Chapter

# Role of Interventional IBD in Management of Ulcerative Colitis(UC)-Associated Neoplasia and Post-Operative Pouch Complications in UC: A Systematic Review

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**Abstract**

Interventional inflammatory bowel disease (IIBD) is going to play a major role in complex IBD including ulcerative-colitis associated neoplasia (UCAN) and postoperative complications after ileal pouch-anal anastomosis (IPAA) in ulcerative colitis (UC). We performed a literature search in PubMed using keywords such as "UCAN" and "endoscopic management of pouch complications," After screening 1221 citations, finally, 91 relevant citations were identified for the systematic review. Endoscopic recognition of dysplasia should be done by high-definition white light endoscopy (HD-WLE) or dye-based/virtual chromoendoscopy (CE) especially in known dysplasia or primary sclerosing cholangitis (PSC). Endoscopically visible lesions without deep submucosal invasion can be resected endoscopically with endoscopic mucosal resection (EMR), endoscopic submucosal dissection (ESD), or using full-thickness resection device (FTRD). Image-enhanced endoscopy (IEE) and IIBD have an emerging role in screening, diagnosis, and management of colitis-associated neoplasia in UC and can avoid colectomy. IIBD can manage a significant proportion of post-IPAA complications. Pouch strictures can be treated with endoscopic balloon dilation (EBD) or stricturotomy, whereas acute and chronic anastomotic leak or sinuses can be managed with through the scope (TTS)/over the scope clips (OTSC) and endoscopic fistulotomy/sinusotomy.

**Keywords:** ulcerative colitis-associated neoplasia, Ileal pouch-anal anastomosis, interventional inflammatory bowel disease, ulcerative colitis, pouch complications

## 1. Introduction

With growing multidisciplinary care model of inflammatory bowel disease (IBD), IIBD is going to play a major role in management of complex IBD. Apart from its major role in management of Crohn's disease-related strictures and fistulas, IIBD has an important role to play in management of colitis-associated neoplasia in ulcerative colitis (UC) and postoperative pouch complications [1, 2]. Ulcerative-colitis associated neoplasia (UCAN) can range from indefinite dysplasia (IND), low-grade dysplasia (LGD), high-grade dysplasia (HGD), invisible dysplasia, and colorectal cancer (CRC). Apart from conventional dysplastic lesions, non-conventional dysplasia (e.g., serrated epithelial change: SEC) can occur in one third. Non-conventional dysplasia increases risk of advanced colorectal neoplasia (aCRN) according to recent meta-analysis and may warrant frequent surveillance [3].

Endoscopic screening should begin at 8–10 years from symptom onset for UCAN in the absence of PSC with subsequent surveillance based on risk stratification. HD-WLE, narrow band imaging (NBI), and CE have similar efficacy in detecting UCAN [4]. The incremental benefit of newer modalities of IEE such as Fuji Intelligent Color Enhancement (FICE), I-SCAN, linked color imaging (LCI), and autofluorescence imaging (AFI) for diagnosis of UCAN compared to conventional screening needs further evaluation. Endocytoscopy and probe-based confocal laser endomicroscopy (pCLE) can be helpful in "in vivo" diagnosis of UCAN [5]. Visible, uni-focal, polypoidal dysplasia of any grade can be resected en bloc using EMR or ESD [6]. For invisible dysplasia, management is dependent on patient-related (e.g., PSC) and histologic factors and includes colectomy. Concurrent inlet strictures in pre-pouch ileitis and anastomotic strictures can be treated with endoscopic balloon dilation or stricturotomy. Stricturing/fistulizing complications of Crohn's disease of the pouch can also be treated endoscopically. Endoscopic sinusotomy and fistulotomy are helpful in treating pouch sinus and fistulas respectively. Endoscopic placement of clips is useful in controlling leaks from pouch. Endoscopic resection can be done for large symptomatic inflammatory polyps in the pouch or polyps in the rectal cuff [2, 7]. We aimed to systematically review all the relevant literature pertaining to endoscopic management of UCAN and pouch complications post IPAA.

## 2. Search strategy

For the purpose of the review, we searched the PubMed using keywords "ulcerative-colitis associated neoplasia (UCAN)" and "endoscopic management of pouch complications" We found 965 citations. We also screened relevant articles with specific searches and selected cross references. Finally, after screening, total of 1238 citations, 91 were identified for the systematic review (**Figure 1**).

## 3. Detection of UCAN

Among various modalities for detection of dysplasia in IBD (**Table 1**), high-definition white light endoscopy (HD-WLE), narrow-band imaging (NBI), and chromoendoscopy (CE) were similar in efficacy in detecting UCAN with minor differences among them according to network meta-analysis [4]. Standard definition

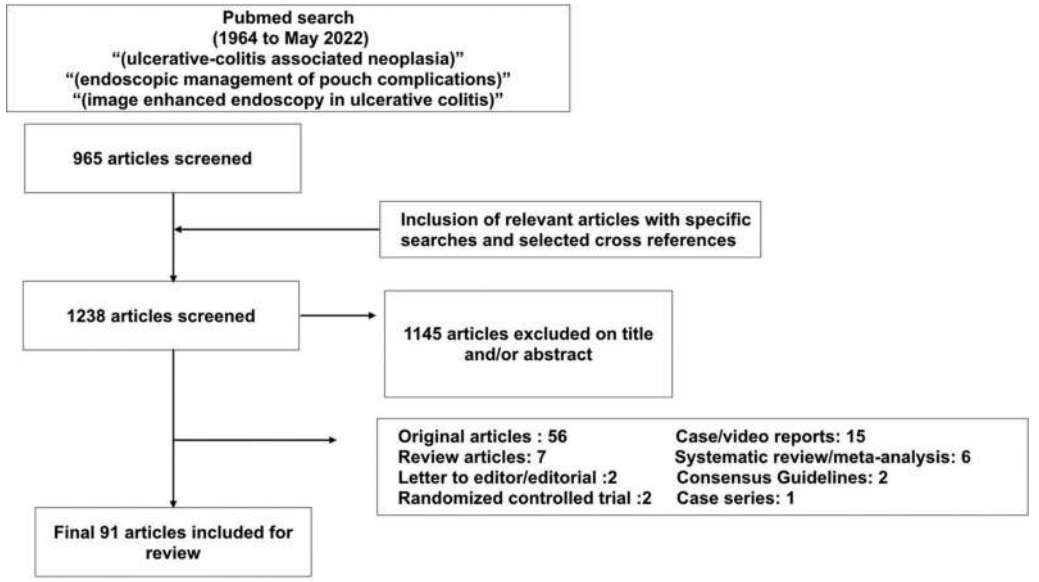


**Figure 1.**
*Consort diagram of systematic review on ulcerative colitis associated neoplasia and post ileal pouch complications.*

white light endoscopy (SD- WLE) was shown to be inferior to all these modalities [4]. Shorter withdrawal time and easy applicability are the advantages of NBI compared to CE whereas dysplasia detection rates are similar [8]. Magnifying endoscopy (ME) has incremental benefits over CE for detecting tumor margins to guide endoscopic resection (ER). ME guided ER has R0 resection rate of 95% (compared to 91% with distinct borders with only CE) [9].

The Japanese NBI expert team (JNET) classification and pit pattern on magnifying virtual/chromoendoscopy can predict histological diagnosis and invasion depth accurately as shown in a retrospective study of UCAN who underwent endoscopic resection or colectomy. JNET 2A, 2B, and 3 lesions imply low grade dysplasia (LGD), LGD/high grade dysplasia (HGD), and submucosal invasive carcinoma (SMIC). Pit pattern III/IV, VI low irregularity, VI high irregularity/VN can predict LGD, LGD/HGD, SMIC respectively [10]. Among image-enhanced endoscopy, (IEE), Fuji Intelligent Color Enhancement (FICE) can help predict histology of raised lesions in IBD apart from NBI [11]. I-SCAN is another modality of IEE which has a similar diagnostic yield with a shorter examination time than conventional CE [12]. Linked color imaging (LCI) with indigo carmine dye spraying can help facilitate UCAN diagnosis [13]. Endocytoscopy may help in "in vivo" diagnosis of intra-mucosal carcinoma (IMC) by observing enlarged nuclei after methylene blue staining [14]. Endocytoscopy irregularly-formed nuclei with pit (EC-IN-PIT) guided diagnosis of UCAN were shown to have better specificity and diagnostic accuracy than pit pattern alone in a pilot study [15]. Probe-based confocal laser endomicroscopy (pCLE, Cellvizio, Mauna Kea Technologies, Paris, France) can differentiate UCAN (carcinoma or dysplasia) with accuracy, sensitivity, and specificity of 92%, 100%, and 83%, respectively [16]. Autofluorescence imaging (AFI) can assess the lesion based on fluorescent intensity rather than analysis of surface pattern [17]. AFI with oral 5-aminolevulinic acid sensitization has incremental diagnostic yield compared to WLE [18]. Prospective randomized controlled trial (RCT) did not show any advantage of high definition

| Imaging modalities | Potential application in detecting Ulcerative colitis associated neoplasia (UCAN) |
|---|---|
| High-definition white light endoscopy (HD-WLE) | 2-fold better than standard definition white light endoscopy (WLE) in detection of neoplasia on targeted biospy |
| Dye Chromoendoscopy (DCE) | 3.2-fold increase in number of detected intraepithelial neoplasia compared to WLE guided random biopsies, 57.4% incremental yield compared to WLE |
| Virtual chromoendoscopy | |
| Narrow band imaging (NBI) | The diagnostic yield is not increased compared to DCE, but shorter withdrawal time and easy applicability are the advantages |
| Linked color imaging (LCI) | Study in IBD is scanty and limited to case reports |
| Blue laser imaging | |
| Dyeless chromoendoscopy | |
| Fuji Intelligent Color Enhancement | FICE can predict histology of polypoid and non-polypoidal raised lesions based on Kudo's classification and presence of fibrin cap |
| Autofluorescence imaging | AFI can have incremental diagnostic benefit over WLE based on fluorescent intensity |
| i-SCAN-OE (Pentax) | Similar diagnostic yield with shorter examination time than conventional CE, combined digital and optical enhancement (OE) |
| Newer techniques | |
| Endocytoscopy | It can help "in vivo" diagnosis of intra-mucosal carcinoma (IMC) by observing enlarged nuclei after methylene blue staining. Endocytoscopy irregularly-formed nuclei with pit (EC-IN-PIT) guided diagnosis of neoplasia can have better diagnostic accuracy than pit pattern alone |
| Probe based confocal laser endomicroscopy | Highly accurate but inflammation and hyperplasia can reduce sensitivity, use of molecular imaging with confocal probes can help in early diagnosis of neoplasia part from predicting response to biologics |

**Table 1.**
*Potential applications of various endoscopic imaging modalities in detection of ulcerative colitis associated neoplasia.*

chromoendoscopy (HDCE) guided targeted biopsy over HD-WLE guided random biopsies [19]. However, targeted biopsy may be cost-effective and time-saving [20]. An inter-observer agreement study has shown poor agreement on intention to biopsy among endoscopists in non-pedunculated potentially dysplastic lesions in UC [21]. Apart from IEE, EUS-guided assessment of depth of invasion can help in treatment selection [22].

## 4. Dysplasia in ulcerative colitis and risk of advanced colorectal neoplasia (aCRN)

### 4.1 Low grade dysplasia

Recurrent low-grade dysplasia (LGD) at first follow-up colonoscopy is a risk factor for aCRN as shown in a population-based registry from Netherlands with a hazard ratio of 1.66. A recurrence-free interval of three years predicts lower probability of subsequent occurrence of aCRN [23]. The risk of progression to aCRN is

0.8% per year. Multifocal LGD, PSC, location in distal colon, and invisible uni-focal low-grade dysplasia are associated with disease progression and hence require colectomy [24]. However, this is not commonly practiced by clinicians with limited experience in surveillance colonoscopy and from non-academic centers [25]. A web-based prediction tool for progression of LGD to aCRN has been recently developed and validated based on these four parameters: endoscopically visible LGD >1 cm, unresectable/incomplete endoscopic resection, moderate/severe histologic inflammation within 5 years of LGD and multifocal LGD [26]. LGD in a case of primary sclerosing cholangitis (PSC) warrants colectomy as the risk of aCRN is considerably high after diagnosis of LGD in PSC (8.4 per patient-years) as compared to LGD in non-PSC patients (3.1 per patient-years). PSC is an independent risk factor for aCRN warranting annual colonoscopic surveillance [27]. Biopsy sampling of surrounding mucosa has limited yield in predicting risk of aCRN whereas the grade of dysplasia predicts aCRN [28].

### 4.2 Indefinite dysplasia

Indefinite dysplasia (IND) found in nearly 4% of patients can increase the risk of aCRN (3.1% per patient-years) by 6.9-fold after adjusting for other confounding factors [29]. On the other hand, post inflammatory polyps (PIP)/pseudo-polyps were predictive of higher severity of colonic inflammation and colectomy but not aCRN [30].

### 4.3 Colonic strictures in UC

Colonic stricture in ulcerative colitis was thought to be associated with neoplasia unless proven otherwise. However, strictures may represent inflammatory sequelae as well. Colonic strictures in long-standing colitis do not independently predict advanced colorectal neoplasia as shown in a retrospective cohort study mainly involving Crohn's colitis [31]. Prospective studies in ulcerative colitis-associated strictures are needed to confirm the finding. Non-passable strictures <4/5 cm on computed tomography (CT)-colonography without any evidence of dysplasia on endoscopic biopsy are candidates for endoscopic dilation [32].

### 4.4 Non-conventional and invisible dysplasia

A study retrospectively evaluating colonoscopic images recorded within last two years prior to diagnosis of UCAN has shown that the mean diagnostic delay for UCAN was nearly 15 months. Visible lesions were present in 25.9%, 18.2%, and 31.3% of UCAN, early- and late-stage cancers, respectively. Invisible lesions were more common in left colon and rectum and was associated with inflammation. UCAN with indistinct margins were more likely to be associated with inflammation than those with distance margins [33]. Two third of the non-conventional dysplasia in IBD (hypermucinous, goblet cell deficient and crypt cell dysplasia) can present with flat/invisible dysplasia (crypt cell:96%, goblet cell deficient-65%, hypermucinous-42%) with equally high risk of subsequent aCRN (HGD or adenocarcinoma: 37% and 23% respectively in those with follow up colonoscopy; goblet cell>hypermucinous>crypt cell) [34]. These findings highlight the need for random biopsies in addition to targeted biopsies as non-conventional dysplasia often co-exist with the conventional dysplasia and can be the only form of dysplasia present. One-fifth of the dysplasias in IBD patients are found on random biopsies [35].

A recent study has highlighted that demarcated red-colored areas histologically characterized by increased vessel density and size (CD 34 positive) can be useful in identifying flat type dysplasia. These areas are common in base of LGD and throughout entire surface of HGD. Targeted biopsy from these areas should be considered [36]. In addition to Kudo's neoplastic pit patterns (III-V), pine-cone/villi pattern on surface morphology are highly specific for neoplasia and hence should be subjected to targeted biopsy [37]. Red in blue sign, pale-whitish mucosa, velvety appearance, ulceration, wall deformity, spontaneous friability and interruption of innominate grooves are signs of non-polypoidal UCAN [38].

### 4.5 CRN in rectal stump post colectomy in UC

Risk of CRN in rectal stump after ileorectal anastomosis (IRA) post-colectomy in UC is 7.1% and 14% after 10 and 20 years respectively. PSC, age at the time of IRA, UC disease duration and history of colorectal cancer are risk factors of CRN and rectal carcinoma after IRA. Hence ileal pouch anal anastomosis (IPAA) should be considered instead of IRA in high-risk patients such as PSC [39]. Acute severe UC decreases risk of IRA failure whereas Pre-colectomy thiopurine use within 12 months does not increase risk of CRN after IPAA in UC or indeterminate colitis [40].

## 5. Endoscopic resection of UCAN

(**Figure 2**)

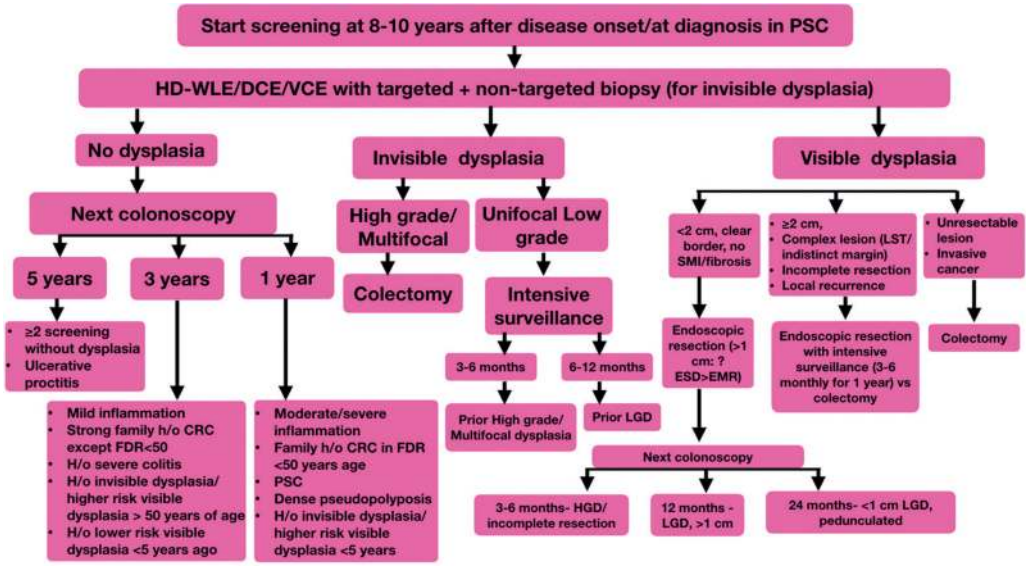


**Figure 2.**
*Algorithm for surveillance and management of ulcerative colitis associated neoplasia. HD-WLE- high-definition white light endoscopy, DCE- dye chromoendoscopy, VCE- virtual chromoendoscopy, CRC- colorectal cancer, FDR- first degree relative, H/o - history of, HGD- high grade dysplasia, LGD- low grade dysplasia, LST- laterally spreading tumor.*

### 5.1 Endoscopic mucosal resection

Earlier colectomy was indicated for any grade of dysplasia until it was recognized that endoscopy resection for polypoidal HGD or endoscopically visible dysplasia (earlier known as dysplasia-associated lesion or mass: DALM) with surveillance can avoid colectomy [41–44]. For polypoidal lesions, there was no difference between outcomes with polypectomy versus proctocolectomy. However, continued close surveillance is mandatory to identify metachronous lesions [45] Similarly it was realized that flat dysplasias can be managed safely with endoscopic mucosal resection (EMR) (**Figure 3** A-D)) [46]. Underwater EMR can be particularly beneficial in resecting UCAN compared to conventional EMR in areas of scarring and severe submucosal fibrosis (SMF) hindering lifting of the lesion [47]. UEMR is safe, effective and time-saving which have shown to remove large polyps in UC with submucosal fibrosis by "heat-sink" and "floating" effects (**Figure 3** E-F) [48].

### 5.2 Endoscopic submucosal dissection (ESD)

For CAN, the en-bloc and Ro resection rates with ESD are 83% and 67%, respectively. However, a study reported that upto 70% can develop metachronous UCAN on long term follow up which may require colectomy or re-ESD according to a small study [49]. The advantage of ESD is total excision biopsy to evaluate the lesion. Compared to non-UC patients, ESD in UC is associated with lower rate of Ro resection (71% vs. 93%) with lower probability of negative horizontal margin [50]. Hence the demarcation line should be ascertained. Technical difficulties can occur due to scarring and excessive submucosal fibrosis (SMF) which can occur in nearly 40% of cases undergoing ESD [51]. Submucosal fatty infiltration is another limiting factor

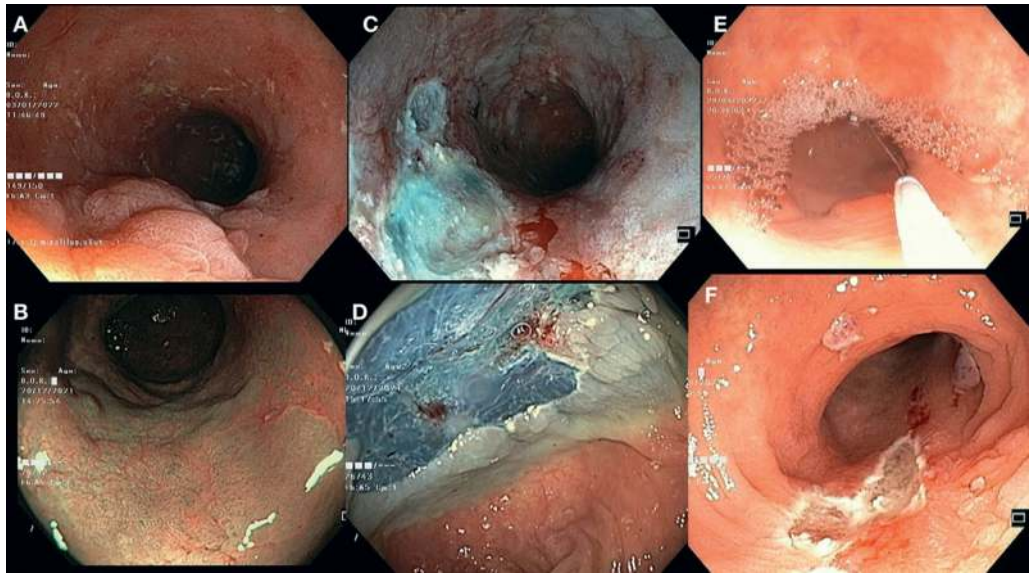


**Figure 3.**
*Endoscopic mucosal resection (EMR) for ulcerative colitis associated neoplasia. A, B- flat visible dysplasias in a case of long-standing ulcerative colitis, C, D- EMR site post resection- biopsy showed high grade dysplasia, D, E- underwater EMR done for residual neoplasia post initial session of EMR.*

for ESD in UCAN [52]. Analysis of colectomy specimens have shown that 21% of the lesions can be invisible endoscopically highlighting the importance of intensive surveillance colonoscopy [51]. To overcome the effect of SMF, multi-traction technique using three intertwined loops with clips have been used to treat recurrence of HGD in UC [53]. Another study in 133 colorectal neoplasms (28 with UC) with submucosal fibrosis (28 had UC) water pressure assisted ESD (WP-ESD) had significantly shorter procedure time related to conventional ESD [54].

In a meta-analysis of 203 dysplastic lesions (mean size 2.7 cm, 83% left colon, 90% non-polypoid,) in 192 UC patients, the en bloc resection, complete resection, and R0 resection rates were 94%, 84%, and 81% respectively. SMF was seen in 71%. Mean procedure time was 83 minutes. The rates of local recurrence, metachronous tumor and additional surgery were 5%, 6%, and 10% respectively. Adverse events like bleeding and perforation were seen in 8% and 6%, respectively [55]. Another systematic review showed comparable en bloc and R0 resection rates (88.4% and 78.2% respectively) [56]. Results of ESD in UCAN is best for those with non-invasive pit/vascular pattern, no surface ulceration, distinct borders and appropriate lifting on submucosal injection [57]. Results of ESD for non-polypoidal UCAN is inferior to those for polypoidal lesions due to SMF in 90–100% patients: en-bloc and curative resection rates are 60–100% and 70–79% respectively. Adverse events and recurrence occurred in <10% and 4–20% respectively [58–60].

Prior to widespread use of ESD, endoscopic piecemeal resection followed by argon plasma coagulation had been described in the past for large, poorly lifting adenomas [61].

### 5.3 Choice of an endoscopic resection technique in UCAN

The choice between ESD and EMR for UCAN can be decided based on a recent study which showed that ESD has higher R0 resection rates than EMR for ≥11 mm lesions (94% vs. 55%) and non-polypoidal lesions (100% vs. 55%). Hence it was concluded that EMR can be preferred for lesions ≤10 mm. 10% patients had intra-procedure perforation during ESD and metachronous HGD noted in 3% [62]. Another study concluded that EMR is indicated for small lesions without fibrosis and ESD for large lesions with fibrosis [63]. Overall, it is important to note that endoscopic resection techniques can help in preventing colectomy by removal of large CRNs [64].

### 5.4 Modalities other than EMR or ESD

Hybrid resection with ESD and FTRD can be useful in lesions with severe submucosal fibrosis. Hybrid ESD can be useful in large laterally spreading tumor [65]. ESD assisted EMR had been described as early as in 2008 in a series of 67 patients, which reported en-bloc resection rate of 78% with R0 resection rate of 94% in those undergoing en-bloc resection [66]. A recent report first described use of FTRD in a case of long-standing UC for a non-lifting, fibrotic adenoma in descending colon [67].

### 5.5 Risk of recurrence

The chance of recurrence of cancer and any dysplasia after endoscopic resection of polypoid dysplasia in UC are 5.3 cases/1000 patient-years and 65 cases/1000 patient-years, respectively [68].

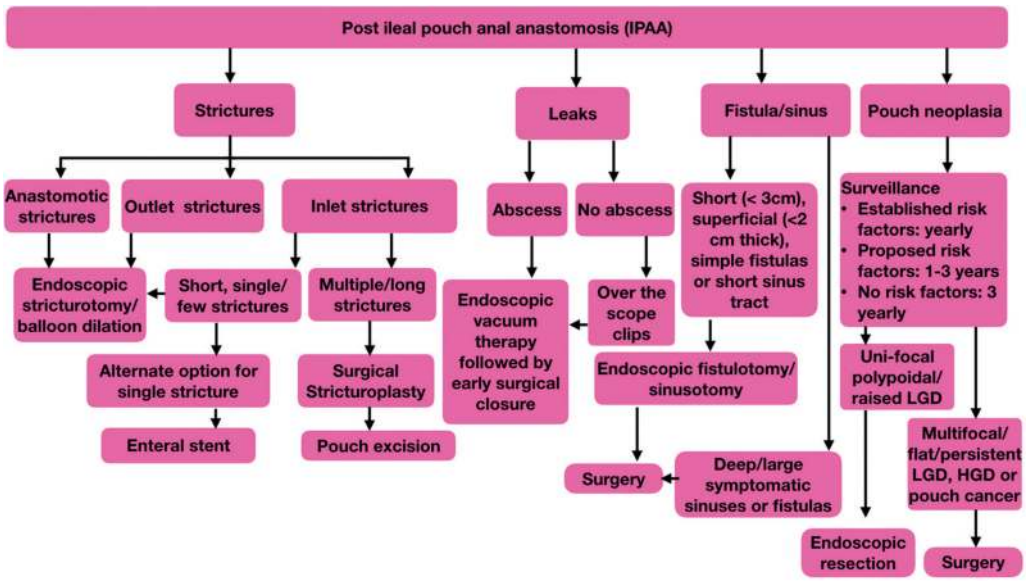


**Figure 4.**
*Management algorithm for endoscopic management of complications after ileal pouch anal anastomosis. HGD-high grade dysplasia, LGD- low grade dysplasia.*

## 6. Role of IIBD in postoperative pouch complications in UC

Among pouch related complications, pouch strictures, floppy pouch complex, acute and chronic anastomotic leak or sinuses can be amenable to endoscopic therapy (**Figure 4**) [69].

### 6.1 Pouch strictures

Pouch outlet stricture related to sealed ileal pouch have been treated with wire guided stricturotomy using insulated tip (IT) knife [70]. Pouch strictures (inlet and outlet) can be successfully dilated with controlled radial expansion (CRE) balloon relieving symptoms, restoring pouch patency and improved quality of life in a study by Shen et al. of 19 patients with pouch strictures (11 had Crohn's disease of the pouch) [71]. The clinical success of endoscopic balloon dilation (EBD) is 66.7% as reported in a study by Kirat et al. with rest requiring excision of pouch. Nearly half require repeat EBD. Pouch inlet/afferent limb strictures can be treated effectively with both EBD and endoscopic stricturotomy (ES) with comparable surgery free survival as shown by Lan et al. (160 EBD, 40 EST) [72]. The risk of bleeding is higher with ES (4.7% vs. 0% with EBD) whereas the risk of perforation is higher with EBD (0.8% vs. 0% with ES). Length of stricture (>5 cm) and pouchitis are predictors of subsequent surgery [72]. Another study reporting 88 dilations in 20 patients (majority 87% had ileo-anal anastomotic strictures, 95% had UC) showed a technical and clinical success of EBD as 98% and 95% respectively without any major adverse events. The study hence concluded that EBD should be the first line for pouch strictures [73]. In the largest study of 150 patients undergoing 646 EBD procedures, perforations and bleeding occurred in less than 1% cases. At a median follow up of nearly 10 years, 87.3% retained their pouches. Multiple strictures and Crohn's disease of the pouch were independent predictors of pouch failure [74].

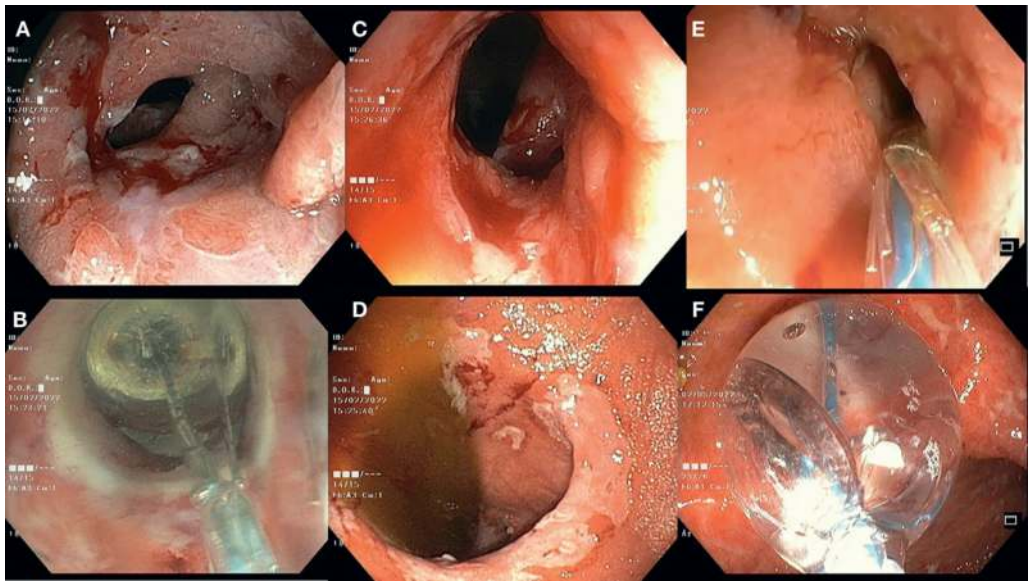


**Figure 5.**
*Endoscopic management of pouch strictures. A. Ileal pouch anastomotic stricture, B. endoscopic balloon dilation (EBD) being performed, C. stricture post EBD, D. Pouchitis noted in ileal pouch post anastomotic dilation, E. pouch inlet stricture, F. EBD for pouch inlet stricture.*

Based on results of various studies, a systematic review has concluded that for pouch anal strictures, bougie dilation followed by balloon dilation (**Figure 5** A-D) are the modalities prior to surgical dilation. Endocarp guided needle knife stricturotomy is another alternative approach [75]. Pouch inlet strictures need to be treated with both medical (for inflammatory stricture) and endoscopic therapy (EBD) (for fibrotic stricture) (Figure E-F) [75]. Mid pouch stricture has been treated with surgical stricturoplasty rather than excision of pouch [75].

### 6.2 Pouch leaks

Successful management of leak from the "tip of the J" have been described with two over the scope clips (OTSCs) [76]. OTSCs have been shown to be successful in nearly two thirds of the patients with one or two sessions in closing such leaks while remaining require revision surgery. 50% patients required re-procedure (OTSC clip or endoscopic suturing) and finally one third required surgery [77]. Apart from direct closure of defects, a short period of endoscopic vacuum therapy (EVT) with periodic sponge changes can help in early surgical closure for treating anastomotic leakage post IPAA. 100% secondary anastomotic healing (median healing time 48 days) was achieved in early closure group (n = 15) compared to 52% (median healing time 70 days) in conventional treatment group (n = 29) [78]. In another series of 8 patients, complete healing of leak was documented in median 2 months-time [79]. Hence EVT can be used for anastomotic leak post IPAA whereas OTSC is to be used if there is leak without any abscess [7].

### 6.3 Pouch fistula

Endoscopic fistulotomy can be used in short (< 3 cm), superficial (<2 cm thick), simple fistulas like pouch-to-pouch body fistula, perianal fistula and ileo-cecal fistula

[7]. In a study of 29 patients (26 IPAA, 21 having UC) with IBD related fistulas, endoscopic fistulotomy (EFT) with needle knife was successful in healing fistula in nearly 90% patients whereas 10% require surgical intervention [80]. Preliminary results of another study comparing EFT with redo-surgery showed complete healing in all cases of redo surgery with complete and partial fistula healing in 78.4% and 21.6% wire EFT respectively. Rate of subsequent surgery and adverse events were lower in EFT arm (n = 40) compared to redo surgery (n = 19) [81]. Combined use of multiple sessions of endoscopic clipping and EFT have been used to completely heal pouch-to-pouch fistula from tip of the "J" to the anastomosis [82].

### 6.4 Pouch sinus

Endoscopic sinusotomy can be successfully used to manage chronic pouch anastomotic sinus after IPAA in UC with fair healing rate (53.2% complete, 15.3% partial) as compared to 94% initial complete healing rate with redo surgery as shown in a historical cohort study (endoscopic sinusotomy 141, surgery 85). However, redo surgery was associated with higher morbidity (43.5%) vs. compared to endoscopic sinusotomy (2.5%). Subsequent recurrence and need for surgery were not significantly higher in endoscopic arm as compared to surgical closure [83]. Like pouch fistulas, EVT can be helpful in treating anastomotic leak post IPAA preventing development of chronic pre-sacral sinus [84]. Multiple sessions of endoscopic sinusotomy under doppler ultrasound guidance have been used along with topical doxycycline (100 mg IV with 10 ml saline) (a matrix metalloproteinase inhibitor which promote fibrosis) injection for refractory sinus post IPAA [85]. However, endoscopic therapy is reserved for small sinus tracts whereas surgery may be required for large, deep symptomatic sinuses [86].

Few studies have evaluated factors influencing sinus healing and pouch survival with endoscopic sinusotomy. Crohn's disease of the pouch is a negative predictor of pouch healing whereas higher BMI and longer intervals between sinusotomy were positive predictors [87]. Conversely, another study by the same group have shown that excess BMI gain (≥ 10%) post sinusotomy was associated with recurrent sinus [88]. With regard to surgery free survival, acute anastomotic leak, toxic megacolon, longer sinus and delayed sinusotomy were risk factors; whereas longer interval between sinusotomies, concurrent 50% dextrose and doxycycline use were protective factors [87]. Endoscopic hemostasis for severe bleeding in diverted ileal pouch have been described with spray of hypertonic saline (50% dextrose) [89]. Incremental number of endoscopic sinusotomy increase the chances of sinus healing whereas delay in sinus diagnosis and complex sinuses are negative predictors of success as shown in another study of 65 patients [90].

### 6.5 Floppy pouch complex

Floppy pouch complex is managed initially with lifestyle modifications like avoidance of excessive straining failing which endoscopic ligation/plication can be considered [69].

### 6.6 Pouch neoplasia

Low grade dysplasia, high grade dysplasia, adenocarcinomas and squamous cell carcinomas are reported to occur in pouch after IPAA. Presence of established

(pre-colectomy cancer or dysplasia) and proposed risk factors (PSC, family history of colon cancer, chronic pouch inflammation, long standing UC, type "C" mucosa- atrophic mucosa with chronic inflammation) predict risk of pouch neoplasia and direct pouch surveillance [91]. Presence of established risk factors warrant annual surveillance pouchoscopy with at least 3 biopsies from cuff/anal transition zone, pouch inlet and body or any endoscopically visible lesion [2]. Presence of proposed risk factors warrant pouchoscopy with biopsy every 1–3 years. Surveillance pouchoscopy is recommended every 3 years in patients without risk factors [2]. Surveillance is important given the fact that pouch neoplasia has poor prognosis and early detection can salvage pouch. After endoscopic resection of uni-focal polypoidal/raised LGD by polypectomy/EMR/ESD, surveillance should be done every 3 months for 2 years. Irrespective of the modality of endoscopic resection (EMR/ESD), the resection should be en-bloc with extensive biopsy of adjacent mucosa. Multifocal/flat/persistent LGD, HGD or pouch cancer should be treated with surgical intervention (excision, mucosectomy or pouch advancement). People with established risk factors of pouch neoplasia may require complete proctectomy [91] .

## 7. Conclusion

The role of interventional endoscopy in diagnosis and management of ulcerative colitis associated neoplasia and pouch complications post colectomy in UC are expanding. While HD-WLE and CE are established methods of screening for UCAN, other modalities of virtual CE are emerging. Endocytoscopy and pCLE have the potential for "in vivo" diagnosis of dysplasia. EMR, ESD and recently FTRD have been employed for endoscopic resection of UCAN. Underwater EMR and traction or water pressure assisted ESD can help in resecting UCAN in the presence of submucosal fibrosis. Among pouch related complications, pouch strictures, leaks, fistula, sinus, pouch neoplasia and floppy pouch can be managed endoscopically. Future prospective and comparative studies are required to further define the role of IIBD in the current management algorithm of UCAN and pouch complications.

## Authors' contribution

**Concept and design:** PP; **Administrative support:** MT, DNR; **Provision of study material/patients:** PP; **Acquisition of data:** PP. **Data Analysis and interpretation:** PP; **Preparation of initial draft:** PP,; **Critical revision of the manuscript:** MT, RB, DNR, **Important intellectual inputs and revision:** MT, RB, ZN, MR, DNR **Manuscript writing:** All authors, **Approval of final manuscript:** All authors.

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