Erythrocyte Sedimentation Rate and C-Reactive Protein Compared in the Elderly

Paul R. Katz,1 Steven I. Gutman,2 Gary Richman,3 Jurgis Karuza,4 William R. Bartholomew,5 and John Baum6

The erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP) concentrations were studied in 101 elderly individuals (mean age 72 y) to determine their utility as diagnostic aids in subjects with underlying infection/inflammation. Whereas ESR and CRP were both significantly increased in patients with infection or inflammation, or both, analysis of variance indicated that those subjects still alive six months later had significantly lower ESR values. Analysis of sensitivity, specificity, and positive predictive values indicated that neither test satisfactorily discriminated between patients with and those without ongoing acute or chronic disease. Receiver-operating characteristic curve analysis confirmed the low true-positive/false-positive ratios of both ESR and CRP. In the elderly, neither CRP nor ESR has distinct advantages over the other, and both tests evidently have limited utility.

Additional Keyphrases: geriatric chemistry • distinguishing acute and chronic disease, functional and organic disease • receiver-operating characteristic curves

Diagnosis of disease processes in the elderly is often confounded by subtle and nonspecific symptomatology. As a result, discriminating between functional and organic conditions in this population may be difficult. Two nonspecific measures for disease activity have been advocated for use in this diagnostic setting: the erythrocyte sedimentation rate (ESR) and the C-reactive protein (CRP) (1-4). Although both are widely available and are used interchangeably, whether one is superior in the elderly remains controversial. Furthermore, the increased cost of CRP relative to ESR raises questions of cost effectiveness. Kenny et al. (5), in a small retrospective study comparing ESR and CRP in acutely ill geriatric patients, found CRP to be superior to ESR as an objective, nonspecific maker for disease activity. Nevertheless, sensitivity, specificity, and predictive values were not reported, and problems with both false-negative and false-positive results were noted. Our study was designed to further evaluate the relative value of CRP vs ESR as diagnostic aids for identifying underlying infection/inflammation in an elderly population receiving different levels of care and with acute and chronic disease.

For the efficacy of a clinical test to be adequately evaluated, a "gold standard" needs to be defined. For the purposes of the present study, a thorough chart review, coupled with patient examination where necessary, defined the gold standard for patients with or without infection/inflammation. It is equally important to consider not only the extent to which the clinical tests are able to detect infection/inflammation when truly present (i.e., test sensitivity) but also the extent to which the clinical test correctly identifies the absence of disease (i.e., specificity). Both of these test properties are stable and do not change when different proportions of diseased and well patients are tested (6).

The primary purpose of this study was not to absolutely quantify the diagnostic utility of ESR or CRP. Rather, it was our intention to consider the relative differences in the sensitivity and specificity of the ESR and CRP in the same population sample. Because ESR and CRP assays were performed on the same population sample, the prevalence of disease was identical and, therefore, subject classification problems were controlled for the two tests.

1 Nonstandard abbreviations: ESR, erythrocyte sedimentation rate; CRP, C-reactive protein; and ROC, receiver-operating characteristic (curve).
Materials and Methods

To ensure a sample of typical geriatric patients at various levels of care, we recruited subjects from both institutional and community-based settings. Some were recruited from the inpatients in the acute- and long-term care geriatric wards at the Buffalo Veterans Administration Medical Center over a one-month period. Of the 85 patients approached in this fashion, nearly all (78) agreed to participate. In addition, so as to have a subset of healthier and vigorous elderly and to provide a greater number of female subjects, we included in the study 23 residents from a nonprofit apartment complex for independent elderly in Buffalo, NY. Informed consent was obtained from each subject (or guardian, in cases of diminished competence). Two of us (G. R. and P. R. K.), who had specific experience and training in assessing medical records, reviewed each inpatient’s chart for basic demographic information and active medical problems and medications. In 10% of the cases, we noted discrepancies between the medical charts and observed medical condition of the patients. These discrepancies were resolved by additional direct examination of patients and/or consultation with the primary-care providers. For >90% of the cases both of us reached the same decisions on assessment of patients.

For the community-based subjects, a standardized brief medical history was elicited by one of us (P. R. K.), with emphasis on current illnesses and medications. These data paralleled the information obtained for the hospitalized subjects. Where required for assessing a subject’s health status, an on-site medical examination was performed. Overall short-term mortality was determined in all subjects by review of status six months after entry into the study.

Infection was noted as present in both community-dwelling and hospitalized subjects if laboratory, clinical, and/or radiographic evidence was sufficient to satisfy one of the following five widely accepted criteria (7) (with or without increased (>38 °C) temperature): (a) culture of body site or fluid demonstrating pathogenic bacteria, (b) radiographic evidence of active pneumonia, (c) osteomyelitis confirmed radiographically or by biopsy, (d) purulent drainage from sinus tract or ulceration, or (e) gastroenteritis, with stool culture demonstrating pathogenic bacteria. Inflammation was considered to be present according to one or more of the following generally accepted criteria: (a) negative culture; (b) objective evidence for erythema, increased warmth, pain, and/or effusion of skin or soft tissue; (c) connective tissue disease or vasculitis meeting criteria of the American Rheumatologic Association; (d) malignancy confirmed by biopsy, radiography, or other objective laboratory data.

Blood was sampled from each study subject, and the ESR of the EDTA-treated samples was measured within 2 h (manual Westergren method). Samples for assay of C-reactive protein were centrifuged and the serum was assayed, either immediately or after storage at −70 °C, by automated rate nephelometry (ICS; Beckman Instruments, Inc., Brea, CA). The normal value for CRP as measured by this method is <8 mg/L. Values for CRP >20 mg/L were repeated for confirmation; no qualitative changes in results were observed. Because the ESR and CRP tests were done after medical chart review, the reviewers were blinded as to the results of the ESR and CRP tests. None of the subjects at the time of the study was presenting in an acute fashion and thus neither ESR nor CRP were considered “first tests” in the classic sense.

To assess correlations between disease states, blood tests, and six-month mortality, we used Pearson’s product–moment correlation coefficient and analysis of variance. Predictive value analysis was according to the method of Galen and Gambino (8). ESR and CRP were also compared by use of receiver-operating characteristic (ROC) curves (9, 10).

Results

The mean age of the sample populations was 72 y (SD 11.7 y). Subjects included 21 women and 80 men. Underlying infections and (or) inflammatory diseases were noted in 33% of the study participants, most often involving the skin, genitourinary tract, or respiratory system. No subjects had evidence of active neoplastic disease at the time of the study. Between-group differences were evaluated by one-way analysis of variance. As expected, values for CRP and ESR were significantly (P <0.05) above normal in the infection and (or) inflammation groups. There were no statistically significant differences in either CRP or ESR as a function of specific disease state or medication. We found no significant sex-related differences in CRP or ESR values, nor any significant positive correlation with age and these values.

Analysis of variance of data on ESR and CRP with mortality at six months (Yes, No) as the between-subject factor showed that ESR values for those patients who died within that period were significantly increased at the time of the study. No such differences in CRP values were found. Sensitivity, specificity, and predictive values for both ESR and CRP at various cutoff values are shown in Table 1. Although sensitivity declined dramatically with increasing CRP and ESR cutoff values, specificity increased. ROC curves for the two assays are shown in Figure 1.

Discussion

The utility of nonspecific tests such as the ESR and CRP in screening for occult disease remains controversial. Clearly, screening for disease in asymptomatic patients rarely results in the discovery of clinically useful information not previously apparent after a careful clinical history and physical and laboratory examination. However, in a patient with vague symptomatology unsubstantiated by clinical data—a not infrequent occurrence in the elderly—tests such as the ESR and CRP may be of value as a so-called “sickness index” in discriminating between functional and organic disease (11).

Surprisingly, comparisons between ESR and CRP in the elderly have been limited and there is no consensus on which is better. Although the ESR has been used in clinical

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decision-making for more than 50 years, its operational characteristics remain incompletely defined (12, 13). This is particularly true for older patients, because results may be influenced by age, sex, renal function, erythrocyte morphology, and a variety of medications (14).

Although CRP is unaffected by age and gender, its use has been limited because the latex agglutination techniques previously available for its measurement were only semiquantitative. Current more-sensitive and automated measurement techniques give highly reproducible quantitative results for CRP, which has renewed interest in CRP as a marker for various infectious and inflammatory conditions (15–17).

Further to clarify whether CRP has distinct advantages over ESR in the elderly, we sought to compare the diagnostic utility of CRP relative to ESR within the same patients, without specifically addressing the usefulness of either test alone in older individuals. Concerns over our possible misclassification of subjects with occult disease and the lack of control over severity of illness must, of course, be raised, but these do not detract from the comparative analysis used in the present series and the conclusions reached: although the predictive values may vary according to the underlying prevalence of disease in a given population, the values we reported here were calculated on the same subjects. Thus, the prevalence rate of infection/inflammation was held constant and allowed the relative comparison of CRP with ESR.

In the present series of subjects, a sensitivity (i.e., the likelihood of observing an increased value for CRP or ESR in an individual with underlying infectious or inflammatory disease, or both) of 75% or more for each test could be obtained only by decreasing the specificity (i.e., the likelihood of observing a normal ESR or CRP in a person without underlying disease) to 60% or less. In the population studied, with a disease prevalence of 32%, even when we used the highest cutoff point for each test (50 mm/h for ESR and 40 mg/L for CRP), we obtained clinically unacceptable positive predictive values: 0.64 for ESR and 0.62 for CRP.

The ROC curve analysis demonstrates particularly well the limited value of either assay for distinguishing individuals with and without disease. Effective diagnostic tests (e.g., tests with high true-positive to false-positive ratios) display hyperbolic curves that fall close to the upper left-hand corner of the ROC graph. Neither ESR nor CRP exhibited this characteristic. However, we found ESR, unlike CRP, to be useful as a predictor for mortality at six months. Of course, confounding variables, such as the presence or absence of anemia, would need to be controlled for before such an independent relationship can be unequivocally accepted.

Because ESR is less expensive to perform, one can argue that it has a slight advantage over CRP as a “sickness index” in the elderly. Indeed, although recognizing its limitations, we continue to utilize the ESR almost exclusively in our own institution because of its low cost. In the final analysis, however, neither ESR nor CRP appears to be very useful as diagnostic tools in unselected geriatric patients.

References