



# What is new for IUS in UC?

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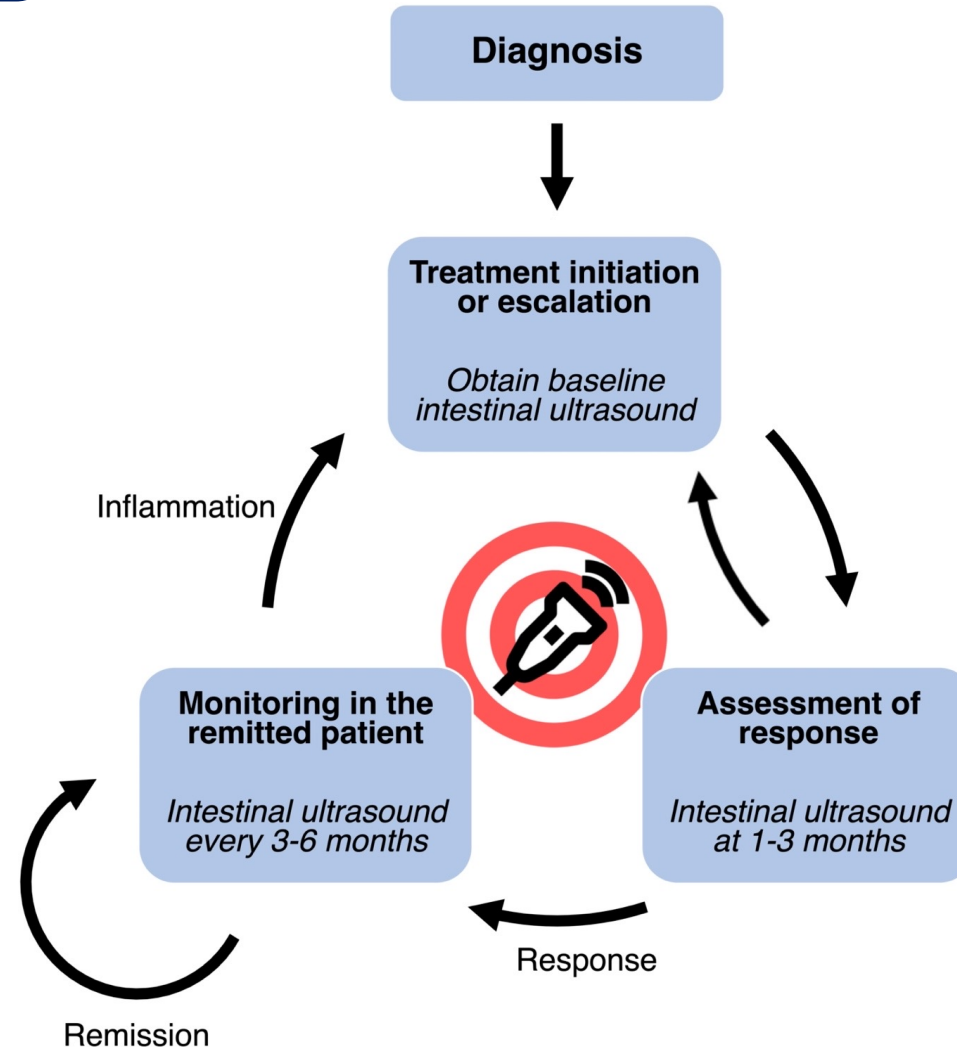
**IBUS Advanced Ultrasound Workshop – Module 3**  
**Washington, DC – May 19th, 2024**



# Disclosures

- Consultant for NeuroLogica (a subsidiary of Samsung Electronics) and Takeda
- Speaker for Bristol Myers Squibb

# Proposed Clinical Approach to Intestinal Ultrasound for Disease Monitoring in IBD

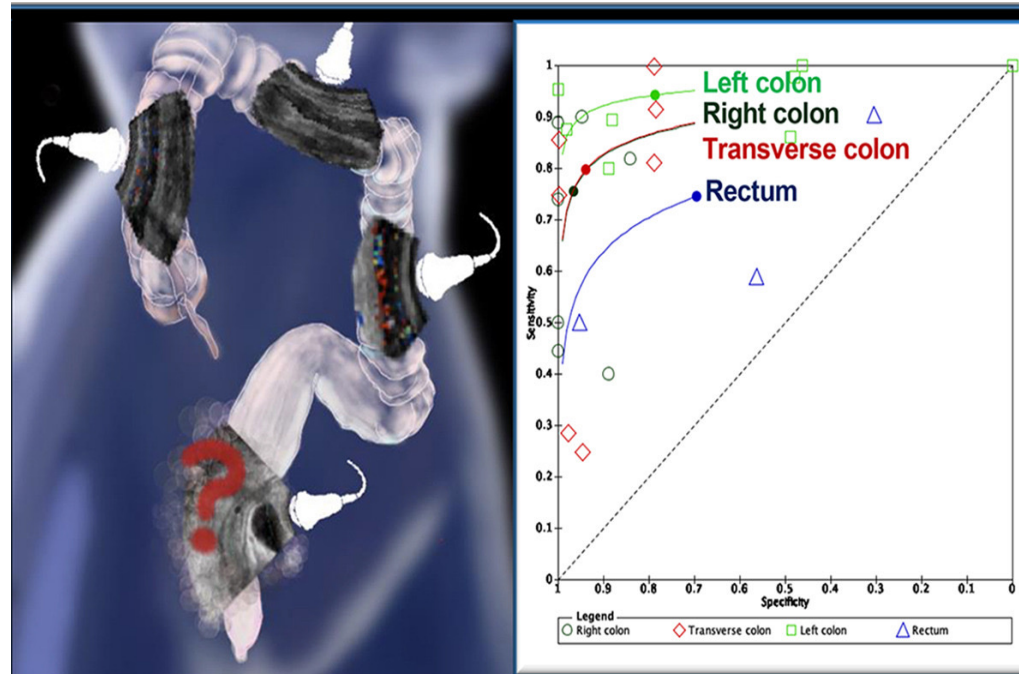


# Transabdominal and Transperineal Ultrasound Accurately Detect Endoscopic Inflammation in the Colon and Rectum

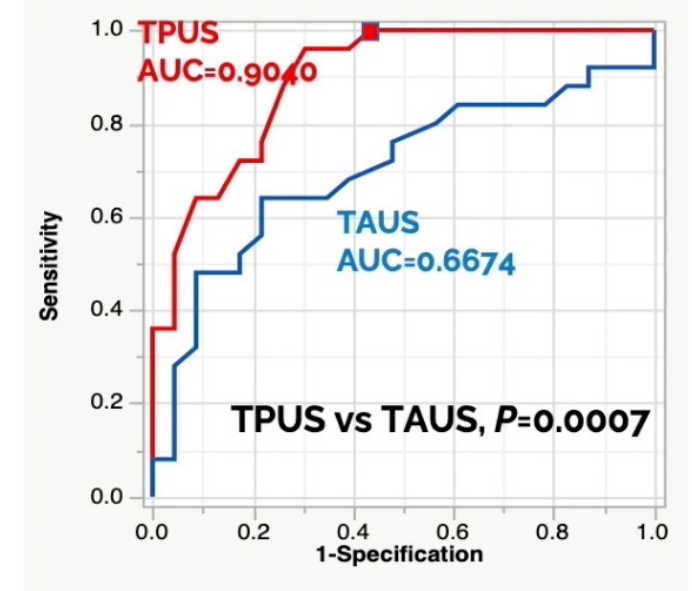


## Meta Analysis:

- 7 studies, 504 patients (420 with UC)
- Compared IUS to gold standard endoscopy by colonic segment
- BWT  $\geq 3$  mm = Inflammation
- **Colon:** sensitivity 86%; specificity 88%
- **Rectum,** sensitivity 74%; specificity 70%



## BWT



BWT (TPUS)  $\geq 4$ mm : Sensitivity 100%, Specificity 45.8%

# IUS is Highly Comparable to Endoscopy

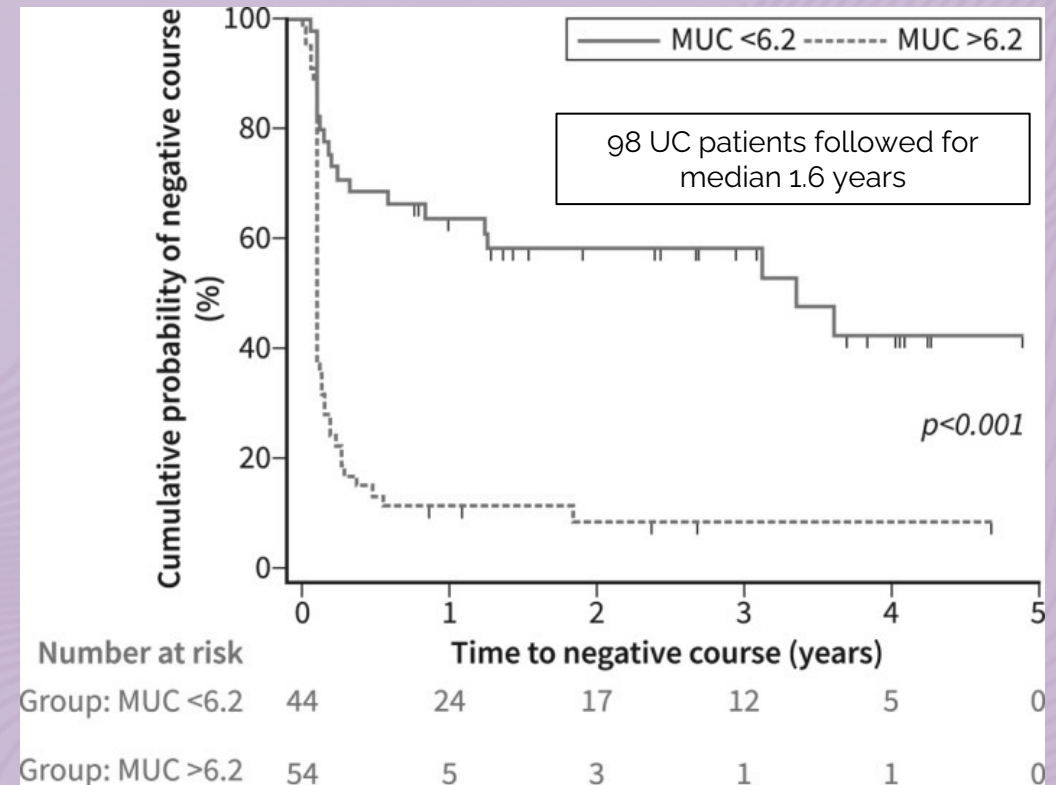
## IUS Scores vs. MES

IUS Score	Bowel Wall Thickness (BWT)	Inflammatory Fat	Hyperemia (mLimberg Score)	Loss of Stratification	Correlation with Endoscopy
UC-IUS (0-7)	✓	✓	✓	✓	$\rho = 0.83$
MUC	✓	✗	✓	✗	$\rho = 0.63$

### Milan Ultrasound Criteria

- EMS:  $\rho = 0.653$ ;  $p < 0.001$
- MUC > 6.2 predicts endoscopic inflammation (Mayo endoscopic subscore >1)
- $\leq 6.2$  – lower cumulative probability of
  - Treatment escalation
  - Need of corticosteroids
  - Hospitalization
  - Colectomy

<b>MUC = 1.4 × BWT + 2 × BWF</b>	
<b>BWT</b>	Bowel wall thickness in mm
<b>BWF</b>	Bowel wall flow (0 = absence; 1 = presence)



# Handheld IUS is a Novel Application of IUS and Comparable to Stationary IUS

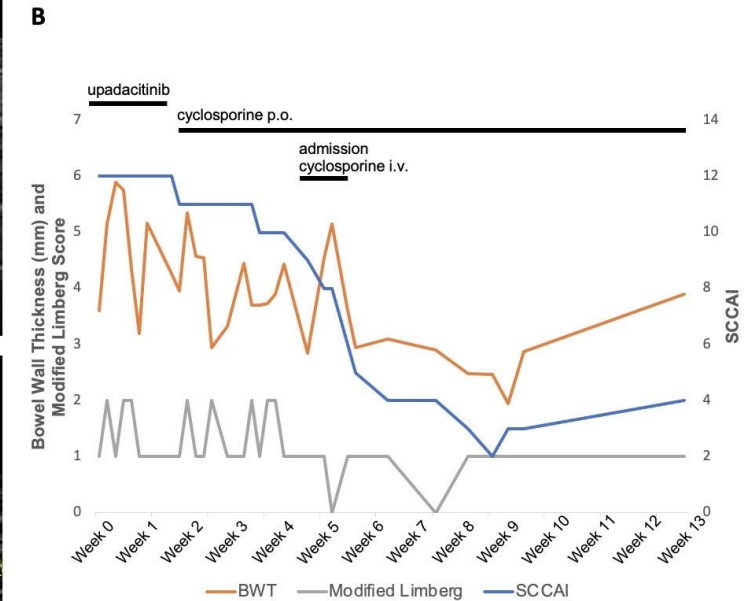
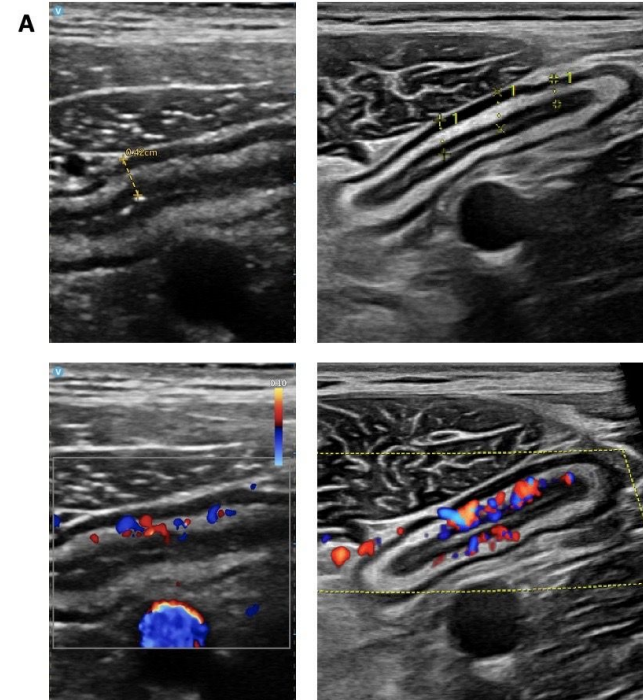
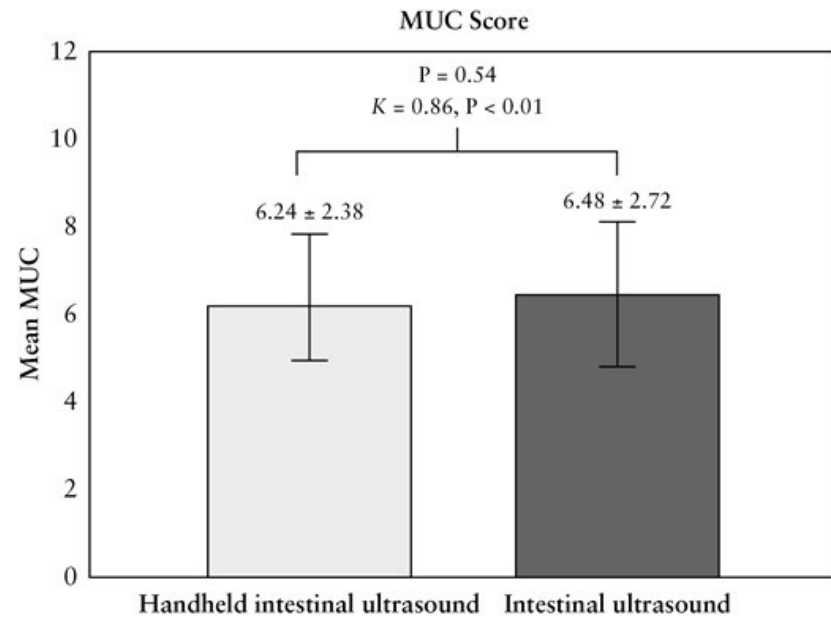


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Handheld IUS is comparable to standing IUS for UC extension definition and MUC evaluation<sup>1</sup>

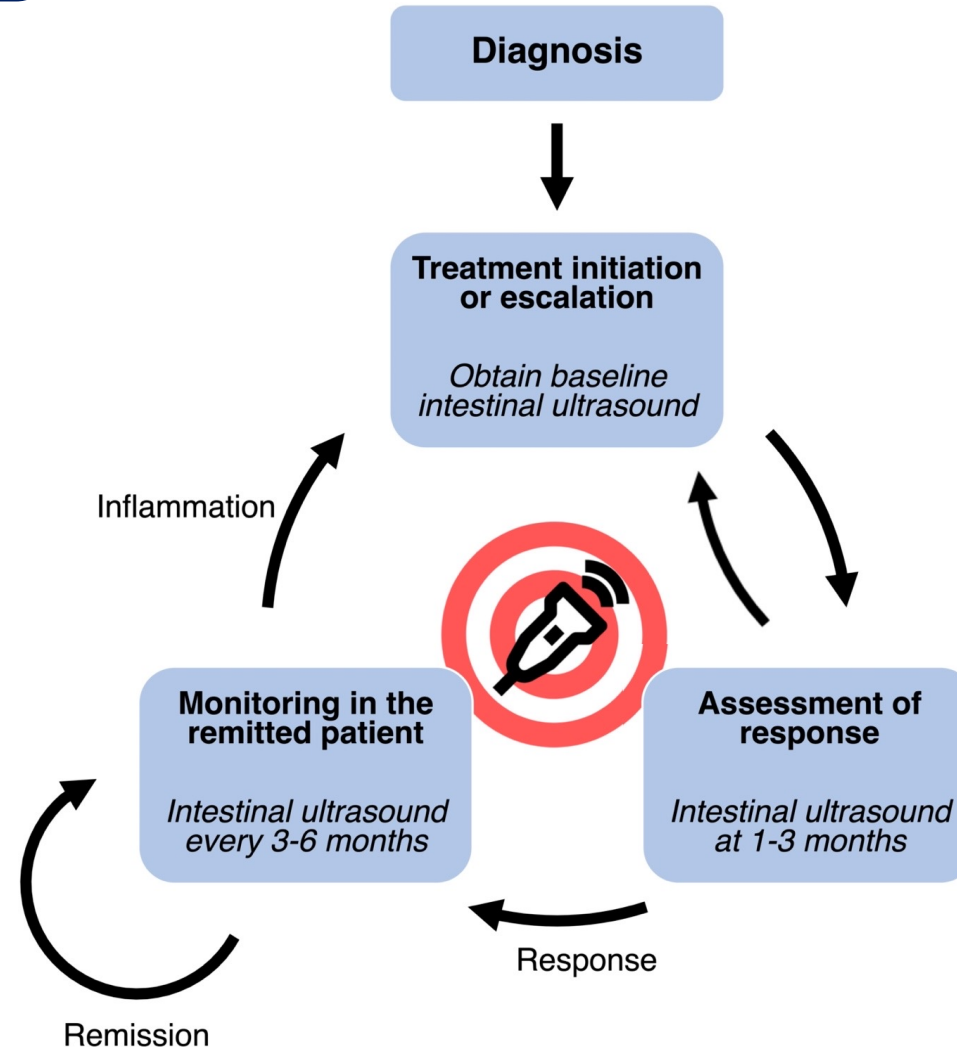


# The Role of the Appendix? Should We Assess in All IUS Exams?



- The appendix has a role in the pathogenesis of ulcerative colitis (UC)
  - Lowered risk of UC post-appendectomy (OR 0.307, 95% CI 0.249–0.377)<sup>1</sup>
- Single-center prospective cohort study<sup>2</sup>
- Included patients with varying levels of UC disease activity: 35 active UC, 30 quiescent UC, and 30 healthy controls (HC)
- Visualized appendix in 63.1% of UC patients and 60% of HCs
- Transverse appendiceal diameter (TAD) significantly higher in UC patients compared to HCs (5.5 vs. 5.0 vs. 4.3 mm)
- TAD >6 mm (indicative of acute appendicitis) significantly more common in active UC (43%) compared to quiescent UC (6%) and HCs (0%) (p = 0.01)

# Proposed Clinical Approach to Intestinal Ultrasound for Disease Monitoring in IBD

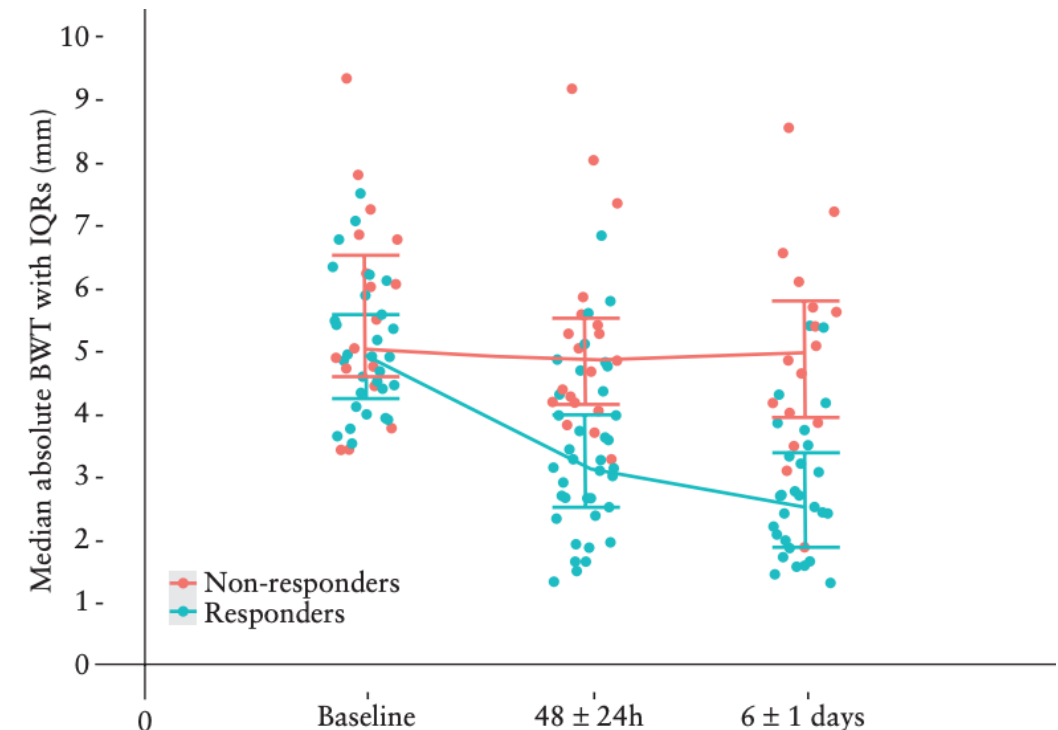






# IUS Predicts Response in ASUC Receiving IV Corticosteroids

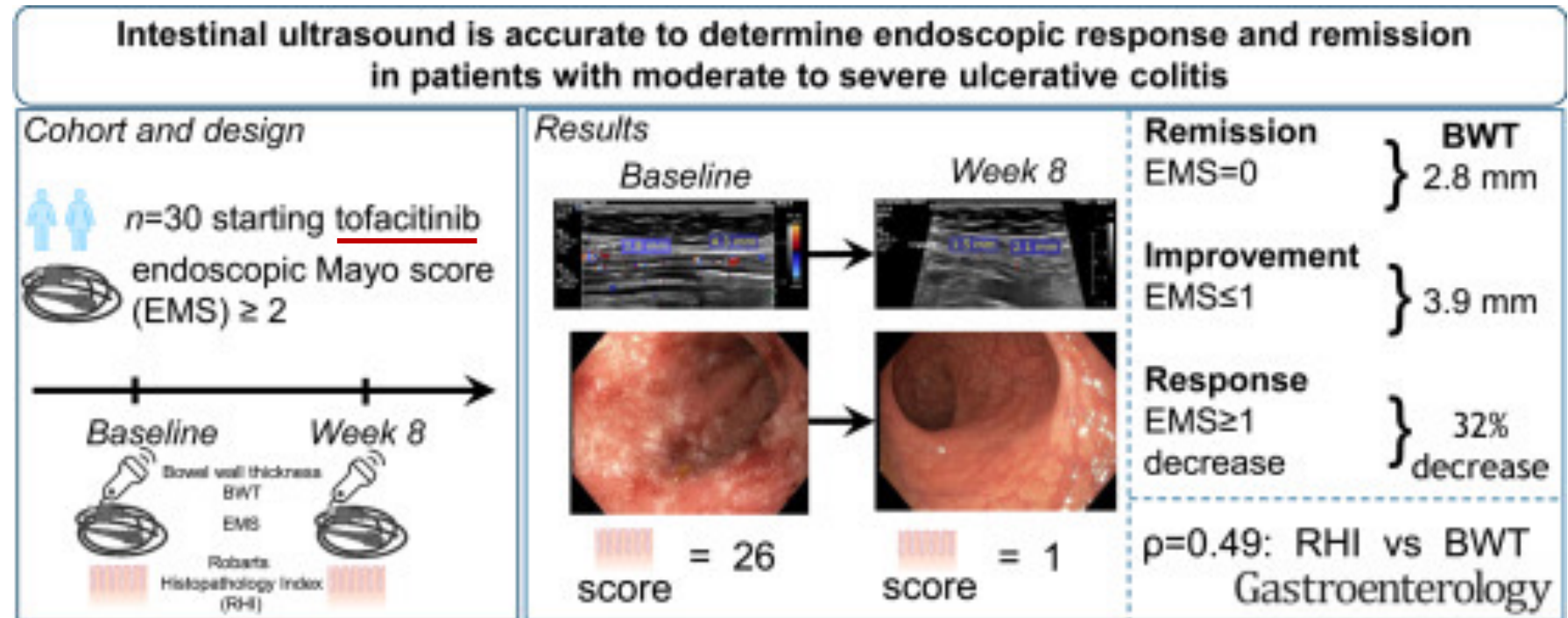
- IUS parameters assessed before treatment initiation, after  $48 \pm 24$  hrs, and  $6 \pm 1$  days.
- **>20% reduction in BWT = OR 22.6 for therapeutic response**
- **$\leq 20\%$  reduction - sensitivity = 84.2%; specificity = 78.4% for determining non-response**



# IUS in UC is Sensitive to Change with Tofacitinib



- BWT as the single most important parameter
- Submucosa was the most responsive wall layer
- BWT correlated with endoscopic scores ( $\rho=0.7$   $p<0.0001$ )



# Consensus on Treatment Response for Intestinal Ultrasound in Ulcerative Colitis



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Original Article

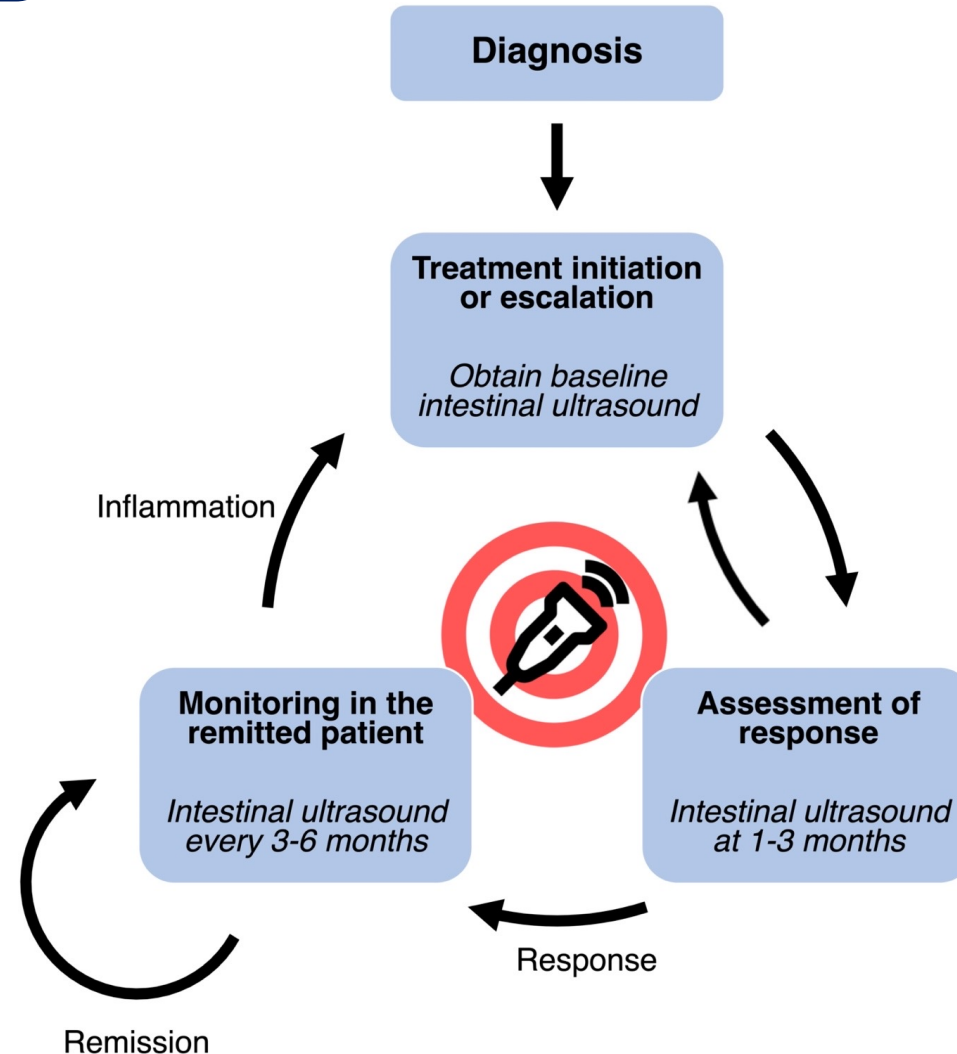
## Defining Transabdominal Intestinal Ultrasound Treatment Response and Remission in Inflammatory Bowel Disease: Systematic Review and Expert Consensus Statement



Johan F. K. F. Ilvemark,<sup>a,\*</sup> Tawnya Hansen,<sup>b</sup> Thomas M. Goodsall,<sup>c,d</sup> Jakob B. Seidelin,<sup>a</sup> Heba Al-Farhan,<sup>e</sup> Mariangela Allocca,<sup>f,g</sup> Jakob Begun,<sup>h,\*</sup> Robert V. Bryant,<sup>i</sup> Dan Carter,<sup>j</sup> Britt Christensen,<sup>k,\*</sup> Marla C. Dubinsky,<sup>l</sup> Krisztina B. Gecse,<sup>m</sup> Torsten Kucharzik,<sup>n</sup> Cathy Lu,<sup>o</sup> Christian Maaser,<sup>p</sup> Giovanni Maconi,<sup>q</sup> Kim Nylund,<sup>r,s</sup> Carolina Palmela,<sup>t</sup> Stephanie R. Wilson,<sup>u</sup> Kerri Novak,<sup>o,\*</sup> Rune Wilkens,<sup>v,w,\*,\*</sup>; on behalf of the International Bowel Ultrasound [IBUS] Group

- > 25% Reduction in BWT
- > 2 mm Reduction in BWT
- $\geq$  1 mm Reduction in BWT and 1 point in CDS

# Proposed Clinical Approach to Intestinal Ultrasound for Disease Monitoring in IBD



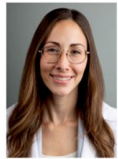
# Should Transmural Healing be a Therapeutic Goal in UC?



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Gastroenterology 2022;162:1396–1408

## What Does Disease Progression Look Like in Ulcerative Colitis, and How Might It Be Prevented?



Noa Krugliak Cleveland<sup>1</sup>



Joana Torres<sup>2,3</sup>



David T. Rubin<sup>1</sup>



Gastroenterology

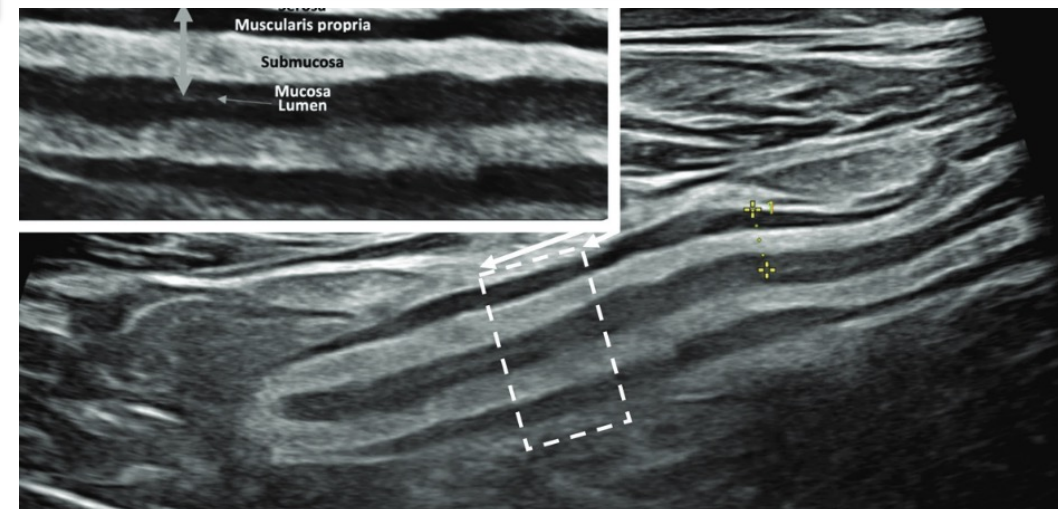
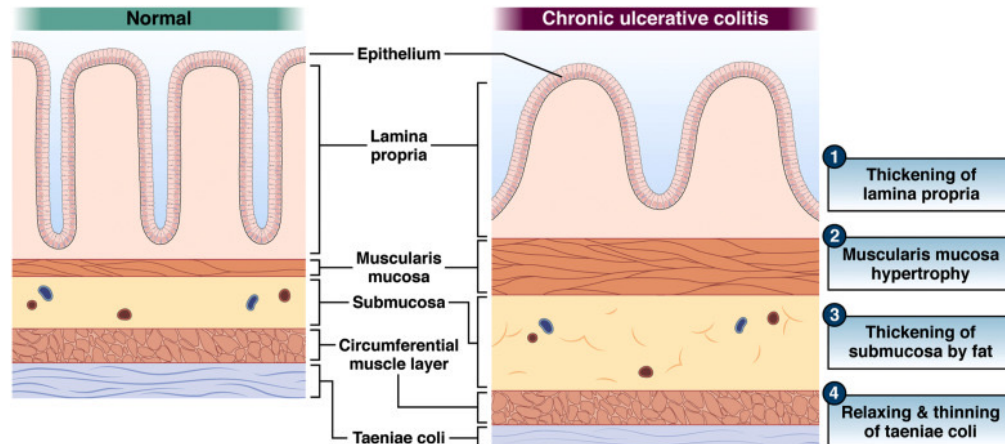
Volume 163, Issue 6, December 2022, Pages 1485-1487



Editorial

## The Use of Intestinal Ultrasound in Ulcerative Colitis—More Than a Mucosal Disease?

Carolina Palmela  , Christian Maaser



# Sonographic Transmural Healing in Ulcerative Colitis



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Original Article

## Defining Transabdominal Intestinal Ultrasound Treatment Response and Remission in Inflammatory Bowel Disease: Systematic Review and Expert Consensus Statement



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- BWT  $\leq$  3 mm AND no color Doppler signal

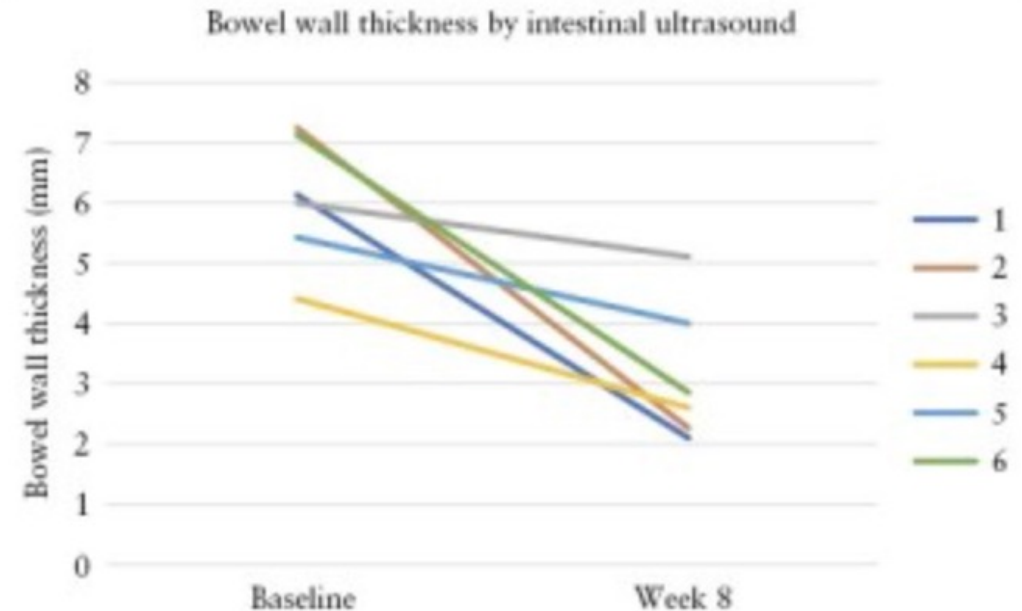
# Upadacitinib Salvage Therapy for Infliximab-Experienced ASUC Patients

- **6 patients who received upa for steroid-refractory ASUC**
  - Followed for up to 16-weeks with clinical, biochemical, and IUS markers
- **Median BWT = 6.1 mm (in most affected segment)**
- **Median mLimberg score = 3**
- **4 patients achieved IUS remission (transmural healing) at week 8**
  - Including a median BWT = 2 mm and median mLimberg score = 0



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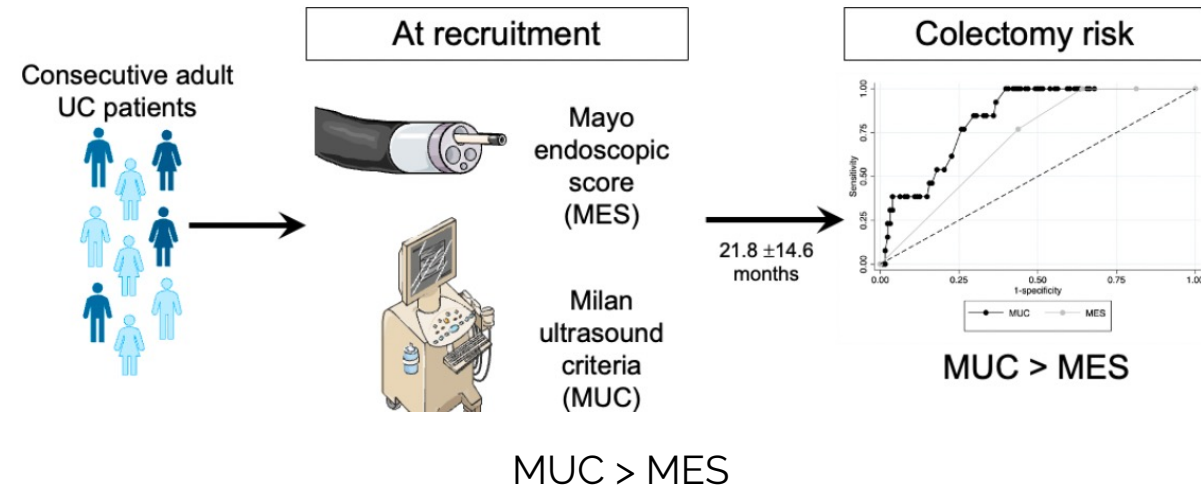
NEW!



# Transmural Severity is a Superior Predictor of Colectomy Risk Compared to Endoscopic Severity



- n=141 pts, 13 colectomies
- MUC was the only independent variable associated with colectomy risk, OR: 1.53 (1.03–2.27)
- MUC demonstrated higher accuracy than MES (AUROC 0.83 vs. 0.71)
- MUC demonstrated better performance for predicting colectomy (p=0.02).
- The optimal MUC score cut- off value for predicting colectomy was 7.7



$$\text{Milan Ultrasound Criteria (MUC)} = 1.4 \times \text{Bowel Wall Thickness (mm)} + 2 \times \text{Bowel Wall Flow}$$

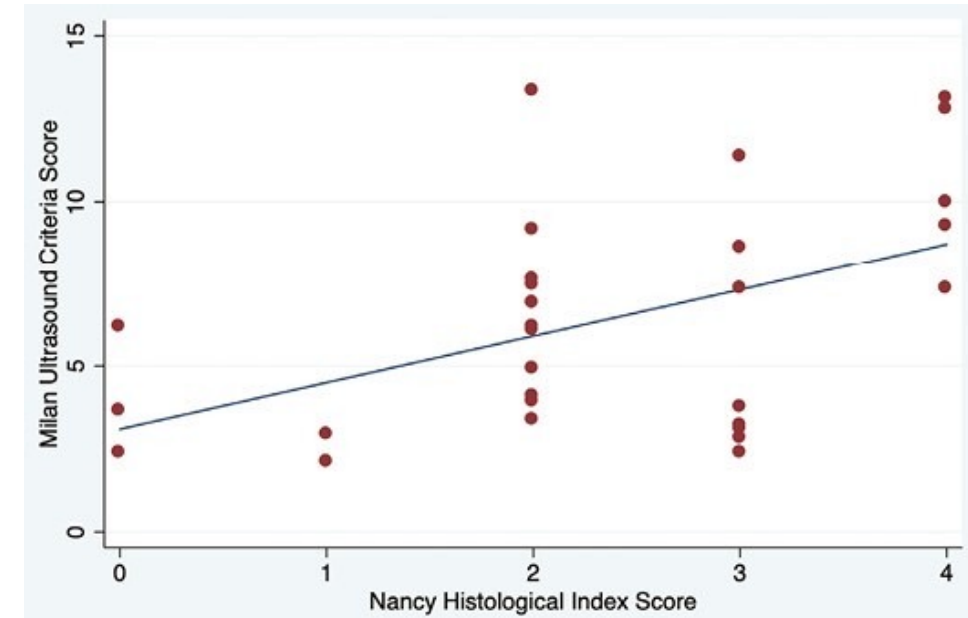


# Composite Assessment with IUS and FCP is Accurate in Predicting Histological Activity



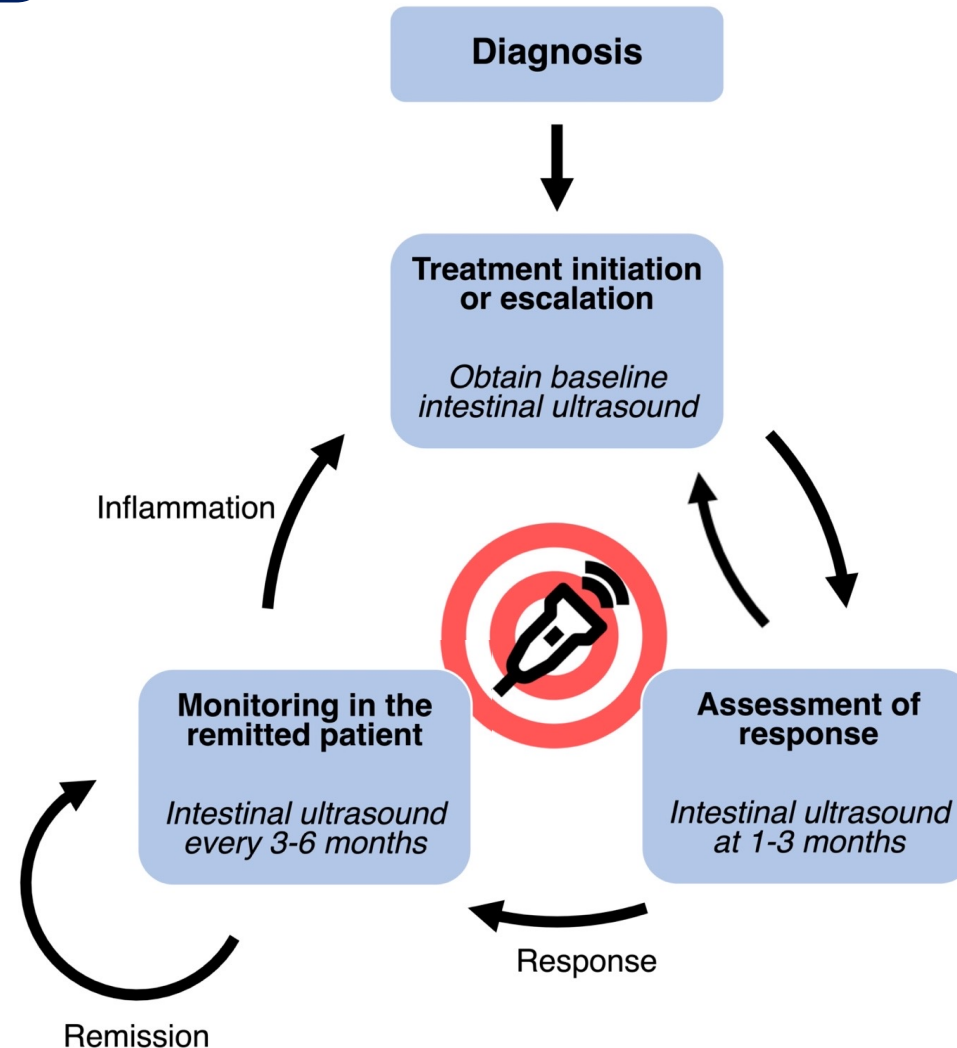
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- 29 prospective, paired patients with same-day IUS/endo/histo/FCP
- **Histological activity had a sig. linear assoc. with overall IUS activity and BWT alone**
- **Composite of IUS and FCP had greatest association and accurately predicted histological activity**
  - sens. 88%, spec. 80%, PPV 95%, NPV 57%
- **In all 5 cases of histological remission, the IUS MUC score was <6.3**



Comparison	<i>P</i>	Sensitivity (%)	Specificity (%)	Positive Predictive Value (%)	Negative Predictive Value (%)
MUC >6.3	.048	55	100	100	31
Calprotectin >50 ug/g	.127	92	40	88	50
Calprotectin >100 ug/g	.022	79	80	95	44
Composite of MUC and calprotectin <sup>a</sup>	.007	88	80	95	57

# Proposed Clinical Approach to Intestinal Ultrasound for Disease Monitoring in IBD



# IUS is Predictive of Disease Relapse in Asymptomatic Patients with IBD

- 40 patients (53 IUS exams)
- Asymptomatic by HBI and SCCAI (HBI $\leq$ 4,SCCAI $\leq$ 2) but with BWT >3 mm and or mLimberg score >0
- 10 patients (18.9%) relapsed within an average of 107.0 ( $\pm$ 108.2) days.

	Not Relapsed (n = 43)	Relapsed (n = 10)	P-Value
Age – mean (SD)	37.5 (2.3)	33.4 (4.9)	
Female sex – n (%)	17 (39.5)	6 (60.0)	
IBD Diagnosis – n (%)			
Crohn's disease	40 (93.0)	7 (70.0)	
Ulcerative colitis	3 (7.0)	2 (20.0)	
IBD-U	0	1 (10.0)	
Had FCP at initial visit – n (%)	16 (37.2)	6 (60.0)	
Elevated FCP > 150 mcg/g – n (%)	9 (56.3%)	6 (100%)	
Maximum Bowel Wall Thickness (mm) – mean (SD)	3.9 (0.5)	4.5 (0.3)	0.112
Maximum Color Doppler Signal (mLimberg) – mean (SD)	1.3 (0.12)	1.7 (0.3)	0.503
Changed treatment – n (%)	31 (72.1)	9 (90.0)	0.842

**NEW!**



# Summary

- Transabdominal ultrasound accurately detects endoscopic inflammation in the colon but the sensitivity for the rectum is decreased (TPUS increases the sensitivity)
- The Milan ultrasound criteria predicts both disease activity and prognosis (>6.2 mm)
- The appendix is challenging to visualize but can indicate active UC when >6.0 mm
- IUS response in ASUC can be seen as early as 24-72 hours with reduction of over 20% in BWT predicting response at 1 week
- Sonographic transmural healing can be achieved by week 8 on JAK-inhibitors
- Transmural severity is a superior predictor of colectomy compared to the Mayo Endoscopic Score
- IUS + FCP together have greater association to accurately predict histologic activity than IUS alone