Cochrane for Clinicians

Putting Evidence into Practice

Noninvasive Diagnostic Tests for *Helicobacter pylori* Infection

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Clinical Question

Which noninvasive diagnostic test—urea breath test, serology, or stool antigen test—provides the most accurate diagnosis of *Helicobacter pylori* infection in symptomatic and asymptomatic patients?

Evidence-Based Answer

When compared with serology or stool antigen tests, the urea breath test has the highest diagnostic accuracy to identify *H. pylori* infection in patients without a history of gastrectomy or recent use of antibiotics or proton pump inhibitors. Use of any of these three methods in a hypothetical cohort with an *H. pylori* prevalence of 53.7% and fixed specificity of 90% resulted in 46 false-positive results out of 1,000 patients tested, and the urea breath test had the lowest false-negative rate.[1] (Strength of Recommendation: B, based on inconsistent or limited-quality patient-oriented evidence.)

Practice Pointers

H. pylori infection affects 50% of the world's population.[2] In the United States, the seroprevalence of *H. pylori* is higher in blacks (53%) and Mexicans (62%) than in whites (26%), and it is more common in groups with lower socioeconomic status.[3] *H. pylori* infection can cause dyspepsia, peptic ulcer disease, and gastric cancers and is associated with iron deficiency anemia, idiopathic thrombocytopenia, and colorectal adenomas. Diagnostic tests used in the primary care office include serology and stool antigen tests, whereas the urea breath test and gastric biopsies require subspecialist referral. Once *H. pylori* has been detected, the treatment with standard therapy results in a 70% to 85% eradication rate.[4]

This review included 101 diagnostic studies involving a total of 11,003 patients, 5,839 (53%) of whom had confirmed *H. pylori* infection.[1] The authors evaluated the diagnostic accuracy of the urea breath test-^{13}C, urea breath test-^{14}C, serology studies, and stool antigen tests. The reference standard was endoscopic biopsy with pathognomonic staining in the same patient. Studies included adults and children (1,508 children in 14 studies) with and without gastrointestinal symptoms, and most studies excluded patients with gastrectomy and recent (not defined) use of antibiotics or proton pump inhibitors. Eight of the studies (with 843 patients) were completed in North America; none of these studies included children. All but one study had a moderate to high risk of bias because of a lack of consecutive or random patient selection, lack of blinding, and variable test diagnostic thresholds.

The urea breath test had the highest diagnostic accuracy and lowest false-negative rate for the detection of *H. pylori*. To enable comparison of the tests in a hypothetical sample of 1,000 patients, the authors calculated false-negative rates at a prevalence of 53.7% and used a median specificity of 90%. At these fixed values, all four tests had a false-positive rate of 46 per 1,000, whereas the urea breath test had the lowest false-negative rate and the stool antigen test had the highest. The positive predictive values were similar.

The American College of Gastroenterology (ACG) recommends testing in patients with active peptic ulcer disease, dyspepsia symptoms, and gastric mucosa–associated lymphoid tissue lymphoma, whereas the Maastricht guidelines also include patients starting long-term nonsteroidal anti-inflammatory drugs, those with idiopathic thrombocytopenic purpura, and those

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CME **This clinical content** conforms to AAFP criteria for continuing medical education (CME). See CME Quiz on page 13.

SUMMARY TABLE: ACCURACY OF *HELICOBACTER PYLORI* TESTING AT A PREVALENCE OF 53.7% AND SPECIFICITY OF 90%

Test	Sensitivity percentage (95% CI)	Diagnostic odds ratio (95% CI)	False-negative rate per 1,000 patients (95% CI)	Positive predictive value percentage
Urea breath test-^{13}C	94 (89 to 97)	153 (73.7 to 316)	30 (15 to 58)	92
Urea breath test-^{14}C	92 (89 to 94)	105 (74 to 150)	42 (30 to 58)	92
Serology	84 (74 to 91)	47.4 (25.5 to 88.1)	86 (50 to 140)	91
Stool antigen	83 (73 to 90)	45.1 (24.2 to 84.1)	89 (52 to 146)	91

who desire testing.[5,6] The ACG states that the urea breath test has the highest sensitivity and specificity overall but, in a low-prevalence population (around 20%), stool antigen testing also performs well. The ACG does not recommend serology testing in a low-prevalence population because of a high false-positive rate. Urea breath testing is easily attainable and can make a rapid diagnosis, although its availability is often limited to subspecialty clinics and can cost $150 to $400. Family physicians should test all patients with dyspepsia for *H. pylori*, and although the urea breath test offers the lowest false-negative rates, the false-negative rates of the more readily available serology and stool antigen tests are only slightly higher.

The practice recommendations in this activity are available at http://www.cochrane.org/CD012080.

Editor's Note: The positive predictive values reported in this Cochrane for Clinicians were calculated by the authors based on raw data provided in the original Cochrane review.

The opinions and assertions contained herein are the private views of the authors and are not to be construed as official or as reflecting the views of the Department of the Navy, the Defense Health Agency, the Department of Defense, or the U.S. government.

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Medication Management for Chronic Heart Failure with Preserved Ejection Fraction

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Clinical Question

Do therapies that help patients who have heart failure with reduced ejection fraction (HFrEF) also improve morbidity and mortality in patients who have heart failure with preserved ejection fraction (HFpEF)?

Evidence-Based Answer

Mineralocorticoid receptor antagonists reduce hospitalizations for patients with HFpEF. Angiotensin-converting enzyme (ACE) inhibitors and angiotensin receptor blockers (ARBs) have not been shown to change the morbidity or mortality in patients with HFpEF. Beta blockers may positively affect cardiovascular mortality, but they do not improve hospitalizations or all-cause mortality.[1] (Strength of Recommendation: A, based on consistent, good-quality patient-oriented evidence.)

Practice Pointers

HFpEF is a heterogeneous clinical syndrome with signs and symptoms of heart failure with left ventricular ejection fraction greater than 40%.[2] Six million adults in the United States have heart failure.[3] Patients with HFpEF account for one-half of this population and share similar mortality rates as those with HFrEF.[1,4] The authors of this

SUMMARY TABLE: TREATMENTS FOR CHRONIC HEART FAILURE WITH PRESERVED EJECTION FRACTION

Outcomes	Assumed risk	Corresponding risk (95% CI)	ARR (95% CI)	NNT (95% CI)
Angiotensin-converting enzyme inhibitors				
Cardiovascular mortality	86 per 1,000	81 per 1,000 (53 to 123)	NA	NA
Heart failure hospitalization	13 per 1,000	11 per 1,000 (8 to 15)	NA	NA
Angiotensin receptor blockers				
All-cause mortality	72 per 1,000	73 per 1,000 (66 to 80)	NA	NA
Cardiovascular mortality	131 per 1,000	133 per 1,000 (118 to 149)	NA	NA
Heart failure hospitalization	171 per 1,000	157 per 1,000 (142 to 174)	NA	NA
Beta blockers				
All-cause mortality	243 per 1,000	199 per 1,000 (163 to 243)	NA	NA
Cardiovascular mortality	173 per 1,000	135 per 1,000 (107 to 171)	0.038 (0.002 to 0.066)	26 (15 to 500)
Heart failure hospitalization	117 per 1,000	86 per 1,000 (55 to 133)	NA	NA
Mineralocorticoid receptor antagonists				
All-cause mortality	133 per 1,000	121 per 1,000 (104 to 141)	NA	NA
Cardiovascular mortality	88 per 1,000	79 per 1,000 (65 to 97)	NA	NA
Heart failure hospitalization	136 per 1,000	112 per 1,000 (94 to 134)	0.024 (0.002 to 0.042)	42 (23 to 500)

ARR = absolute risk reduction; NA = not applicable; NNT = number needed to treat.

Cochrane review sought to determine if therapies that improve morbidity and mortality in patients with HFrEF (i.e., beta blockers, mineralocorticoid receptor antagonists, ACE inhibitors, and ARBs) have similar benefits in those with HFpEF.[1]

This review included 37 randomized controlled trials with 18,311 patients. Primary outcomes were cardiovascular mortality and heart failure hospitalization, and secondary outcomes included all-cause mortality and quality of life. A limitation of this review was that a range of left ventricular ejection fraction cutoffs were used for HFpEF diagnosis (between 40% and 50%).

Beta blockers (i.e., carvedilol [Coreg], nebivolol [Bystolic], propranolol, metoprolol succinate, and bisoprolol) were compared with placebo in five studies and with usual care in five studies for a total of 3,087 patients. None of these studies were conducted in the United States or Canada. Only a few studies were included in the meta-analysis because of different outcome measures reported. There was an apparent reduction in cardiovascular mortality when examining the data across three studies (absolute risk reduction [ARR] = 0.038; 95% CI, 0.002 to 0.066; number needed to treat [NNT] = 26). However, the authors were cautious about drawing conclusions from this because when they removed the two studies that were considered to be at high risk of bias, the one remaining low-risk study did not demonstrate a difference in cardiovascular mortality between outcomes with beta blockers and placebo (relative risk = 0.81; 95% CI, 0.50 to 1.29; 643 participants).

Mineralocorticoid receptor antagonists (i.e., spironolactone, eplerenone [Inspra], and canrenone [not available in the United States]) were compared with placebo in eight studies and to usual care in four studies for a total of 4,408 participants. Some of these studies were conducted in the United States and Canada. Although most findings were driven by one trial with 3,445 patients, treatment with mineralocorticoid receptor antagonists led to a reduction in heart failure hospitalization (ARR = 0.024; 95% CI, 0.002 to 0.042; NNT = 42) with an increased risk of hyperkalemia. There was, however, no benefit on cardiovascular or all-cause mortality.

ACE inhibitors (i.e., enalapril [Vasotec], benazepril [Lotensin], perindopril [Aceon], ramipril [Altace], and quinapril [Accupril]) were compared with placebo in three studies and with usual care in five studies for a total of 2,061 patients with HFpEF. None of the studies were conducted in the United States or Canada, and the findings were again driven by one trial with 850 patients. ACE inhibitors showed no benefits

on cardiovascular mortality, heart failure hospitalizations, all-cause mortality, or quality of life.

ARBs (i.e., candesartan [Atacand], irbesartan [Avapro], valsartan [Diovan], and olmesartan [Benicar]) were compared with placebo in five studies and with usual care in three studies for a total of 8,755 patients with HFpEF. There were no benefits with regard to cardiovascular mortality, heart failure hospitalizations, all-cause mortality, or quality of life.

Guidelines on the treatment of HFpEF call for consideration of mineralocorticoid receptor antagonists to decrease hospitalization in patients who meet the following criteria: ejection fraction of 45% or more, elevated brain natriuretic peptide or heart failure hospitalization within one year, estimated glomerular filtration rate greater than 30 mL per minute, creatinine levels less than 2.5 mg per dL (221 µmol per L), and potassium levels less than 5.0 mEq per L (5 mmol per L). The American College of Cardiology also continues to recommend that ARB treatment be considered to decrease hospitalizations, consistent with previous guidelines.[5]

The practice recommendations in this activity are available at http://www.cochrane.org/CD012721.

Editor's Note: The absolute risk reductions and numbers needed to treat reported in this Cochrane for Clinicians were calculated by the author based on raw data provided in the original Cochrane review.

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