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Agreement between high-sensitivity C-reactive protein and C-reactive protein assays

Han E[1], Fritzer-Szekeres M[2], Szekeres T[2], Gyöngyösi M[1], Bergler-Klein J[1]

[1]Department of Internal Medicine II, Division of Cardiology, Medical University Vienna, Austria
[2]Department of Laboratory Medicine, Medical University Vienna, Austria

Introduction

High sensitivity C-reactive protein (hs-CRP) is a biomarker used for risk prediction for cardiovascular disease (CVD) by assessing low concentrations of inflammatory markers. Measurements of regular CRP assays have become very sensitive as well, with a detection limit of 0.03 mg/dL, as well as being more available and cheaper. Existing studies link chronic subclinical systemic inflammation with a higher degree of atherosclerosis, a known cause of pathogenesis for acute myocardial infarction or other CVDs. The aim of this study is to compare the association between CRP and hs-CRP.

Methods

This study compared CRP and hs-CRP serum concentrations and data acquired by medical chart review of 590 patients from 11/2017 to 10/2018 of our cardiology outpatient clinic who were divided into hs-CRP and CRP risk groups for cardiovascular events: low < 0.1 mg/dL, average 0.1-0.3 mg/dL, high > 0.3 mg/dL. Both hs-CRP and CRP were measured by automated latex-particle enhanced immunoturbidimetric assay kit (Roche Diagnostics) on a COBAS 702 analyser (Roche/Hitashi). CRP measurements used CRPL3 (C-Reactive Protein Gen.3, Roche Diagnostics), while hs-CRP measurements used CRPHS (Cardiac C-Reactive Protein (Latex) High Sensitive, Roche Diagnostics). Blood samples were centrifuged and measurements done on the same day of the sample collection, as per routine procedure. Detection limits for hs-CRP measurements were 0.015-2.0 mg/dL and for CRP measurements 0.03-35 mg/dL. The agreement of classification in hs-CRP risk groups and CRP risk groups was assessed by kappa statistic, with Kappa coefficient of < 0.20, 0.21– 0.40, 0.41–0.60, 0.61–0.80, 0.81–0.99 interpreted as slight, fair, moderate, substantial and almost perfect agreement, respectively. Bland-Altman analysis was used to assess agreement between hs-CRP and CRP.

Results

Out of all 590 patients, 37.7% were in low risk, 33.9% in average risk and 28.5% in high risk hs-CRP group. Some group changes occurred after reclassification of the patients according to CRP measurements. Eight percent of patients were categorised into a higher risk group, 0.7% reclassified into a lower risk group, while 91.4% remained in the same risk group as determined by hs-CRP (kappa: 0.87; p < 0.001) **(Table 1).** Important to note, there was a 100% agreement between the high-risk CRP and hs-CRP group patient classification.

Bland-Altman plot displayed a fixed bias with an average difference between the two laboratory tests for CRP and hs-CRP of 0.02 mg/dL ± 0.09 SD with only sporadic outliers. The upper limit of agreement was 0.12 and lower limit of agreement was -0.07 **(Figure 1).** In the lower range of CRP values, measurements were tightly clustered around the average difference. Greater variability could be observed at higher serum level of the inflammatory biomarker in the Bland-Altman plot with a bias to higher CRP concentrations than hs-CRP concentrations at values greater than 0.5 mg/dL. This proportional bias, which was further demonstrated by linear regression analysis, does not affect the risk predicting qualities of hs-CRP or CRP for CVD because the cut-off values for risk groups (0.1 mg/dL for low risk, 0.3 mg/dL for high risk) are all below this threshold.

Conclusion

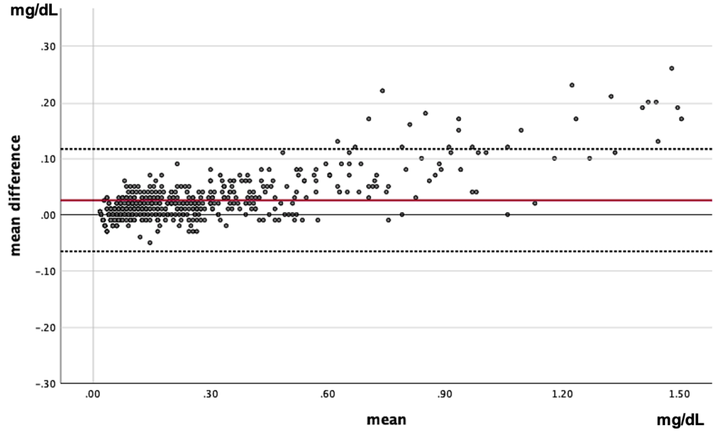
A close agreement between measurements of hs-CRP and CRP assays was identified, therefore regular CRP assays could replace hs-CRP for cardiac risk assessment. Benefits for clinical implementation are: First, CRP assessment is routinely available in most laboratories compared to hs-CRP. Second, CRP is less costly than hs-CRP, since no further laboratory acquisitions are necessary, which is especially relevant in regions where cost efficiency is of importance.

Table 1: Number of patients reclassified into risk groups according to CRP and hs-CRP.

	hs-CRP			
CRP	Low risk; n (%)	Average risk; n (%)	High risk; n (%)	**Total**
Low risk; n (%)	191 (86.0)	4 (2.0)	0 (0.0)	195
Average risk; n (%)	31 (14.0)	180 (90.0)	0 (0.0)	211
High risk; n (%)	0 (0.0)	16 (8.0)	168 (100.0)	184
Total	222	200	168	590

91.4 % (539/590) of patients were classified into the same risk group (kappa 0.87; p < 0.001).

Figure 1: Bland-Altman plot of CRP versus hs-CRP measurements.



Average difference (red line) 0.02 ± 0.09 SD; upper LOA: 0.12; lower LOA: -0.07; y = 0 is the line for perfect average agreement; mean difference calculated by CRP – hs-CRP.

Conflict of interest: None to declare.