**Current Practices in Ileal Pouch Surveillance for Patients with Ulcerative Colitis:**

**A Multinational, Retrospective Cohort Study**

Mark A Samaan1\*, Katrina Forsyth1,2\*, Jonathan P Segal3, 4, Djuna de Jong5,

Jasper LA Vleugels5, Soad Elkady3, 6, Misha Kabir7, Samantha Campbell7, Klaartje Kok8, David G Armstrong2, Lawrence Penez3, Aitor P Arenaza3, Edward Seward7, Roser Vega7, Shameer Mehta7, Farooq Rahman7, Sara McCartney7, Stuart Bloom7, Kamal Patel2, Richard Pollok2,

Edward Westcott9, Amir Darakhshan9, Andrew Williams9, Ioannis Koumoutsos1, Shuvra Ray1, Joel Mawdsley1, Simon Anderson1, Jeremy D Sanderson1, Evelien Dekker5, Geert R D’Haens5,

Ailsa Hart3, 4, Peter M Irving1

***Author affiliations***

1Department of Gastroenterology, Guy’s & St. Thomas’ NHS Foundation Trust, London, UK

2Department of Gastroenterology, St George’s University Hospitals NHS Foundation Trust, London, UK

3Department of Gastroenterology, St Mark's Hospital, London, UK

4Imperial College, London, UK

5Department of Gastroenterology, Amsterdam University Medical Centre, Academic Medical Centre, Amsterdam, The Netherlands

6University of Alexandria, Alexandria, Egypt

7Department of Gastroenterology, University College London Hospitals NHS Foundation Trust, London, UK

8Department of Gastroenterology, Barts Health NHS Foundation Trust, London, UK

9Department of Surgery, Guy’s & St. Thomas’ NHS Foundation Trust, London, UK

\*Authors contributed equally

***Running title***

UC Pouch Surveillance

***Correspondence to***

Mark A Samaan

IBD Clinical Research Fellow

Department of Gastroenterology

First Floor College House, North Wing, St Thomas' Hospital

Westminster Bridge Road

London, SE1 7EH

United Kingdom

markasamaan@gmail.com Tel: 020 7188 2499

***Word count***

3823

***Disclosures***

Mark A Samaan Advisory fees: Takeda, Janssen

Lecture fees: Takeda, MSD, Janssen, Falk

Katrina Forsyth None

Jonathan P Segal None

Djuna de Jong None

Jasper LA Vleugels None

Soad Elkady None

Misha Kabir None

Samantha Campbell None

Klaartje Kok None

David G Armstrong None

Lawrence Penez None

Aitor P Arenaza None

Edward Seward None

Roser Vega None

Shameer Mehta None

Farooq Rahman None

Sara McCartney Lecture fees: Abbvie, Janssen, Takeda, MSD, Actavis

Stuart Bloom None

Kamal Patel None

Richard Pollok None

Evelien Dekker None

Geert R D’Haens Consultant and/or lecturer for AbbVie, ActoGeniX, AIM, Boehringer Ingelheim GmbH, Centocor, Chemo Centryx, Cosmo Technologies, Elan Pharmaceuticals, enGene, Dr Falk Pharma, Ferring, Galapagos, Giuliani SpA, Given Imaging, GlaxoSmithKline, Janssen Biologics, MSD, Neovacs, Novo Nordisk, Otsuka, PDL BioPharma, Pfizer, Receptos, Salix, SetPoint, Shire Pharmaceuticals, Schering-Plough, Takeda, Tillotts Pharma, UCB Pharma, Versant, and Vifor Pharma

Research grant recipient from AbbVie, Janssen, Given Imaging, MSD, Dr Falk Pharma, and PhotoPill

Speaker for AbbVie, Tillotts, Tramedico, Ferring, MSD, UCB Pharma, Norgine, and Shire

Edward Westcott None

Amir Darakhshan None

Andrew Williams None

Ionnis Koumoutsos None

Shuvray Ray None

Joel Mawdsley None

Simon Anderson None

Jeremy D Sanderson None

Ailsa Hart None

Peter M Irving Advisory fees: Abbvie, Warner Chilcott, Takeda, MSD, Vifor Pharma, Pharmacosmos, Topivert, Genentech, Hospira, Samsung Bioepis

Lecture fees: Abbvie, Warner Chilcott, Ferring, Falk Pharma, Takeda, MSD, Johnson and Johnson, Shire

Financial support for research: MSD, Takeda

***Author Contributions***

Guarantor of the article: MAS. Development of study concept and design: MAS, JPS, KF, KK, SC, MK, DdJ, JV, EW, AD, AW, AH, PMI. Study supervision: PMI. Acquisition, analysis, and interpretation of the data: MAS, JPS, KF, KK, DGA, SC, MK, DdJ, JV, SE, APA, LP. Statistical analysis: KF, MAS. Drafting of the manuscript: MAS, JP, KF, PMI. Critical revision of the manuscript for important intellectual content: ES, RV, FR, SC, SM, SB, KP, RP, ED, GRD, AD, EW, AW, IK, SR, JM, SA, JDS, AH, PMI.

***Grant Support***

None

**ABSTRACT**

***Background & Aims***

There are no universally accepted guidelines regarding surveillance of UC patients after restorative proctocolectomy and ileal pouch-anal anastomosis (IPAA). There also exists a lack of validated quality assurance standards for performing pouchoscopy. To better understand IPAA surveillance practices in the face of this clinical equipoise, we carried out a retrospective cohort study at five IBD referral centres.

***Methods***

Records of patients who underwent IPAA for UC or IBD-U were reviewed and patients with <1-year follow-up after restoration of intestinal continuity were excluded. Criteria for determining the risk of pouch dysplasia formation were collected as well as the use of pouchoscopy, biopsies and completeness of reports.

***Results***

We included 272 patients. Median duration of pouch follow-up: 10.5 (3.3-23.6) years. 95/272 (35%) had never undergone pouchoscopy for any indication and 191/272 (70%) had never undergone pouchoscopy with surveillance as the specific indication. 3/26 (12%) high-risk patients had never undergone pouchoscopy. Two cases of adenocarcinoma were identified, occurring in the rectal cuff of low-risk patients.Patients under the care of surgeons appeared more likely to undergo surveillance but rates of incomplete reporting were higher amongst surgeons (78%) than gastroenterologists (54%, p=0.002).

***Conclusions***

We observed wide variation in surveillance of UC/IBDU-IPAA patients. In addition, the rate of neoplasia formation amongst ‘low-risk’ patients was higher than may have been expected. We therefore, concur with previous recommendations that pouchoscopy be performed at one year post-operatively to refine risk-stratification based on clinical factors alone. Reports should document findings in all regions of the pouch and biopsies should be taken.

***Key words***

Ileal pouch, Ileoanal pouch, Ileal pouch-anal anastomosis, surveillance, ulcerative colitis

**INTRODUCTION**

There are currently no universally accepted guidelines regarding the surveillance of inflammatory bowel disease (IBD) patients after restorative proctocolectomy (RPC) with ileal pouch-anal anastomosis (IPAA). Both the European Crohn’s and Colitis Organization (ECCO) and the British Society of Gastroenterology (BSG) suggest that clinicians should ‘consider’ surveillance with annual pouchoscopy and biopsy in patients with risk factors such as: dysplasia or colorectal cancer (CRC) at time of pouch surgery, pouches exhibiting type C mucosa (persistent atrophy and severe inflammation) or primary sclerosing cholangitis1, 2. However, the guidelines differ in their approach to managing IPAA patients without risk factors whom, it must be noted, form the majority of patients undergoing pouch surgery. Whilst accepting that ‘there is no clear evidence that pouch surveillance is beneficial and thus cannot be strongly recommended’, the BSG suggests that 5 yearly surveillance should be considered in the low risk group1, whereas ECCO guidance does not appear to support any program of planned surveillance in patients without risk factors2. Clarity of advice with regards to this group is no more forthcoming from the US, where neither the American Gastroenterology Association (AGA)3 nor the American Society for Gastrointestinal Endoscopy (ASGE)4 have issued specific recommendations (table 1). Compared with guidelines for patients with an intact colon (where surveillance may reduce colorectal cancer and mortality5, 6), this relative paucity of guidance for clinicians has the potential to lead to variation in practice and controversy7. In lieu of clear recommendations and the evidence on which to base them, several groups have proposed rational and pragmatic surveillance algorithms7-9. However, these too differ from one another.

In addition to the variation in guidance relating to surveillance practices, the reported rates of neoplasia or cancer within ileal pouches also vary widely. Some series have shown these occurrences to be very rare10, 11. Most recently a population-based study of 1723 UC-IPAA patients was carried out using the Danish Cancer Registry and appeared to confirm this notion with a demonstrated pouch cancer rate of 0.12% (just 2 occurrences) over a median follow-up of 12.9 (interquartile range 7.7–19.6) years12. This led the authors to conclude that generalised pouch cancer screening appeared unjustified. However, when investigating rates of neoplasia (dysplasia or cancer) a prior retrospective cohort study of over 3000 IBD-IPAA patients demonstrated cumulative incidences of 0.9%, 1.3%, 1.9%, 4.2%, and 5.1% at 5, 10, 15, 20, and 25 years from pouch formation, respectively13. In addition, a prospective study showed it to be as high as 4.5% after a mean of 8.6 years amongst patients with co-existing dysplasia in their colectomy specimen14.

To investigate how clinicians interpret these conflicting messages Gu et al. carried out a study surveying the self-reported practice patterns of 52 clinicians in academic centres in the US15. They found that the majority (79%) felt that pouch surveillance was indeed necessary, that the combination of pouchoscopy with biopsy was an effective method for detecting neoplasia (69%) and that almost all agreed on taking biopsy samples from the pouch body (92%) and rectal cuff/anal transition zone (ATZ) (86%). However, consensus was less evident regarding the frequency of surveillance, where “great variation” was described with some clinicians favouring annual surveillance and others suggesting that a five-year interval was adequate. Their reported practice also appeared discrepant with regards to whether biopsy samples should be taken from the afferent limb15.

In addition to the sometimes-conflicting advice regarding surveillance for pouch patients, there also exists a lack of performance indicators or quality assurance standards for pouchoscopy procedures. These are now widely accepted for both upper16 and lower17 GI endoscopy, and although expert consensus recommendations exist for performing and reporting pouchoscopy18, these are yet to be formally adopted by national or international societies. Indeed, a recent publication from a joint medico-surgical group from St Mark’s Hospital demonstrated clearly not only that pouchoscopy reports were often suboptimal but also that standardisation using a reporting template can result in a significant improvement19.

It is probable that there exists variation in practice between individual clinicians, specialties, institutions and geographic regions with regards to IPAA surveillance practices. In addition, we hypothesised that endoscopic pouchoscopy practices and reporting would also be variable due to a combination of lack of clear guidance and relative infrequency of these procedures. Some of this variation may not necessarily be captured by the type of aforementioned self-reporting study. We therefore, carried out a retrospective cohort study to investigate the UC-IPAA surveillance practices of IBD clinicians in Amsterdam and at several centres in London.

**MATERIALS & METHODS**

***IBD Centres***

Our study included four IBD centres in London: Guy’s & St. Thomas’ Hospital (GST), St. Mark’s Hospital, University College London Hospital (UCLH) and St. George’s Hospital (SGH). Data was also collected from the Amsterdam University Medical Centre (UMC), Amsterdam Medical Center (AMC).

***Patient Identification***

In centres with pre-existing, electronic pouch databases (AMC and St. Mark’s), these were used to identify potential patients for inclusion. In both cases the databases were produced and maintained prospectively. In centres where such databases were paper-based (GST and SGH), these were converted to electronic format with the addition of information from prospectively maintained medical records. Where no such database existed (UCLH), pouch patients were identified via medical coding and an electronic database was generated, again using information from prospectively maintained medical records.

***Inclusion Criteria***

Patients with confirmed UC or IBD unclassified (IBDU) having undergone RPC with IPAA were included.

***Exclusion Criteria***

Patients with a documented post-surgical follow-up period of less than one year after restoration of intestinal continuity, those followed-up at institutions other than the institution in which their surgery was performed and those who underwent pouch formation for a diagnosis of Crohn’s disease, were excluded.

***Data Collection***

For centres with relatively smaller numbers of eligible UC-IPAA patients (GST, UCLH, SGH) the entire cohort was included, from inception to the time of data collection in June 2016. For centres with large numbers of eligible patients (St Mark’s, AMC), data was collected from a ‘representative’ cohort of 50 consecutive patients, beginning at the earliest surgical date. Thereby, giving the greatest amount of follow-up data. Only pouchoscopies recorded on electronic endoscopy software were included, meaning that ‘on table’ pouchoscopies performed in the operating theatre were not.

***Outcomes of Interest***

Standard demographic information was collected in addition to UC-specific data such as disease extent, concurrent PSC, age at diagnosis and at time of colectomy, as well as the use of biologic treatment prior to surgery. Surgery-related data included the indication for colectomy, pouch configuration, number of surgical stages and interval between stages 2 and 3 (where relevant). A clinical history of pouchitis was considered present when described by the patients supervising clinician in clinical correspondence or medical records.

Data regarding the use of pouchoscopy overall and specifically for the indication of dysplasia surveillance were collected, including time to first pouchoscopy and frequency of procedures. In addition, the specialty of the primary supervising clinical team was also collected (surgical, gastroenterology or joint-care). Data regarding endoscopic practices at pouchoscopy were also collected. This included the documented description and use of endoscopic biopsy sampling of the following three pouch regions: *anal transition zone, pouch body and pre-pouch ileum*. We defined a patient as having undergone a ‘complete’ pouchoscopy if endoscopic findings (normal or abnormal) in *all* three regions had been described in at least one procedure they underwent. In terms of biopsy samples, we considered a patient having had a ‘complete’ set of biopsies if they were taken from the pouch body *and* rectal cuff/ATZ during at least one pouchoscopy they underwent. The finding of dysplasia or neoplasia in histological specimens was collected but other histological findings, such as degree of inflammatory activity, were not uniformly reported and, therefore, were not included in the study.

***Statistical analysis***

Fisher's exact, Pearson’s chi-squared and Wilcoxon signed-rank tests were used to compare sub-groups (GraphPad Prism v7.0a). Continuous data is summarised as medians with ranges in brackets.

**RESULTS**

Our study included a total of 272 patients (258 with UC and 14 with IBDU) with a median duration of pouch follow-up of 10.5 (3.3-23.6) years. The cumulative number of years of pouch follow-up for the entire cohort was 3266. The demographics and disease-related characteristics can be seen in table 2 and details relating to their surgery in table 3. Factors associated with a high risk of neoplasia (previous dysplasia or CRC, or the presence of PSC) 1, 2, 4 were present in 26 patients (10%).

***Use of pouchoscopy***

Of the 272 patients, 95 (35%) did not undergo pouchoscopy for any indication during the follow-up period. Amongst the 177 (65%) who had undergone at least one pouchoscopy, the median number of procedures was 2 (1-11) and the median interval between restoration of GI continuity via a pouch and first pouchoscopy was 1.6 years (0.1-16.2). Amongst the 113 patients who had undergone two or more pouchoscopies, the median interval between scopes was 15 (2-58) months.

Only 81/272 (30%) had undergone pouchoscopy with surveillance as the specific indication, the remainder having not had a dedicated surveillance pouchoscopy. Amongst the 81 patients who had undergone surveillance, the median number of pouchoscopies carried out with surveillance as the specific indication was 1 (1-7).

***Factors associated with surveillance***

We investigated a range of factors that could possibly have influenced the likelihood of surveillance pouchoscopy being carried out. These included: a diagnosis of PSC, documented clinical history of pouchitis, indication for colectomy, duration of disease and duration with pouch as well as the specialty of the supervising clinician. The results of our univariate analysis can be seen in table 4. Patients with a longer UC duration, under the care of a surgeon or with a clinical history of pouchitis appeared significantly more likely to have undergone at least one surveillance pouchoscopy. In addition, patients with PSC and those having undergone colectomy for dysplasia or CRC were also more likely to undergo surveillance. Based on BSG guidance, patients with a history of PSC or dysplasia/CRC would qualify as high-risk, meaning annual pouchoscopy with biopsy should be considered. Based on these criteria, 26 patients in our cohort would be considered high-risk (22 with a history of CRC/dysplasia, 4 PSC, including 5 patients with both). This group had a median pouch duration of 11.2 (7.2-14.6) years. Of the 26 high-risk patients 23 (88%) had undergone at least one pouchoscopy, whilst 3 (12%) had none (one PSC patient with a pouch for 9.9 years, one patient with previous CRC and a pouch for 14.1 years and one patient with previous HGD and a pouch for 18.9 years). 21/26 (81%) had undergone at least one pouchoscopy specifically for surveillance. For the 18 high-risk patients who had undergone more than one pouchoscopy (for any indication), the median interval between pouchoscopies was 23.3 months (12-122).

***Endoscopic practices at pouchoscopy***

We identified a total of 464 pouchoscopy procedures carried out on the 177 patients in our cohort who underwent endoscopic evaluation. The documentation of examination of the various pouch regions (divided into body, ATZ and pre-pouch ileum) can be seen in figure 1 and frequency of use of endoscopic biopsies in figure 2. As would be expected, findings within the pouch body were described in all cases but documentation of the ATZ and particularly the pre-pouch ileum was less frequent. Similarly, biopsies were taken from the body in almost all procedures (90%). However, they were taken from the ATZ in only 32% of procedures and from the pre-pouch ileum in 29%. The overall mean number of biopsies taken from the pouch body was 3.3, rectal cuff/ATZ 0.5 and pre-pouch ileum 0.5.

Based on our definition of ‘completeness of pouchoscopy’ (patient having undergone at least one pouchoscopy describing the anal transition zone, pouch body and pre-pouch ileum), only 65/177 (37%) had undergone a complete pouchoscopy. Based on our definition of ‘completeness of biopsies’ (patient having undergone at least one pouchoscopy with biopsy samples from the pouch body and rectal cuff/ATZ), only 56/177 (32%) had undergone a complete set of biopsies. When considering the 26 high-risk patients, of the 23 who had undergone pouchoscopy, the completeness of procedures was 13/23 (57%) and biopsy sampling was 13/23 (57%).

***Factors associated with completeness of pouchoscopy reporting and the use of endoscopic biopsies***

We analysed factors that we predicted may have influenced completeness of pouchoscopy reporting and biopsy sampling. These included, speciality and level of experience of the endoscopists performing the procedures (table 5). We observed that gastroenterologists were significantly more likely than surgeons to report procedures completely (46% vs 21%, p=0.002) and take a complete set of biopsy samples (40% vs 16%, p=0.001). Trainees/nurses were also found to be more likely to take a complete set of biopsies than consultants/specialists (42% vs 23%, p=0.01).

**Neoplasia found at pouchoscopy**

Two (0.7% of total cohort) cases of cancer were found within the rectal cuff/ATZ. Neither patient had high-risk features and both underwent colectomy for chronic active/medically refractory UC. One patient was aged 60 at the time of cancer diagnosis and had had a pouch for 13 years, the other was 52 and had had a pouch for 3 years. In addition, one case of ‘indefinite dysplasia’ was observed in the pouch body but no other cases of dysplasia were identified in the pouch body, rectal cuff/ATZ or pre-pouch ileum. Both patients with adenocarcinoma of the cuff were treated with chemotherapy. One had local lymph node metastases at the time of diagnosis, subsequently developed distant metastases and died of her cancer. The other case developed an anal mucinous adenocarcinoma and underwent extensive pelvic surgery including to his prostate and bladder in view of local tumour invasion. He received neoadjuvant chemotherapy and had survived for over a year from the time of cancer diagnosis by the time of writing.

**DISCUSSION**

Our results demonstrate wide variation in endoscopic surveillance of UC/IBDU-IPAA patients, even amongst experienced IBD clinicians. Some patients underwent several pouchoscopies for surveillance, whereas others had none. As widely recommended (table 1) where colectomy was carried out for dysplasia/CRC or in patients with PSC, clinicians were significantly more likely to perform surveillance pouchoscopy. The likelihood of patients undergoing surveillance pouchoscopy also appeared to be increased by a longer UC duration, as per independent recommendations (figure 3) as well as by a clinical history of pouchitis and being under follow-up with a surgeon. These results appear to suggest that clinicians are indeed following recommendations regarding pouch surveillance in high-risk groups but perhaps not in others; for example, it would be impossible to know whether a patient had type C mucosal changes without performing pouchoscopy with biopsies which were only taken in 95 patients (35%) in our cohort. In addition, the incidence of pouchoscopy carried out specifically for surveillance was predictably lower at 30% of our cohort. Although pouchitis does not necessarily predict the presence of type C mucosa20 it makes sense that patients with pouchitis would have undergone more frequent pouchoscopies for assessment of inflammatory activity. In addition, it has been demonstrated elsewhere that pouchitis significantly increases the risk of progression from low to high grade dysplasia over the course of 6-8 years (odds ratio, 13.48; 95% confidence interval, 1.48-122.86; p=0.021 for n=276). Nonetheless, as is the case for surveillance endoscopy for the intact colon, the sensitivity of identifying subtle mucosal changes is likely to be impaired by the presence of active inflammation21.

Increasing duration of IBD may also have been expected to increase the likelihood of surveillance as this is one of the key factors determining the need for surveillance in the intact colon21. Although patients with pouches clearly have very little (or no) colonic mucosa remaining, it remains unclear whether surveillance of the cuff (if present) using the standard timelines for patients with long-standing UC and an intact colon is appropriate. This is further complicated by the fact that surveillance in patients with disease limited to the rectum is considered unnecessary by some authorities1, 22.

As may have been predicted based on the lack of clear recommendations regarding management of low risk patients, wide variation in practice was found across the five centres. This becomes even more relevant when considering the facts that low risk patients represented the large majority in this cohort (246, 90%) and, secondly, that both patients who developed neoplasia were in the low risk group (although their type C mucosal status was unknown). Although no gastroenterology societies strongly suggest a formal plan of surveillance in this cohort, other groups have recommended a pouchoscopy with biopsies at one year to help risk stratify patients based on the presence or absence of type C mucosa8. Characterised by persistent atrophy and severe inflammation, type C mucosa has been shown to have a strong positive predictive value for the subsequent development of dysplasia20, 23. In a study by Gullberg et al that included 7 patients with type C and 14 with type A mucosa (no, or only slight, atrophy), the rate of dysplasia formation was 71% in the type C group compared to 0% in the type A group (p<0.001)20. In view of the appreciable rate of neoplasia formation in our cohort (2/272, 0.7%), we believe that routine screening for type C mucosa at one-year post restoration of intestinal continuity, as per the flow diagram shown in figure 3 (adapted from McLaughlin et al8), is worthwhile. Although the broad adoption of such an approach would help to unify practice, it should be noted that no specific pouch surveillance strategy has yet been proved to confer a more favourable outcome or earlier detection of dysplasia. To demonstrate the benefit of an intervention of this type would require a prospective, randomised study with a large number of patients and long-term follow-up, and this type of study appears unlikely to take place. By contrast, there exists relatively clear guidance regarding the surveillance of high-risk patients. It is therefore concerning that 3/26 (12%) of this cohort had never undergone pouchoscopy. It is also noteworthy that endoscopic pouch assessments could be considered incomplete in a significant proportion of patients, with no description of the prepouch ileum or rectal cuff/ATZ being documented. This finding is concerning, especially in the context of surveillance pouchoscopy where careful and comprehensive examination is essential if it is to be of real value in detecting early or subtle changes. However, even for symptomatic patients undergoing pouchoscopy to confirm endoscopic evidence of pouchitis, findings in the pre-pouch ileum and rectal cuff/ATZ should still be documented, as inflammation in these regions is associated with worse outcomes and requires different management to pouchitis in isolation24-26.

It has been demonstrated elsewhere that lesion detection at the ATZ is positively associated with the degree of endoscopic experience of the operator27. Our results did not demonstrate a difference between consultants/specialists and trainees/nurses in terms of reporting completeness and, in fact, the latter were more likely to take a complete set of biopsies. We also observed that gastroenterologists were more likely to produce complete pouchoscopy reports and more likely to take a complete biopsy set than surgeons. The relative low frequency of pouchoscopy procedures may also have led to technical issues which could impact on completeness. For example, despite evidence suggesting it may improve lesion detection rates28, some endoscopists may be uncomfortable with performing retroflexion in a pouch for fear of causing trauma. This manoeuvre is also more difficult to perform when using an adult colonoscope (rather than an upper GI or paediatric scope) and, although not formally collected in our cohort, the use of colonoscopes for at least some cases seems likely based on other studies15. Whatever the reason, these findings highlight the need for performance indicators and/or quality assurance standards to be defined and implemented for pouchoscopy, as has been the case for other endoscopic procedures. Quality of reporting (and presumably assessments) has previously been demonstrated to be enhanced by the introduction of a pouchoscopy reporting template and this low-cost and relatively straight-forward intervention is therefore recommended19. In addition, concentrating pouchoscopies on dedicated endoscopy lists with experienced, IBD-interested endoscopists, and perhaps even centralisation of pouch care at specialist centres (as has been recommended for other conditions requiring specific endoscopic assessment, e.g. Barrett’s oesophagus29) may also be beneficial.

Our study has several strengths including a relatively large cohort which has been carefully phenotyped collected from several centres spanning two countries. It gives a historic perspective with assessments going back over 2 decades and encompasses a total of over 3266 years of pouch follow up. It is also likely to reflect practice patterns regarding attitudes to surveillance and endoscopic practices more accurately than previous studies which have relied upon self-reporting15. However, it also has several limitations including, most notably, its retrospective nature and the potential for biases (e.g. selection and misclassification) which are inherent in this study design. It is also limited by the potential for missing data, such as pouchoscopies carried out at centres other than those involved in the study, which would not have been included in our analysis. In the larger datasets (AMC and St Mark’s) we studied a ‘representative’ consecutive 50 patients beginning from the earliest in their cohorts; whilst this maximised data for analysis, it may have skewed data if practices at those particular centres had changed significantly over time for any reason. And although consistent eligibility criteria were used across all centres, this type of sampling clearly has the potential to introduce selection bias. Nonetheless, it was not considered feasible to review the larger cohorts in their entirety given the resources available for this type of study. Potentially important confounding factors such as smoking, mucosectomy at the time of pouch formation and the presence of type C histological changes, were not included due to inconsistencies in reporting. However, mucosectomy does not appear to significantly influence cancer rates30 and we attempted to use pouchitis as proxy for type C mucosa (although the two entities are clearly different, with relatively few pouchitis sufferers actually going on to develop type C changes20). Due to the retrospective nature of the study, we were unable to further sub-divide pouchitis phenotypes (e.g. antibiotic-responsive/dependent/refractory or Crohn’s-like), so were unable to assess whether this has any influence on outcomes. Finally, we have attributed incompleteness of endoscopic assessments based on reporting of the procedures when it is likely that, at least some cases, we are identifying incomplete reporting rather than incomplete examination. However, even if this is the case, it is worthy of note as incomplete reporting in standard upper and lower GI endoscopy is no longer considered acceptable16, 17, a fact which should also apply to pouchoscopy.

In conclusion, our retrospective cohort study has demonstrated wide variation in the endoscopic surveillance of UC/IBDU-IPAA patients. In addition, the demonstrated rate of neoplasia formation amongst low risk patients was higher than may have been expected. We would therefore concur with previous recommendations suggesting that this group should undergo pouchoscopy with biopsy at one year for further risk stratification8. Where possible, pouchoscopy should be carried out by an IBD-interested endoscopist, at which time findings in all regions of the pouch (body, pre-pouch ileum and rectal cuff/ATZ) should be documented and biopsies taken.

**REFERENCE**

1. Cairns SR, Scholefield JH, Steele RJ, et al. Guidelines for colorectal cancer screening and surveillance in moderate and high risk groups (update from 2002). Gut 2010;59:666-89.

2. Annese V, Beaugerie L, Egan L, et al. European Evidence-based Consensus: Inflammatory Bowel Disease and Malignancies. J Crohns Colitis 2015;9:945-65.

3. Farraye FA, Odze RD, Eaden J, et al. AGA technical review on the diagnosis and management of colorectal neoplasia in inflammatory bowel disease. Gastroenterology 2010;138:746-74, 774 e1-4; quiz e12-3.

4. American Society for Gastrointestinal Endoscopy Standards of Practice C, Shergill AK, Lightdale JR, et al. The role of endoscopy in inflammatory bowel disease. Gastrointest Endosc 2015;81:1101-21 e1-13.

5. Ananthakrishnan AN, Cagan A, Cai T, et al. Colonoscopy is associated with a reduced risk for colon cancer and mortality in patients with inflammatory bowel diseases. Clin Gastroenterol Hepatol 2015;13:322-329 e1.

6. Lutgens MW, Oldenburg B, Siersema PD, et al. Colonoscopic surveillance improves survival after colorectal cancer diagnosis in inflammatory bowel disease. Br J Cancer 2009;101:1671-5.

7. Derikx LA, Nissen LH, Oldenburg B, et al. Controversies in Pouch Surveillance for Patients with Inflammatory Bowel Disease. J Crohns Colitis 2016;10:747-51.

8. McLaughlin SD, Clark SK, Tekkis PP, et al. Review article: restorative proctocolectomy, indications, management of complications and follow-up--a guide for gastroenterologists. Aliment Pharmacol Ther 2008;27:895-909.

9. Zhu H, Wu XR, Queener E, et al. Clinical value of surveillance pouchoscopy in asymptomatic ileal pouch patients with underlying inflammatory bowel disease. Surg Endosc 2013;27:4325-32.

10. Herline AJ, Meisinger LL, Rusin LC, et al. Is routine pouch surveillance for dysplasia indicated for ileoanal pouches? Dis Colon Rectum 2003;46:156-9.

11. Nilubol N, Scherl E, Bub DS, et al. Mucosal dysplasia in ileal pelvic pouches after restorative proctocolectomy. Dis Colon Rectum 2007;50:825-31.

12. Mark-Christensen A, Erichsen R, Brandsborg S, et al. Long-term Risk of Cancer Following Ileal Pouch-anal Anastomosis for Ulcerative Colitis. J Crohns Colitis 2017.

13. Kariv R, Remzi FH, Lian L, et al. Preoperative colorectal neoplasia increases risk for pouch neoplasia in patients with restorative proctocolectomy. Gastroenterology 2010;139:806-12, 812 e1-2.

14. Kuiper T, Vlug MS, van den Broek FJ, et al. The prevalence of dysplasia in the ileoanal pouch following restorative proctocolectomy for ulcerative colitis with associated dysplasia. Colorectal Dis 2012;14:469-73.

15. Gu J, Remzi FH, Lian L, et al. Practice pattern of ileal pouch surveillance in academic medical centers in the United States. Gastroenterol Rep (Oxf) 2016;4:119-24.

16. Beg S, Ragunath K, Wyman A, et al. Quality standards in upper gastrointestinal endoscopy: a position statement of the British Society of Gastroenterology (BSG) and Association of Upper Gastrointestinal Surgeons of Great Britain and Ireland (AUGIS). Gut 2017;66:1886-1899.

17. Rees CJ, Thomas Gibson S, Rutter MD, et al. UK key performance indicators and quality assurance standards for colonoscopy. Gut 2016;65:1923-1929.

18. Devlin SM, Melmed GY, Irving PM, et al. Recommendations for Quality Colonoscopy Reporting for Patients with Inflammatory Bowel Disease: Results from a RAND Appropriateness Panel. Inflamm Bowel Dis 2016;22:1418-24.

19. van der Ploeg VA, Maeda Y, Faiz OD, et al. Standardising assessment and documentation of pouchoscopy. Frontline Gastroenterology 2018.

20. Gullberg K, Stahlberg D, Liljeqvist L, et al. Neoplastic transformation of the pelvic pouch mucosa in patients with ulcerative colitis. Gastroenterology 1997;112:1487-92.

21. Mowat C, Cole A, Windsor A, et al. Guidelines for the management of inflammatory bowel disease in adults. Gut 2011;60:571-607.

22. Eaden JA, Mayberry JF, British Society for G, et al. Guidelines for screening and surveillance of asymptomatic colorectal cancer in patients with inflammatory bowel disease. Gut 2002;51 Suppl 5:V10-2.

23. Thompson-Fawcett MW, Marcus V, Redston M, et al. Risk of dysplasia in long-term ileal pouches and pouches with chronic pouchitis. Gastroenterology 2001;121:275-81.

24. Samaan MA, de Jong D, Sahami S, et al. Incidence and Severity of Prepouch Ileitis: A Distinct Disease Entity or a Manifestation of Refractory Pouchitis? Inflamm Bowel Dis 2016;22:662-8.

25. Pardi DS, D'Haens G, Shen B, et al. Clinical guidelines for the management of pouchitis. Inflamm Bowel Dis 2009;15:1424-31.

26. Segal JP, McLaughlin SD, Faiz OD, et al. Incidence and Long-term Implications of Prepouch Ileitis: An Observational Study. Dis Colon Rectum 2018;61:472-475.

27. Lan B, Kalady M, Remzi F, et al. Missing the boat: Underestimating the incidence of ATZ neoplasia after IPAA in patients with familial adenomatous polyposis. Annual Meeting of the American Society of Colon and Rectal Surgeons, ACSRS. Los Angeles, CA United States, 2016.

28. Man RFS, Fraser C, Saunders BP. Retroflexion in flexible pouchoscopy can increase adenoma detection in patients with familial adenomatous polyposis after restorative proctocolectomy. Gut 2006;55:A68-A69.

29. Weusten B, Bisschops R, Coron E, et al. Endoscopic management of Barrett's esophagus: European Society of Gastrointestinal Endoscopy (ESGE) Position Statement. Endoscopy 2017;49:191-198.

30. Selvaggi F, Pellino G, Canonico S, et al. Systematic review of cuff and pouch cancer in patients with ileal pelvic pouch for ulcerative colitis. Inflamm Bowel Dis 2014;20:1296-308.

**FIGURE LEGENDS**

**TABLES**

Table 1. Overview of pouch surveillance guidelines. AGA, American Gastroenterology Association; BSG, British Society of Gastroenterology; ASGE, American Society for Gastrointestinal Endoscopy; ECCO, European Crohn’s and Colitis Organisation (adapted from Derikx et al7)

\*Type C pouch mucosa is defined as exhibiting permanent persistent atrophy and severe inflammation

Table 2. Demographic and UC/IBDU disease related characteristics

Table 3. Surgical details

Table 4. Univariate analysis of factors associated with surveillance pouchoscopy

Table 5. Factors associated with completeness of pouchoscopy reporting and the use of endoscopic biopsies.

\*169 patients for whom all procedures were undertaken by a single specialty (an additional 8 underwent procedures under both specialties)

\*\*169 patients for whom all procedures were undertaken by an endoscopist of a single level of training

**FIGURES**

Figure 1. Rates of documentation of each individual pouch region on at least one occasion for the 177 patients who underwent pouchoscopy

Figure 2. Rates of biopsy sampling of each individual pouch region on at least one occasion for the 177 patients who underwent pouchoscopy

Figure 3. Suggested surveillance protocol (adapted from McLaughlin at al8)

**TABLES**

Table 1.Overview of pouch surveillance guidelines. AGA, American Gastroenterology Association; BSG, British Society of Gastroenterology; ASGE, American Society for Gastrointestinal Endoscopy; ECCO, European Crohn’s and Colitis Organisation

\*Type C pouch mucosa is defined as exhibiting permanent persistent atrophy and severe inflammation

|  |  |  |  |
| --- | --- | --- | --- |
| Guideline | Year of publication | Risk stratification | Surveillance strategy |
| Yes/No | Risk categories |
| AGA3 | 2010 | N/A | N/A | No recommendations |
| BSG1 | 2010 | Yes | **High risk:**- Previous rectal dysplasia- Dysplasia/cancer at the time of pouch surgery - Primary sclerosing cholangitis- Type C pouch mucosa\* | Yearly |
| **Low risk:**- Absence of high risk factors  | 5-yearly |
| ASGE4 | 2015 | Yes | **Highest risk:**- History of dysplasia or cancer.  | Yearly surveillance should be considered |
| **High risk:** - Primary sclerosing cholangitis - Type C pouch mucosaa- Refractory pouchitis  | Yearly surveillance may be considered |
| **Other patients**  | No recommendations |
| ECCO2 | 2015 | Yes | **High risk:**- Dysplasia/cancer at the time of pouch surgery - Primary sclerosing cholangitis- Type C pouch mucosa\*- Unremitting pouchitis  | Yearly |
| **Absence of high risk factors**  | No evidence that supports routine surveillance |

Table 2. Demographic and UC/IBDU disease related characteristics

|  |  |
| --- | --- |
| Characteristic | Number |
| Number of patients | 272 |
| Gender, male:female | 153:119 (56%:44%) |
| Mean age (±SD), years | 46 (± 14.5) |
| IBD phenotype |  |
| *UC* | 258 (95%) |
| *IBDU* | 14 (5%) |
| Disease extent |  |
| *Proctitis* | 12 (4%) |
| *Left-sided colitis* | 40 (15%) |
| *Extensive colitis* | 199 (73%) |
| *Unknown* | 20 (7%) |
| PSC |  |
| *Present* | 9 (3%) |
| *Absent* | 263 (97%) |

Table 3. Surgical details

|  |  |
| --- | --- |
| Characteristic | Number |
| Number of patients | 272 |
| Indication for colectomy |  |
| *Acute severe UC* | 87 (32%) |
| *Chronic active UC* | 157 (58%) |
| *Colorectal Cancer* | 9 (3%) |
| *High-grade dysplasia* | 11 (4%) |
| *Low-grade dysplasia* | 3 (1%) |
| *Unknown* | 5 (2%) |
| Mean duration of IBD prior to colectomy (n=238) | 10.9 (± 12.6) |
| Mean age at time of colectomy (±SD), years | 35.0 (± 13.8) |
| Mean duration since completion of pouch surgery and restoration of GI continuity (±SD), years | 11.6 (± 5.3) |
| Number of surgical stages for pouch surgery |  |
| *One* | 16 (6%) |
| *Two* | 92 (34%) |
| *Three* | 164 (60%) |
| Pouch configuration |  |
| *J-pouch* | 144 (53%) |
| *S-pouch* | 24 (9%) |
| *W-pouch* | 3 (1%) |
| *Unknown* | 101 (37%) |
| Clinical history of pouchitis  |  |
| *Present* | 111 (41%) |
| *Absent* | 161 (59%) |

Table 4. Univariate analysis of factors associated with surveillance pouchoscopy

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
|  |  | Patients having undergone at least one pouchoscopy with surveillance as stated indication (n=81) | Patients having undergone no pouchoscopy with surveillance as stated indication (n=191) | p-value |
| **Department supervising care**‡ | Gastroenterology | 13 (16%) | 40 (39%) | 0.0323\* |
| Surgery | 43 (53%) | 75 (21%) |
| Joint care | 25 (31%) | 31 (16%) |
| Unknown | 0 (0%) | 45 (24%) |
| **Median IBD disease duration, years**† (n=239) | 18 | 14 | <0.0001\* |
| **Duration elapsed since completion of pouch surgery, median (years)***†* | 10 | 11 | <0.0001\* |
| **Previous clinical history of pouchitis**‡ | Present | 47 (58%) | 64 (34%) | 0.0002\* |
| Absent | 34 (42%) | 127 (66%) |
| **Primary sclerosing cholangitis**‡ | Present | 8 (10%) | 1 (1%) | <0.0001\* |
| Absent | 73 (90%) | 190 (99%) |
| **Indication for colectomy**‡ | Acute severe UC | 26 (32%) | 61 (32%) |  |
| Chronic active UC | 36 (44%) | 121 (63%) |  |
| Colorectal Cancer | 8 (10%) | 1 (1%) | <0.0001\* |
| HGD | 8 (10%) | 3 (2%) |  |
| LGD | 0 (0%) | 3 (2%) |  |
| Unknown | 3 (4%) | 2 (1%) |  |

Table 5. Factors associated with completeness of pouchoscopy reporting and the use of endoscopic biopsies

\*169 patients for whom all procedures were undertaken by a single specialty (an additional 8 underwent procedures under both specialties)

\*\*169 patients for whom all procedures were undertaken by an endoscopist of a single level of training

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
|  |  | Complete pouchoscopy reported on at least one occasion | Complete pouchoscopy *never* reported | p-value | Pouchoscopy with biopsies taken from body and rectal cuff/ATZ on at least one occasion | No pouchoscopy with biopsies taken from body and rectal cuff/ATZ | p-value |
| Endoscopist specialty\*(n=169) | Gastroenterology | 48 (46%) | 57 (54%) | 0.002\* | 42 (40%) | 63 (60%) | 0.001\* |
| Surgery | 14 (22%) | 50 (78%) | 10 (16%) | 54 (84%) |
| Level of training\*\*(n=169) | Specialist/Consultant | 37 (36%) | 65 (64%) | >0.9 | 23 (23%) | 79 (77%) | 0.01\* |
| Trainee/Nurse Endoscopists | 25 (37%) | 42 (63%) | 28 (42%) | 39 (58%) |