal contractions), and we tailor the myotomy to the length of the spastic segment on manometry, esophagram, and Endoflip. Patients who have had prior esophageal surgery or LHM and need a redo myotomy are often best served by POEM due to the difficulty of repeat operation. Patients who are newly diagnosed with achalasia in a practice where POEM is not offered should be referred to a center where POEM is performed. As of January 2022, there is a CPT code for POEM so this is recognized and reimbursesd by insurance carriers and getting approval should not be an issue.

The Achilles heel remains post-POEM reflux and the possibility for significant silent GERD and catastrophic complications such as erosive esophagitis, Barrett's esophagus, and even cancer. For my anti-reflux POEM, I use a modified posterior approach with a navigational tunnel method that allows for predictable navigation of the myotomy to finish at the lesser curve of the stomach and avoid disruption of the gastric sling fibers. We have adapted our technique to do a shorter myotomy on both the esophageal and cardia side. We are even moving towards only cutting the circular muscle rather than disrupting the longitudinal fibers (full thickness) as we learn more about the physiology of dysphagia and GERD. All patients come back at 3-6 months for endoscopic evaluation and esophageal pH testing. Patients with significant acid reflux who do not wish to continue lifelong medication may benefit from transoral incisionless fundoplication which recreates and lengthens the gastroesophageal flap valve.

For Future Research

The technique of POEM continues to be refined as we learn more about risk factors for post-POEM reflux. Further studies are needed to determine the indications and timing for antireflux interventions—whether at the same time as POEM analogous to a LHM with fundoplication or at a subsequent session. Another topic of ongoing investigation is determining the optimal therapy for non-achalasia spastic esophageal disorders and what role POEM plays in these conditions.

Conflict of Interest

Drs. Kolb and Chang reported no potential conflict of interest.

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EVIDENCE-BASED GI
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Does Choice of Anticoagulant Influence Risk of Gastrointestinal Bleeding?

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Associate Editor

This summary reviews Ingason AB, Hreinsson JP, Agustsson AS, et al. Rivaroxaban is Associated with Higher Rates of Gastrointestinal Bleeding than Other Direct Oral Anticoagulants. Ann Intern Med 2021; 174:1493-1502. https://pubmed.ncbi.nlm.nih.gov/34633836

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STRUCTURED ABSTRACT

Question: Is rivaroxaban (Xarelto), a direct-acting oral anticoagulant (DOAC), associated with higher rates of gastrointestinal (GI) bleeding compared to other frequently used DOACs, apixaban (Eliquis) and dabigatran (Pradaxa)?

Design: Retrospective cohort study, 2014-2019.

Setting: Icelandic national healthcare system.

Patients: New DOAC users.

Interventions/Exposure: Treatment with apixaban, dabigatran, or rivaroxaban at anticoagulation-level doses.

Outcome: Clinically relevant GI bleeding. This was defined as a GI bleed that led to a medical intervention, unscheduled physician visit, or temporary cessation of anticoagulation. These were identified by

International Classification of Diseases, Tenth Revision codes and manual verification through chart review.

Data Analysis: The main results of interest were the rates of GI bleeding associated with each anticoagulant. To adjust for factors that could confound the rates, the investigators used inverse probability of treatment weighting (IPTW). IPTW is a form of propensity score adjustment that estimates how likely an individual is to receive an exposure of interest (a given DOAC in this study). The likelihood of receiving the exposure is then used to weight how much each individual contributes to the study results. Individuals who are very likely to receive or not receive the exposure contribute less to the results. Because of this adjustment, the results should approximate the effect of the exposure of interest in the general population.

Funding: Icelandic Centre for Research and the Landspítali University Hospital Research Fund.

Results: Overall, 5,868 individuals met inclusion criteria. Two thousand one hundred fifty-seven (37%) were treated with apixaban, 494 (8%) with dabigatran, and 3,217 (55%) with rivaroxaban. Atrial fibrillation was the indication for anticoagulation in 80% of individuals. Investigators identified 241 GI bleeding events among the cohort. Seventy-two (30%) were upper GI bleeding, 135 (56%) were lower GI bleeding, and 34 (14%) could not be classified. One hundred forty-six (61%) of the events were classified as major GI bleeding.

Rivaroxaban was associated with the highest rate of GI bleeding at 3.2 events per 100 person-years, compared to apixaban and dabigatran at 2.5 and 1.9 events per person-year, respectively. The hazard ratio (HR) of GI bleeding for rivaroxaban and dabigatran relative to apixaban were 1.42 (95% CI 1.04-1.93) and 0.87 (0.46-1.65), respectively. In subgroup analyses, rivaroxaban was associated with higher rates of major GI bleeding and lower GI bleeding, but these were not statistically significant relative to apixaban (**Table 1**).

	Overall	Major	Upper	Lower
Apixaban	2.4	1.4	0.8	1.3
Dabigatran	1.6	1.1	0.4	1.2
Rivaroxaban	**3.2**	2.0	1.0	1.6

Table 1: Rates of GI bleeding per 100 person-years by DOAC

Note: Bold denotes statistically significant 95% confidence interval relative to apixaban.

COMMENTARY

Why Is This Important?

This study[1] uses real-world evidence to support prior observational studies that demonstrated that rivaroxaban is associated with higher GI bleeding risk compared to other DOACs.[2,3] In particular, the strengths of this study include a high-quality database with very little missing data or loss to follow-up due to the nationalized healthcare system in Iceland. Furthermore, the investigators manually confirmed all cases of GI bleeding, giving confidence to the study conclusions. The findings are potentially consistent with the hypothesis that rivaroxaban has higher GI bleeding risk due to its pharmacokinetics. Rivaroxaban (Xarelto) is dosed daily instead of twice daily like apixaban (Eliquis) and dabigatran (Pradaxa). As such, rivaroxaban achieves higher levels of factor Xa inhibition.[4]

Key Study Findings

Rivaroxaban was associated with slightly higher rates of GI bleeding compared to apixaban (3.2 vs 2.5 per 100 person-years, respectively). One hundred forty-two individuals would need to be treated for 1 year with apixaban instead of rivaroxaban to prevent 1 case of GI bleeding (number needed to harm). Whether this benefit is sufficient to justify

potential decreased adherence from twice daily dosing should be discussed between patients and their prescribers.

Caution

Relative to prior observational studies of DOAC-associated GI bleeding, the number of individuals included in the study was relatively small. This reduces the power and precision of the analyses. Furthermore, because of the relative recency of DOAC availability, the mean follow-up time was only about 1.5 years. The outcomes described in this study should be considered short term and not necessarily representative of risk for long-term users.

My Practice

In my luminal gastroenterology practice, I most commonly encounter DOACs in preparation for elective gastrointestinal endoscopy. I recommend anticoagulation holds consistent with recent joint clinical practice guidelines from the American College of Gastroenterology and Canadian Association of Gastroenterology.[5] That is, I do not recommend holding anticoagulation for low-risk procedures such as diagnostic endoscopy with mucosal biopsies. However, if the procedure is a screening colonoscopy, I usually recommend an anticoagulation hold because of the possibility of endoscopic mucosal resection of large polyps. I practice in an integrated care delivery network, so I am privileged to work with the prescribers of the anticoagulant and anticoagulation pharmacists in determining the duration of pre-procedure anticoagulation holds. In gen-

Creatinine clearance (ml/min)	Apixaban	Dabigatran	Rivaroxaban
≥60	2 days	2-3 days	2 days
30-59	3 days	3-4 days	3 days
15-29	4 days	4-6 days	4 days
<15 or on dialysis	Consult a pharmacist		

Table 2: Number of days to hold DOAC prior to endoscopy for procedures with high risk of GI bleeding
Note: Adapted from (6)

eral, our recommendations align with clinical practice guidance based on renal function from the American Society for Gastrointestinal Endoscopy (**Table 2**).[6] In the few cases where patients arrive for their endoscopy without holding anticoagulation, I discuss the risks and benefits of performing the procedure versus rescheduling. In particular, for colonoscopies performed on anticoagulation, this includes the possibility of need for a second colonoscopy to remove large polyps by endoscopic mucosal resection after the anticoagulant has been held.

Another scenario where I encounter DOACs is during inpatient consultation for patients who require anticoagulation but have high risk of GI bleeding. Based on the results of this study and other studies demonstrating higher GI bleeding rates for rivaroxaban, I recommend apixaban over rivaroxaban for new anticoagulation starts. However, because the number needed to harm for rivaroxaban versus apixaban is relatively high at 142, I do not recommend prophylactic DOAC changes from rivaroxaban to prevent GI bleeding.

For Future Research

Resumption of anticoagulants post endoscopy is a corollary to the topic of this study. Notably, the authors of the 2022 ACG-CAG Clinical Practice Guideline on anticoagulation management did not make a recommendation on this topic based on lack of relevant high-quality evidence. Future studies that determine rates of post-endoscopy bleeding by timing of DOAC resumption may help standardize clinical practice.

Disclosures

Dr. Vajravelu has no disclosures to report. This commentary does not represent the views of the U.S. Department of Veterans Affairs or the United States Government.

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CRC SCREENING

Adenoma Detection Rate in 45-49 Year-Olds Is Lower Compared to 50-54 Year-Olds, But Still Higher Than 25% Benchmark

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This summary reviews: Bilal M, Holub J, Greenwald D, et al. Adenoma Detection Rates in 45-49 Year-Old Persons Undergoing Screening Colonoscopy: Analysis from the GIQuIC Registry. Am J Gastroenterol 2022; 117: 806-808. https://pubmed.ncbi.nlm.nih.gov/35169107/

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STRUCTURED ABSTRACT

Question: What is the adenoma detection rate (ADR) in average-risk 45-49 year-olds undergoing their first screening colonoscopy?

Design: Retrospective database analysis using the GI Quality Improvement Consortium Ltd (GIQuIC) registry.

Setting: Participants in the GIQuIC registry include US endoscopists from multiple patient settings, including outpatient ambulatory endoscopy centers, hospital-based and office-based endoscopy units.

Participants: The study included individuals aged 45-49 years, 50-54 years, and 50-75 years who underwent colonoscopy between 2014 and 2020 who met the meeting following criteria: average-risk screening as only indication, adequate bowel preparation, and photo-documentation of cecum performed. Only procedures from endoscopists who performed at least 30 screening exams were included.

Intervention/Exposure: The GIQuIC registry was queried to

identify screening colonoscopies among average-risk individuals aged 45 to 75 years. ADR for these procedures were calculated. Only the first colonoscopy per patient was included in the study.

Outcomes: ADR was stratified by age group (45-49 years old, 50-54 years old, and 50-75 years old) and gender for the screening population. For completeness, ADR was also calculated for those in the 45-49 years old group undergoing screening colonoscopy regardless of family history of CRC.

Data Analysis: One-way ANOVA testing was used to determine differences in ADR among individuals aged 45-49 years, 50-54 years, and 50-75 years.

Funding: None

Results: Of the 2,806,539 screening colonoscopies performed by 814 endoscopists, 1.6% (n = 47,213) were performed in patients in the 45-49 age group, and 36% (n = 1,014,193) were in the 50-54 age group. As expected, the number of screening colonoscopies in patients aged 45 to 49 years increased over time, especially after 2018. The mean ADR was significantly lower in the 45-49 age group vs 50-54 age group (28.6% vs 31.8%, respectively, P <0.001; Table 1). After stratification for gender, mean ADR was still significantly lower in 45-49 age group vs 50-54 age group for men (32.9% vs 37.0%, respectively, P < 0.0001) and women (22.8% vs 25.6%, P < 0.0001). The overall ADR for patients aged 45 to 49, regardless of family history of CRC, was 28.5% (mean ADR in men: 32.8%; mean ADR in women: 22.9%).

COMMENTARY

Why Is This Important?

Recent data has shown that while CRC incidence has declined in the United States, there is an uptick in new cases among individuals younger than 50 years with a 13% increase in colon adenocarcinoma and 16% increase in rectal adenocarcinoma in those aged 40-49 years.[1] In fact, the current rates of incident CRC cases among 45 to 49-year-olds are comparable with rates in 50 year-olds before the adoption of nationwide CRC screening.[2] This has led major US societies to recommend the initiation

	45-49 years	50-54 years	*P*-value	50-75 Years	*P*-value
Overall mean ADR% (SD) among 814 endoscopists	28.63 (10.34)	31.87 (9.34)	<0.0001	36.32 (9.78)	<0.0001
Total procedures	47,213	1,014,193		2,759,326	
Mean ADR% (SD) in men	32.9 (10.74)	37.0%(9.96)	<0.0001	41.5 (9.89)	<0.0001
Total procedures	9,928	470,146		1,270,382	
Mean ADR% (SD) in women	22.84 (9.87)	25.57 (8.48)	<0.0001	30.10 (9.18)	<0.0001
Total procedures	16,372	529,084		1,477,418	

Table 1: Mean ADR stratified by age and gender

ADR, adenoma detection rate ; SD, standard deviation.

of CRC screening from age 45.[2,3] These recommendations have also been supported by data from simulation modelling studies which show that earlier CRC screening from age 45 is cost-effective.[4] However, while ADR in patients undergoing screening from age 50 have been established and benchmarked, ADRs in patients aged 45 to 49 years have not been rigorously studied.

Key Study Findings

Although the mean ADRs were significantly lower in the 45 to 49 year age cohort vs 50 to 54 year age cohort (28.6% vs 31.8%, respectively, $P< 0.001$), the mean ADR in the 45 to 49 age group still exceeds national ADR benchmark of $\geq$ 25%, which further supports guideline recommendations to initiate screening at age 45.

Caution

The presence or absence of a family history of CRC in the screening cohort could not be reliably ascertained. Also, Black patients might have been overrepresented in the 45 to 49 age group as they accounted for 18% of this subgroup, compared with 8% in the over 50 cohort, which

most likely occurred because some societal guidelines had previously recommended screening from age 45 in Black patients.[3]

My Practice

While we routinely report endoscopist ADRs at my institution as part of quality improvement, we are yet to report this metric in the 45-49 age group. The interesting results by Bilal et al do provide a benchmark for comparison when we review our data.

For Future Research

This excellent study provides some national estimates of mean ADRs in patients aged 45 to 49 years undergoing their first screening colonoscopy. However, more work needs to be done since potentially higher risk groups may be overrepresented in this cohort. In addition, benchmarks for other screening colonoscopy quality metrics including serrated lesion detection rates, advanced adenomas detection rates, and advanced serrated lesion detection rate will need to be described in the 45 to 49 age group.

Disclosures

Dr. Okafor has no disclosures to report.

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