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Q/ How best to diagnose iron-deficiency anemia in patients with inflammatory disease?

EVIDENCE-BASED ANSWER

A/ THE SERUM FERRITIN LEVEL is the most sensitive and specific initial laboratory test for iron-deficiency anemia (IDA) in patients with inflammation. Serum ferritin levels <45 ng/dL confirm IDA, and levels of ≥100 ng/dL essentially rule it out (strength of recommendation [SOR]: **B**, systematic review of prospective validating cohort studies with heterogeneity).

For patients with intermediate serum ferritin levels (45-99 ng/dL), the soluble transferrin receptor (sTfR) level and the sTfR-ferritin index (ratio of sTfR to log ferritin) are highly sensitive and specific. An sTfR-ferritin index of ≥1.5 is diagnostic of IDA, even in the presence of acute or chronic inflammation (SOR: **B**, systematic review of prospective validating cohort studies that lacked standardized reference values).

Evidence summary

A systematic review of 55 studies that included 45 validating prospective studies (total 2579 patients, of whom 919 had inflammatory, liver, or neoplastic disease) found that a low serum ferritin level was the most sensitive and specific initial test to diagnose IDA, even in the presence of inflammation.[1] More than 80% of patients studied had confirmatory bone marrow aspiration.

Serum ferritin <45 ng/dL performed well for identifying IDA in all patients combined (sensitivity=85%; specificity=92%; positive likelihood ratio=11), although the authors didn't calculate sensitivity and specificity for the subgroup of patients with an inflammatory disease process.

A serum ferritin level ≥100 ng/dL made IDA unlikely (sensitivity=5.5%; specificity=29%; negative likelihood ratio=0.08). Serum ferritin levels between 45 and 99 ng/dL weren't useful in evaluating IDA. The subgroup analysis of the patients with inflammatory, liver, or neoplastic disease found that serum ferritin outperformed measurements of mean cell volume, transferrin saturation, red cell protoporphyrin, and red cell volume for diagnosing IDA.[1]

Follow up with the sTfR-ferritin index if necessary

The sTfR-ferritin index is sensitive and specific for diagnosing IDA in patients with concomitant inflammation, including those with intermediate serum ferritin levels of 45 to 99 ng/dL. A systematic review of 9 prospective validating cohort studies (total 818 patients, of whom 678 had inflammatory disease) compared sTfR levels and sTfR-ferritin index (sTfR-to-log ferritin ratio) values against bone marrow biopsy for identifying IDA.[2]

A mean sTfR level ≥2.5 mg/L diagnosed IDA with a sensitivity of 68% to 97% and a specificity of 47% to 100%. In patients with acute and chronic inflammation, a mean sTfR-ferritin index ≥1.5 mg/L had a higher sensitivity (88%-100%) and specificity (93%-100%). The studies were limited by heterogenous populations, small sample sizes, and

nonstandardized techniques and reference ranges for sTfR levels.

Recommendations

No major professional organizations in the United States have issued recommendations or clinical guidelines for diagnosing iron deficiency in patients with chronic inflammation.

The British Society of Gastroenterology suggests that a serum ferritin level <50 ng/dL is consistent with iron deficiency but lists the use of sTfR as promising, but unproven, in the clinical setting.[3] JFP

References

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