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CLINICAL AND GENETIC FACTORS PREDICT SEVERE DISEASE: A NOVEL COMPOSITE SEVERITY INDEX

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Introduction Crohn's disease is an incurable progressive disease with marked heterogeneity in outcome. Identifying patients at diagnosis (Dx) at high risk of poor outcomes would allow treatment stratification. Current definitions of severe disease lack discrimination. A more discriminant composite severity score would benefit clinical research and aid clinical decision making.

Methods Based on a consensus of 5 clinicians, the authors designed a composite severity score, assessed over the 5 years after Dx, with a total possible score 1–16. The score was applied retrospectively in 367 CD patients who were also genotyped for 32 CD susceptibility loci. The severity score that would encompass the 50% of patients with the highest score was defined, and factors present at Dx – both clinical and genetic – were assessed by the χ^2 test for their ability to predict being in the more severe disease category. CD was classified according to the Montreal classification.

Results 367 CD patients (median age at Dx 30.8 (IQR 22.9–46.1)) were assessed. 249 patients had full data available for the first 5 years after Dx. The mean severity score was 6.3 (95% CI 5.9 to 6.6). Patients with a score >6 were defined as having more severe disease. Patients with more severe disease were younger at Dx ($p=0.0004$ for trend, OR A1 vs A2=4.42 (95% CI 1.4 to 13.9)) and had an ileal ($p=0.0025$, OR=2.2 (95% CI 1.32 to 3.68)) and upper GI location disease location at Dx ($p=0.0008$, OR=5.3 95% CI 1.9 to 14.7). Perianal disease at Dx approached but did not achieve statistical significance ($p=0.052$). Only rs9286879 ($p=0.0085$) and rs17582416 ($p=0.0448$) were observed more frequently in patients with severe disease. The need for steroids at Dx, having a first degree relative with IBD, needing surgery at Dx or smoking status at Dx did not differ between the groups.

Conclusion This index discriminates more effectively between severity groups. Disease location, age at Dx and genetic markers are associated with more severe disease but validation of these factors is needed in a separate cohort.

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