

CT Colonography as a Triage Examination After a Positive Fecal Immunochemical Test: A Retrospective Cohort Study in a Chilean Screening Program

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Abstract

Purpose:

To evaluate computed tomography colonography (CTC) as a triage examination for colonoscopy within a fecal immunochemical test (FIT)-based colorectal cancer screening program in a resource-limited region of Chile.

Methods:

This retrospective cohort study included asymptomatic FIT-positive individuals aged 45–75 years who underwent CTC between January 2019 and November 2022. Patients with CT Colonography Reporting and Data System (C-RADS) C2–C4 findings were referred for optical colonoscopy. The primary outcome was the per-patient positive predictive value (PPV) of CTC for polyps measuring ≥ 6 mm among patients with an evaluable colonoscopy.

Results:

The cohort comprised 675 patients (mean age 64.0 years, SD 9.2; 443 women, 65.6%). Overall, 473 patients (70.1%) were classified as C1 and were not referred for immediate colonoscopy, 62 (9.2%) had C3–C4 findings and 71 (10.5%) had unresolved C0 examinations. Of 131 patients referred for colonoscopy, 115 (87.8%) underwent the procedure and 108 had an evaluable examination. Colonoscopy confirmed at least one polyp measuring ≥ 6 mm in 93 patients, yielding a PPV of 86.1% (95% CI 78.3–91.4). Advanced colorectal neoplasia was confirmed in 48 patients (PPV 44.4%, 95% CI 35.4–53.8). The detection rates was 42/675 (6.2%) for advanced adenoma and 6/675 (0.9%) for colorectal cancer.

Conclusion:

Among FIT-positive patients with CTC findings warranting colonoscopy, clinically relevant colorectal lesions were frequently confirmed. CTC may help prioritize colonoscopy in settings with limited endoscopic capacity. Further evaluation of the complete screening pathway is warranted.

INTRODUCTION

Colorectal cancer (CRC) is a leading cause of cancer-related mortality worldwide. It is the third most commonly diagnosed cancer globally, with more than 2 million new cases and over 900,000 deaths annually [1]. In Chile, CRC accounts for 13.3% of newly diagnosed cancers and is the second leading cause of cancer-related death [2]. Screening may be performed using both invasive and non-invasive methods [3]. Colonoscopy remains the reference standard for detecting colorectal polyps and CRC, and the removal of precancerous lesions has been shown to reduce CRC incidence and mortality [4]. Among

non-invasive methods, fecal occult blood testing is effective for screening asymptomatic populations and has been shown to reduce long-term CRC mortality [5]. In particular, the fecal immunochemical test (FIT) has been adopted in preference to guaiac-based testing in many screening programs because of its greater sensitivity and specificity; both quantitative and qualitative FITs are commercially available [6]. However, the increasing implementation of CRC screening programs has increased the demand for colonoscopy, resulting in waiting lists and delays in access, particularly in healthcare systems with limited endoscopic capacity.

Computed tomography colonography (CTC), also known as virtual colonoscopy, is a validated examination with high sensitivity and specificity for detecting advanced colorectal neoplasia, comprising advanced adenomas and colorectal adenocarcinoma. Its detection rates are comparable with those of colonoscopy in screening and surveillance settings [7–10]. CTC has traditionally been recommended for FIT-positive patients in whom colonoscopy is incomplete or contraindicated [11]. However, evidence supporting its incorporation as a triage examination following a positive FIT remains limited, particularly in Latin America.

The aim of this study was to evaluate CTC as an endoscopic triage strategy within a FIT-based CRC screening program and to determine its ability to identify clinically relevant colonic lesions in a resource-limited Latin American region.

METHODS

Study design and population

This retrospective observational cohort study included asymptomatic individuals aged 45–75 years who entered a regional colorectal cancer screening program following a positive fecal immunochemical test (FIT) and underwent computed tomography colonography (CTC) at a tertiary hospital in Arica, Chile, between January 2019 and November 2022. Individuals were ineligible for the screening program if they had a personal history of colorectal cancer, one first-degree relative diagnosed with colorectal cancer before the age of 60 years, two first-degree relatives diagnosed at any age, colorectal polyps under surveillance, or inflammatory bowel disease. Patients with a contraindication to optical colonoscopy (OC) and those with incomplete records that precluded confirmation or exclusion of the CTC findings were excluded from the analysis. No formal a priori sample-size calculation was performed because the study sample comprised all consecutive eligible FIT-positive individuals who underwent CTC during the defined study period.

Fecal immunochemical testing

The FIT used was a qualitative lateral-flow chromatographic immunoassay employing antibodies specific for human hemoglobin (ABON Biopharm Co. Ltd, Hangzhou, China). The test required a single fecal sample and provided a qualitative positive or negative result. It had a nominal detection threshold of 50 ng Hb/mL of buffer, reported by the manufacturer as equivalent to 6 µg Hb/g of feces.

CTC protocol

CTC protocol

CTC examinations were performed using an 80-detector-row CT scanner capable of acquiring 160 slices per rotation. Bowel preparation comprised a low-residue diet for 72 h before the examination and polyethylene glycol, 17 g dissolved in 250 mL of water, administered three times daily during the 3 days preceding the procedure. For fecal tagging, a water-soluble iodinated contrast agent containing 300 mg iodine/mL was administered on the evening before and 2 h before the examination. Immediately before image acquisition, 1 mg of glucagon was administered intramuscularly unless contraindicated. Colonic distension was achieved by manual insufflation of room air through a rectal catheter until the maximum distension tolerated by the patient was reached. Images were acquired with the patient in both the supine and prone positions. When distension or visualization of a colonic segment was inadequate, additional acquisitions were obtained in the right or left lateral decubitus position at the discretion of the supervising radiologist.

All CTC examinations were interpreted and reported by a single radiologist with specific training in CTC interpretation. Each examination was categorized according to the CT Colonography Reporting and Data System (C-RADS) [12]. CTC examinations categorized as C2, C3 or C4 according to the size and number of the detected colonic lesions were considered positive.

C0 examinations were considered non-diagnostic, and repeat CTC was recommended. Patients classified as C1 were scheduled for CTC surveillance at 5 years, whereas those with C2, C3 or C4 findings were referred for optical colonoscopy. When an initial C0 examination was repeated, the result of the repeat CTC was used as the patient's definitive C-RADS classification, and the initial C0 result was not included in the final distribution. Patients who did not undergo repeat CTC retained their C0 classification. Each patient was counted only once in the analysis.

Colonoscopy and histopathology

Optical colonoscopies were performed by endoscopists at the participating institution according to routine clinical practice. Bowel preparation comprised 2 L of polyethylene glycol administered on the day before the procedure. Procedure completeness, bowel preparation quality, and the size, number and location of identified lesions were recorded. An evaluable reference-standard examination was defined as a complete colonoscopy with cecal intubation and adequate bowel preparation, defined as a total Boston Bowel Preparation Scale score ≥ 6 with a score ≥ 2 in each colonic segment. Examinations not meeting either criterion were considered non-evaluable, and repeat colonoscopy was recommended. Resected or biopsied lesions were assessed by institutional pathologists, and the most clinically significant histopathological finding was retained for the per-patient analysis. Endoscopists had access to the CTC report before performing the procedure.

Definitions

Advanced adenomas were defined as adenomas measuring ≥ 10 mm or smaller adenomas with high-grade dysplasia or a villous component. Advanced colorectal neoplasia was defined as either an advanced adenoma or colorectal adenocarcinoma.

Outcomes

The primary outcome was the per-patient positive predictive value (PPV) of CTC for polyps measuring ≥ 6 mm. Secondary outcomes included the detection rates of advanced adenoma and colorectal cancer, the distribution of colonic findings according to the C-RADS classification, the per-patient PPV of CTC for advanced colorectal neoplasia and the exploratory association between sex and the presence of C-RADS C3–C4 findings.

PPV calculation

PPV was calculated on a per-patient basis among patients with C2–C4 findings who completed an evaluable optical colonoscopy. For the primary outcome of polyps measuring ≥ 6 mm, a patient was considered a true positive if colonoscopy confirmed at least one polyp of this size, irrespective of the availability of histopathological assessment. As the analysis was performed on a per-patient basis, exact agreement between CTC and colonoscopy regarding the total number of lesions was not required. In patients with multiple lesions, confirmation of at least one polyp measuring ≥ 6 mm was sufficient for the patient to be classified as positive.

For the calculation of PPV for advanced colorectal neoplasia, histopathological confirmation of at least one lesion meeting the previously defined criteria was required. An evaluable colonoscopy showing no polyps measuring ≥ 6 mm was considered a false-positive result for the primary outcome, even when no tissue sample had been obtained. Colonoscopies with a Boston Bowel Preparation Scale score ≥ 6 and those that were initially inadequate but subsequently repeated with adequate bowel preparation were included. Colonoscopies with a score < 6 that were not repeated were considered non-evaluable and excluded from the PPV calculation. Patients who did not complete colonoscopy were also excluded from this analysis.

Statistical analysis

Categorical variables were reported as absolute frequencies and percentages, whereas continuous variables were summarized using the mean and standard deviation. PPVs were reported with corresponding 95% confidence intervals calculated using the Wilson score method. The exploratory association between sex and the presence of C3–C4 findings was assessed using Pearson's chi-square test after excluding patients with unresolved C0 examinations. The magnitude of this association was expressed as an unadjusted prevalence ratio (PR), with women as the reference group, and its

corresponding 95% confidence interval was calculated on the logarithmic scale. All expected cell counts exceeded five. All tests were two-sided, and a P value < 0.05 was considered statistically significant. Analyses were performed using IBM SPSS Statistics, version 28.0 (IBM Corp., Armonk, NY, USA).

Ethical considerations

The study was approved by the Scientific Ethics Committee of the Universidad de Tarapacá (approval No. 14/2025). Owing to the retrospective design and use of anonymized data, the requirement for individual informed consent was waived by the committee. The study was conducted in accordance with the principles of the Declaration of Helsinki.

RESULTS

A total of 685 patients enrolled in the regional screening program were initially assessed. Seven patients were excluded because of incomplete records and three because of contraindications to optical colonoscopy, leaving a final cohort of 675 FIT-positive patients who underwent CTC and were included in the analysis. The mean age was 64 years (SD 9.2), and 443 patients (65.6%) were women.

Regarding the final colonic C-RADS classification, 473 patients (70.1%) were classified as C1, 69 (10.2%) as C2, 50 (7.4%) as C3 and 12 (1.8%) as C4. Overall, 62 patients (9.2%) had high-priority findings warranting endoscopic evaluation, corresponding to categories C3–C4.

At the initial assessment, 78 of the 675 patients (11.6%) had a non-diagnostic CTC examination classified as C0. Seven of these patients underwent repeat CTC (7/78, 9.0%); in these cases, the result of the second examination replaced the initial classification in the per-patient analysis. The remaining 71 patients did not undergo repeat CTC during the study period and retained their C0 classification, representing 10.5% of the cohort. The final C-RADS distribution is presented in Table 1.

Table 1
Demographic characteristics and distribution of colonic CT colonography findings. C-RADS, CT Colonography Reporting and Data System; CTC, computed tomography colonography; SD, standard deviation.

Variable	n = 675
Mean age (SD), years	64 (9.2)
Sex, n (%)	
Male	232 (34.4)
Female	443 (65.6)
Colonic C-RADS findings, n (%)	
C0	71 (10.5)
C1	473 (70.1)
C2	69 (10.2)
C3	50 (7.4)
C4	12 (1.8)

Of the 131 patients with C2–C4 findings and therefore an indication for optical colonoscopy, 115 (87.8%) completed the procedure. Colonoscopy was performed in 57 of 69 patients classified as C2 (82.6%), 47 of 50 classified as C3 (94.0%) and 11 of 12 classified as C4 (91.7%).

Of the 115 colonoscopies performed, 103 (89.6%) had adequate bowel preparation, defined as a Boston Bowel Preparation Scale score ≥ 6 , whereas 12 (10.4%) had inadequate preparation. Five of the latter were subsequently repeated with adequate preparation. The remaining seven colonoscopies—five in patients classified as C2 and two in patients classified as C3—were not repeated during the follow-up period and were considered non-evaluable. Consequently, 108 patients had an adequate reference-standard examination for the PPV analysis: 52 classified as C2, 45 as C3 and 11 as C4 (Fig. 1).

Among the 108 evaluable patients, colonoscopy confirmed at least one polyp measuring ≥ 6 mm in 93, corresponding to a per-patient PPV of 86.1% (95% CI 78.3–91.4). Advanced colorectal neoplasia was confirmed in 48 patients, yielding a PPV of 44.4% (95% CI 35.4–53.8). The PPV for advanced colorectal neoplasia was 19.2% among patients classified as C2 (10/52; 95% CI 10.8–31.9), 75.6% among those classified as C3 (34/45; 95% CI 61.3–85.8) and 36.4% among those classified as C4 (4/11; 95% CI 15.2–64.6).

In the overall cohort, the 48 patients with advanced colorectal neoplasia comprised 42 with advanced adenoma and six with colorectal cancer. This corresponded to program-level detection rates of 6.2% for advanced adenoma, 0.9% for colorectal cancer and 7.1% for advanced colorectal neoplasia.

The 71 patients with unresolved C0 examinations were excluded from the exploratory analysis of the association between sex and C3–C4 findings. Among the 604 patients with diagnostic CTC examinations, C3–C4 findings were identified in 30 of 199 men (15.1%) and 32 of 405 women (7.9%). Men had a higher prevalence of C3–C4 findings than women, with an unadjusted prevalence ratio of 1.91 (95% CI 1.19–3.05; Pearson’s $\chi^2(1) = 7.46$; $P = 0.006$) (Table 2).

Table 2
Association between sex and high-priority C-RADS findings among patients with diagnostic CT colonography. *PR, prevalence ratio. Women were used as the reference group. The P value was obtained using Pearson’s chi-square test. Seventy-one patients with unresolved C0 examinations were excluded.*

Sex	C3–C4, n (%)	C1–C2, n (%)	Total, n	Unadjusted PR (95% CI)	P value
Male	30 (15.1)	169 (84.9)	199	1.91 (1.19–3.05)	0.006
Female	32 (7.9)	373 (92.1)	405	1.00 (reference)	-
Total	62 (10.3)	542 (89.7)	604	-	-

DISCUSSION

This study evaluated a FIT-positive screening pathway in which CTC was used to triage patients for optical colonoscopy. CTC achieved a per-patient PPV of 86.1% for polyps measuring ≥ 6 mm, consistent with the available evidence. Liedenbaum et al. reported a PPV of 87% among FIT-positive patients [13], whereas Pickhardt et al. reported a PPV of 92% in a primary CTC screening program [14]. A systematic review including more than 600 patients reported PPVs ranging from 62% to 88% among FIT-positive patients and from 92% to 93% in screening programs involving asymptomatic populations [15]. Although differences in patient selection, positivity criteria and units of analysis limit direct comparisons, our findings support the ability of CTC to identify patients with polyps of clinically relevant size.

The per-patient PPV for advanced colorectal neoplasia was 44.4%. This was similar to the 38.8% reported by Pickhardt et al. in a study including more than 1600 patients [16], but lower than the values reported in other studies [17–19]. This difference may be attributable to methodological variation, the criteria used to define a positive CTC examination and differences in the characteristics of the study populations. In our study, PPV was estimated within a FIT-positive screening program using CTC as a triage examination. Furthermore, the use of a qualitative FIT with a low positivity threshold (approximately 6 μg Hb/g feces), below that used in many screening programs, may have resulted in the inclusion of a greater proportion of FIT-positive patients at relatively low risk, thereby reducing the PPV for advanced colorectal neoplasia.

The PPV for advanced colorectal neoplasia varied considerably across C-RADS categories: 19.2% for C2, 75.6% for C3 and 36.4% for C4. The PPV observed for C3 supports the usefulness of this category for prioritizing access to colonoscopy. By contrast, the lower PPV observed for C4 should be interpreted

cautiously because of the small number of patients in this subgroup and because most of these findings proved to be benign mural thickening or strictures of diverticular or inflammatory origin.

The program-level detection rates were 6.2% for advanced adenoma and 0.9% for colorectal cancer. These values are comparable with those reported in colonoscopy-based screening studies [9, 20] and fall within the range of advanced colorectal neoplasia detection rates reported in CTC-based screening programs, which range from 3.2% to 8.7% [9, 21, 22]. Among FIT-positive patients, Liedenbaum et al. reported a colorectal cancer detection rate of 7% (22/308 patients) [13]. This difference may reflect variation in study design, the type of FIT used and the characteristics of the populations evaluated.

In our study, 70.1% of FIT-positive patients were classified as C1 and were therefore not referred immediately for optical colonoscopy. This finding illustrates the potential of CTC to reduce immediate demand for endoscopy, although it does not establish that colonoscopy would have been unnecessary in all these patients. The decision not to refer patients immediately for lesions measuring ≤ 5 mm is supported by their low risk of malignancy. In a longitudinal study with almost 5 years of follow-up, Kim et al. reported a malignancy risk of 0.1%–0.2% among diminutive polyps (< 6 mm) [23]. Similarly, a review by Hassan and Pickhardt found that lesions measuring < 6 mm showed no clinically significant short-term growth or progression to invasive cancer [24]. In a study of more than 42,000 subcentimeter polyps, Ponugoti et al. reported an advanced adenoma rate of 2.1% among polyps measuring < 6 mm, with high-grade dysplasia present in only 0.3% of adenomas [25]. Restricting polypectomy to lesions measuring ≥ 6 mm has therefore been associated with substantial cost reductions while potentially identifying approximately 95% of individuals with advanced adenomas [21, 26]. CTC surveillance of polyps measuring 6–9 mm has also been shown to be a safe alternative that may improve the medium-term yield of screening programs without delaying the diagnosis of clinically relevant lesions [27]. However, much of this evidence derives from primary CTC screening in average-risk populations, and its extrapolation to FIT-positive patients should be approached with caution.

Regarding the safety of CTC surveillance, Pickhardt et al. reported an advanced colorectal neoplasia rate of 2.8% and an interval colorectal cancer rate of 0.14% following an initially negative CTC examination [28]. Within primary screening populations, these findings support a 5-year rescreening interval and the practice of not reporting lesions measuring ≤ 5 mm. Appropriate training and experience in CTC interpretation remain essential, as up to 61% of interval colorectal cancers have been reported to have been visible and potentially detectable on the preceding CTC examination [29]. Long-term follow-up of patients classified as C1 in our cohort is required to establish the safety of this protocol in a FIT-positive population and to determine whether outcomes are consistent with those reported in other settings.

In the exploratory analysis restricted to patients with diagnostic CTC examinations, the prevalence of high-priority C3–C4 findings was almost twice as high in men as in women (15.1% vs. 7.9%; unadjusted PR 1.91, 95% CI 1.19–3.05). This finding is consistent with previous studies reporting a higher prevalence of advanced colorectal neoplasia among men [20, 30]. Nevertheless, the association should be interpreted cautiously because the analysis was exploratory, was not adjusted for age or other

potential confounders, and excluded patients with unresolved C0 examinations. Further studies are required to determine whether sex independently predicts high-priority CTC findings in FIT-positive populations.

This study has several limitations. First, its retrospective, single-center design limits the generalizability of the findings. Optical colonoscopy, which served as the reference standard, was performed only in patients with positive CTC findings (C-RADS C2–C4). This introduces potential verification bias and precludes estimation of the sensitivity, specificity and negative predictive value of CTC. The absence of a comparator group managed by direct referral to optical colonoscopy precludes direct comparison of the two screening strategies. In addition, some patients did not undergo the indicated colonoscopy, and seven had inadequate bowel preparation without subsequent repeat examination. Their exclusion from the PPV analysis may have introduced further verification bias. The use of a qualitative FIT with a low positivity threshold and the absence of a formal cost-effectiveness analysis also limit the applicability of these findings to other screening programs. Finally, the absence of long-term follow-up among patients classified as C1 precludes assessment of the oncological safety of foregoing immediate colonoscopy after a negative CTC examination.

In conclusion, among FIT-positive patients, CTC showed a high PPV for polyps measuring ≥ 6 mm and demonstrated potential as a tool for prioritizing referral to colonoscopy in a healthcare system with limited endoscopic capacity. These findings support further evaluation of CTC as a second-line examination in this setting. However, prospective studies incorporating long-term follow-up of patients with negative CTC findings and direct comparison with colonoscopy are required to establish the safety and cost-effectiveness of this strategy.

Declarations

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Competing Interests

The authors have no relevant financial or non-financial interests to disclose.

Author contributions

Conceptualization: Francisco Navarro Subiabre, Renato Alarcón Elgueta ; Methodology: Francisco Navarro Subiabre, Renato Alarcón Elgueta. Formal analysis and investigation: Francisco Navarro Subiabre, Ignacio Heyer Salinas, Rocío Chanampa Vitali, Paz Bello Villalobos. Supervision: Francisco Navarro Subiabre Writing - original draft preparation: Francisco Navarro Subiabre, Renato Alarcón Elgueta; Writing - review and editing: Ignacio Heyer Salinas, Rocío Chanampa Vitali, Paz Bello Villalobos, Roxana Carmago Varela.

Data Availability

The datasets generated during and/or analyzed during the current study are available from the corresponding author on reasonable request.

Ethics approval

The study was approved by the Scientific Ethics Committee of the Universidad de Tarapacá (approval No. 14/2025). Owing to the retrospective design and use of anonymized data, the requirement for individual informed consent was waived by the committee. The study was conducted in accordance with the principles of the Declaration of Helsinki.

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Figures

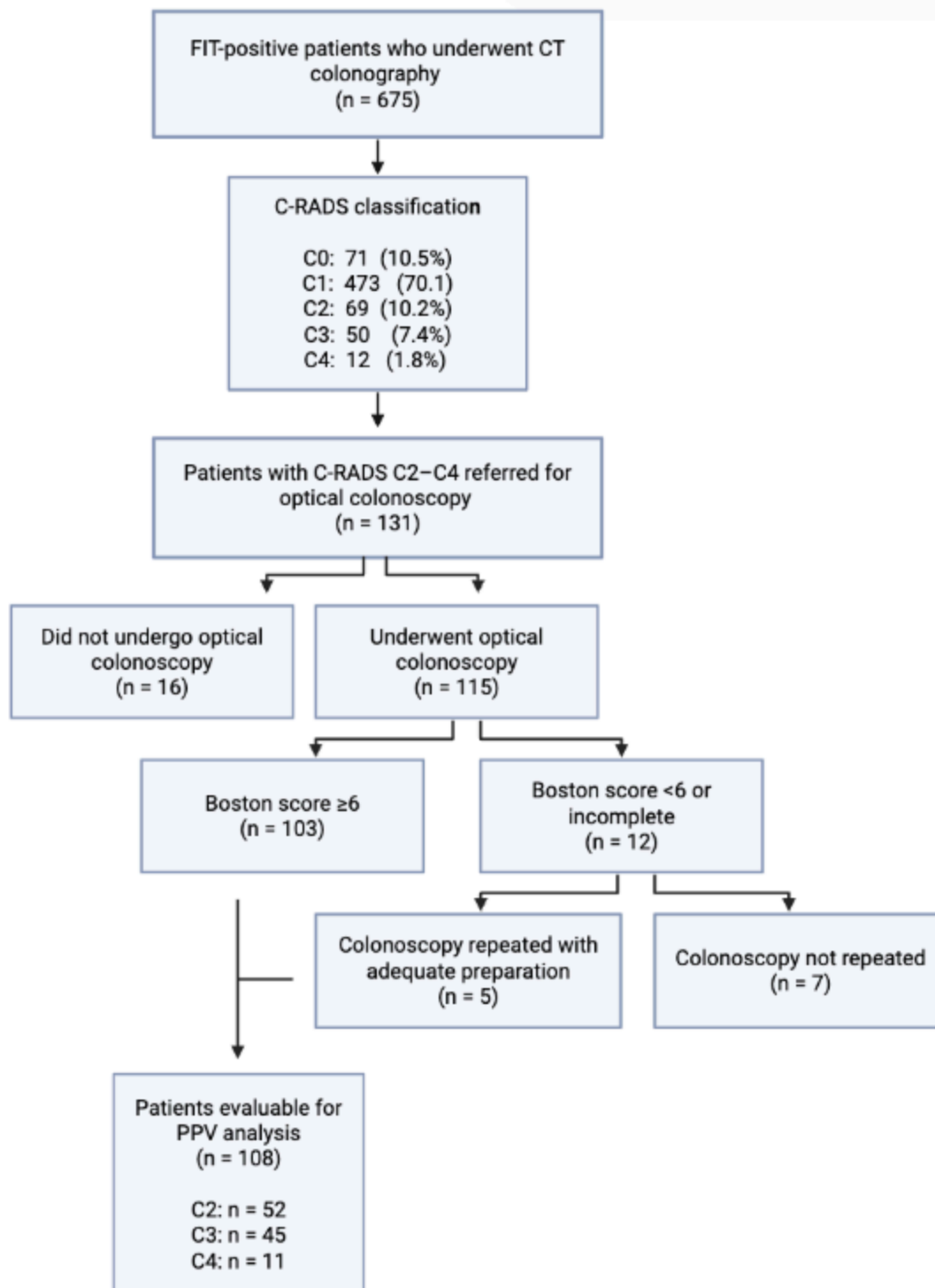


Figure 1

Flow diagram of the study population and selection of patients evaluable for positive predictive value analysis. *CTC*, computed tomography colonography; *FIT*, fecal immunochemical test; *PPV*, positive predictive value.