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Is CRP, like ESR, Age and Gender Dependent?

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Abstract

C-reactive protein (CRP) and the erythrocyte sedimentation rate (ESR) are often ordered together in patients suspected of having inflammatory or infectious disorders. ESRs are higher in women than in men and they also increases with age, although most laboratory reference ranges only take gender into account. It is unclear whether CRP, like ESR, differs between women and men and/or increases with age. We analyzed 382 consecutive patients in whom the CRP and ESR were both within the laboratory's reference range. ESR was, as expected, ≈5 mm/h higher in the 236 women than in the 146 men (P<0.0001). ESR was significantly correlated with patient age (P=0.0012). In contrast to ESR, CRP levels were identical in women and men and there was no correlation between CRP and patient age. Thus, laboratories should adjust the ESR reference range for gender and age, but this adjustment is not necessary for CRP.

Keywords: C-reactive protein; Age dependent; Erythrocyte

Introduction

The erythrocyte sedimentation rate (ESR) and the serum C-reactive protein (CRP) level are popular tests of inflammation. The ESR tends to be slightly higher in women than in men [1,2] and laboratory reference ranges typically reflect this gender difference. ESR also increases with advancing age [2]. However, age-adjustments to the ESR reference range are uncommon.

In contrast to ESR, CRP is not believed to differ in women and men. The effect of age on serum CRP is debated: some argue it is age-independent [3] and while others believe it, like ESR, increases with advancing age, albeit minimally [4]. Thus, most laboratories employ the same reference CRP range in women and men regardless of their age.

We studied patients in whom CRP and ESR had been measured simultaneously in our hospital's laboratory. The CRP and ESR were found to be within their respective references ranges, thereby minimizing the likelihood of underlying inflammation. Our objective was to further explore the effects or age and gender on serum CRP levels in these patients.

Methods

THPD's laboratory performed simultaneous CRP and ESR assays in 1,753 consecutive patients during 2011 [5]. The laboratory's reference range for CRP is 0-0.49 mg/dl and for ESR are 0-20 mm/h in men and 0-30 mm/h in women. In some batches, the lower detection limit for CRP was 0.2 mg/dl and in others it was 0.5 mg/dl. When serum CRP levels were undetectable (i.e., below the detection limit), we arbitrarily assigned them values of either 0.10 or 0.25 mg/dl, respectively.

Of the 1,753 patients, 382 (22%) had CRP and ESR measurements in the reference ranges. The ages and genders of these 382 patients (236 women and 146 men) were not significantly different (Table 1). Some patients were tested on more than occasion, but only the first pair of CRP and ESR measurements was included in this study.

Pearson correlation coefficients were determined using Excel 2010 software (Microsoft Corp., Redmond, WA). Two-sided probability (P) values for these Pearson correlation coefficients and their 95% confidence intervals (CIs) were determined [6,7]. Continuous variables (age, CRP, ESR) in women or men were expressed as means ± one standard error of the mean. Between-gender differences in these variables were tested for significance by group t tests [6], with 2-sided P values less than 0.05 considered to be significant. The research conformed to the relevant ethical guidelines for human research and was approved by the Institutional Review Board of Texas Health Resources, Arlington, Texas on August 23, 2013.

Results

In this cohort of 382 patients with normal ESRs and CRPs, there was a modest but nevertheless statistically significant direct correlation between CRP and ESR (r=0.18, 95% CI, 0.09 to 0.28; P=0.0003). This correlation between CRP and ESR is shown in Figure 1.

Gender effects on ESR and CRP

ESR. As shown in Table 1, the mean ESR was approximately 5 mm/h higher in the women than the men (P<0.0001), likely because of the wider reference range in the women.

CRP. The mean CRP was identical in the women and men (Table 1).

Age effects on ESR and CRP

ESR. As shown in Figure 2, there was a modest but statistically significant correlation between age and ESR (r=0.17, 95% CI, 0.07 to 0.26; P=0.0012).

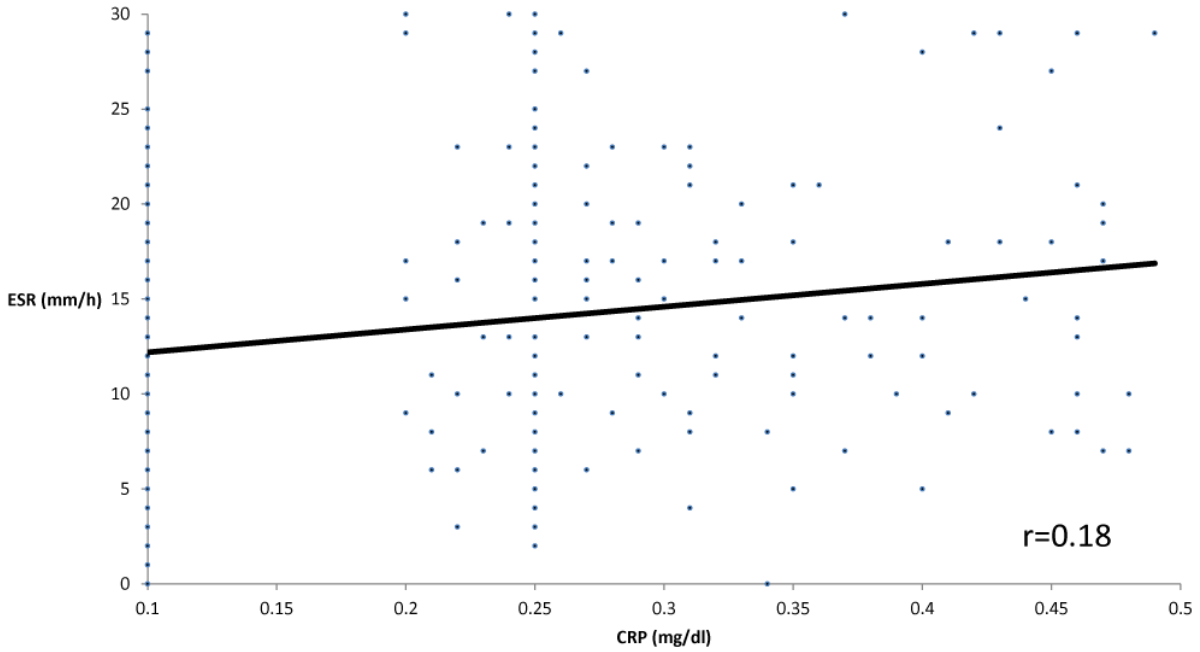

Figure 1: Plot of C-reactive protein (CRP) level versus erythrocyte sedimentation rate (ESR) in 382 patients. The Pearson correlation coefficient was 0.18 (P=0.003).

	WOMEN (n=236)	MEN (n=146)	P
AGE (years)			
Mean	56.63	54.27	0.264
SEM	1.31	1.65	
Range	18-97	18-94	
ESR (mm/h)			
Mean	15.58	10.16	<0.0001
SEM	0.48	0.39	
Range	0-30	1-20	
CRP (mg/dl)			
Mean	0.21	0.21	1.000
SEM	0.01	0.01	
Range	0.10-0.49	0.10-0.47	

Table 1: Ages of 382 Patients with CRPs and ESRs within the Laboratory's Reference Range[a,a] 0 – 0.49 mg/dl for CRP; 0-20 mm/h for ESR (men) and 0-30 mm/h for ESR (women). CRP, C-reactive protein; ESR, erythrocyte sedimentation rate; SEM, standard error of the mean

CRP. As shown in Figure 3, unlike with ESR there was no correlation between age and serum CRP (r=0.00; 95% CI, -0.10 to 0.10).

Discussion

This study confirms the findings of Miller et al. [2] that ESR is higher in women and men and that ESR is correlated significantly with advancing age. According to their method, the upper limit of normal (ULN) for ESR should be established in each woman and man [2]. Thus, the ULN for ESR in men (mm/h) should be the patient's age divided by 2 and for women the patient's age plus 10 years, divided by 2. For patients who are the same age, the ESR, by the Miller formulas, should be 5 mm/h higher in women than men. In our study, in which the women were slightly older than the men, the observed difference in ESR was 5.4 mm/h, close to the 6.2 mm/h difference predicted from the Miller formula. Laboratories should consider reporting individualized reference ranges for ESR based on the patient's gender and age. This could easily be accomplished by an automated system and formula, much like EGFR is reported.

In striking contrast to ESR, serum CRP levels were neither affected by the gender of the patient or by their age among the 382 adults in this study. Thus, unlike ESR, serum CRP levels do not require adjustment for gender or age.

Our conclusions are derived from a cohort of patients whose physicians ordered both CRP and ESR for some indication. Although the CRP and ESR results were normal in these patients, making underlying inflammation and infection unlikely, our results are not derived from a random sample of a healthy, asymptomatic population, but from patients with symptoms or signs that led their physician to order these tests that proved to be negative.

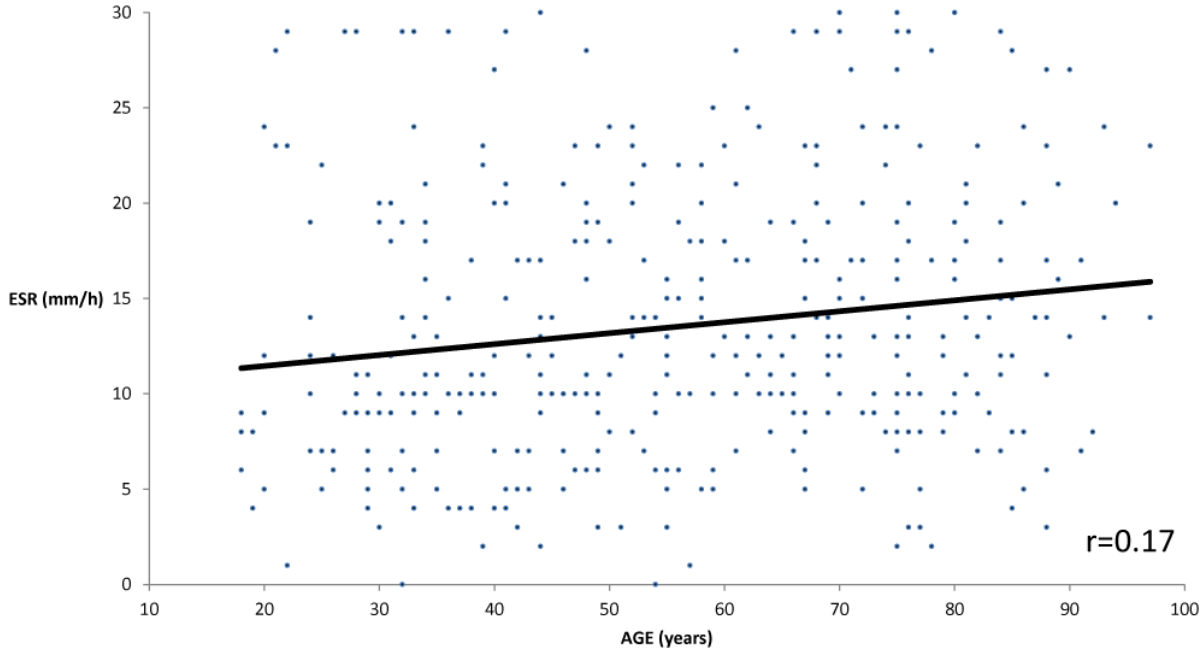

Figure 2: Plot of age versus erythrocyte sedimentation rate (ESR) in 382 patients. The Pearson correlation coefficient was 0.17 (P=0.0012).

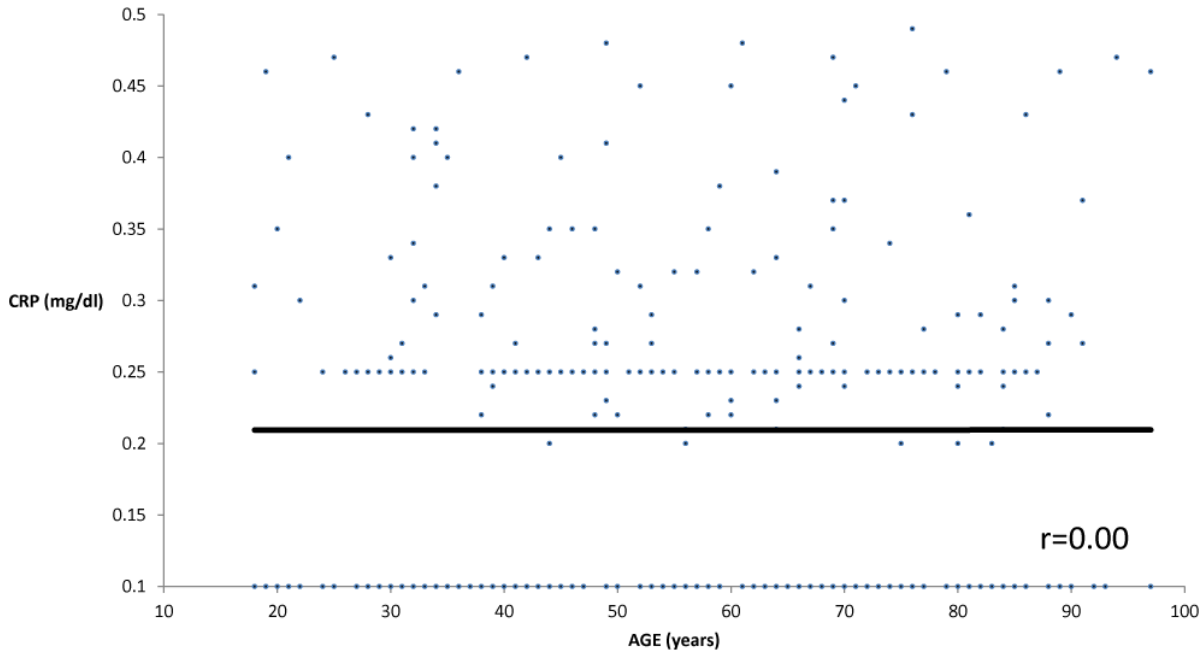

Figure 3: Plot of age versus the serum C-reactive protein (CRP) level in 382 patients. The Pearson correlation coefficient was 0.

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