Elevated C-Reactive Protein in Asymptomatic Crohn's Disease Patients: Listen to the Sound of Silence

To the Editor:

Bhattacharya et al[1] confirmed and extended their previous finding[2] indicating that "silent" Crohn's disease (CD) patients (i.e., asymptomatic patients with elevated C-reactive protein [CRP] level) are a subgroup of patients at the higher risk of hospitalization and of more disabling disease. We completely agree with the relevant role of CRP in asymptomatic CD management, and we conducted a cross-sectional observational study at our institution that showed that such patients are at the higher risk, even in the short time, of clinical flare.

In fact, from an electronic database of prospectively collected data of patients visited at the Inflammatory Bowel Disease Outpatient Clinic of S. Andrea Hospital in Rome, Italy, we evaluated a cohort of CD patients at regular follow-up visit, from January 2013 to December 2014. Inclusion criteria were firm diagnosis of CD, availability of clinical (age, sex, disease location and duration, presence of extraintestinal manifestation, smoking status) and biochemical (CRP, hemoglobin level) data, Harvey–Bradshaw index ≤ 4 (clinical remission), and 1 year of recorded follow-up from the index visit. From a total of 97 CD patients with complete data reports, 64 fulfilled inclusion criteria for the study. Among those, 15 (23%) had a CRP level at least 2-fold above the normal laboratory-reported value ("silent" CD patients). Thirteen (20%) of 64 CD patients in clinical remission experienced a clinical flare of disease (empirically defined by the onset of clinical symptoms related to CD [abdominal pain and/or diarrhea] that required a medical consultation). In that group, 6 patients (46%) required steroids administration, and no hospitalization was recorded. In a multivariate analysis, only elevated CRP value showed independent association with disease flare onset at 1 year of follow-up ($P < 0.05$). Patient with "silent" CD had a significantly lower remission rate at 1 year compared with those with normal CRP (60% versus 86%; log-rank test, $P < 0.05$), with a 4-fold higher risk of flare (odds ratio, 4; 95% confidence interval, 1.0829–14.7754; $P = 0.038$; Fig. 1).

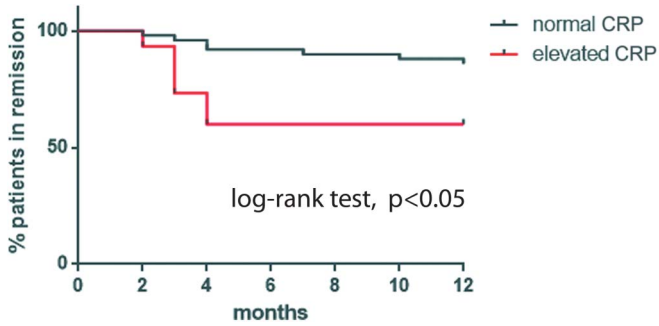

FIGURE 1. Cumulative probability of remission rate at 1 year of follow-up (Kaplan–Meier curve) in asymptomatic CD patients with normal or elevated CRP.

In conclusion, despite the fact that the relevance of CRP in the monitoring of CD patients has been recognized from a long time,[3] CRP is not currently indicated as a treatment target.[4] Nonetheless, because assessing bowel inflammation burden could be challenging, we believe that the results of the study of Bhattacharya et al, further confirmed by the present retrospective investigation, underline the important role of CRP as a "surrogate" marker in CD management, even in the absence of clinical symptoms. For the future, those findings may open the door to the consideration of specific treat-to-target trials to evaluate possible influence on disease course of treatment optimization aiming to normalize CRP level in CD patients.

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Reply:

Thank you Dr Pagnini et al. for your observations. Your letter to the Editor confirms our findings regarding silent Crohn's disease—specifically that patients who feel no symptoms have no "early warning" mechanism to warn them to seek care. The result is presenting with

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