AGA Iron Deficiency Anemia – Draft Quality Indicators

Diagnosis

1. Use readily available laboratory parameters for diagnosis of iron deficiency anemia. Anemia is defined as Hgb ≤13 g/dL in men and ≤12 g/dL in non-pregnant women.

   Rationale: The World Health Organization defines anemia as a hemoglobin ≤13 g/dL in men and ≤12 g/dL in nonpregnant women.

2. In patients with anemia, additional testing is needed to identify iron deficiency, most commonly ferritin. AGA suggests a ferritin cutoff of <45 ng/mL, but different thresholds may be appropriate in specific patient populations, such as those with underlying inflammatory disorders, chronic kidney disease, or heart failure. Additional tests, such as transferrin saturation, may be needed to clarify the diagnosis.

   Rationale: Serum ferritin is the most commonly used test for diagnosing iron deficiency, but different organizations have proposed cutoff values ranging from 15 to 100 ng/mL. In AGA's guideline and accompanying technical review for the gastrointestinal evaluation of iron deficiency anemia, a ferritin threshold of <45 ng/mL was felt to maximize sensitivity with an acceptable number of false-positive diagnoses. In some patient populations, ferritin studies may not accurately reflect body iron stores, and other tests, such as transferrin saturation, may be needed to assist in the diagnosis of iron deficiency.

Evaluation

3. Perform a thorough history and physical examination to identify potential etiologies of iron deficiency.

   Rationale: Patient history and exam findings can guide whether evaluation is indicated. Eliciting dietary intake, menstrual history (in women), and other sources of blood loss, such as frequent blood donation, can help guide evaluation.

4. Patients with iron deficiency anemia and potential alarm features, such as gastrointestinal bleeding, abdominal pain, or unexplained weight loss, warrant further diagnostic evaluation.

   Rationale: Alarm features may indicate the presence of serious gastrointestinal disorders, including gastrointestinal malignancy, celiac disease, and inflammatory bowel disease, and should be investigated as clinically appropriate.

5. Perform bidirectional endoscopy in men and postmenopausal women without other obvious causes of iron deficiency anemia, such as poor dietary intake, non-gastrointestinal blood loss, or frequent blood donation.

   Rationale: The overall risk of gastrointestinal malignancy is significantly higher in asymptomatic patients with iron deficiency anemia compared to an average-risk

DRAFT

colorectal cancer screening cohort, as noted in AGA Technical Review for Gastrointestinal Diagnosis of Iron Deficiency Anemia. Bidirectional endoscopy is indicated in these patient populations for the detection of colorectal or upper gastrointestinal cancer. It may also detect other potential etiologies of iron deficiency, such as peptic ulcer disease, celiac disease, erosive esophagitis, or inflammatory bowel disease. The benefits of detecting gastrointestinal disorders and malignancy outweigh the risks of bidirectional endoscopy.

6. Perform bidirectional endoscopy in premenopausal women without a clear cause of iron deficiency or those with alarm features or worsening anemia.

   Rationale: Premenopausal women with iron deficiency anemia merit special consideration. While there is a baseline prevalence of iron deficiency in this population due to menstrual bleeding, there is clinical value in further risk-stratifying this group based on the severity of iron deficiency anemia, presence of gastrointestinal symptoms, family history of gastrointestinal cancer, indication of occult GI blood loss, or if anemia is new or significantly changed from baseline. Given the increasing incidence of early-onset colorectal cancer, a lower threshold for pursuing endoscopic evaluation in this population is warranted. In premenopausal women with higher risk for underlying gastrointestinal causes of iron deficiency anemia, the benefits of bidirectional endoscopy are felt to outweigh the potential risks.

7. Patients with iron deficiency anemia should be evaluated for *Helicobacter pylori* (*H. pylori)* infection by noninvasive testing (urea breath test or stool antigen test) or by gastric biopsies taken during endoscopy.

   Rationale: *H. pylori* infection has been associated with iron deficiency in observational studies, and the addition of *H. pylori* treatment to iron supplementation can result in greater improvement in mean hemoglobin compared to iron supplementation alone. There is a lack of strong evidence to support the selection of a particular diagnostic strategy for *H. pylori* infection in this patient population; therefore, any of the commonly recommended strategies is likely acceptable. If proceeding with bidirectional endoscopy, gastric biopsies can be readily obtained.

8. Patients with iron deficiency anemia should be evaluated for celiac disease by serologic testing and/or duodenal biopsies during endoscopy.

   Rationale: Celiac disease is a well-recognized cause of iron deficiency, and patients may not present with overt symptoms. Identification and treatment of celiac disease can lead to resolution of iron deficiency, improvement of subtle gastrointestinal symptoms, and correction of other nutritional deficiencies, while preventing potential complications. In practice, Celiac disease may be evaluated by obtaining serologic studies with endoscopic confirmation if positive, or by taking duodenal biopsies during upper endoscopy.

Management

DRAFT

9. Patients with iron deficiency anemia should have iron repletion to ameliorate symptoms and prevent possible complications.

   Rationale: Iron repletion can ameliorate symptoms of iron deficiency, such as fatigue, shortness of breath, pica, alopecia, brain fog, and decreased exercise tolerance, and improve hemoglobin and iron stores.

10. In most patients, a trial of oral iron, dosed every day to every other day, is the initial first-line therapy.

    Rationale: Oral iron supplementation can result in improvements in fatigue and iron stores, and some studies have shown comparable rates of iron repletion with every other day dosing compared to daily dosing with improved tolerability. There is no substantial evidence that one formulation of oral iron is superior in effectiveness or tolerance. While some patients will not tolerate or have an inadequate response to oral iron, the benefits, acceptability, and lower cost compared to intravenous iron support an initial trial of oral supplementation.

11. In patients with more severe iron deficiency or anemia-related symptoms, intravenous iron should be considered for first-line therapy.

    Rationale: Intravenous iron will lead to more rapid replenishment of iron stores with more rapid improvement in anemia or anemia-related symptoms (e.g., fatigue, shortness of breath, etc.) compared to oral iron.

12. Intravenous iron is indicated in patients who do not respond to or who are intolerant of oral iron.

    Rationale: Intravenous iron is effective at increasing iron stores and hemoglobin and allows avoidance of packed red blood cell transfusions. These potential benefits outweigh the low risk of adverse events with currently used intravenous iron formulations.

13. Intravenous iron is indicated as first-line therapy for specific patient populations, including those who have undergone malabsorptive bariatric procedures (e.g., Roux-en-Y gastric bypass or duodenal switch), have comorbidities including inflammatory bowel disease with active inflammation, chronic kidney disease (CKD), or heart failure, or are in the 3rd trimester of pregnancy.

    Rationale: Patients with underlying malabsorptive conditions, including certain bariatric procedures or active inflammatory bowel disease, are unlikely to respond to oral iron. Patients with active inflammatory bowel disease may not absorb oral iron due to impaired gut function or inflammation-driven blockade of iron absorption. Patients with chronic kidney disease or heart failure may also have poor iron absorption due to functional blockades and impaired gut function and have a better response to intravenous iron compared to oral iron without an increase in adverse events. Thus, intravenous iron should be considered as first-line therapy in these patient populations. In pregnant individuals in the 3rd trimester, intravenous iron can lead to improvements in

DRAFT

fatigue, reduced need for blood transfusion, and higher maternal hemoglobin and iron stores compared with oral iron.

14. Response to oral or intravenous iron should be monitored by hemoglobin and iron parameters at least one month after initiating therapy.

    Rationale: Hemoglobin and iron parameters will typically improve rapidly after iron supplementation. These parameters should be monitored about a month after initiation of oral iron and at least one month after initiation of intravenous iron to ensure an adequate response and guide further therapy.

DRAFT