

**Title:**

**Risk factors associated with recurrent ischemic colitis – A 10-year retrospective study**

**Authors:**

Luís Relvas, Isabel Carvalho, Pedro Baltazar, Tânia Gago, Francisco Velasco, Paulo Caldeira, Bruno Peixe

DOI: 10.17235/reed.2025.11631/2025

Link: [PubMed \(Epub ahead of print\)](#)

Please cite this article as:

Relvas Luís, Carvalho Isabel, Baltazar Pedro, Gago Tânia, Velasco Francisco, Caldeira Paulo , Peixe Bruno. Risk factors associated with recurrent ischemic colitis – A 10-year retrospective study. Rev Esp Enferm Dig 2025. doi: 10.17235/reed.2025.11631/2025.

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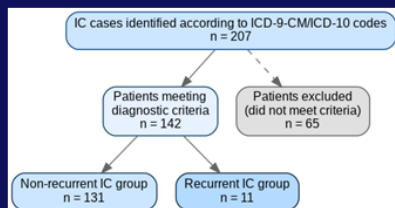
# RISK FACTORS ASSOCIATED WITH RECURRENT ISCHEMIC COLITIS: A 10-YEAR RETROSPECTIVE STUDY

Recurrent IC is uncommon but clinically relevant, and its risk factors remain poorly defined.

**AIM:** To assess the prevalence of recurrence and identify associated clinical predictors.

## METHODS

### Patients selection



- **Recurrent IC** was defined as a new episode after a  $\geq 30$ -day symptom-free interval.
- *Demographic, clinical, imaging, and outcomes* data were collected.
- Associations with recurrence were analyzed using odds ratios (OR) with 95% confidence intervals (CI).

## RESULTS

- 142 patients, **recurrence in 11 (7.7%)**.
- **Risk factors:**
  - Smoking (OR 5.6)
  - Coronary artery disease (OR 4.1)
  - Prior laparotomy (OR 5.8)
  - Clopidogrel use (OR 5.2)
- **Outcomes:**
  - More transfusions (OR 7.8)
  - Less hematochezia (OR 0.16)
- **Imaging/endoscopy:** similar across groups.

Accepted

## **Risk factors associated with recurrent ischemic colitis – A 10-year retrospective study**

Luís Miguel Relvas, Serviço de Gastrenterologia, Unidade Local de Saúde do Algarve – Hospital de Faro, Faro, Portugal

Isabel Malta Carvalho, Serviço de Gastrenterologia, Unidade Local de Saúde do Algarve – Hospital de Faro, Faro, Portugal

Pedro Baltazar, Faculdade de Medicina e Ciências Biomédicas da Universidade do Algarve, Faro, Portugal

Tânia Gago, Serviço de Gastrenterologia, Unidade Local de Saúde do Algarve – Hospital de Faro, Faro, Portugal

Francisco Velasco, Serviço de Gastrenterologia, Unidade Local de Saúde do Algarve – Hospital de Faro, Faro, Portugal

Paulo Caldeira, Serviço de Gastrenterologia, Unidade Local de Saúde do Algarve – Hospital de Faro, Faro, Portugal

Bruno Peixe, Serviço de Gastrenterologia, Unidade Local de Saúde do Algarve – Hospital de Faro, Faro, Portugal

### **List of abbreviations:**

IC - Ischemic colitis;

CT – Compute tomography;

ICU – Intensive care unit;

OR - odds ratios.

**Lay summary:** Ischemic colitis happens when blood flow to the colon is reduced, causing inflammation and damage. Most cases occur only once, but some patients develop recurrences, which make diagnosis and management more challenging.

We reviewed all cases of ischemic colitis diagnosed at a regional hospital over 10 years. Among 142 patients, 11 (7.7%) had recurrent disease. These patients were generally younger and more likely to have a history of smoking, coronary artery disease, prior

abdominal surgery (laparotomy), and treatment with clopidogrel (a blood thinner). Their scans and colonoscopies looked similar to those without recurrence. However, they needed blood transfusions more often and were less likely to show obvious rectal bleeding.

This suggests that recurrent ischemic colitis may be linked to specific risk factors and present with subtler symptoms, which can delay recognition. Greater awareness of these patterns could help clinicians identify high-risk patients earlier. Further studies are needed to confirm these findings and guide preventive care.

#### **Abstract:**

**Background:** Recurrent ischemic colitis (IC) is uncommon but clinically relevant, and its risk factors remain poorly defined. We aimed to assess the prevalence of recurrence and identify associated clinical predictors.

**Methods:** We conducted a retrospective single-center cohort study including all patients diagnosed with IC at the Algarve Local Health Unit (Faro, Portugal) between January 2011 and December 2021. Cases were identified using ICD-9/ICD-10 codes and confirmed by clinical presentation and at least one diagnostic modality (computed tomography, colonoscopy, or histology). Patients younger than 18 years, pregnant women, and those with mechanical or inflammatory causes of colitis were excluded. Recurrent IC was defined as a new episode after a  $\geq 30$ -day symptom-free interval. Demographic, clinical, imaging, and outcome data were collected. Associations with recurrence were analyzed using odds ratios (OR) with 95% confidence intervals (CI).

**Results:** Of 142 patients, 11 (7.7%) had recurrent IC. Recurrence was associated with smoking (OR 5.6, 95% CI 1.5–20.3), coronary artery disease (OR 4.1, 95% CI 1.1–15.6), prior laparotomy (OR 5.8, 95% CI 1.3–26.0), and clopidogrel use (OR 5.2, 95% CI 1.3–20.1). Patients with recurrence required blood transfusion more often (OR 7.8, 95% CI 1.9–31.5) but presented with hematochezia less frequently (OR 0.16, 95% CI 0.04–0.57). Imaging and endoscopic findings were comparable across groups, although colonic necrosis was absent in recurrent cases.

**Conclusions:** Recurrent IC occurred in 7.7% of patients and was linked to smoking, cardiovascular disease, prior laparotomy, and clopidogrel therapy. Its presentation was

often less typical, which may hinder early recognition. Prospective, multicenter studies are required to confirm these findings.

**Keywords:** Ischemic colitis. Recurrent ischemic colitis. Risk factors.

## INTRODUCTION

Ischemic colitis (IC) is a vascular disorder caused by reduced blood flow to the colon, which impairs cellular metabolism and may lead to inflammation, ischemia, and necrosis of colonic tissue (1). Clinically, it may present as a reversible lesion with subepithelial hemorrhage and edema (ischemic colopathy) or as mucosal ulceration (ischemic colitis). In severe cases, however, it can progress to gangrene, fulminant colitis, stricture formation, chronic ischemic colitis, or sepsis (2).

IC is the most frequent form of intestinal ischemia, with higher prevalence among women and older adults (3,4). Its annual incidence ranges from 15.6 to 17.7 cases per 100,000 population (2). Diagnostic rates have increased in recent decades, likely reflecting broader use of computed tomography (CT) and colonoscopy as well as population aging, which raises susceptibility to ischemic events (5).

Patients typically report lower abdominal pain, often in the left quadrants, which may improve after defecation. Hematochezia is a frequent symptom, although presentation can be nonspecific (3,6). While most cases resolve with conservative treatment, IC carries a higher 30-day mortality than other colonic disorders (5). It also accounts for 8.7–18% of acute lower gastrointestinal bleeding (LGIB) cases, ranking among the most common causes (5,7,8).

The colon is particularly vulnerable to ischemia because of its relatively poor collateral supply, reduced blood flow during functional activity, and high sensitivity to autonomic regulation (2). The left colon is most commonly affected, particularly the splenic flexure (Griffith's point) and the rectosigmoid junction (Sudeck's point), which correspond to watershed areas supplied by the superior and inferior mesenteric arteries and by the inferior mesenteric and internal iliac arteries, respectively (2). The right colon can also be involved, especially in individuals with an underdeveloped marginal artery of Drummond—present in about half the population—which increases

the risk of IC (9).

Risk factors are generally divided into intestinal and vascular. Intestinal factors include constipation, irritable bowel syndrome, fecal impaction, colonic obstruction, and other conditions that raise intraluminal pressure, thereby compromising mucosal perfusion. Vascular factors include systemic hypoperfusion, vasoconstriction, and mesenteric thromboembolism, as well as prior abdominal surgery, particularly when arterial clamping is required (5).

IC has also been linked to cardiovascular disease and related risk factors such as diabetes mellitus, hypertension, hyperlipidemia, and smoking (6). Still, in many patients no predisposing condition is identified, which complicates management and limits prevention of recurrence (2). Sherid et al. (2014) reported smoking and abdominal aortic aneurysm as predictors of recurrent IC (5). Beyond this study, most available evidence on recurrence is limited to case reports.

The objective of this study was to determine the prevalence and potential risk factors for recurrent IC.

## **METHODS**

### Study design and population

We conducted a retrospective cohort study at the Algarve Local Health Unit – Faro Unit (Portugal). All patients diagnosed with ischemic colitis (IC) between January 2011 and December 2021 were included. The study protocol was approved by the Institutional Ethics Committee (protocol ID: 068/2025).

### Case identification and selection

Cases were identified using ICD-9-CM codes 557.0 (acute vascular insufficiency of intestine) and 557.9 (unspecified vascular insufficiency of intestine) and ICD-10 codes K55.x (vascular disorders of intestine). Each hospitalization was individually reviewed, and the diagnosis confirmed by compatible clinical presentation plus at least one diagnostic modality (colonoscopy, computed tomography [CT], or histology). Two investigators independently validated all cases to minimize misclassification.

Recurrent IC was defined as a new episode after a symptom-free interval of  $\geq 30$  days, clearly distinct from persistent or chronic disease. Only episodes captured within our institutional database were included; recurrences treated elsewhere may have been missed.

#### Exclusion criteria

Exclusion criteria were age  $< 18$  years, pregnancy, gastrointestinal infections, colonic ischemia of mechanical origin (e.g., obstruction, volvulus, hernia), acute or chronic mesenteric ischemia, inflammatory bowel disease flare, diverticulitis, or absence of objective diagnostic confirmation.

#### Data collection

Data were retrieved from electronic medical records using a standardized form and included demographics, comorbidities, home medications, clinical presentation, laboratory values, imaging, endoscopic and histological findings, and clinical outcomes (surgery, transfusion, hospital length of stay, intensive care unit [ICU] admission, mechanical ventilation, and 30-day all-cause mortality). Smoking history was recorded whenever any use was documented; pack-years and current versus former status were not consistently available.

#### Sample size and power

No a priori sample size calculation was performed due to the retrospective design. Post hoc, given the recurrence rate of 7.7% (11/142), the study had limited power to detect modest associations.

#### Statistical analysis

Data were entered into a secure database and analyzed using IBM SPSS Statistics for Windows, version 23.0 (IBM Corp., Armonk, NY, USA). Categorical variables were compared with chi-square or, when any expected cell count was  $< 5$ , Fisher's exact test,

and continuous variables with Student's t-test or Mann–Whitney U test, as appropriate. Results are presented as mean  $\pm$  standard deviation or counts with percentages. Percentages for computed tomography (CT) and colonoscopy findings were calculated among patients who underwent the respective procedure (procedure-specific denominators).

Associations with recurrence were expressed as odds ratios (OR) with 95% confidence intervals (CI). A multivariable logistic regression model adjusting for age, sex, and cardiovascular comorbidities was performed and should be interpreted cautiously given the small number of recurrent events. Sensitivity analyses excluding patients with prior colectomy or severe comorbidities were conducted to test robustness. Two-sided  $p < 0.05$  was considered statistically significant.

Time to recurrence was analyzed using the Kaplan–Meier estimator. The index date was the first IC episode during the study period. Patients without recurrence were censored at their last documented follow-up. Ninety-five percent CIs were derived using Greenwood's method. A number-at-risk line is provided beneath the curve at predefined time points.

## RESULTS

From the 207 patients initially identified with IC in the medical records, 65 did not meet the diagnostic criteria and were excluded. The final cohort therefore comprised 142 patients: 11 (7.7%) with recurrent IC and 131 (92.3%) without recurrence (Fig. 1). Demographic and comorbidity data are presented in Table 1, clinical presentation and outcomes in Table 2, and imaging and endoscopic findings in Table 3.

### Baseline characteristics

The overall mean age was  $75.6 \pm 13.2$  years. Patients who later developed recurrence tended to be younger ( $68.1 \pm 15.0$  vs.  $76.2 \pm 12.9$  years,  $p = 0.069$ ). Women predominated in both groups (54.5% vs. 62.6%).

A history of smoking was much more common among recurrent cases (45.5% vs. 13.0%; OR 5.6, 95% CI 1.5–20.3;  $p = 0.014$ ). Coronary artery disease also showed a higher frequency in this group (36.4% vs. 12.2%; OR 4.1, 95% CI 1.1–15.6;  $p = 0.050$ ).

Other comorbidities such as hypertension and diabetes were prevalent across the cohort but did not differ substantially between groups.

Previous abdominal surgery emerged as another relevant factor: prior laparotomy was documented more often in recurrent IC (27.3% vs. 6.1%; OR 5.8, 95% CI 1.3–26.0;  $p=0.041$ ). Appendectomy showed a similar pattern (18.2% vs. 3.1%), although this trend was not statistically significant ( $p=0.069$ ).

In terms of chronic medication, clopidogrel use was significantly more frequent among recurrent patients (36.4% vs. 10.0%; OR 5.2, 95% CI 1.3–20.1;  $p=0.029$ ). Statin therapy was also common in this group (72.7% vs. 39.2%), with a borderline association (OR 4.2, 95% CI 1.0–17.6;  $p=0.052$ ).

Additional baseline comorbidities, medications, and less frequent clinical features are provided in Supplementary Table S1.

#### Clinical presentation and outcomes

Abdominal pain was the leading symptom overall (81.8% vs. 80.2%). By contrast, hematochezia was reported in just over half of recurrent cases compared with nearly nine out of ten patients without recurrence (54.5% vs. 88.5%; OR 0.16, 95% CI 0.04–0.57;  $p=0.009$ ).

Blood transfusion was required more frequently in recurrent IC (36.4% vs. 6.9%; OR 7.8, 95% CI 1.9–31.5;  $p=0.010$ ). ICU admission was also more common in this group (27.3% vs. 7.6%), although this difference narrowly missed statistical significance (OR 4.5, 95% CI 1.0–20.2;  $p=0.065$ ). The average length of stay was shorter in recurrent patients ( $6.1 \pm 3.6$  vs.  $9.5 \pm 9.8$  days), but without statistical relevance. Thirty-day mortality and the composite endpoint of severe IC (surgery or death) were comparable between groups.

#### Time to recurrence

The Kaplan–Meier analysis (Fig. 2) demonstrated low cumulative recurrence over follow-up, and the median recurrence-free survival was not reached. Censoring marks indicate patients free of recurrence at last follow-up, with the number at risk displayed

at predefined intervals. In total, 11 of 142 patients (7.7%) experienced a recurrent episode.

#### Imaging and endoscopic findings

CT was performed in 5/11 (45.5%) recurrent and 50/131 (38.2%) non-recurrent patients, while colonoscopy was available in 9/11 (81.8%) and 123/131 (93.9%), respectively. Findings are expressed as proportions among those examined.

On CT, bowel-wall thickening was the predominant abnormality in both groups. Pericolic fat stranding and free intra-abdominal fluid were also observed, with no clear differences between groups.

At colonoscopy, edematous mucosa, erythema, and ulcerations were the most frequent features. Notably, none of the recurrent cases showed necrosis, compared with 18.7% of non-recurrent patients.

#### Anatomical distribution

Overall, left-sided disease predominated (90.9% vs. 95.4%). Right colon involvement (18.2% vs. 5.3%) and pancolitis (9.1% vs. 1.5%) occurred more often among recurrent cases, though these findings did not reach statistical significance.

### **DISCUSSION**

This study examined factors associated with recurrent ischemic colitis (IC), a relatively uncommon but clinically relevant entity. We observed a recurrence rate of 7.7%, which lies within the range reported in earlier series (5,10,11). As described previously, IC occurred more often in women and older adults; in our cohort, however, recurrent cases tended to be younger.

Smoking history was strongly associated with recurrence (OR 5.6, 95% CI 1.5–20.3). Because the records did not consistently distinguish active from former smoking and pack-years were unavailable, we could not explore dose–response or current use. Sherid et al. identified active smoking as a predictor of recurrent IC, which is concordant with our findings (5). Mechanistically, smoking promotes endothelial dysfunction, hypercoagulability, inflammation, platelet activation, and atherosclerosis,

offering a biologically plausible link to recurrent ischemia (12). These data underscore the importance of documenting tobacco exposure and counseling cessation.

Coronary artery disease was more frequent among recurrent cases (OR 4.1, 95% CI 1.1–15.6). Clopidogrel use was likewise more common (OR 5.2, 95% CI 1.3–20.1). Because clopidogrel is typically prescribed to patients with ischemic heart disease, this association likely reflects confounding by indication rather than a direct drug effect (13). Larger datasets will be needed to determine whether antiplatelet therapy independently influences recurrence risk.

Prior laparotomy was also associated with recurrence (OR 5.8, 95% CI 1.3–26.0). Adhesion-related alterations in mesenteric perfusion or regional hypoperfusion may contribute (14), although the small number of recurrent events mandates caution in interpreting this signal.

Clinically, recurrent IC presented less typically: hematochezia was less frequent (OR 0.16, 95% CI 0.04–0.57), whereas transfusion requirements were higher (OR 7.8, 95% CI 1.9–31.5). Severe IC is often linked to bleeding and anemia requiring transfusion (16,17). The combination of fewer overt bleeding reports but greater transfusion needs may reflect a subtler or delayed presentation, potentially contributing to under-recognition in practice.

Endoscopic and imaging features were largely comparable between groups. Notably, necrosis was not observed among recurrent cases, whereas it occurred in nearly one-fifth of non-recurrent patients, which is consistent with a less fulminant course in recurrent disease. Left-sided involvement predominated overall, in line with prior literature (10,11).

Time-to-event analysis supports a low cumulative recurrence over follow-up: in our Kaplan–Meier curve, the median recurrence-free survival was not reached, and estimates carried wide confidence intervals given the small number of events. Substantial censoring further advises cautious interpretation. Even so, the shape of the curve is compatible with infrequent mid-term recurrence in this setting.

This study adds contemporary data on recurrent IC, an area with limited evidence. Strengths include a 10-year time frame and stringent case verification using clinical, radiological, and endoscopic criteria. Limitations include the retrospective, single-

center design; incomplete granularity of smoking exposure; possible underascertainment of events managed outside our institution; and the small number of recurrent cases, which restricted multivariable modeling and widened confidence intervals, increasing the risk of type II error. Not all patients underwent CT or colonoscopy; therefore, proportions for imaging and endoscopic findings were calculated among examined patients, which may introduce selection effects. Several comparisons involved small cell counts; accordingly, Fisher's exact test was used and some estimates are imprecise, with wide confidence intervals, warranting cautious interpretation. Residual confounding cannot be excluded. Prospective, multicenter cohorts with standardized follow-up are warranted to refine risk stratification and to test targeted prevention strategies—particularly smoking cessation—among patients at risk of recurrence.

## CONCLUSION

Recurrent IC occurred in 7.7% of patients and was associated with smoking, coronary artery disease, prior laparotomy, and clopidogrel use. Presentations were often less typical, with lower rates of hematochezia but higher transfusion needs, which may complicate timely diagnosis. Larger multicenter prospective studies are needed to confirm these findings and improve risk stratification.

### Key points box:

- Recurrent ischemic colitis (IC) was identified in 7.7% of patients over a 10-year retrospective cohort.
- Recurrence was associated with smoking history, coronary artery disease, prior laparotomy, and clopidogrel use.
- Recurrent cases showed less hematochezia but required blood transfusion more often.
- Imaging and endoscopic findings were comparable, with no necrosis reported in recurrent IC.
- The less typical presentation may delay recognition, underscoring the need for vigilance in at-risk patients.

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**Table 1.** Demographics and comorbidities by recurrence status

| Variable                       | Recurrent IC<br>(n=11) | Non-recurrent IC<br>(n=131) | OR   | 95% CI         | p-value |
|--------------------------------|------------------------|-----------------------------|------|----------------|---------|
| Age, years<br>(mean ± SD)      | 68.1 ± 15.0            | 76.2 ± 12.9                 | —    | —              | 0.069   |
| Female sex                     | 6/11 (54.5%)           | 82/131 (62.6%)              | —    | —              | —       |
| Smoking<br>history             | 5/11 (45.5%)           | 17/131 (13.0%)              | 5.59 | 1.54–20.3<br>3 | 0.014   |
| Hypertension                   | 7/11 (63.6%)           | 102/131 (77.9%)             | 0.50 | 0.14–1.82      | 0.281   |
| Dyslipidemia                   | 7/11 (63.6%)           | 63/131 (48.1%)              | 1.89 | 0.53–6.76      | 0.363   |
| Coronary<br>artery<br>disease* | 4/11 (36.4%)           | 16/131 (12.2%)              | 4.11 | 1.08–15.6<br>1 | 0.050   |
| Diabetes<br>mellitus*          | 4/11 (36.4%)           | 41/131 (31.3%)              | 1.25 | 0.35–4.52      | 0.743   |
| Heart failure*                 | 2/11 (18.2%)           | 19/131 (14.5%)              | 1.31 | 0.26–6.54      | 0.667   |
| Chronic kidney<br>disease*     | 3/11 (27.3%)           | 16/131 (12.2%)              | 2.70 | 0.65–11.2<br>2 | 0.167   |
| Peripheral<br>arterial         | 1/11 (9.1%)            | 4/131 (3.1%)                | 3.17 | 0.32–31.1<br>6 | 0.336   |

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| disease* |  |  |  |  |  |
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| Peripheral arterial disease* |              |                |      |                |       |
| Laparotomy (any)*            | 3/11 (27.3%) | 8/131 (6.1%)   | 5.77 | 1.28–26.0<br>3 | 0.041 |
| Clopidogrel*                 | 4/11 (36.4%) | 13/131 (9.9%)  | 5.19 | 1.34–20.1<br>2 | 0.029 |
| Statin                       | 8/11 (72.7%) | 51/131 (38.9%) | 4.18 | 1.06–16.5<br>0 | 0.052 |
| Beta-blocker*                | 4/11 (36.4%) | 20/131 (15.3%) | 3.17 | 0.85–11.8<br>4 | 0.095 |

**Footnote:** Odds ratios from univariate logistic regression. Chi-square or Fisher's exact tests used as appropriate.

Rows with \* include small cell counts (<5); results should be interpreted cautiously.

**Table 2.** Clinical presentation and outcomes by recurrence status

| Variable                      | Recurrent IC<br>(n=11) | Non-recurrent IC<br>(n=131) | OR   | 95% CI     | p-value |
|-------------------------------|------------------------|-----------------------------|------|------------|---------|
| Abdominal pain                | 9/11 (81.8%)           | 105/131 (80.2%)             | —    | —          | 1.000   |
| Hematochezia                  | 6/11 (54.5%)           | 116/131 (88.5%)             | 0.16 | 0.04–0.57  | 0.009   |
| Diarrhea*                     | 3/11 (27.3%)           | 52/131 (39.7%)              | 0.57 | 0.14–2.25  | 0.530   |
| Fever*                        | 1/11 (9.1%)            | 7/131 (5.3%)                | 1.77 | 0.20–15.86 | 0.484   |
| Blood transfusion*            | 4/11 (36.4%)           | 9/131 (6.9%)                | 7.75 | 1.91–31.50 | 0.010   |
| ICU admission*                | 3/11 (27.3%)           | 10/131 (7.6%)               | 4.54 | 1.04–19.84 | 0.065   |
| Surgery*                      | 1/11 (9.1%)            | 7/131 (5.3%)                | 1.77 | 0.20–15.86 | 0.484   |
| 30-day mortality*             | 1/11 (9.1%)            | 9/131 (6.9%)                | 1.36 | 0.16–11.80 | 0.566   |
| Severe IC (surgery or death)* | 1/11 (9.1%)            | 15/131 (11.5%)              | 0.77 | 0.09–6.47  | 1.000   |

**Footnote:** Odds ratios from univariate logistic regression. Fisher's exact test used when cell counts <5; results should be interpreted cautiously.

**Table 3.** Imaging, endoscopic, and anatomical findings by recurrence status

| Variable                          | Recurrent IC (n=11) | Non-recurrent IC (n=131) | p-value |
|-----------------------------------|---------------------|--------------------------|---------|
| Imaging (CT)                      |                     |                          |         |
| Normal CT                         | 0/11 (0.0%)         | 2/131 (1.5%)             | 1.000   |
| Wall thickening                   | 5/11 (45.5%)        | 45/131 (34.4%)           | 1.000   |
| Pericolic fat stranding           | 3/11 (27.3%)        | 22/131 (16.8%)           | 0.658   |
| Free intra-abdominal fluid        | 2/11 (18.2%)        | 16/131 (12.2%)           | 1.000   |
| Pneumatosis coli                  | 0/11 (0.0%)         | 1/131 (0.8%)             | 1.000   |
| Portal/mesenteric venous gas      | 0/11 (0.0%)         | 1/131 (0.8%)             | 1.000   |
| Bowel loop dilation               | 1/11 (9.1%)         | 6/131 (4.6%)             | 0.522   |
| Endoscopic findings               |                     |                          |         |
| Edematous mucosa                  | 6/11 (54.5%)        | 83/131 (63.4%)           | 1.000   |
| Erythema / purplish discoloration | 6/11 (54.5%)        | 71/131 (54.2%)           | 0.734   |
| Erosions / ulcerations            | 7/11 (63.6%)        | 116/131 (88.5%)          | 0.116   |
| Friability / active bleeding      | 3/11 (27.3%)        | 39/131 (29.8%)           | 1.000   |
| Exudate / necrosis                | 0/11 (0.0%)         | 23/131 (17.6%)           | 0.358   |
| Stenosis                          | 1/11 (9.1%)         | 2/131 (1.5%)             | 0.192   |
| Anatomical location               |                     |                          |         |
| Right colon                       | 2/11 (18.2%)        | 7/131 (5.3%)             | 0.146   |
| Cecum                             | 2/11 (18.2%)        | 7/131 (5.3%)             | 0.146   |
| Ascending colon                   | 1/11 (9.1%)         | 8/131 (6.1%)             | 0.527   |
| Hepatic flexure                   | 1/11 (9.1%)         | 3/131 (2.3%)             | 0.278   |
| Transverse colon                  | 2/11 (18.2%)        | 15/131 (11.5%)           | 0.622   |
| Splenic flexure                   | 3/11 (27.3%)        | 28/131 (21.4%)           | 0.705   |

|                       |               |                 |       |
|-----------------------|---------------|-----------------|-------|
| Descending colon      | 3/11 (27.3%)  | 49/131 (37.4%)  | 0.746 |
| Sigmoid colon         | 7/11 (63.6%)  | 98/131 (74.8%)  | 0.477 |
| Rectosigmoid junction | 6/11 (54.5%)  | 60/131 (45.8%)  | 0.755 |
| Rectum                | 3/11 (27.3%)  | 16/131 (12.2%)  | 0.167 |
| Left colon (any)      | 10/11 (90.9%) | 125/131 (95.4%) | 0.439 |
| Pancolitis            | 1/11 (9.1%)   | 2/131 (1.5%)    | 0.216 |

**Footnotes:** Percentages are based on group totals. CT was performed in 5/11 recurrent and 50/131 non-recurrent patients; colonoscopy in 9/11 and 123/131, respectively. Patients could have involvement of multiple segments. Chi-square or Fisher's exact test used as appropriate. Odds ratios were not reported for imaging, endoscopic, or anatomical findings given low cell counts and variable denominators.

**Supplementary Table S1.** Comprehensive characteristics, medications, presentation, and outcomes by recurrence status

| Variable                              | Recurrent IC (n=11) | Non-recurrent IC (n=131) | Total (n=142)   | p-value |
|---------------------------------------|---------------------|--------------------------|-----------------|---------|
| <b>Demographics</b>                   |                     |                          |                 |         |
| Age, years (mean $\pm$ SD)            | 68.1 $\pm$ 15.0     | 76.2 $\pm$ 12.9          | —               | 0.069   |
| Sex: Female                           | 6/11 (54.5%)        | 82/131 (62.6%)           | 88/142 (62.0%)  | —       |
| Sex: Male                             | 5/11 (45.5%)        | 49/131 (37.4%)           | 54/142 (38.0%)  | —       |
| Race: White                           | 11/11 (100.0%)      | 130/131 (99.2%)          | 141/142 (99.3%) | 1.000   |
| Race: Other                           | 0/11 (0.0%)         | 1/131 (0.8%)             | 1/142 (0.7%)    | 1.000   |
| Smoking history                       | 5/11 (45.5%)        | 17/131 (13.0%)           | 22/142 (15.5%)  | 0.014   |
| <b>Comorbidities</b>                  |                     |                          |                 |         |
| Hypertension                          | 7/11 (63.6%)        | 102/131 (77.9%)          | 109/142 (76.8%) | 0.281   |
| Dyslipidemia                          | 7/11 (63.6%)        | 63/131 (48.1%)           | 70/142 (49.3%)  | 0.363   |
| Coronary artery disease               | 4/11 (36.4%)        | 16/131 (12.2%)           | 20/142 (14.1%)  | 0.050   |
| Diabetes mellitus                     | 4/11 (36.4%)        | 41/131 (31.3%)           | 45/142 (31.7%)  | 0.743   |
| Heart failure                         | 2/11 (18.2%)        | 19/131 (14.5%)           | 21/142 (14.8%)  | 0.667   |
| Atrial fibrillation                   | 0/11 (0.0%)         | 14/131 (10.7%)           | 14/142 (9.9%)   | 0.602   |
| Deep vein thrombosis                  | 0/11 (0.0%)         | 2/131 (1.5%)             | 2/142 (1.4%)    | 1.000   |
| Cerebrovascular disease               | 0/11 (0.0%)         | 24/131 (18.3%)           | 24/142 (16.9%)  | 0.211   |
| Chronic obstructive pulmonary disease | 0/11 (0.0%)         | 4/131 (3.1%)             | 4/142 (2.8%)    | 1.000   |



|                                     |               |                 |                 |       |
|-------------------------------------|---------------|-----------------|-----------------|-------|
| Chronic kidney disease              | 3/11 (27.3%)  | 16/131 (12.2%)  | 19/142 (13.4%)  | 0.167 |
| Peripheral arterial disease         | 1/11 (9.1%)   | 4/131 (3.1%)    | 5/142 (3.5%)    | 0.336 |
| Irritable bowel syndrome            | 1/11 (9.1%)   | 1/131 (0.8%)    | 2/142 (1.4%)    | 0.149 |
| Cancer (any)                        | 3/11 (27.3%)  | 17/131 (13.0%)  | 20/142 (14.1%)  | 0.187 |
| Anemia (baseline)                   | 2/11 (18.2%)  | 18/131 (13.7%)  | 20/142 (14.1%)  | 0.654 |
| Abdominal aortic aneurysm           | 1/11 (9.1%)   | 2/131 (1.5%)    | 3/142 (2.1%)    | 0.216 |
| Obesity                             | 0/11 (0.0%)   | 5/131 (3.8%)    | 5/142 (3.5%)    | 1.000 |
| Constipation                        | 0/11 (0.0%)   | 6/131 (4.6%)    | 6/142 (4.2%)    | 1.000 |
| Abdominal surgery                   |               |                 |                 |       |
| Appendectomy                        | 2/11 (18.2%)  | 4/131 (3.1%)    | 6/142 (4.2%)    | 0.069 |
| Cholecystectomy                     | 2/11 (18.2%)  | 12/131 (9.2%)   | 14/142 (9.9%)   | 0.296 |
| Hysterectomy                        | 1/11 (9.1%)   | 14/131 (10.7%)  | 15/142 (10.6%)  | 1.000 |
| Laparotomy (any)                    | 3/11 (27.3%)  | 8/131 (6.1%)    | 11/142 (7.7%)   | 0.041 |
| <b>Medications</b>                  |               |                 |                 |       |
| Clopidogrel                         | 4/11 (36.4%)  | 13/131 (9.9%)   | 17/142 (12.0%)  | 0.029 |
| Aspirin                             | 6/11 (54.5%)  | 44/131 (33.6%)  | 50/142 (35.2%)  | 0.197 |
| Statin                              | 8/11 (72.7%)  | 51/131 (38.9%)  | 59/142 (41.5%)  | 0.052 |
| Calcium channel blocker             | 3/11 (27.3%)  | 50/131 (38.2%)  | 53/142 (37.3%)  | 0.534 |
| Beta-blocker                        | 4/11 (36.4%)  | 20/131 (15.3%)  | 24/142 (16.9%)  | 0.095 |
| ACE inhibitor                       | 4/11 (36.4%)  | 52/131 (39.7%)  | 56/142 (39.4%)  | 1.000 |
| ARB                                 | 0/11 (0.0%)   | 26/131 (19.8%)  | 26/142 (18.3%)  | 0.217 |
| Diuretic                            | 5/11 (45.5%)  | 46/131 (35.1%)  | 51/142 (35.9%)  | 0.529 |
| NSAIDs                              | 1/11 (9.1%)   | 9/131 (6.9%)    | 10/142 (7.0%)   | 0.571 |
| Digoxin                             | 1/11 (9.1%)   | 2/131 (1.5%)    | 3/142 (2.1%)    | 0.219 |
| Warfarin                            | 1/11 (9.1%)   | 3/131 (2.3%)    | 4/142 (2.8%)    | 0.282 |
| Antidepressant/antipsychotic        | 4/11 (36.4%)  | 57/131 (43.5%)  | 61/142 (43.0%)  | 0.756 |
| <b>Clinical presentation</b>        |               |                 |                 |       |
| Abdominal pain                      | 9/11 (81.8%)  | 105/131 (80.2%) | 114/142 (80.3%) | 1.000 |
| Nausea                              | 1/11 (9.1%)   | 27/131 (20.6%)  | 28/142 (19.7%)  | 0.693 |
| Vomiting                            | 0/11 (0.0%)   | 26/131 (19.8%)  | 26/142 (18.3%)  | 0.216 |
| Diarrhea                            | 3/11 (27.3%)  | 52/131 (39.7%)  | 55/142 (38.7%)  | 0.530 |
| Hematochezia                        | 6/11 (54.5%)  | 116/131 (88.5%) | 122/142 (85.9%) | 0.009 |
| Abdominal distension                | 2/11 (18.2%)  | 7/131 (5.3%)    | 9/142 (6.3%)    | 0.146 |
| Fever                               | 1/11 (9.1%)   | 7/131 (5.3%)    | 8/142 (5.6%)    | 0.484 |
| Peritoneal signs                    | 0/11 (0.0%)   | 5/131 (3.8%)    | 5/142 (3.5%)    | 1.000 |
| <b>Outcomes</b>                     |               |                 |                 |       |
| Hospital stay, days (mean $\pm$ SD) | 6.1 $\pm$ 3.6 | 9.5 $\pm$ 9.8   | —               | 0.143 |
| Prophylactic antibiotics            | 6/11 (54.5%)  | 81/131 (61.8%)  | 87/142 (61.3%)  | 0.750 |
| ICU admission                       | 3/11 (27.3%)  | 10/131 (7.6%)   | 13/142 (9.2%)   | 0.065 |
| Invasive mechanical ventilation     | 1/11 (9.1%)   | 3/131 (2.3%)    | 4/142 (2.8%)    | 0.278 |
| IC during hospitalization           | 1/11 (9.1%)   | 9/131 (6.9%)    | 10/142 (7.0%)   | 0.566 |

|                              |              |                |                |       |
|------------------------------|--------------|----------------|----------------|-------|
| Blood transfusion            | 4/11 (36.4%) | 9/131 (6.9%)   | 13/142 (9.2%)  | 0.010 |
| Surgery                      | 1/11 (9.1%)  | 7/131 (5.3%)   | 8/142 (5.6%)   | 0.484 |
| 30-day mortality             | 1/11 (9.1%)  | 9/131 (6.9%)   | 10/142 (7.0%)  | 0.566 |
| Severe IC (surgery or death) | 1/11 (9.1%)  | 15/131 (11.5%) | 16/142 (11.3%) | 1.000 |

**Abbreviations:** IC, ischemic colitis; CT, computed tomography; ICU, intensive care unit; ACE, angiotensin-converting enzyme; ARB, angiotensin receptor blocker; NSAIDs, nonsteroidal anti-inflammatory drugs. P-values from chi-square or Fisher's exact tests as appropriate.

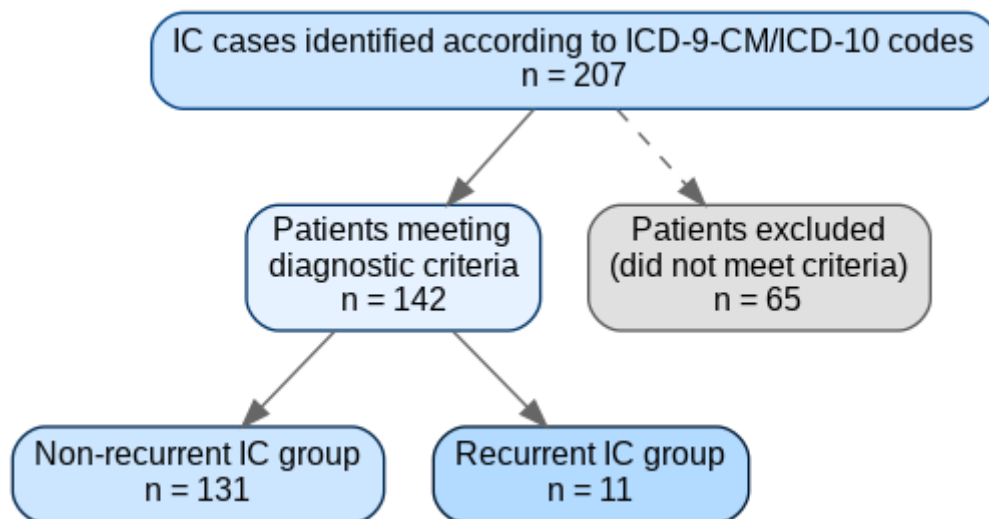


Fig. 1. Study flowchart showing patient selection and exclusion