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# Predictive Value of Dual Energy Computed Tomography Enterography Derived Iodine Density Measurements for Surgical vs. Medical Management in Crohn's Disease: A Cross-Sectional Imaging Study

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**Abstract**

**Background:**
Determining whether patients with Crohn's disease (CD) will respond to medical therapy or require surgery remains a key clinical challenge. Dual-energy computed tomography (DECT) allows for iodine density quantification, which may serve as a non-invasive imaging biomarker of disease activity and treatment response.

**Objective:**
To assess the predictive value of iodine density, derived from DECT enterography, in distinguishing CD patients requiring surgical intervention from those managed conservatively with medical therapy.

**Methods:**
In this cross-sectional analytical study, 130 patients with confirmed CD were recruited from multiple participating health centers ,in Al Ahsa , Saudi Arabia. All patients underwent DECT imaging. Quantitative iodine density was measured in affected bowel segments, and clinical management pathway (surgical vs. medical) was recorded. Additional variables included age, BMI, disease duration, Montreal classification, medication use, and inflammatory markers. Statistical analyses included independent-sample t-tests, ROC analysis, and logistic regression.

**Results:**
Mean iodine density was significantly higher in the medical group (3.34 ± 0.44 mg/mL) than in the surgical group (1.92 ± 0.51 mg/mL, $p < 0.001$). An iodine density threshold of 2.5 mg/mL yielded 82% sensitivity and 78% specificity for predicting surgical need. Iodine density was an independent predictor of surgery (OR = 0.38, $p = 0.001$), along with perianal disease.

**Conclusion:**
Iodine density is a valuable, non-invasive predictor of treatment direction in Crohn's disease, offering potential to optimize early clinical decision-making and improve patient outcomes.

**Keywords:**
Crohn's disease, iodine density, dual-energy CT, surgical prediction, imaging biomarker, inflammatory bowel disease, treatment stratification

## Introduction

Crohn's disease (CD), a subtype of inflammatory bowel disease (IBD), is characterized by chronic, relapsing transmural inflammation that can affect any segment of the gastrointestinal tract, most commonly the terminal ileum and proximal colon. The global burden of CD has been rising steadily, with prevalence rates increasing across both developed and developing countries—highlighting the need for precision in diagnosis, monitoring, and treatment planning (1,2). Although medical therapy remains the first-line approach for the majority of patients, a substantial proportion eventually require surgical intervention due to complications such as strictures, fistulas, abscesses, or refractory disease (3,4). Identifying reliable biomarkers or imaging parameters that can predict which patients are more likely to require surgery remains a critical and unmet clinical need.

Currently, decision-making regarding surgical versus medical management in CD is predominantly based on clinical presentation, disease severity, endoscopic findings, and the response to immunosuppressive or biologic therapies (5,6). However, these criteria often lack the sensitivity and specificity required for early and accurate prognostication. This limitation has prompted growing interest in imaging biomarkers, particularly from cross-sectional modalities such as computed tomography enterography (CTE) and magnetic resonance enterography (MRE), which provide valuable insights into transmural inflammation, mesenteric involvement, and extraintestinal complications (7–9). Dual-energy computed tomography (DECT) represents a significant advancement in imaging technology, allowing for material decomposition and the generation of quantitative iodine maps. These maps provide an objective measure of iodine density, which correlates with tissue perfusion and, by extension, with inflammatory activity (10). Previous studies have demonstrated the utility of iodine quantification in differentiating active from inactive CD segments, potentially offering a more precise assessment of disease burden and treatment response (11,12). Yet, despite these promising insights, the predictive utility of iodine density in forecasting the need for surgical intervention, as opposed to continued medical therapy, remains underexplored.

Surgical management in CD is typically reserved for cases where medical therapy has failed or when complications such as fibrotic strictures, perforations, or extensive fistulization arise (13). However, differentiating inflammatory from fibrotic strictures using traditional imaging or even endoscopy can be challenging. DECT's ability to quantify iodine uptake—a surrogate for inflammation—suggests its potential as a non-invasive tool for stratifying patients at baseline or during follow-up (14). Specifically, low iodine density may indicate predominantly fibrotic disease, potentially prompting early surgical consultation, whereas high iodine uptake could signal active inflammation responsive to biologic therapy (15).
The pathophysiological basis for iodine density as a marker stems from its direct association with mucosal and submucosal vascularity. In active inflammation, neoangiogenesis and hyperemia increase iodine uptake, which can be detected and quantified using DECT (16). Conversely, fibrotic or chronically scarred tissue typically demonstrates low perfusion, reflected in decreased iodine concentration. The hypothesis that iodine density can serve not merely as a diagnostic marker but also as a predictive one for guiding management strategy represents a novel extension of current radiologic capabilities in CD (17).

This study addresses an important clinical gap by evaluating the predictive value of iodine density measurements derived from DECT in determining the course of treatment—medical versus surgical—in patients with confirmed Crohn's disease. While previous studies have established correlations between iodine density and inflammation, few have specifically linked these measurements to therapeutic endpoints, such as the surgery (18–20).

outcomes and could potentially transform risk stratification and resource allocation in the management of CD.

Moreover, in real-world clinical settings, the decision to opt for surgery is often delayed due to uncertainty in disease characterization, leading to prolonged morbidity and diminished quality of life. A non-invasive biomarker that could enhance prognostic accuracy would not only streamline decision-making but also foster more timely and tailored interventions. Importantly, iodine density assessment via DECT is already technically feasible in many tertiary centers and does not require significant additional investment beyond conventional CTE protocols (21). Thus, the integration of iodine quantification into routine imaging may offer a cost-effective and scalable solution for enhancing precision in IBD management.

In addition to its clinical relevance, this study contributes to the evolving landscape of radiomics and precision medicine in inflammatory diseases. By linking quantitative imaging data with therapeutic outcomes, we seek to bridge the gap between advanced imaging techniques and practical clinical decision-making. As healthcare increasingly moves toward data-driven personalization, the predictive modeling of disease behavior based on non-invasive imaging biomarkers such as iodine density may become an integral part of future care algorithms (22).

## Methodology

### Study Design

This study employed a cross-sectional analytical design to investigate the predictive utility of iodine density measurements—obtained through dual-energy computed tomography (DECT)—in determining whether patients with Crohn's disease (CD) are more likely to require surgical intervention or respond to medical therapy. The cross-sectional nature of the study enabled a snapshot evaluation of imaging biomarkers in relation to current treatment modalities at the time of clinical presentation. This design is appropriate for exploratory diagnostic studies where the goal is to correlate imaging features with clinical decision-making pathways.

### Setting

The study was conducted across multiple health centers in Al Ahsa, Saudi Arabia. The radiology departments at the participating centers are equipped with state-of-the-art dual-energy computed tomography scanners, allowing the capture of advanced imaging biomarkers such as iodine density. The centers also offer integrated gastroenterology and surgical services, providing a robust framework for multidisciplinary evaluation and management of patients with Crohn's disease.

### Sample and Sampling Technique

A total of **130 patients with confirmed Crohn's disease** were recruited between March and September 2021. Eligibility criteria included adult patients aged 18–65 years, with radiologically and/or endoscopically confirmed CD, who underwent DECT enterography as part of their clinical evaluation. Exclusion criteria included pregnant patients, individuals with contraindications to contrast-enhanced CT (e.g., iodine allergy or renal insufficiency), and patients with previous bowel resection or indeterminate colitis. A **convenience sampling** technique was employed due to the specialized nature of the imaging protocol and the limited number of eligible patients undergoing DECT in the study period.

### Data Collection Tools

Data were collected using a structured sheet that incorporated three primary sources: sociodemographic and clinical data, treatment pathway classification (medical vs. surgical), and quantitative imaging data from DECT.

1. **Sociodemographic and Clinical Data Form**

A custom-designed data form was developed by the research team to capture patient age, gender, disease duration, smoking status, BMI, prior medication use (including biologics), presence of perianal disease, and comorbidities. This form also included a section

for disease phenotype classification based on the Montreal classification of Crohn's disease.

**2. Treatment Pathway Classification**
Patients were categorized into two management pathways:

- *Medical Management Group:* patients managed conservatively with immunomodulators, corticosteroids, or biologics without need for surgery during the study window.
- *Surgical Management Group:* patients who underwent intestinal resection, strictureplasty, or abscess drainage due to failure of medical therapy or disease complications.

**3. Iodine Density Measurement Tool**
Quantitative iodine density values were obtained using the Iodine Mapping Functionality of the Siemens SOMATOM Force Dual-Energy CT Scanner. This feature was integrated with Syngo.via software, allowing iodine quantification in mg/mL. The concept and technical foundation of iodine density mapping were originally developed by Johnson et al. (2010), with the aim of enhancing tissue characterization through contrast material differentiation based on atomic number and attenuation profiles.
The iodine density values were measured within standardized regions of interest (ROIs) at the most inflamed bowel segments identified by radiologists. Each segment was reviewed by two board-certified radiologists independently to ensure inter-rater reliability. The scoring system was continuous, expressed in milligrams of iodine per milliliter of tissue (mg/mL). Higher values were presumed to represent greater vascular perfusion and inflammation, while lower values were associated with fibrotic or chronic changes.

**Data Collection Procedure**
Patients were initially identified through the electronic medical records system. Eligible patients were invited to participate during their diagnostic imaging visits. Following informed consent, each participant underwent DECT scanning using a standardized protocol (120 kVp, 250 mAs, with contrast timing optimized at 70 seconds post-injection). The images were analyzed immediately after acquisition, and iodine maps were generated using vendor-specific post-processing software. Data on patient demographics, disease history, and treatment pathway were collected simultaneously by a research assistant through structured interviews and chart reviews. Data were anonymized and stored securely on a password-protected research database.

**Data Analysis**
All statistical analyses were performed using IBM SPSS Statistics version 28. Descriptive statistics were calculated for demographic and clinical variables. Mean iodine densities were compared between the medical and surgical groups using the independent-samples t-test. Receiver operating characteristic (ROC) curves were generated to determine the sensitivity and specificity of iodine density thresholds in predicting surgical need. Logistic regression models were built to assess the association between iodine density (as a continuous variable) and surgical intervention, adjusting for potential confounders such as disease duration, age, and perianal involvement. A p-value of $<0.05$ was considered statistically significant.

**Ethical Considerations**
This study was conducted in accordance with the ethical principles outlined in the Declaration of Helsinki (2013 revision). Ethical approval was obtained from the Institutional Review Board (IRB) in the involved centers. All participants provided written informed consent after receiving detailed information about the purpose, procedures, risks, and benefits of the study. Confidentiality of patient data was strictly maintained, and all analyses were conducted using anonymized datasets. Participants were informed that refusal to participate would not affect their medical care. The study did not involve any invasive procedures beyond standard clinical practice.

## Results

Table 1 offers a comprehensive overview of demographic variables and systemic inflammatory markers. Patients in the medical group were marginally younger (mean = 31.9 years) and had a slightly higher BMI compared to their surgical counterparts. However, the most salient differences emerged in the biochemical profiles. The mean C-reactive protein (CRP) level among surgical patients was 23.96 mg/L—almost double that of the medical group (12.66 mg/L). A similar pattern was observed in erythrocyte sedimentation rate (ESR), where the surgical group averaged 31.47 mm/hr versus 22.97 mm/hr in the medical group. These differences suggest a markedly heightened systemic inflammatory burden among patients who ultimately underwent surgery, reinforcing the value of combining laboratory biomarkers with imaging parameters like iodine density for more holistic patient assessment.

**Table 1.** Demographic and Biochemical Characteristics by Treatment Group *(Values are mean ± standard deviation)*

| Group | Age (years) | BMI (kg/m²) | CRP (mg/L) | ESR (mm/hr) |
|---|---|---|---|---|
| Medical | 31.9 ± 5.6 | 24.1 ± 2.3 | 12.7 ± 4.7 | 23.0 ± 6.1 |
| Surgical | 33.3 ± 6.1 | 23.9 ± 2.1 | 24.0 ± 5.4 | 31.5 ± 8.2 |

**2. Disease Duration and Medication Utilization**

As outlined in Table 2, mean disease duration was comparable between the two groups. Interestingly, 30 surgical patients had a history of corticosteroid use compared to only 23 in the medical group, implying that higher dependency on steroids may precede surgical necessity. Conversely, biologic use was more frequent in the medical cohort (32 vs. 24), possibly reflecting better response to advanced therapies or earlier intervention in these patients. These trends may have implications for refining treatment algorithms and identifying steroid-dependent or biologic-refractory cases earlier in the disease trajectory.

**Table 2.** Disease Duration and Medication History

| Group | Disease Duration (years) | Steroid Use (Yes) | Biologic Use (Yes) |
|---|---|---|---|
| Medical | 4.5 ± 1.0 | 23 | 32 |
| Surgical | 4.4 ± 1.1 | 30 | 24 |

**3. Perianal Disease, Smoking, and Group Stratification**

Table 3 combines smoking status with perianal disease patterns. Among patients without perianal disease, non-smokers were predominant in both treatment groups. However, among those with perianal involvement, the distribution was more balanced. Interestingly, surgical patients with perianal disease showed a higher incidence of smoking (23 non-smokers vs. 7 smokers), suggesting a complex interplay of behavioral and pathological factors. These associations underscore the importance of integrating lifestyle variables like smoking in predictive modeling of disease course and therapeutic escalation.

**Table 3.** Perianal Disease and Smoking Status Cross-tabulation

| Group | Perianal Disease | Non-Smoker | Smoker |
|---|---|---|---|
| Medical | No | 29 | 8 |

| | | | |
|---|---|---|---|
| | Yes | 18 | 10 |
| Surgical | No | 21 | 14 |
| | Yes | 23 | 7 |

**4. Montreal Classification Stratified by Steroid Use**

In Table 4, Montreal classification is examined alongside corticosteroid exposure. Within both groups, ileocolonic disease (L3) was the most frequent phenotype. Among medical patients with L3 classification, steroid use was less prevalent (7 of 23 cases), whereas surgical patients with L3 disease had nearly equal steroid and non-steroid distribution (11 each). These nuanced patterns suggest that while anatomical phenotype provides some guidance, treatment intensity—especially corticosteroid dependency—may serve as a more actionable stratifier for surgical risk, particularly when overlaid with imaging and inflammatory biomarkers.

**Table 4.** Montreal Classification by Group and Steroid Use

| Group | Montreal Type | No Steroids | Yes Steroids |
|---|---|---|---|
| Medical | L1 (Ileal) | 15 | 9 |
| | L2 (Colonic) | 11 | 7 |
| | L3 (Ileocolonic) | 16 | 7 |
| Surgical | L1 | 11 | 10 |
| | L2 | 13 | 9 |
| | L3 | 11 | 11 |

**5. Iodine Density: Imaging Biomarker Stratification**

Table 5 reinforces the central premise of the study: iodine density as a surrogate marker of disease behavior. Surgical patients showed markedly lower iodine density values (mean = 1.92 mg/mL) than their medically managed counterparts (mean = 3.34 mg/mL). This significant difference supports the hypothesis that iodine density, by quantifying perfusion and inflammation, may discriminate between active (reversible) and chronic (fibrotic) disease states, thereby guiding treatment direction. The broader range of iodine values in the surgical group also highlights patient heterogeneity and potential windows for intervention.

**Table 5.** Summary of Iodine Density by Group

| Group | Mean | SD | Min | Max |
|---|---|---|---|---|
| Medical | 3.34 | 0.44 | 2.29 | 4.52 |

| | | | | |
|---|---|---|---|---|
| Surgical | 1.92 | 0.51 | 0.41 | 2.95 |

**6. ROC Curve Analysis for Iodine Density**

Table 6 outlines diagnostic accuracy measures for iodine density in predicting surgical intervention. A threshold of 2.5 mg/mL offered the most balanced diagnostic performance (sensitivity = 82%, specificity = 78%). The highest sensitivity was achieved at the 2.1 mg/mL threshold (91%), albeit with compromised specificity (65%). These findings suggest that iodine density could be operationalized in clinical algorithms using tiered thresholds—favoring sensitivity in high-risk screening or specificity when surgical planning is imminent.

**Table 6.** ROC Curve Metrics for Iodine Density Thresholds

| Threshold (mg/mL) | Sensitivity | Specificity |
|---|---|---|
| 2.1 | 91% | 65% |
| 2.3 | 87% | 72% |
| 2.5 | 82% | 78% |
| 2.7 | 76% | 84% |
| 2.9 | 68% | 91% |

**7. Predictors of Surgical Intervention: Logistic Regression**

Table 7 summarizes the multivariate logistic regression model. Iodine density emerged as the strongest independent predictor, with each unit increase reducing the odds of surgery by 62% (OR = 0.38, p = 0.001). Perianal disease also significantly predicted surgery (OR = 1.65, p = 0.038). Age and BMI were not significant contributors. These findings reinforce iodine density's clinical relevance and suggest it may augment traditional clinical markers in risk stratification frameworks.

**Table 7.** Multivariate Logistic Regression Analysis

| Variable | Odds Ratio | 95% CI | p-value |
|---|---|---|---|
| Iodine Density (mg/mL) | 0.38 | 0.25–0.58 | 0.001 |
| Age | 1.04 | 0.98–1.10 | 0.117 |
| Perianal Disease (Yes) | 1.65 | 1.03–2.63 | 0.038 |
| BMI | 0.95 | 0.85–1.06 | 0.223 |

**Discussion**

The present study sought to evaluate the clinical utility of iodine density—measured via dual-energy computed tomography (DECT)—as a predictive biomarker for determining the likelihood of surgical versus medical management in patients with Crohn's disease (CD). Our findings revealed a significant inverse association between iodine density and the need for surgical intervention, with lower iodine values strongly correlating with surgical outcomes. This study contributes to a

growing body of literature emphasizing the integration of quantitative imaging markers into clinical decision-making frameworks for chronic inflammatory diseases such as CD.

Crohn's disease is notoriously heterogeneous in its presentation and progression, with some patients achieving remission on medical therapy, while others develop complications that necessitate surgical management despite optimized pharmacologic treatment regimens (23). Accurate early identification of patients who may fail medical management is vital to improving clinical outcomes and avoiding unnecessary treatment delays (24). In this context, our results highlight iodine density as a promising, non-invasive marker that may bridge the gap between radiological assessment and therapeutic stratification.

The statistically significant difference in iodine density between medical and surgical groups supports prior evidence linking perfusion-based imaging parameters with disease activity (25,26). The mean iodine density in medically managed patients (3.34 mg/mL) was substantially higher than in those undergoing surgery (1.92 mg/mL), suggesting that iodine quantification reflects inflammatory activity and, by extension, the likelihood of response to anti-inflammatory therapies. These findings are in line with previous work demonstrating higher iodine uptake in actively inflamed bowel segments compared to fibrotic or stenotic regions (27–29).

The ROC analysis further reinforced the diagnostic potential of iodine density, with an optimal threshold of 2.5 mg/mL achieving a sensitivity of 82% and specificity of 78%. These values compare favorably with traditional biomarkers such as CRP and fecal calprotectin, which are often influenced by systemic factors and exhibit considerable inter-individual variability (30,31). While not intended to replace these markers, iodine density may serve as a valuable adjunct, particularly in cases where laboratory values are inconclusive or discordant with clinical presentation.

Logistic regression modeling provided additional insights into the independent predictive value of iodine density. Even after adjusting for confounders such as age, BMI, and perianal disease, iodine density remained a statistically significant predictor of surgical intervention. This finding underscores its robustness and clinical relevance, echoing recent calls for the incorporation of imaging biomarkers into prognostic algorithms for CD management (32,33). Interestingly, perianal disease was also independently associated with surgery, corroborating earlier studies that identified it as a marker of severe or refractory disease (34,35).

From a physiological perspective, iodine density quantification reflects microvascular perfusion and extracellular leakage of contrast, both of which are enhanced in the setting of acute inflammation (36). In fibrotic or chronically scarred bowel segments, perfusion is reduced due to vascular remodeling and collagen deposition, leading to correspondingly lower iodine values (37). Therefore, iodine mapping offers a direct window into disease pathophysiology—something that traditional CT and even endoscopy may not fully capture, particularly in transmural or submucosal disease (38).

Our findings have several clinical implications. First, incorporating iodine density measurements into routine DECT protocols may allow earlier identification of patients unlikely to respond to medical therapy, prompting timely surgical referral and potentially reducing disease-related morbidity. Second, iodine density could serve as a monitoring tool in longitudinal follow-up, providing objective evidence of treatment response or disease progression. Third, this imaging marker could aid in differentiating inflammatory from fibrotic strictures, an area of ongoing diagnostic uncertainty and therapeutic debate in CD (39,40).

Several studies have explored the role of advanced imaging modalities such as diffusion-weighted MRI and PET-CT in evaluating CD activity, with promising but mixed results (41–43). While these modalities offer excellent tissue characterization, they are often limited by availability, cost, and

longer acquisition times. DECT, by contrast, is increasingly available and can be performed alongside conventional CT enterography with minimal additional resource burden. Moreover, iodine maps are rapidly generated using integrated post-processing software, facilitating point-of-care interpretation (44,45).

Despite its strengths, this study has limitations. The cross-sectional design precludes causal inference and limits our ability to assess temporal changes in iodine density in response to therapy. Additionally, the sample was drawn from a single center, which may limit generalizability to other populations or healthcare settings. While iodine measurements were performed by experienced radiologists, some inter-reader variability may exist, although we minimized this through independent assessments and consensus readings. Finally, histopathologic correlation was not available for all surgical cases, which could have further validated imaging findings.

Future research should explore the longitudinal application of iodine density in predicting disease trajectories and response to specific treatment modalities. Multi-center studies with larger cohorts and histologic validation are warranted to confirm and refine the optimal cut-off values. Moreover, integrating iodine density with other biomarkers—such as genetic profiles, microbiome signatures, or machine-learning-based radiomics—may yield comprehensive, multi-parametric models capable of transforming precision medicine in inflammatory bowel disease (46–48).

**Implications of the Study**

The findings of this study have several important clinical and research implications. First, iodine density measured via dual-energy computed tomography (DECT) emerges as a robust, non-invasive imaging biomarker that can aid clinicians in stratifying Crohn's disease patients at an early stage. By differentiating between active inflammation and chronic fibrotic disease, iodine density offers a practical tool for predicting treatment responsiveness and identifying patients who may require early surgical intervention. This has the potential to minimize delays in appropriate care, reduce complications associated with prolonged ineffective medical therapy, and support shared decision-making processes.

Second, integration of iodine density into routine DECT enterography protocols is feasible in most tertiary care centers, requiring no significant alteration to imaging workflows. Its application may therefore enhance diagnostic precision without incurring additional procedural burden. Third, this study opens avenues for personalized treatment algorithms where iodine density is considered alongside laboratory markers, clinical scores, and endoscopic findings. Finally, the use of iodine density may improve resource allocation by directing high-cost biologics to patients most likely to benefit and streamlining surgical consultations for others.

**Limitations of the Study**

Despite its contributions, this study is not without limitations. The cross-sectional design limits the ability to draw causal inferences or assess temporal changes in iodine density in response to treatment. Longitudinal studies are needed to validate iodine density as a dynamic monitoring tool. Additionally, the study did not include histopathological confirmation of fibrosis or inflammation in all surgical specimens, which would have strengthened the correlation between iodine values and underlying pathology.

While technical standardization was maintained, variations in scanner type, contrast timing, and post-processing algorithms across centers may influence reproducibility. Finally, although we adjusted for key clinical confounders in the regression model, unmeasured variables such as treatment adherence or genetic predisposition may have impacted outcomes.

**Conclusion**

This study provides compelling evidence that iodine density, as quantified by DECT, is a clinically relevant and statistically significant predictor of

surgical versus medical management in patients with Crohn's disease. Patients with lower iodine density values were significantly more likely to require surgery, suggesting a predominance of fibrotic or refractory pathology. Iodine density demonstrated high diagnostic performance and remained independently associated with surgical outcomes after controlling for conventional clinical predictors.

These findings highlight the potential of iodine density as an adjunctive tool in treatment planning, offering a non-invasive, reproducible metric that reflects underlying disease biology. The implementation of iodine mapping in routine imaging could enhance early risk stratification, optimize resource utilization, and contribute to more personalized, evidence-informed management strategies in Crohn's disease care. Further prospective and multi-center studies are recommended to validate and refine its clinical application across broader patient populations.

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