NARRATIVE REVIEW

Iron Deficiency Anemia in Postmenopausal Women: A Practical Approach to Diagnosis, Gastrointestinal Evaluation, and Management

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KEY POINTS

- IDA in a postmenopausal woman should not be attributed to diet alone without evaluation for an underlying cause.
- The AGA recommends a ferritin cutoff of <45 ng/mL in anemic patients when diagnosing iron deficiency.
- Bidirectional endoscopy is the standard initial gastrointestinal evaluation for unexplained IDA in postmenopausal women and men.
- Celiac disease should be considered, and noninvasive Helicobacter pylori testing is appropriate when no cause is identified after initial endoscopic evaluation.
- Oral iron is appropriate for most patients; intravenous iron is useful when oral therapy is not tolerated, ineffective, or unlikely to be adequately absorbed.
- After negative bidirectional endoscopy, response to iron therapy and recurrence of IDA should guide the need for further small-bowel or alternative evaluation.

Abstract

Background. Iron deficiency anemia (IDA) has a broad differential diagnosis. In postmenopausal women, the absence of menstrual blood loss increases the likelihood that iron deficiency reflects occult gastrointestinal blood loss or impaired absorption. Gastrointestinal malignancy is the most serious consideration, although nonmalignant conditions and normal examinations are more common.

Objective. To summarize current evidence and guideline recommendations for the diagnosis, gastrointestinal evaluation, and treatment of IDA in postmenopausal women.

Methods. Narrative synthesis of contemporary clinical practice guidelines, systematic reviews, meta-analyses, and selected primary studies.

Results. A ferritin concentration below 45 ng/mL is a useful diagnostic threshold for iron deficiency in patients with anemia, although ferritin rises with inflammation. The American Gastroenterological Association (AGA) recommends bidirectional endoscopy as the initial gastrointestinal evaluation for unexplained IDA in postmenopausal women and men. In the AGA technical review, pooled diagnostic yield was 8.9% for lower-gastrointestinal malignancy and 2.0% for upper-gastrointestinal malignancy. Oral iron remains appropriate for most patients; intravenous iron is preferred when oral iron is not tolerated, ineffective, or unlikely to be adequately absorbed.

Conclusions. Unexplained IDA in a postmenopausal woman warrants evaluation for an underlying cause rather than iron replacement alone. Bidirectional endoscopy is the central initial investigation. Subsequent evaluation should be individualized according to response to iron therapy, recurrence, initial findings, and the likelihood of small-bowel or non-gastrointestinal disease.

Keywords: *iron deficiency anemia; postmenopausal women; gastrointestinal malignancy; bidirectional endoscopy; colonoscopy; fecal immunochemical testing; iron replacement.*

1. Introduction

Iron deficiency is the most common nutritional deficiency worldwide and a major cause of anemia. Its clinical significance varies with age, sex, menstrual status, comorbidity, and the presence or absence of anemia.[4]

In postmenopausal women, menstrual blood loss is no longer an expected physiologic source of iron loss. Newly identified IDA without an obvious alternative explanation therefore warrants investigation for occult gastrointestinal blood loss or impaired absorption. Gastrointestinal malignancy is the most serious potential cause, but peptic ulcer disease, erosive disease, angioectasia, inflammatory bowel disease, celiac disease, and Helicobacter pylori infection are also encountered, and many endoscopic examinations are normal.[1–3]

The clinical task is to balance under-investigation of a potentially important source of blood loss against unnecessary invasive testing in patients without significant gastrointestinal disease. This review emphasizes practical decision-making, particularly after the initial gastrointestinal evaluation.

2. Illustrative Clinical Case

A 58-year-old postmenopausal woman presents with three months of progressive fatigue, exertional dyspnea, and ice craving (pagophagia). She denies melena, hematochezia, hematemesis, abdominal pain, altered bowel habits, and weight loss. She has no NSAID use, prior bariatric surgery, celiac disease, or inflammatory bowel disease, and eats meat regularly. Her last menstrual period was six years earlier. On examination she is pale with conjunctival pallor; vital signs are otherwise normal and the abdomen is unremarkable.

Laboratory Results — Illustrative Case

Parameter	Result
Hemoglobin	
MCV	
Ferritin	
Serum iron	
TIBC	
Transferrin saturation	
Reticulocyte count	
TSH, creatinine, WBC, platelets	

The findings establish IDA: markedly reduced ferritin, low transferrin saturation, elevated TIBC, and microcytosis. The absence of gastrointestinal symptoms does not exclude gastrointestinal pathology, and a negative fecal occult blood test would not reliably exclude intermittent or clinically relevant gastrointestinal lesions. Bidirectional endoscopy is indicated, with iron replacement initiated concurrently; celiac serology and noninvasive H. pylori testing should be incorporated according to the results of the initial evaluation.[1,2] This case is illustrative rather than a report of an actual patient.

3. Diagnosis of Iron Deficiency Anemia

Diagnosis requires both anemia and iron deficiency. The AGA recommends a ferritin threshold below 45 ng/mL in patients with anemia; this threshold is more sensitive than the traditional <15 ng/mL cutoff.[1] In patients with inflammation, ferritin may be misleadingly high, and transferrin saturation and other markers should be interpreted alongside ferritin.[3,4]

Laboratory Diagnosis of Iron Deficiency Anemia

Parameter	Typical Finding
Hemoglobin	Decreased
MCV	Decreased
Ferritin	Decreased
Serum iron	Decreased
TIBC / transferrin	Increased
Transferrin saturation	Decreased
RDW	Often increased

A therapeutic response can provide supportive diagnostic information: a hemoglobin rise of approximately 1 g/dL within two to four weeks of adequate iron therapy is generally consistent with iron-responsive iron deficiency, although response depends on adherence, ongoing blood loss, absorption, and competing diagnoses.[4,12]

4. Why IDA in Postmenopausal Women Requires Gastrointestinal Evaluation

For postmenopausal women and men with unexplained IDA, clinically important gastrointestinal pathology may be present even without gastrointestinal symptoms, so gastrointestinal investigation is recommended.[1–3] The AGA technical review pooled studies of bidirectional endoscopy in men and postmenopausal women with IDA and reported lower-gastrointestinal malignancy in 8.9% and upper-gastrointestinal malignancy in 2.0%; the panel emphasized that inclusion of some symptomatic patients likely overestimates the true prevalence in asymptomatic populations.[2] These estimates justify evaluation without implying that malignancy is the most likely finding in an individual patient.

A 2026 systematic review and meta-analysis of 9,807 patients with IDA further illustrates the range of findings: upper-gastrointestinal H. pylori gastritis was the most common upper-tract diagnosis, while colorectal cancer was identified in approximately 8% overall; 52% of upper endoscopies and 66% of lower endoscopies were normal.[5] These pooled estimates should not be interpreted as individual risk estimates because study populations and referral patterns varied substantially.

5. Bidirectional Endoscopy

Bidirectional endoscopy — esophagogastroduodenoscopy and colonoscopy, ideally performed in the same setting — provides complementary evaluation of the upper and lower gastrointestinal tracts.[1,2] Colonoscopy is central because colorectal neoplasia is a recognized cause of chronic occult blood loss; upper endoscopy can identify peptic ulcer disease, erosive gastritis, gastric malignancy, and other lesions. The decision to proceed should rest on confirmed iron deficiency and clinical context rather than on overt bleeding or stool blood testing alone.

When colonoscopy is unsuitable or incomplete, alternative large-bowel imaging may be considered according to local expertise and patient factors.[11]

6. Fecal Immunochemical Testing

FIT has been proposed as a tool to triage colonoscopy in patients with IDA. A 2024 systematic review and meta-analysis of 1,761 iron-deficient patients found that, at a threshold of 10 µg hemoglobin/g feces, FIT was approximately 88% sensitive and 83.4% specific for colorectal cancer in patients with IDA.[6]

FIT may help prioritize colonoscopy where endoscopic capacity is constrained, but it should not be considered a universal substitute for endoscopic evaluation in postmenopausal women with confirmed IDA. FIT evaluates fecal hemoglobin and does not assess the upper gastrointestinal tract. A 2026 single-center retrospective study reported a high negative predictive value for colorectal cancer in IDA, but residual risk remained; the study therefore supports risk stratification rather than exclusion of disease.[7] Older fecal occult blood testing performs inadequately as a diagnostic test in IDA and should not determine whether endoscopic evaluation is performed.[8]

7. Celiac Disease and Helicobacter pylori

Celiac disease can cause iron deficiency through impaired absorption and may present without classic gastrointestinal symptoms. The AGA supports serologic testing rather than routine small-bowel biopsy in every patient; tissue transglutaminase IgA with total IgA is a practical initial approach, with biopsy guided by positive serology or persistent clinical suspicion.[1,9]

H. pylori may contribute to iron deficiency through chronic gastritis and impaired iron absorption. The AGA recommends noninvasive H. pylori testing when no cause is identified after bidirectional endoscopy rather than routine gastric biopsies in every patient.[1]

8. Iron Replacement

Iron replacement should generally begin once IDA is recognized and need not await completion of the gastrointestinal evaluation. Ferrous sulfate is a reasonable first choice because it is inexpensive; no single oral formulation has demonstrated a clear overall advantage.[3]

The AGA advises oral iron no more than once daily. Alternate-day dosing may improve tolerability and can increase fractional absorption in physiologic studies, although clinical trials have not

established a consistent hemoglobin advantage over daily dosing.[3,10] Thus, alternate-day dosing is best viewed as a practical option when tolerability or adherence is a concern rather than as a proven superior regimen.

Intravenous iron should be considered when oral iron is not tolerated, ineffective despite adherence, or unlikely to be adequately absorbed, including selected patients with malabsorptive disorders such as prior bariatric surgery, celiac disease, or active inflammatory bowel disease.[3] Severity of anemia, symptoms, ongoing blood loss, comorbidity, and the need for timely repletion may also influence the choice of route.

Iron Replacement: Route by Clinical Situation

Clinical Situation	Preferred Approach
Newly diagnosed uncomplicated IDA	Oral iron, generally once daily
GI intolerance to daily dosing	Consider alternate-day dosing
Poor response to oral iron	Reassess adherence, ongoing blood loss, diagnosis, and absorption
Malabsorption likely (e.g. bariatric surgery, celiac, IBD)	Consider IV iron
Oral iron not tolerated or stores fail to improve	Consider IV iron
Need for rapid repletion or substantial ongoing loss	Consider IV iron based on clinical context

9. Management After Negative Bidirectional Endoscopy

Negative EGD and colonoscopy do not mandate immediate capsule endoscopy. For uncomplicated patients, the AGA suggests a trial of iron replacement before routine small-bowel evaluation because the yield of capsule endoscopy for small-bowel malignancy is low and evidence for routine use after negative bidirectional endoscopy is limited.[1,2]

Patients with persistent or recurrent IDA despite adequate iron therapy should undergo reassessment of adherence, ongoing blood loss, absorption, and the adequacy of the initial studies. Small-bowel evaluation, particularly capsule endoscopy, becomes more appropriate in persistent or recurrent unexplained IDA and when clinical features increase suspicion for small-bowel disease.[3,11]

10. Common Clinical Pitfalls

- Assuming absence of gastrointestinal symptoms excludes gastrointestinal disease.
- Using a negative FIT or older fecal occult blood test to exclude gastrointestinal pathology.
- Attributing IDA to NSAIDs, antiplatelet agents, or anticoagulants alone without considering an underlying lesion.
- Equating hemoglobin normalization with resolution of the underlying cause.
- Performing capsule endoscopy reflexively after every negative bidirectional endoscopy.
- Failing to reassess adherence, ongoing blood loss, absorption, or the original diagnosis when the hemoglobin response is inadequate.

11. Practical Diagnostic Algorithm

Confirm anemia → confirm iron deficiency → assess history, medications, diet, bleeding risk, and non-gastrointestinal sources → for unexplained IDA in a postmenopausal woman, perform bidirectional endoscopy while initiating iron replacement → if a cause is found, treat it and replace iron → if no cause is identified, perform celiac serology and noninvasive H. pylori testing as appropriate → assess hematologic response → for persistent or recurrent IDA, reassess the initial studies and consider small-bowel evaluation.

12. Discussion

The importance of IDA in postmenopausal women lies less in the anemia itself than in the possibility that it signals an unrecognized disease process. The evidence supports gastrointestinal evaluation but not the assumption that every patient harbors malignancy; normal and nonmalignant findings are common.[1–5] Three practical points follow: iron replacement should not routinely be withheld pending evaluation; hemoglobin normalization does not establish the cause; and a negative initial evaluation should lead to response-guided follow-up rather than indiscriminate escalation.

The most useful strategy is sequential — confirm the diagnosis, investigate the likely source, replace iron, assess response, and escalate when the clinical course warrants.

13. Limitations

This is a narrative review, not a systematic review; it did not use a prespecified search protocol, duplicate screening, or formal risk-of-bias assessment. Reported malignancy and diagnostic-yield rates vary across studies because of differences in population, referral patterns, definitions, and study design, and should be interpreted as population-level estimates rather than individual probabilities. The review also relies substantially on guidelines and expert reviews for management recommendations; these recommendations may evolve as newer evidence becomes available.

14. Conclusion

IDA in a postmenopausal woman warrants investigation because menstrual loss is no longer an expected explanation and clinically important gastrointestinal disease may be present despite the absence of symptoms. After iron deficiency is confirmed and non-gastrointestinal causes are considered, bidirectional endoscopy is the standard initial gastrointestinal evaluation. Most patients will not have malignancy, but the prevalence of important gastrointestinal disease is high enough to justify investigation. Iron replacement and etiologic evaluation should proceed concurrently, with small-bowel or alternative investigation reserved for persistent, recurrent, or otherwise unexplained IDA.

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