COLLEGE of AMERICAN PATHOLOGISTS

C-Reactive Protein and Erythrocyte Sedimentation Rate Test Use for Clinicians

SYNOPSIS AND RELEVANCE

Erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP) are the most widely used markers in the clinical evaluation of acute and chronic inflammatory conditions. This module addresses the clinical scenarios in which ESR and CRP are most appropriately used to assess acute and chronic inflammatory conditions to reduce routine ordering of both tests simultaneously.

- CRP is a more sensitive and specific reflection of the acute phase response than ESR.
- ESR is not recommended as a screening test for acute inflammation in patients with undiagnosed conditions.
- Routine ordering of both ESR and CRP is unnecessary and risks clinical misinterpretation if the tests give discrepant results.

INSIGHTS

1. CRP has superior sensitivity, specificity and kinetics than ESR and is the preferred screening test for acute inflammation.
2. ESR remains useful in the diagnosis and monitoring of chronic rheumatologic diseases (eg, rheumatoid arthritis (RA), polymyalgia rheumatica, and giant cell arteritis).
3. Simultaneous ESR and CRP testing has unique utility in systemic lupus erythematosus (SLE), giant cell arteritis (GCA), and orthopedic infection, and requires judicious planning of combined result interpretation.

BACKGROUND

ESR and CRP are the most common laboratory tests used in the screening of inflammatory conditions. Both tests are widely available and easy to perform.[1] Elevations in the ESR are an indirect measurement influenced by the amount of protein in the plasma,[2] whereas CRP is a specific measurement produced by the liver in the acute phase response. Therefore, CRP is far more sensitive and specific than ESR in the evaluation of acute inflammation, precluding the need for routine ordering of both ESR and CRP which can be discrepant in approximately one-fourth of cases.[3]

For the initial evaluation of idiopathic acute inflammation, CRP testing alone is recommended.[4] ESR, in contrast, remains useful in certain clinical conditions, such as monitoring chronic rheumatologic diseases (eg, rheumatoid arthritis, polymyalgia rheumatica and giant cell arteritis).[1] There are some notable situations in which simultaneous ESR and CRP testing can be useful, including RA, SLE, GCA, Kawasaki disease, and orthopedic infection.[5] In RA, ESR and CRP are used in the classification system to classify a patient with definite RA.[6] In SLE patients presenting with a fever, each unit increase in the ratio of ESR:CRP is associated with a 17% increase in the odds of the fever being attributable to SLE flare compared to infection.[7] In GCA most patients have both an elevated ESR and CRP, but there can be discordance of the two tests (usually elevated CRP and normal ESR), so the use of both tests provides a greater sensitivity for the diagnosis of GCA than either test alone.[8] In Kawasaki disease, ESR and CRP levels are usually elevated at presentation and return to normal in 6-10 weeks, where the diagnosis is unlikely if ESR and CRP return to normal without treatment after one week.[9] In orthopedic infection, simultaneous ESR and CRP testing can improve diagnostic accuracy, particularly at reducing false positive rates in clinical scenarios with a low-pretest probability for infection.[10]

Careful interpretation of individual and combined tests is key in proper assessment of results, including unique confounding factors and discrepant findings between the two tests. For confounding variables, CRP is notably influenced by obesity and related metabolic abnormalities, while ESR is well-known to be influenced by age and gender (higher in ages >50 years and women).[11] Discrepant results between the two tests may be due to timing of inflammation, where CRP quickly rises and falls in contrast to ESR which slowly rises and falls following an inciting inflammatory event. Furthermore, ESR would remain elevated in settings of Intravenous immunoglobulin (IVIG) therapy, given increased immunoglobulins. CRP is also much more sensitive than ESR in detecting low-level inflammation, in which ESR may not increase much if at all. In summary, concurrent ordering of both ESR and CRP should be avoided except in certain clinical scenarios, and ordering physicians should understand how to interpret possible discrepant results.

MODULE REFERENCES

1. Lapić I, Padoan A, Bozzato D, Plebani M. Erythrocyte sedimentation rate and C-reactive protein in acute inflammation. Am J Clin Pathol. 2020;153(1):14-29. doi:10.1093/ajcp/aqz142

2. Alende-Castro V, Alonso-Sampedro M, Vazquez-Temprano N, et al. Factors influencing erythrocyte sedimentation rate in adults: new evidence for an old test. *Medicine (Baltimore)*. 2019;98(34):e16816. doi:10.1097/MD.0000000000016816
3. Assasi N, Blackhouse G, Campbell K, et al. *Comparative Value of Erythrocyte Sedimentation Rate (ESR) and C-Reactive Protein (CRP) Testing in Combination Versus Individually for the Diagnosis of Undifferentiated Patients With Suspected Inflammatory Disease or Serious Infection: A Systematic Review and Economic Analysis*. Ottawa (ON): Canadian Agency for Drugs and Technologies in Health. November 2015.
4. Colombet I, Pouchot J, Kronz V, et al. Agreement between erythrocyte sedimentation rate and C-reactive protein in hospital practice. *Am J Med*. 2010;123(9). doi:10.1016/j.amjmed.2010.04.021
5. Harrison M. Erythrocyte sedimentation rate and C-reactive protein. *Aust Prescr*. 2015;38(3):93-94. doi:10.18773/austprescr.2015.034
6. Kay J, Upchurch KS. ACR/EULAR 2010 rheumatoid arthritis classification criteria. *Rheumatology (Oxford)*. 2012;51 Suppl 6:vi5-vi9. doi:10.1093/rheumatology/kes279
7. Littlejohn E, Marder W, Lewis E, et al. The ratio of erythrocyte sedimentation rate to C-reactive protein is useful in distinguishing infection from flare in systemic lupus erythematosus patients presenting with fever. *Lupus*. 2018;27(7):1123-1129. doi:10.1177/0961203318763732
8. Parikh M, Miller NR, Lee AG, et al. Prevalence of a normal C-reactive protein with an elevated erythrocyte sedimentation rate in biopsy-proven giant cell arteritis. *Ophthalmology*. 2006;113(10):1842-1845. doi:10.1016/j.ophtha.2006.05.020
9. Bayers S, Shulman ST, Paller AS. Kawasaki disease: part I. Diagnosis, clinical features, and pathogenesis. *J Am Acad Dermatol*. 2013;69(4):501.e1-512. doi:10.1016/j.jaad.2013.07.002
10. Barrack R, Bhimani S, Blevins JL, et al. General assembly, diagnosis, laboratory test: proceedings of international consensus on orthopedic infections. *J Arthroplasty*. 2019;34(2S):S187-S195. doi:10.1016/j.arth.2018.09.070
11. Alende-Castro V, Alonso-Sampedro M, Fernández-Merino C, et al. C-reactive protein versus erythrocyte sedimentation rate: implications among patients with no known inflammatory conditions. *J Am Board Fam Med*. 2021;34(5):974-983. doi:10.3122/jabfm.2021.05.210072