1	Efficient diagnosis for endoscopic remission in Crohn's diseases
2	by the combination of three non-invasive markers
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15	Short title: Three non-invasive markers for CD remission diagnosis
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## ABSTRACT

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26 **Background:** Serum C-reactive protein (CRP), leucine-rich alpha-2 glycoprotein (LRG), and 27 fecal calprotectin (Fcal) are non-invasive markers used to assess Crohn's disease (CD) 28 severity. However, the accuracy of these markers alone is often limited, and most previous 29 reports have evaluated the efficacy of each marker individually. We aimed to improve the diagnostic performance of endoscopic remission (ER) of CD by combining these 3 markers. 30 31 Methods: We tested the diagnostic ability of various combinations of these 3 markers for 32 endoscopic severity in 230 consecutive patients with CD from September 2014 to July 2023. 33 The modified Simple Endoscopic Score for Crohn's disease (mSES-CD) was used to 34 determine endoscopic severity. 35 **Results:** Each of the 3 markers was correlated with mSED-CD (LRG: r = 0.69, CRP: r = 0.60, and Fcal: r = 0.67). A combination of 2 of the 3 markers did not increase the diagnostic 36 37 accuracy of ER. However, by combining all 3 markers, the diagnostic ability for ER was 38 improved in comparison to the diagnostic ability of the 3 individual markers, assuming that 39 ER was obtained if 2 or 3 markers were negative. The sensitivity, specificity, and accuracy 40 were 89%, 83%, and 86%, respectively. Additionally, we established a 2-step method using 41 Fcal values after evaluating the 2 serum markers. This method was most useful for reducing 42 both the patient burden and costs. 43 Conclusions: The newly established 2-step method allowed for a higher accuracy in the noninvasive diagnosis of ER when the 3 markers were combined. 44

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46 **Keywords:** CD, Crohn's disease; LRG, leucine-rich alpha-2 glycoprotein; Fcal, fecal calprotectin; CRP, C-reactive protein; ER, endoscopic remission.

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