

strategies can improve these measures and their impact on overall quality of care among patients with ulcerative colitis.

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#### Sex Differences in Cancer Risk Among Patients With Inflammatory Bowel Diseases Treated With Biologics: A Large Retrospective Analysis

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**Introduction:** Biologic therapies have transformed the treatment of inflammatory bowel disease (IBD), providing targeted control of chronic inflammation, a major factor in malignancy in this population. However, little is known about their long-term impact on the risk of cancer in the IBD population. Particularly, it remains unclear if the association between biologic therapy and malignancy varies by sex among IBD patients. We aim to investigate sex-specific cancer risk among patients with IBD treated with biologics.

**Methods:** We conducted a retrospective, multi-center cohort study at Northwell Health between 2008 and 2023. We included 11,325 patients with IBD including ulcerative colitis (UC) and Crohn's disease (CD). Patients younger than 18 years or with a history of cancer prior to IBD diagnosis were excluded ( $n = 370$ ). Data on demographics and IBD medications were extracted from medical records. Logistic regression estimated odds ratios (ORs) for any cancer associated with biologic use, adjusting for age, sex, IBD subtype, and steroid use. Analyses were stratified by sex and IBD subtypes, and propensity score matching was performed as a sensitivity analysis.

**Results:** Among 10,955 patients with IBD, 54.6% were females and 5.3% were on biologics. Biologics were associated with a 50% reduction in the odds of any cancer (aOR 0.50, 95% CI 0.33-0.76). This protective effect was stronger with dual biologics therapy (aOR 0.44, 95% CI 0.19-0.88). In males, the use of biologics was associated with a significantly lower risk of any cancer (aOR 0.40, 95% CI 0.21-0.77), whereas in females, this risk was not statistically significant (aOR 0.61, 95% CI 0.36-1.04). Only males with UC had lower odds of developing cancer (aOR 0.38, 95% CI 0.16-0.91). For colorectal cancer specifically, there was no significant association with biologic use in either sex.

**Conclusion:** Biologic therapy in IBD patients was associated with a lower risk of developing malignancy only in males, suggesting possible underlying sex-related biological or hormonal attributes which could influence long-term cancer outcomes. Additional research is warranted on this subject to validate these sex-specific differences and to clarify their underlying mechanisms.

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#### Is the Use of Systemic Corticosteroid Associated With Increased Risk of Colorectal Cancer in Inflammatory Bowel Diseases: A Large Retrospective Cohort Study

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**Introduction:** Chronic inflammation in inflammatory bowel disease (IBD) is a well-established risk factor for colorectal cancer (CRC). While immunosuppressive and biologic therapies have been studied for their potential favorable impact on CRC risk, the role of systemic glucocorticoids remains unclear, and the published data show conflicting results. We aim to investigate the association between the use of systemic glucocorticoids and CRC risk in the IBD population.

**Methods:** We conducted a retrospective, multi-center cohort study at Northwell Health between 2008 and 2023. Among 11,325 patients with IBD, ulcerative colitis (UC) and Crohn's disease (CD), we excluded patients under 18 years, and if they had indeterminate colitis, or history of cancer prior to IBD diagnosis ( $n = 370$ ). Demographics and IBD medication data were extracted from the Northwell Health Information Exchange (HIE) database. The primary exposure was systemic corticosteroid use, and the primary outcome was CRC. Adjusted odds ratios (aORs) were estimated by logistic regression, controlling for age, sex, IBD type, and use of biologic and immunomodulator therapies. Analyses were stratified by sex, IBD type, and age group ( $\leq 50$  and  $> 50$  years).

**Results:** Of the 10,955 study patients, 196 (1.8%) were diagnosed with CRC, and 4,375 (40%) were on chronic corticosteroid. The use of corticosteroids was associated with a more than twofold increase in the odds of CRC (aOR 2.03, 95% CI 1.49-2.77). This elevated risk was consistent across IBD types, with similar associations in Crohn's disease (aOR 1.91, 95% CI 1.17-3.13) and ulcerative colitis (aOR 2.09, 95% CI 1.27-3.42). Stratified analysis showed that both males (aOR 2.01, 95% CI 1.27-3.19) and females (aOR 1.90, 95% CI 1.16-3.11) experienced significantly higher risk of CRC with steroid exposure. Notably, the association was strongest among patients older than 50 years (aOR 2.16, 95% CI 1.48-3.15), while no significant association was seen in those 50 years or younger (aOR 1.29, 95% CI 0.64-2.62).

**Conclusion:** Our study shows that corticosteroid use may be independently associated with a twofold increase in risk of CRC in patients with IBD, across sex and disease type. The risk was greatest in older patients. This finding may be explained by the inability to achieve deep remission and mucosal healing with steroid therapy. Future controlled studies are warranted to shed more light on this subject and further underscore the practice of steroid-sparing strategies in IBD management.

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#### Validating Calibration of an Artificial Intelligence Assessment of Endoscopic Severity in Ulcerative Colitis

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**Introduction:** Regulatory guidance recommends the endoscopy subscore as the index to assess the endoscopic component of the primary endpoint in ulcerative colitis (UC) trials. Inter-reader

variability in assessments may impact the reliability of trial results. Currently, there is no metric in place to assess the certainty by which a reader is assigning an endoscopy subscore. Machine learning (ML) provides an opportunity to assess the endoscopy subscore and provide a measurement of its certainty in a standardized manner. Artificial Intelligence Assessment of Endoscopic Severity (AI-ES) accurately assesses the endoscopy subscore. The objective of this study is to evaluate the calibration of AI-ES - how well its predicted probabilities reflect true likelihoods - to assess the reliability of its measurement of certainty in endoscopy subscore assessments in UC trials.

**Methods:** AI-ES is a deep learning algorithm that assesses the endoscopy subscore in UC endoscopic videos. AI-ES measures probability for the 4 ordinal endoscopy subscore classes. The endoscopy subscore with the highest probability is assigned as the final score by AI-ES. We assessed calibration on a holdout test set of 639 videos (~25%) from the Phase 3 induction trial for mirikizumab in UC (NCT03518086). Videos had a 2 + 1 centrally read endoscopy subscore, randomly selected from week 0 and 12 with a distribution of endoscopic severity similar to the overall study population. Calibration plots were generated across endoscopy subscore classes with probabilities grouped into septiles (~100 videos per group) for primary analysis and deciles for confirmation. Brier scores, ranging from 0 (perfect calibration) to 1 (worst calibration), were calculated, with values  $< 0.25$  considered informative.

**Results:** AI-ES demonstrated strong calibration, with Brier scores below  $< 0.25$  for each endoscopy subscore (0: 0.037, 1: 0.082, 2: 0.162, 3: 0.112). The Brier score for evaluation of endoscopic improvement (0,1 vs 2,3) also showed excellent calibration (0.066). Findings were consistent when assessing probabilities by deciles.

**Conclusion:** Whereas data on the certainty of human readers in endoscopy subscore assessments are elusive, AI-ES is calibrated across all endoscopy subscore classes, providing reliable data on score probabilities. This novel measurement of certainty by AI-ES added to the score assessment may enable novel AI-based multi-reader or consensus workflows in trials, potentially improving the reliability of UC endpoint assessments.

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#### Machine Learning Classification of Ulcers in the Colon and Ileum in Crohn's Disease

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**Introduction:** Artificial intelligence has been extensively applied to assess endoscopic disease severity in ulcerative colitis; however, its use in Crohn's disease (CD) is limited. In CD, the presence of ulcers is a key marker of active mucosal inflammation and has emerged as an endpoint, with recent therapeutic trials reporting ulcer-free remission rates. We aim to develop a machine learning (ML) model to classify the presence or absence of ulcers in both the colon and the ileum to support more standardized endoscopic evaluations in CD.

**Methods:** A dataset of endoscopic recordings was sampled from the Phase 2 SERENITY trial for mirikizumab in patients with active CD. Videos were randomly stratified by patient into a training ( $n = 472$ ) and validation ( $n = 119$ ) cohort, which was used for model selection. Each video was assigned a Simple Endoscopic Score for Crohn's disease by one to 3 readers, per protocol, from which binary distinction of presence or absence of ulcers in the ileum and colon was derived. We developed a multi-stage deep learning model consisting of convolutional image classifiers and a transformer-based video classification model to classify the presence or absence of ulcers in the colon and ileum. Receiver Operating Characteristic (ROC) curves and confusion matrices were used to evaluate sensitivity and specificity of model assessments.

**Results:** Of the 119 videos in the validation cohort, all had at least one segment of the colon assessed and 104 videos had the ileum assessed. Among videos with the segment assessed, a consensus annotation was reached in 91% of videos for the colon (51% ulcers present) and 98% of videos for the ileum (31% ulcers present) among readers. In cases with more than one read, 2 randomly selected readers agreed on their assessment of ulcer presence or absence in the colon and ileum in 75% and 79% of cases, respectively. Model assessment of ulcer presence or absence in the colon showed an accuracy of 89% and area under ROC curve (AUC) of 0.94. Model assessment of ulcer presence or absence in the ileum showed an accuracy of 83% and AUC of 0.87.

**Conclusion:** We developed an ML model to assess the presence or absence of ulcers in the colon and ileum in CD. The model demonstrated strong performance in both locations and may be utilized to aid in the assessment standardization of endoscopic severity. Future research will investigate the use of ML to provide more granularity into endoscopic disease severity in patients with CD.

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#### Perceptions and Barriers to the Use of Intestinal Ultrasound in Inflammatory Bowel Disease: A Survey of Gastroenterologists in Panama

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**Introduction:** Intestinal ultrasound (IUS) is a validated, non-invasive modality for real-time assessment and monitoring of inflammatory bowel disease (IBD). Although widely adopted internationally, its clinical use in Panama remains limited. IUS became locally available in November 2023 at a single private center. This study aimed to assess Panamanian gastroenterologists' (GIs) awareness, perceptions, and barriers to implementing IUS in clinical practice.

**Methods:** A cross-sectional survey was distributed in May 2025 to 63 members of the Panamanian Gastroenterology Association. The anonymous, self-administered questionnaire explored awareness, knowledge, perceived utility, barriers, and practice intentions regarding IUS. Responses were analyzed descriptively and by subgroup based on years of experience, IBD patient volume, and reported barriers.

**Results:** Thirty-one GIs responded (response rate: 49.2%). Most practiced in mixed public-private settings (61.3%) and 71% had more than 10 years of experience. Only 16.1% reported seeing multiple IBD patients per week. While 96.8% were aware of IUS, only 48.4% reported detailed knowledge, and 67.7% knew it was available locally. Most respondents (87.1%) believed patients prefer non-invasive monitoring tools, and 90.3% agreed that IUS could complement or replace other modalities in selected cases. Despite this, only 25.8% intended to pursue IUS training, and 58.1% planned to refer