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STATISTICS AND EPIDEMIOLOGY OF INFLAMMATORY BOWEL DISEASE ASSOCIATED COLORECTAL NEOPLASIA

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Abstract

Inflammatory bowel diseases (IBD), namely ulcerative colitis (UC) and Crohn’s disease (CD), are linked to a heightened risk of developing intestinal neoplasia, which represents one of the most serious long-term consequences of persistent inflammation. This review outlines recent epidemiological patterns and the clinicopathological characteristics of colorectal cancer (CRC) and dysplasia arising in patients with UC and CD.

In patients with UC, the cumulative incidence of CRC has decreased over recent decades, likely due to advances in therapeutic approaches and improved surveillance programs. Nevertheless, significant risk factors remain, including prolonged disease duration, extensive colonic involvement, coexisting primary sclerosing cholangitis, a history of dysplasia, and a familial background of CRC. Neoplasia associated with UC commonly appears as flat, poorly demarcated lesions, frequently surrounded by dysplastic mucosa and often demonstrating multifocal or infiltrative histological patterns. Outcomes tend to be less favorable compared with sporadic CRC, particularly in advanced disease stages.

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Although the overall incidence of cancer in CD patients is comparatively lower, their relative risk of colorectal and small intestinal malignancies remains substantially elevated compared to the general population. Marked geographic differences have been observed, with anorectal and fistula-related carcinomas occurring more frequently in East Asian populations. Key risk factors for CD-associated neoplasia include early disease onset, long disease duration, extensive colonic inflammation, intestinal strictures, and a family history of CRC. Prognosis in CD-associated neoplasia is generally poorer than in sporadic CRC, with a higher tendency for local recurrence.

Overall, intestinal neoplasia related to IBD demonstrates unique epidemiological and pathological features distinct from sporadic colorectal cancer. Large-scale multicenter studies conducted in Japan have contributed valuable data on UC- and CD-associated neoplasia, highlighting the need for region-specific strategies to enhance surveillance and clinical management.

Keywords: Inflammatory bowel diseases, Ulcerative colitis, Crohn's disease, UC-associated neoplasia, CD-associated neoplasia, Colorectal cancer, Dysplasia, Epidemiology, Risk factors, Intestinal neoplasia, Surveillance strategies, Clinicopathological features, Geographic variations.

Introduction

Inflammatory bowel diseases (IBD), including ulcerative colitis (UC) and Crohn's disease (CD), are chronic inflammatory disorders of the gastrointestinal tract that are well established to increase the risk of colorectal neoplasia [1–3]. UC is characterized as a diffuse, continuous mucosal inflammation limited to the colon, leading to erosions, ulcerations, and long-term structural changes of the colonic mucosa. In contrast, CD is a transmural inflammatory disorder that can involve any segment of the gastrointestinal tract, from the mouth to the anus, and

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is associated with complications such as strictures, fistulas, perforations, and deep mucosal ulcerations.

Chronic inflammation in IBD induces persistent oxidative stress, cytokine release, and immune dysregulation, which in turn contribute to the accumulation of genetic mutations, epigenetic modifications, and dysregulated cellular signaling pathways. These molecular alterations promote the transformation of normal intestinal epithelium into dysplastic and neoplastic tissue, a process often referred to as the "dysplasia–carcinoma sequence" [4, 5]. The term IBD-associated intestinal neoplasia encompasses both carcinoma and its precursor lesions, dysplasia.

With the increasing global prevalence of IBD, the clinical burden of IBD-associated intestinal neoplasia, particularly colorectal cancer (CRC) and dysplasia, has become an urgent concern for gastroenterologists and oncologists [6, 7]. Epidemiological studies indicate that patients with long-standing disease, extensive colitis, coexisting primary sclerosing cholangitis, prior dysplasia, or a family history of CRC are at higher risk for neoplastic transformation. Furthermore, surveillance strategies, including colonoscopic monitoring, targeted biopsies, and the use of advanced imaging techniques, play a critical role in early detection and prevention of progression to CRC.

In Japan, the Japanese Society for Cancer of the Colon and Rectum (JSCCR) released the 2024 guidelines for the clinical management of IBD-associated intestinal neoplasia, offering evidence-based recommendations for diagnosis, endoscopic surveillance, and therapeutic interventions [8]. Complementing these guidelines, a nationwide multicenter database project conducted by JSCCR has provided valuable insights into the clinicopathological features, treatment outcomes, and long-term survival of patients with UC- and CD-associated neoplasia [9].

This review aims to provide a comprehensive overview of the current understanding of the statistics, epidemiology, risk factors, and clinical

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characteristics of IBD-associated intestinal neoplasia, with a particular focus on colitis-associated CRC and dysplasia in both UC and CD. Additionally, we discuss emerging trends in molecular biomarkers, preventive strategies, and region-specific variations that may inform optimized surveillance and management approaches worldwide.

UC-associated neoplasia (UCAN) – Epidemiology (Expanded Version, Meaning Preserved)

Chronic mucosal inflammation associated with long-standing ulcerative colitis (UC) is a well-established risk factor for colorectal carcinogenesis. The first case of UC-associated neoplasia (UCAN) was reported by Crohn and Rosenberg in 1925 [10], and subsequent studies have consistently confirmed this association.

The risk of UCAN, which includes both colorectal cancer (CRC) and dysplasia, increases with the duration of UC. In a meta-analysis conducted by Eaden et al., the cumulative incidence of invasive CRC was reported as 1.8% at 10 years, 8.3% at 20 years, and 18.4% at 30 years of disease duration [11]. More recent studies indicate lower incidences, possibly reflecting improved medical management and enhanced surveillance strategies. For example, in the United Kingdom, Choi et al. reported cumulative incidences of 0.1% at 10 years, 2.9% at 20 years, and 6.7% at 30 years [12]. Similarly, in Japan, Kishikawa et al. observed a cumulative incidence of invasive cancer of 0.7% at 10 years, 3.2% at 20 years, and 5.2% at 30 years, which is comparable to the findings of Choi et al. (Fig. 1A).

The cumulative incidence of dysplasia in UC patients was reported to increase to 3.3%, 12.1%, and 21.8% at 10, 20, and 30 years, respectively, emphasizing the importance of long-term surveillance [13] (Fig. 1B). A meta-analysis in Asian populations reported a pooled prevalence of CRC of 0.85% (95% confidence interval [CI], 0.65–1.04) across Asian countries [6]. Another meta-analysis by Jess et al. indicated that patients with UC have a 2.4-fold higher risk of developing CRC than the general population [14].

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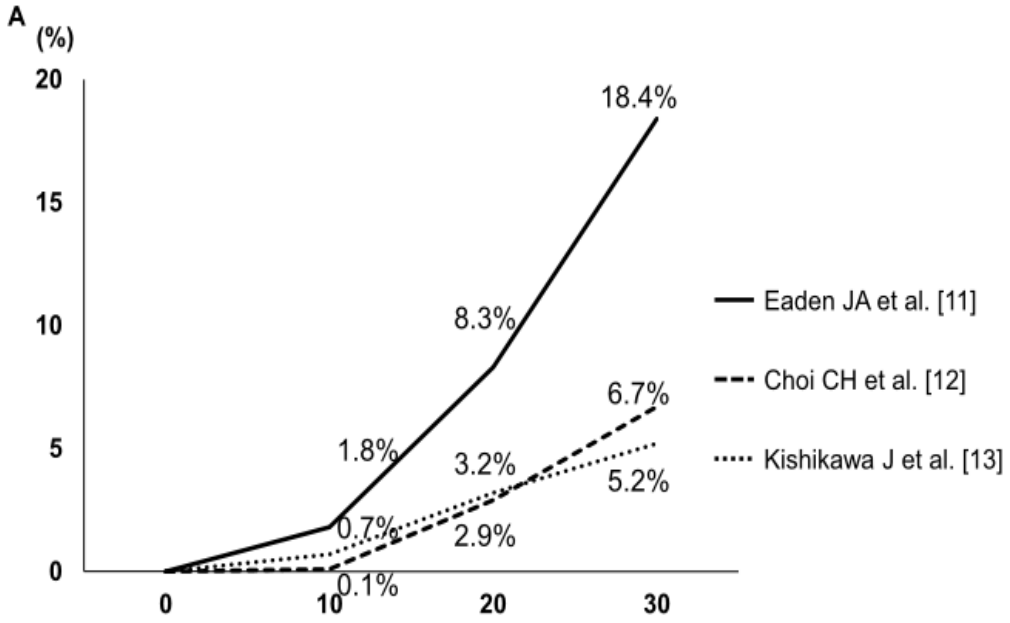
In addition to disease duration, the extent of colonic inflammation is a major determinant of cancer risk. Ekbom et al. reported relative risks (RR) of CRC as 1.7 for proctitis, 2.8 for left-sided colitis, and 14.8 for extensive colitis compared with the general population [1]. These findings highlight the necessity of careful and frequent surveillance in patients with widespread disease.

Overall, long-term, extensive mucosal inflammation remains a key risk factor for the development of UCAN. Regular colonoscopic monitoring and surveillance are essential to detect dysplasia and prevent progression to invasive colorectal cancer in UC patients.

In addition to conventional risk factors, persistent mucosal inflammation may promote genetic and epigenetic alterations that accelerate neoplastic transformation.

Patients with coexisting primary sclerosing cholangitis (PSC) are reported to have a significantly higher risk of UCAN compared with UC patients without PSC.



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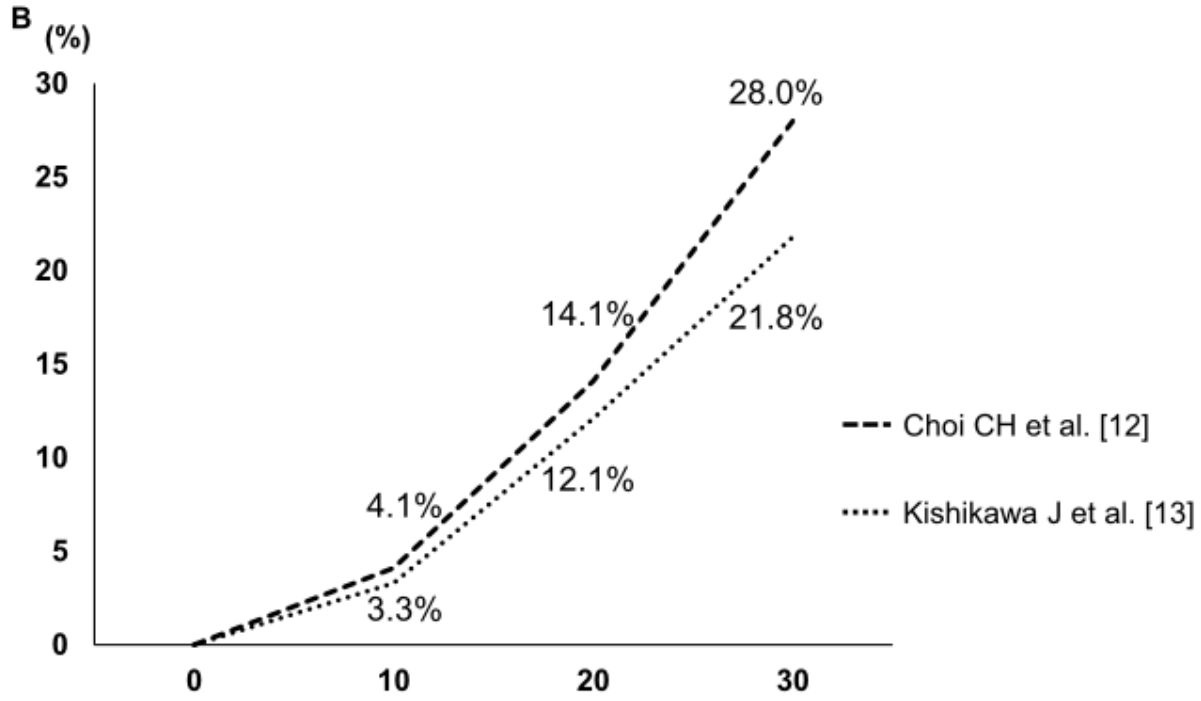

Fig. 1 Cumulative incidence of invasive colorectal cancer (A) and neoplasia, including low- and high-grade dysplasia (B). A Eaden et al. reported cumulative incidences of 1.8%, 8.3%, and 18.4% at 10, 20, and 30 years, respectively [11]. In contrast, Choi et al. reported lower rates of 0.1%, 2.9%, and 6.7% at 10, 20, and 30 years, respec-tively [12], whereas Kishikawa et al. reported rates of 0.7%, 3.2%, and 5.2% at 10, 20, and 30 years, respectively [13]. B When dysplasia was included, Choi et al. reported cumula-tive incidences of 4.1%, 14.1%, 28.0% at 10, 20, and 30 years, respectively [12], whereas Kishikawa et al. reported 3.3%, 12.1%, and 21.8% at 10, 20, and 30 years, respectively [13]

Risk Factors

In addition to disease duration and the extent of colonic involvement, several other risk factors contribute significantly to the development of UC-associated neoplasia (UCAN). These include the severity of inflammation, with moderate to

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severe inflammation increasing risk (odds ratio [OR], 2.51; 95% confidence interval [CI], 1.75–3.61), coexistence of primary sclerosing cholangitis (PSC) (OR, 4.05; 95% CI, 2.15–7.64), a history of dysplasia (OR, 3.64; 95% CI, 1.81–7.32), family history of colorectal cancer (CRC), especially when diagnosed before 50 years of age (OR, 2.42; 95% CI, 1.14–5.16), and the presence of strictures (OR, 7.78; 95% CI, 3.74–16.18) [15, 16]. Patients presenting with one or more of these risk factors require close monitoring, typically including annual surveillance colonoscopies.

In particular, patients with coexisting PSC are at high risk for early development of CRC, prompting many clinical guidelines to recommend initiating surveillance at the time of PSC diagnosis [17]. Recent secondary analyses from the JSCCR multicenter database in Japan indicated that UC patients with PSC tend to develop UCAN at a younger age and that lesions are more frequently located in the right-sided colon [18]. Surveillance intervals for IBD-associated colorectal neoplasia vary slightly across major international guidelines. The American Society for Gastrointestinal Endoscopy (ASGE) and the American Gastroenterological Association (AGA) generally recommend starting colonoscopic surveillance 8–10 years after disease onset in patients with extensive or left-sided colitis, with follow-up intervals adjusted according to individual CRC risk. The European Crohn's and Colitis Organization (ECCO) guidelines advocate a more risk-stratified approach, recommending annual surveillance for high-risk patients, every 2 years for intermediate-risk patients, and every 3 years for low-risk patients. Despite these regional differences, all guidelines emphasize personalized surveillance based on disease extent, inflammatory burden, and additional risk factors such as PSC or prior dysplasia [17, 19].The patient was ultimately diagnosed with acute PE. The PL occlusion identified during CAG was considered a chronic total occlusion in the context of CCS rather than an acute total occlusion associated with ACS. She was discharged two weeks later without

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complications. At six-month follow-up, the patient remained asymptomatic, and repeat CTPA and echocardiography findings were normal.

Clinicopathological Features

UCAN exhibits several features that distinguish it from sporadic CRC. Lesions often appear flat with indistinct margins, making detection and tumor delineation challenging under conventional endoscopy. UCAN frequently shows multifocality, with some lesions demonstrating diffuse infiltration into deeper layers of the colon wall, even when surface epithelial changes are minimal. Invisible dysplastic foci may surround the main tumor, requiring careful inspection. High-resolution endoscopy and chromoendoscopy with agents such as indigo carmine have been recommended to improve lesion detection [19].

In Japan, a multicenter randomized trial demonstrated that targeted biopsies of suspicious areas achieved similar detection rates (11.4% vs. 9.3%) compared with random biopsies but required fewer samples and shorter procedure times [21]. Therefore, targeted biopsy guided by detailed endoscopic evaluation—including chromoendoscopy or magnifying endoscopy—is recommended, although random biopsies remain useful in certain cases depending on clinical history and endoscopic findings.

Macroscopically, UCAN lesions can appear as flat, low-elevated, granular, nodular, or irregularly elevated areas, whereas advanced UC-associated CRCs are often diffusely infiltrating with undermined ulcers (Fig. 2). Secondary analysis of the JSCCR database revealed that type 3 (ulcerated with infiltration), type 4 (diffusely infiltrating), and type 5 (unclassified) tumors occur more frequently in UCAN than type 2 (ulcerated with clear margins), which dominates in sporadic CRC (46.5% vs. 24.2%) [22, 23]. Notably, invasive cancers may be misclassified preoperatively, with 13.8% initially categorized as type 0.

Histologically, UCAN shows a higher frequency of poorly differentiated adenocarcinoma, mucinous adenocarcinoma, and signet-ring cell carcinoma

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compared with sporadic CRC, particularly in the left-sided color. Chronic inflammation in UC induces oxidative stress, DNA damage, and accumulation of genomic and epigenomic alterations, including TP53 mutations, which drive the dysplasia–carcinoma sequence. Dysplasia is classified as indefinite, low-grade, or high-grade according to the Riddell system, with characteristic features including mucosal dedifferentiation, disordered differentiation, and increased glandular density. Proliferative zones identified by Ki-67 staining show a bottom-up pattern (basal to middle crypt layers) in UCAN, contrasting with the top-down pattern seen in sporadic adenomas. Overexpression of p53 is frequently observed, even at the low-grade dysplasia stage.

A comprehensive assessment of these macroscopic and histological features is crucial for distinguishing UCAN from sporadic CRC. Detection of dysplasia in biopsy specimens indicates either synchronous carcinoma elsewhere in the colon or a high risk of rapid malignant transformation. Consequently, early detection of dysplasia remains critical for timely diagnosis and management of CRC in UC patients.

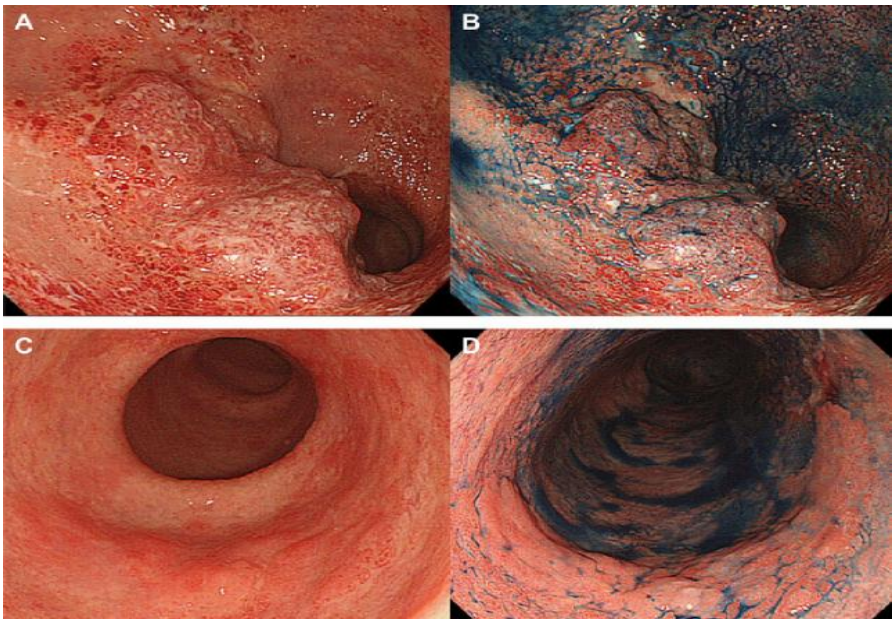

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Fig. 2 Representative endo-scopic findings of UCAN. Upper row: A representative case of type 3 advanced-stage UCAN located in the rectum, observed with A white-light endoscopy and B indigo car-mine chromoendoscopy. Lower row: A representative case of type 0–IIa early-stage UCAN located in the sigmoid colon, observed with C white-light endoscopy and D indigo car-mine chromoendoscopy. Indigo carmine chromoendoscopy is helpful for delineating tumor margins, which are sometimes difficult to identify using white-light endoscopy alone

Prognosis

The prognosis of UC-associated neoplasia (UCAN) is generally worse than that of sporadic colorectal cancer (CRC), largely due to its more aggressive histological features. This is particularly evident in patients with stage III disease, where the 5-year overall survival (OS) has been reported as 43.3% for UCAN compared with 57.4% for sporadic CRC ($p = 0.032$) [23]. However, a recent analysis of the JSCCR multicenter database indicated a relatively higher 5-year OS rate of 68% among stage III UCAN patients in Japan [9] (Table 1), reflecting advances in detection and management strategies.

Intensive surveillance colonoscopy at shorter intervals, combined with the use of biological agents, has been associated with a reduced incidence of advanced-stage UCAN (Fig. 7) [9, 31]. Early detection allows for timely intervention and can enable less invasive treatment approaches, such as endoscopic resection, in selected cases. This was demonstrated in a recent large-scale Japanese study, which included a substantial cohort of UCAN patients [32].

These findings emphasize the importance of appropriate surveillance strategies, individualized risk assessment, and the optimal use of biological therapies in improving long-term outcomes for patients with UCAN. Early identification of dysplasia or early-stage carcinoma not only improves survival rates but also

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expands therapeutic options, potentially reducing the need for extensive surgical procedures.

Early detection of UCAN through regular surveillance colonoscopy significantly improves long-term survival outcomes.Patients with multifocal or infiltrative lesions generally have a poorer prognosis compared to those with localized lesions.

The integration of advanced endoscopic techniques and targeted biopsies has facilitated the identification of early-stage UCAN, allowing les invasive interventions.

Postoperative monitoring and continued surveillance are essential to detect recurrence or new neoplastic lesions in UC patients. Optimisming medical therapy, including the use of biological agents to control chronic inflammation, may reduce progression to advanced-stage UCAN.

Table 1 Summary of characteristics of UCAN and CDAN

	UCAN	CDAN	*P* value
Tumor location [24]			
Ileum	0%	9%	< 0.01
Right-sided colon (C/A/T)	16%	8%	
Left-sided colon (D/S)	31%	7%	
Rectum	51%	28%	
Anal canal/anus	2%	48%	
Macroscopic classification [22]			
Type 0/1/2/3/4/5	14/16/24/13/14/19%	N.A	N.A
Histological type [9]			
wel/mod	73%	43%	< 0.01
por/muc/sig	16%	50%	
Others	11%	7%	
Pathological stage [9]			
0/I/II/III/IV	32/29/17/17/5%	10/17/37/22/14%	< 0.01
Stages in surveillance cases [9]			
0/I	73%	42%	< 0.01
II/III/IV	27%	58%	
Prognosis (5-year OS) [9]			
All stage	87%	59%	< 0.01
Stage 0	97%	100%	0.89
Stage I	95%	90%	0.73
Stage II	89%	76%	0.01
Stage III	68%	18%	< 0.01
Stage IV	13%	0%	0.04

UCAN ulcerative colitis-associated colorectal neoplasia, *CDAN* Crohn's disease-associated neoplasia, *C* cecum, *A* ascending colon, *T* transvers colon, *D* descending colon, *S* sigmoid colon, *wel* well-differentiated adenocarcinoma, *mod* moderately-differentiated adenocarcinoma, *por* poorly differentiated adenocarcinoma, *muc* mucinous adenocarcinoma, *sig* signet-ring cell carcinoma, *OS* overall survival

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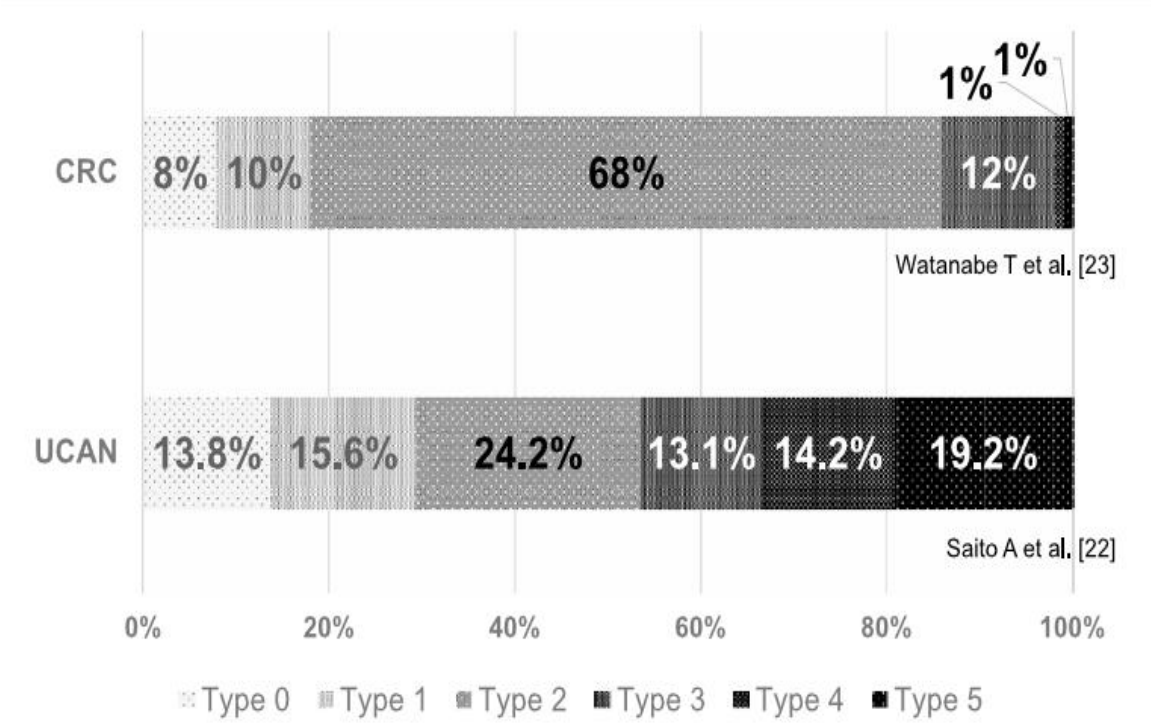

Fig. 3 Comparison of macroscopic findings between UCAN and spo-radic CRC. In UCAN, type 3, 4, and 5 tumors were more frequent than type 2 tumors (46.5% vs. 24.2%) [22], although type 2 tumors were dominant in sporadic CRC (68%) [23]. UC, ulcerative colitis; UCAN, ulcerative colitis-associated colorectal neoplasia; CRC, colo-rectal cancer

CD-Associated Neoplasia (CDAN)

Epidemiology

Crohn's disease (CD) affects various parts of the gastrointestinal tract, including the small intestine and perianal region, leading to a wide range of clinical manifestations. Despite these differences, the risk of malignancy over the long-term disease course remains an important clinical issue. Jess et al. reported that patients with CD have a standardized incidence ratio (SIR) of 1.9 (95% CI, 1.4–

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2.5) for colorectal cancer (CRC) and 27.1 (95% CI, 14.9–49.2) for small bowel cancer, both significantly exceeding the rates in the general population [2]. Likewise, Canavan et al. found SIRs of 2.5 (95% CI, 1.3–4.7) for CRC and 31.2 (95% CI, 15.9–60.9) for small bowel cancer, reporting cumulative CRC incidences of 2.9% at 10 years, 5.6% at 20 years, and 8.3% at 30 years. The risk was particularly elevated in patients with colonic involvement [3].

A comprehensive review of 24 studies published between 2005 and 2021 confirmed that CD patients face a higher overall risk of gastrointestinal neoplasia compared with the general population (RR 1.56; 95% CI 1.10–2.23) [33]. Site-specific analyses revealed especially increased risks in the small intestine (RR 11.9; 95% CI 8.07–17.7), colon (RR 2.30; 95% CI 1.73–3.06), rectum (RR 1.85; 95% CI 1.58–2.17), and anus (RR 4.52; 95% CI 1.19–17.1). Despite the high relative risk of small bowel cancer, it accounts for only about 2% of all gastrointestinal cancers in CD patients.

The anatomical distribution of CD-associated neoplasia varies by region and ethnicity. In Western countries, tumors are more often observed in the right-sided colon, whereas in Japan, rectal and anal canal tumors, including those associated with fistulas, are more frequent [34]. A meta-analysis in Asia found that 84.1% of CD-related CRC cases occurred in the left-sided colon, compared with 63.1% in Western populations [35]. Similarly, a Japanese multicenter study showed that 83% of lesions were left-sided, with nearly half (48%) involving the anal region (Fig. 5B, Table 1).

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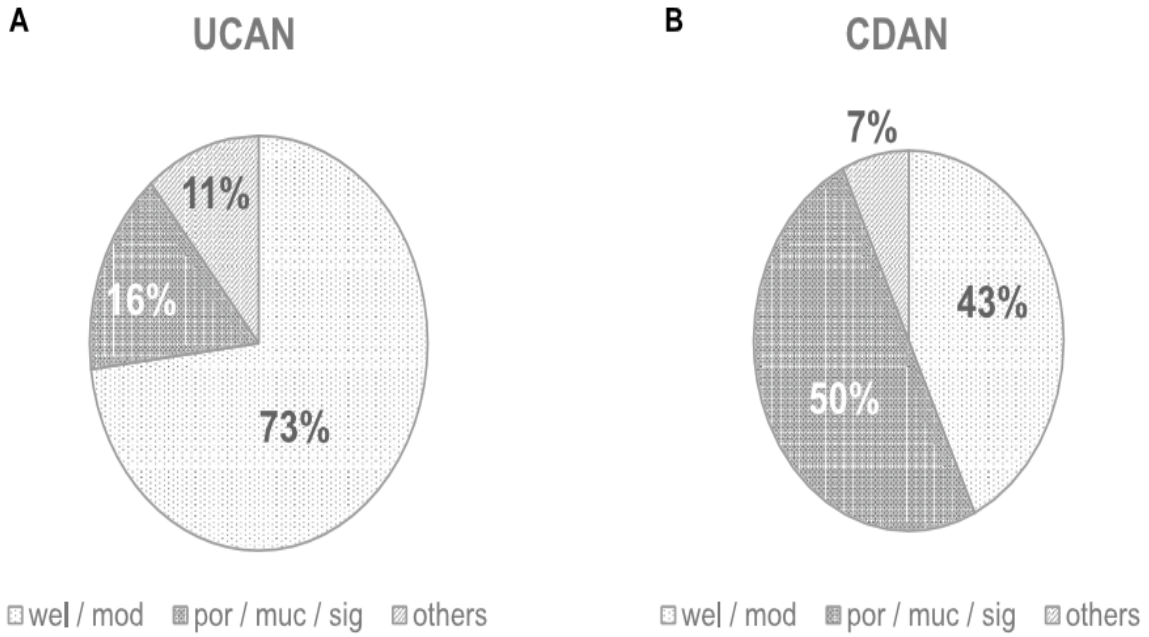

Fig. 4 Histological types of UCAN and CDAN. **A** In UCAN, well- or moderately-differentiated adenocarcinomas (wel/mod) accounted for the majority (73%), whereas poorly differentiated adenocarcinoma (por), mucinous adenocarcinoma (muc), and signet-ring cell carcinoma (sig) comprised approximately 16% of cases [9]. **B** In CDAN, por, muc, or sig accounted for about 50% of cases [9]. UCAN, ulcerative colitis-associated colorectal neoplasia; CDAN, Crohn's disease-associated neoplasia

Consequently, in Japan, it is recommended that patients with perianal CD and disease duration of 10 years or more undergo annual surveillance of the anorectal canal. Clinicians should be vigilant for warning signs such as increased mucous discharge, rectal bleeding, or worsening anal pain, which may indicate the presence of malignancy and require prompt investigation.

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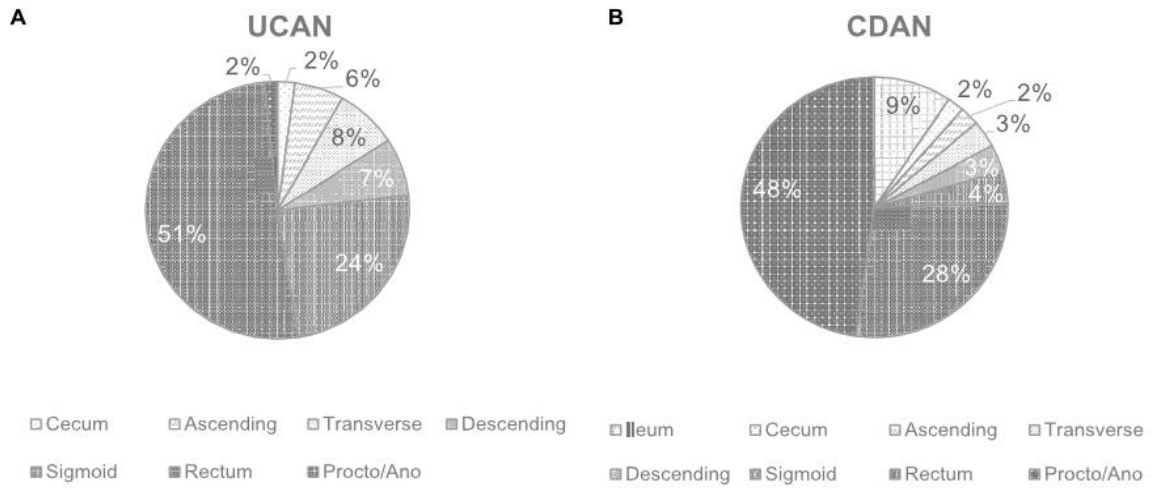

Fig. 5 Location of main tumor of UCAN and CDAN. A In UCAN, a large majority of tumors were located in the left-sided colon com-pared with the right-sided colon (84% vs. 16%) [24]. B In CDAN, 83% of lesions were located in the left-sided colon, with particularly high involvement of the anal region (48%) [24]. UCAN, ulcerative colitis-associated colorectal neoplasia; CDAN, Crohn's disease asso-ciated neoplasia

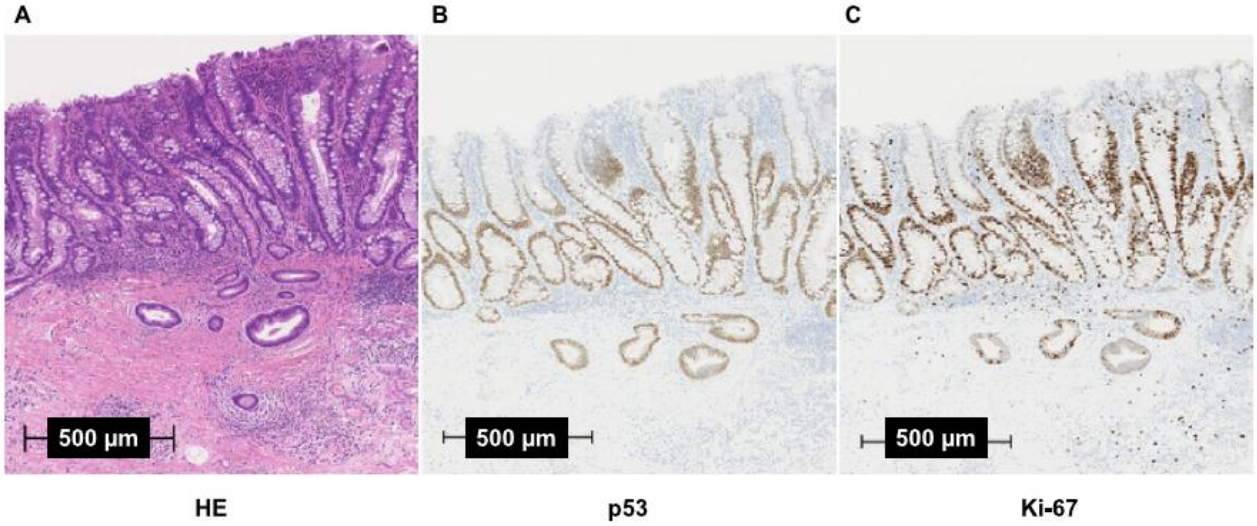

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Fig.6 Immunohistochemical examination of UCAN using p53 and Ki-67. A Hematoxylin and eosin (HE) staining demonstrates submu-cosal invasion of UCAN. B p53 protein overexpression is predominantly observed in the deep portion of the atypical glands in UCAN at an early phase of carcinogenesis. C Ki-67 immunostaining in the same UCAN lesion shows that the cellular proliferation zone is located in the deep to middle layers of the mucosa (bottom-up pat-tern), whereas in sporadic adenoma, the proliferation zone is typically distributed from the surface to the middle layers of the glands (top-down pattern). UCAN, ulcerative colitis-associated colorectal neopla-sia

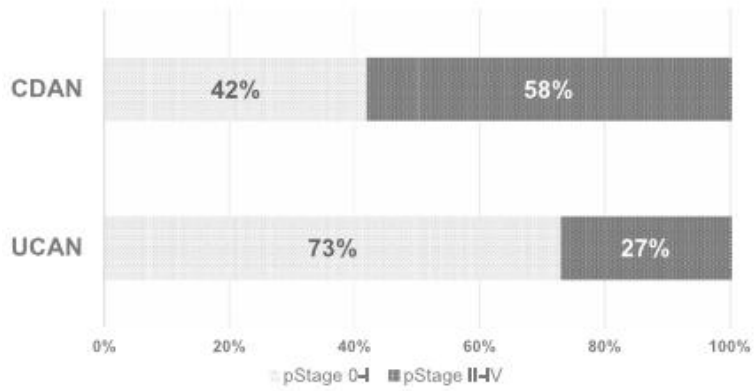

Fig. 7 Cancer stages of UC and CD in surveillance cases. The proportion of early-stage cancers (stage 0 or I) was high among patients with UC detected during surveillance, whereas more advanced-stage cancers (stage II, III, or IV) were frequently observed in CD, even during surveillance. UC, ulcerative colitis; CD, Crohn's disease

Risk factors

Risk factors for CDAN include disease duration, young age at onset, family history of CRC, extensive colonic involvement, and strictures. Long-standing CD has been reported as a risk factor for CRC in CD [3]. Similarly, patients with early-onset CD (before 30 years of age) have been shown to carry a significantly

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increased risk of developing CD-associated CRC (SIR, 8.2; 95% CI, 1.8–14.6) [36]. In patients with CD having a family his-tory of CRC, the risk of developing CRC is higher com-pared with those without such a history (RR, 3.7; 95% CI, 1.4–9.4) [15].

Additionally, colonic strictures have been reported to increase the risk of CRC in patients with CD (odds ratio, 8.03; 95% CI, 3.50–18.45) [16]. Regarding anorectal cancer, a Danish nationwide cohort study dem-onstrated that patients with CD and anorectal fistula have a significantly increased risk of anorectal cancer compared with the general population (hazard ratio, 2.85; 95% CI, 1.80–4.53) [37]. Moreover, chronic perianal disease-par-ticularly long-standing fistulas persisting for more than 10 years-has been recognized as conferring a small but increased risk of perianal and anorectal malignancies, as outlined in a systematic review and expert consensus on perianal fistulizing CD [38]. These findings indicate that perianal disease represents a key site-specific risk factor for CD-associated anorectal cancer and supports the need for careful long-term surveillance.

Clinicopathological features

CDAN (including CRC, fistula-associated carcinoma of the anal canal, and small intestinal cancer) often presents with atypical macroscopic features owing to the coexist-ence of non-neoplastic strictures, fistulas, or inflamma-tory changes caused by CD. In particular, lesions arising in the rectum and anal canal are frequently accompanied by strictures, and their macroscopic classification is not always consistent (Fig. 8). Another characteristic feature of CDAN is the relatively high incidence of adenocar-cinoma, which is thought to arise from fistulas (fistula-associated carcinoma). Histologically, these cancers often exhibit heterogeneous patterns, with a higher frequency of poorly differentiated adenocarcinoma, signet-ring cell carcinoma, and mucinous carcinoma (Fig. 4B) (Table 1).

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Pelvic contrast-enhanced computed tomography (CT) and magnetic resonance imaging are useful for assessing advanced fistula-associated cancer, but are not always reliable for detecting early-stage disease. Similarly, PET/CT has limited utility, particularly for mucinous carcinomas, which are relatively common in fistula-associated cancers. Regular and repeated colonoscopic biopsies of indurated areas, secondary fistula openings, fistula tracts, and strictures are essential. In cases in which strictures or pain preclude adequate endoscopic evaluation, examination of the anorectal canal under regional or general anesthesia should be considered. For fistula-associated lesions, seton drainage combined with periodic review and tissue sampling is recommended. Therefore, an early histopathological diagnosis is critical.

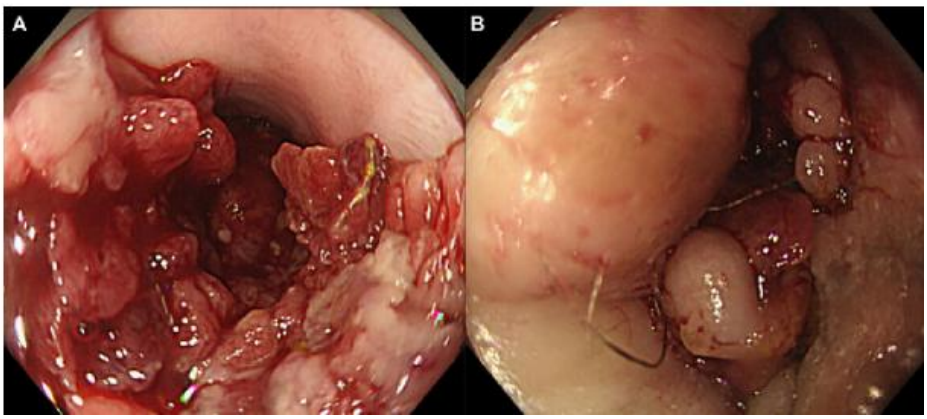

Fig. 8 Endoscopic findings of a representative case of CDAN. **A** A protruded villous tumor located in the anorectal region of a patient with CD. CDAN may occasionally exhibit a villous surface pattern. **B** The tumor extends toward the anal side and protrudes outside the anus. Careful inspection of the anorectal region is essential for the early detection of CDAN. CD, Crohn's disease; CDAN, Crohn's disease-associated neoplasia

Prognosis

The JSCCR database study reported a significantly worse 5-year OS rate for CDAN than for UCAN, particularly in advanced stages (stage II, 76% vs. 89%, $p = 0.01$; stage III, 18% vs. 68%, $p = 0.0009$; and stage IV, 0% vs. 13%, $p = 0.04$). Moreover, a higher proportion of advanced-stage CDAN cases have been diagnosed even under surveillance than UCAN cases [9] (Fig. 7) (Table 1). Furthermore, the survival outcome of CDAN was significantly poorer than that of sporadic CRC (5-year OS: 54.0% vs. 71.2%, $p < 0.001$), with a higher local

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recurrence rate (5-year RFS: 57.9% vs. 71.8%, p = 0.007). As for site-specific prognosis, anorectal cancer is associated with a poorer outcome, with a 5-year OS of 51.6% and a 5-year RFS of 53.0%. Notably, the rate of local recurrence is significantly higher than that of sporadic anorectal cancer (22.3% vs. 5.1%, p < 0.001) [39]. CD-associated small bowel adenocarcinoma also carries a poor prognosis. A systematic review and meta-analysis reported a 5-year OS of approximately 29% (95% CI 18–41%) for CD-associated small bowel adenocarcinoma patients, compared with around 33% for de novo small bowel adenocarcinoma. [40]. Regarding the underlying disease behavior of CD, patients with a penetrating disease phenotype have significantly worse outcomes [41]. Younger age at cancer onset has also been reported as a risk factor for poor prognosis [42]. Similar to UC, early detection through appropriate surveillance and timely therapeutic intervention are essential for improving outcomes in patients with CDAN.

Conclusion

This review provides an overview of the epidemiological patterns and clinicopathological characteristics of intestinal neoplasia associated with inflammatory bowel diseases (IBD), including ulcerative colitis (UC) and Crohn's disease (CD). These malignancies demonstrate distinct epidemiological trends and pathological features that clearly differentiate them from sporadic colorectal cancers (CRCs).

As the global prevalence of IBD continues to rise, neoplastic complications are becoming an increasingly significant clinical concern. Therefore, the implementation of appropriate surveillance programs and the promotion of early detection strategies are critical but remain challenging in routine clinical practice. Although the exact mechanisms of inflammation-related carcinogenesis are not yet fully clarified, ongoing research is necessary to improve risk assessment

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models, optimize diagnostic approaches, and ensure timely therapeutic intervention.

A more comprehensive understanding of the biological and clinical processes involved in IBD-associated neoplasia will contribute to earlier diagnosis, better prognostic evaluation, and improved patient survival. Ultimately, these advances will help shape more effective and individualized management strategies for patients with IBD-associated intestinal neoplasia.

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