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Summary

FECAL MICROBIOME AND METABOLOME SIGNATURES ARE ASSOCIATED WITH FUTURE DISEASE BEHAVIOR IN INFLAMMATORY BOWEL DISEASE

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Baseline fecal metagenomic and metabolomic signatures predict therapy intensification in IBD beyond clinical risk factors, with a combined model achieving AUC 0.76 versus 0.61 for clinical factors alone in 386 patients followed up to 5 years.

KEY POINTS

- Among 386 IBD patients followed prospectively, 105 (27%) underwent therapy intensification; fecal-derived risk scores improved discrimination compared to clinical risk factors alone (AUC 0.76 vs 0.61).
- Species-based risk scores consistently separated high- and low-risk groups across cohorts, with 2.1-fold higher risk in the internal test subset (log-rank p=0.046) and 2.2-fold higher risk in the external cohort (log-rank p=0.03).
- The species-based score comprised 12 species, including Ruminococcus gnavus and Veillonella parvula (higher risk) and Bacteroides uniformis and Alistipes communis (lower risk).
- Metabolite-based signatures best separated moderate disease behavior (therapy intensification) with HR 3.3 in the test subset (log-rank p=0.006), while pathway-based signatures best separated severe disease behavior (intensive escalation) in advanced disease with HR 2.6 in the external cohort (log-rank p=0.016).
- Fecal-derived scores provided added prognostic value particularly in long-term follow-up, with the combined model outperforming the clinical model over the entire follow-up period in internal validation.

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