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## Continence



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# Implications of Inflammatory Bowel Disease for reconstructive surgery in non-malignant urinary tract dysfunction: An International Continence Society working group report



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## ABSTRACT

**Introduction:** Potential consequences of inflammatory bowel disease (IBD) need evaluation for patients considering urinary tract reconstruction for benign disease. A working group was formed by the International Continence Society, which considered urinary tract reconstruction in IBD.

**Methods:** Nominal group technique was used to derive consensus. Principal aspects of IBD assessment and surgery decision-making were agreed. A questionnaire was used to facilitate the generation of statements by a core focus group of experts, which were modified and ratified by the wider working group. This was followed by final voting by the full working group.

**Results:** General considerations included identifying the importance of the specialist IBD multi-disciplinary team. Peri-operative considerations recommended avoiding pre-operative fasting from midnight, and using an enhanced recovery after surgery (ERAS) protocol. Selection of bowel segment, pre-operative optimisation and post-operative issues were considered for both Ulcerative colitis (UC) and Crohn's disease. UC is not an absolute contraindication to urinary tract reconstruction using small or large bowel. Elective reconstructive surgery should wait at least three months following resolution of any acute UC flare-up to correct all abnormalities. Crohn's disease is a high-risk disease for urinary tract reconstruction, even if in remission. In Crohn's, reconstructive surgical options are limited by the location and extent of gastrointestinal segment(s) affected and the phenotype of disease.

**Conclusion:** The consensus opinion indicates that urinary tract reconstruction using bowel segments is feasible in carefully selected and optimised patients with IBD lacking alternative management options, provided there is access to appropriate multidisciplinary skills. UC is relatively low risk for surgical procedures, whereas Crohn's has considerably increased risk of morbidity. The potential risks must be properly discussed with patients considering reconstructive urological procedures. Outcomes should be carefully monitored and published to identify the safety and efficacy of reconstructive surgery in IBD, including full description of the disease status.

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## 1. Introduction

Urinary diversion and urinary tract reconstruction often employ bowel isolated on a vascular pedicle to augment the bladder, create a new urinary reservoir or conduit, act as a continent catheterisable channel, or an interposition chute for ureteric reconstruction. Such surgery requires the ability to safely harvest a segment of healthy bowel to help achieve good surgical outcomes for the urinary tract reconstruction and ensure effective gastrointestinal healing without compromising bowel function.

Although there is literature available on the sequelae of lower urinary tract reconstruction using bowel, the potential consequences of pre-existing bowel disease or dysfunction also need to be considered. There are many complications that can occur following urinary tract reconstruction using bowel [1], including infection, anastomotic leaks, bowel obstruction, metabolic disturbance, change in bowel habit, renal impairment, stricture formation, urolithiasis and malignancy. Risks may be exacerbated if the patient has pre-existing bowel disease, such as inflammatory bowel disease (IBD), notably ulcerative colitis (UC) and Crohn's disease. Crohn's disease, in particular, is associated with post-operative intra-abdominal septic complications related to anastomotic breakdown, especially in patients with low serum albumin, re-operative surgery and steroid use [2]. Appropriate patient selection and post-operative medical treatment and follow-up are therefore pertinent to any bowel surgery in such patients [3]. Due to the relatively high risk of post-operative complications, patients must undergo a thorough assessment beforehand and must be fully optimised, addressing areas specifically related to peri- and post-operative morbidity, such as malnutrition, active inflammation and immunosuppression [4]. UC is not considered as high risk for surgery, but outcomes after elective surgery are variably defined [5]. Nonetheless, appropriate precautions must be taken in patients with this condition, as there is still a recognised risk of morbidity [6].

Concerns that the underlying bowel disease may affect the outcomes when used for urinary tract reconstruction further compound the challenges of such procedures [7]. The high rate of complications from surgery in IBD, and the uncertain implications for the reconstruction, necessitate caution. Accordingly, a working group was set up under the auspices of the International Continence Society (ICS) to develop recommendations regarding the safe use of bowel for urinary reconstruction in adult patients with IBD.

## 2. Methods

A working group was formed by open advertisement to members of the International Continence Society (ICS), European Society of Coloproctology (ESCP) and the American Society of Colon and Rectal Surgeons (ASCRS) with the remit of developing consensus documents on the use of bowel in disease states for urinary tract reconstruction. Detailed literature searches were conducted using Ovid MEDLINE and PubMed databases from inception until December 2021.

A core focus group of experts in the fields of IBD and urinary tract reconstruction was assembled from this working group. The working group considered the use of bowel for urinary tract reconstruction in patients with IBD under the subheadings of 'General considerations' and 'Peri-operative considerations' for all patients with IBD and then specifically 'Pre-operative' and 'Post-operative considerations' for Ulcerative Colitis and Crohn's disease individually.

The nominal group technique (NGT), a semi-quantitative structured interview procedure [8,9], was used to identify the principal aspects of IBD assessment and surgery decision-making, and for prioritisation to achieve consensus on urinary tract reconstruction. In order to facilitate the generation of the initial statements, a questionnaire was drawn up under the headings: General Considerations, Pre-operative, Intra-operative and Post-operative (supplementary material). Online meetings were structured to include: 1. Introduction and explanation, 2. Silent generation of ideas (as individuals), 3. Sharing ideas (round-robin format), until saturation of concepts, 4. Group discussion, 5. Ranking. This process enabled generation of an initial series of statements, which were revised on serial rounds of review by the focus group. It was followed by ratification by the wider working group and final voting by the sub-specialist expert focus group and working group (Fig. 1). All members of the working group and focus group voted and agreed on the final statements. In total the consensus statements underwent nine rounds of discussion.

#### 3. Results

#### 3.1. General considerations in IBD

3.1.1 All patients must be discussed with a specialist IBD multidisciplinary team (MDT) to provide an assessment on the feasibility of surgery and on the segment and length of bowel that can be harvested, whilst weighing up the risk of current or future problems pertaining to risk of progression and likelihood of short bowel syndrome.

The MDT should ideally include a team of colorectal surgeons and gastroenterology physicians. Input from dietetics, radiologists, specialist nurses and pathologists may also be required. This MDT discussion is in addition to the specialist urology MDT discussion, which also involves continence nurses and pelvic floor physiotherapists.

3.1.2 A plan from the IBD MDT should be sought pre-operatively regarding medical therapy and may require re-discussion should the clinical course change in the post-operative setting.

3.1.3 Anyone with a history of complex peri-anal disease or fistulae, arthropathy, ankylosing spondylitis or a family history of Crohn's disease should be referred for a review by a gastroenterologist or colorectal surgeon with a special interest in Crohn's disease to exclude the possibility of undiagnosed Crohn's disease prior to use of bowel in urinary tract reconstruction.

Features suggestive of Ankylosing Spondylitis include a history of lower back pain and stiffness, typically worse after recumbency with a hallmark 'stooped' posture.

## 3.2. Peri-operative considerations in IBD

3.2.1 In IBD, pre-operative overnight fasting should be avoided and an enhanced recovery after surgery (ERAS) protocol should be used instead.

Prolonged pre-operative fasting can exacerbate an insulin resistant state resulting in increased morbidity in the peri-operative period. Following the recommendations of the ERAS protocol, solid food should not be consumed beyond 6 h pre-surgery. However, clear fluids are permitted up to 2 h presurgery [10]. Carbohydrate loading drinks can also be administered at 2 h pre-surgery to further minimise the morbidity associated with this transient insulin resistant state, resulting in a quicker post-operative recovery [11].

3.2.2 In IBD, bowel preparation products should not be routinely administered pre-operatively, as per the ERAS protocol. They can be considered in select cases, such as when performing a colonic conduit or colonic augmentation cystoplasty.

The role of pre-operative mechanical bowel preparation (MBP) remains controversial. There is limited evidence to support the role of MBP reducing complications in patients undergoing cystectomy and ileal conduit or ileal neobladder urinary diversion [12,13]. The concern is that it can impact electrolyte haemostasis and bowel motility.

As there is some emerging evidence to support the role of MBP (coupled with oral antibiotics) in elective colorectal surgery, the working group have recommended that MBP can be considered in select cases using colonic reconstruction.

A full colon can also pose a challenge during major pelvic surgery. Hence, MBP can be considered in select cases, e.g. patients with congenital anomalies and more challenging anatomy.

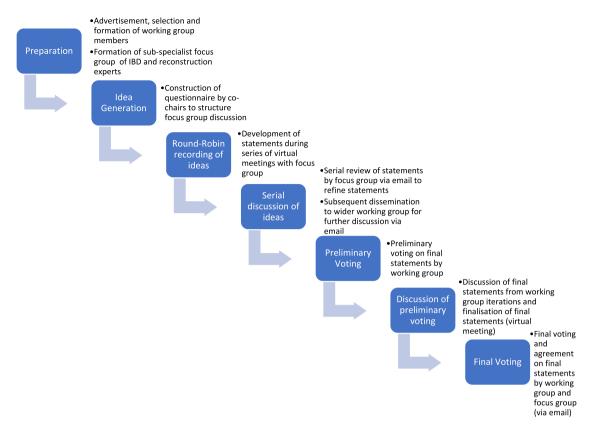


Fig. 1. Process for generation of consensus statement.

3.2.3 Nasogastric tubes may be used intra-operatively in IBD, but should be removed at the end of the case, unless at high risk of post-operative ileus.

Recent evidence suggests that routine nasogastric tube insertion does not significantly reduce the risk of peri-operative morbidity but instead can result in delayed gut recovery.

The working group recommend that nasogastric tubes should be left in situ in patients with an increased risk of post-operative ileus to minimise risk of pulmonary aspiration and pneumonia. Risk factors for postoperative ileus include those with a prior history of delay in resolution of gut function, polypharmacy including anti-cholinergics and opiates, pre-existing electrolyte abnormalities and obesity.

## 3.3. Ulcerative colitis

## 3.3.1 Disease specific pre-operative considerations in UC

3.3.1.1 Ulcerative colitis is not an absolute contraindication to urinary tract reconstruction using small or large bowel.

Urinary tract reconstruction using bowel can be performed in patients with UC, but must only be performed when the disease is in a stable state, preferentially utilising ileum.

3.3.1.2 Ulcerative colitis is considered to be a low-risk disease in those due to undergo urinary tract reconstruction using bowel, provided the disease is in remission.

The overall morbidity in patients with stable disease is thought to be low, especially when compared to those with Crohn's disease.

3.3.1.3 Ulcerative colitis can be a progressive disease. The disease is often contiguous from the rectum, extending to a variable extent proximally, and can result in pan-colitis. There are, however, different phenotypes, and there may be sparing of the rectum in rare cases.

This highlights the importance of a specialist assessment by the colorectal and/or gastroenterology specialists to assess which segment of bowel can be safely harvested.

3.3.1.4 An acute UC flare is an absolute contraindication to any urinary tract reconstructive procedure using bowel. All elective reconstructive surgery should be performed after a minimum of three months following resolution of the acute flare, to allow for correction of all abnormalities, including protein and electrolyte deficiencies, and appropriate weaning of steroids.

A specialist colorectal or gastroenterology opinion is advisable to confirm if the patient is fit to proceed with elective bowel surgery.

## 3.2.2 Selection of UC bowel segment

3.3.2.1 Ileum is the preferred choice for bowel harvest, as it is rarely affected by ulcerative colitis. However, backwash ileitis can be seen in rare cases. When using ileum for reconstruction, the length harvested should be kept to the minimum required and should be proximal to the terminal ileum. This allows for the possibility that the patient may later require a total colectomy and ileal pouch-anal anastomosis if they were to develop advanced pan-colitis.

Ileum should be harvested ideally >30 cm proximal to the ileo-caecal valve, to reduce the risk of bile acid malabsorption and subsequent diarrhoea.

Although it is generally safe to use ileum in patients with UC, a specialist assessment is still mandatory, as there is a risk of backwash ileitis which may contraindicate use of ileum. Patients with advanced UC may end up requiring a total colectomy and accordingly may be more heavily reliant on their small bowel function, again re-iterating the importance of a specialist assessment.

3.3.2.2 Using colonic segments in UC is a relative contraindication and should be avoided whenever possible. Previous colonoscopic evidence of pan-colitis is a contraindication to using colon, unless limited small bowel is available and colonic disease has been quiescent for a prolonged period of time.

There is no specified time frame for which the disease must remain quiescent. We recommend at least one year as a guide to the minimum suitable period of disease quiescence. 3.3.2.3 Reconstruction using colonic segments can be performed in select cases with isolated proctitis as the only manifestation of UC. The small bowel should be preserved in case a pan-proctocolectomy becomes necessary.

3.3.2.4 In the rare circumstances of using colon in patients with isolated proctitis, patients must be counselled of the risk of disease progression affecting the colonic segment utilised for reconstruction, whereby they may require further medical therapy with or without the need for additional surgery. A full colonoscopy should be performed within three months prior to the surgery to identify disease activity and extent of involvement.

The use of colonic segments should always be ratified after discussion with a specialist IBD MDT and only used in the absence of a viable alternative.

## 3.3.3 Pre-operative optimisation in UC

3.3.3.1 Concurrent steroid use is an absolute contraindication to elective reconstructive surgery, due to an increased risk of poor tissue healing. Steroids should be stopped at least six weeks prior to proceeding with reconstructive surgery.

This is particularly relevant to patients that are on 20mg once daily Prednisolone (or equivalent) for more than six months [6].

A plan from the IBD MDT should be sought pre-operatively regarding medical therapy and may require re-discussion should the clinical course change in the post-operative setting.

3.3.3.2 Biologics (e.g. anti-TNF-alpha drugs Infliximab and Adalimumab) and most immune modulators (e.g. Methotrexate and Azathioprine) can be continued pre-, intra- and post-operatively at their normal dose.

A plan from the IBD MDT should be sought pre-operatively regarding medical therapy and may require re-discussion should the clinical course change in the post-operative setting.

3.3.3.3 In addition to the pre-operative correction of any underlying electrolyte abnormalities, anaemia, diabetic control and renal insufficiency, patients should be strongly encouraged regarding smoking cessation, and referred to available smoking cessation support services if necessary.

3.3.3.4 A nutritional assessment should always be conducted. Dietetic input must be sought pre-operatively in patients with extremes of BMI or a recent history of rapid weight loss or weight gain.

The validated Malnutrition Universal Screening Tool (MUST; https:// www.bapen.org.uk/pdfs/must/must\_full.pdf) can be used to help identify malnutrition. However if there is any concern, an expert opinion should be obtained.

## 3.3.4 Post-operative complications in UC

3.3.4.1 Abdominal wall hernias are more common in patients with a history of prolonged steroid use and those deconditioned pre-operatively. Accordingly, efforts must be made to discontinue steroids and improve muscle mass pre-operatively through early involvement of physiotherapists.

3.3.4.2 There is an increased risk of adhesions and subsequent adhesional bowel obstruction in those with a history of previous extensive colonic disease and/or prior surgery.

3.3.4.3 UC with concomitant primary sclerosing cholangitis suggests an aggressive form of disease. These patients may be at higher risk of anastomotic complications (i.e. anastomotic leak).

These patients should be counselled accordingly and fully optimised before embarking on any elective surgery. All reasonable alternatives should be explored first.

3.3.4 The risk of anastomotic complications can be modest, providing a disease-free segment has been harvested and the patient is not on concomitant steroid treatment. The presence of renal failure or liver derangement can increase the risk of anastomotic breakdown and therefore requires specialist input and optimisation pre-operatively. This risk is considerably higher in patients requiring dialysis. It is important to note that both renal impairment (usually defined as a GFR  $<30mL/min/1.73m^2$ ) and hepatic dysfunction are contraindications to performing urinary tract reconstruction using bowel [14].

3.3.4.5 The presence of bowel in a reconstructed urinary tract will often result in mucus production. Excessive mucus production can occur when larger segments of bowel are harvested or when actively diseased bowel segments are used. In those with excessive mucus production and inadequate bladder emptying, there is a resultant increased risk of infection, stones and pyocystis.

A specialist assessment as part of the surgical planning can help to mitigate this risk. If patients are using clean intermittent self-catheterisation (ISC), the ISC regimen (e.g. number of catheterisations, type of catheter) may need to be reviewed to cope with mucus production and poor bladder emptying, and minimise risk of complications such as rupture of the reconstructed bladder.

3.3.4.6 The incidence and severity of urinary tract infections may be exacerbated by the concurrent use of immunosuppressive treatment.

3.3.4.7 Patients must be counselled about the increased risk of post-operative morbidity and sepsis whilst taking any form of immunosuppressive therapy. Clinicians must have a low threshold for suspecting sepsis in these patients.

3.3.4.8 Trimethoprim should be avoided for the treatment of UTIs in patients on Methotrexate, due to significantly increased risk of myelosuppression and nephrotoxicity.

3.3.5Post-operative follow-up and management in UC

3.3.5.1 Patients with UC are often hypercoagulable. Although there is limited evidence in the literature, we recommend that UC patients undergoing major pelvic surgery should be given extended pharmacological thromboprophylaxis (e.g. low molecular weight heparin for 28 days post-operatively), provided there are no contraindications.

Due to limited evidence, the working group recommend venous thromboembolism prophylaxis to reflect the practice of pelvic oncological surgery.

3.3.5.2 Bile acid malabsorption can occur in patients who have undergone terminal ileum resection. Hence, those with significant bowel disturbance after surgery need gastroenterology input. Due to this risk, it is recommended to retain the terminal ileum in continuity with the gastrointestinal tract where possible.

Bile salt diarrhoea becomes increasingly likely for longer extents of terminal ileum harvesting. Fat malabsorption is likely to be encountered additionally when more than 100 cm is harvested.

3.3.5.3 All patients with diarrhoea persisting for more than six weeks following their procedure should be referred for a gastroenterology review, with a view to commencing therapy.

This is often treated with bile acid sequestrants (e.g. cholestyramine) but is best managed by the gastroenterologists.

3.3.5.4 Vitamin B12 deficiency is also common following terminal ileum resection. B12 should be monitored with annual blood tests and replaced as necessary. Terminal ileum should be spared in any reconstructive surgery where possible. Follow-up should be lifelong, as it can take several years for this to become evident.

Management needs to recognise the importance of early identification of vitamin deficiency to prevent serious complications, notably anaemia or neurological problems, and should be undertaken in accordance with applicable guidance, e.g. [15]. For those with no neurological involvement, 1mg intramuscular hydroxcobalamin is required three times a week for two weeks. This is usually continued every two to three months for life but specialist haematology input should be sought [15]. If neurological involvement is evident, urgent specialist advice from a haematologist is needed.

3.3.5.5 Folate should be monitored and replaced as necessary in those who have had extensive small bowel resection.

Management needs to recognise the importance of identifying vitamin deficiency to prevent serious complications, notably pancytopenia and megaloblastic anaemia in severe folate deficiency. Treatment should be undertaken in accordance with applicable guidance, e.g. [15]. Patients should be prescribed 5mg oral folic acid once daily and will often require this lifelong. Dietary advice can also be given and a specialist haematology opinion should be sought [15].

3.3.5.6 A mild, subclinical hyperchloraemic metabolic acidosis is encountered in almost all patients undergoing urinary diversion using bowel segments. Monitoring of bicarbonate and chloride is recommended when there are concerns about clinical metabolic acidosis (e.g. those with resorptive bone disease).

3.3.5.7 Although there is an increased risk of colorectal adenocarcinoma with UC, robust evidence is lacking to support mandatory surveillance following reconstructive surgery. We therefore recommend following local unit surveillance policies pertaining to method of urinary reconstruction, pending further research. Nonetheless, all patients must be counselled about the importance of seeking urgent medical advice if they were to develop any red flag symptoms.

There is no clear consensus on the frequency and duration of surveillance following urinary tract reconstruction with bowel but it is recommended due to the small risk of developing adenocarcinoma. Common surveillance protocols involve lifelong annual cystoscopic surveillance of the reconstructed bladder after 10 years [15] but earlier cystoscopy should be performed in the presence of any red flag symptoms, such as haematuria or recurrent urinary tract infections.

All patients with UC should undergo specialist investigation to determine the extent of their disease. This would also provide the opportunity to exclude any overt malignancy prior to reconstruction.

### 3.4. Crohn's disease

3.4.1 Disease specific pre-operative considerations in Crohn's disease

3.4.1.1 Crohn's disease *per se* is not an absolute contraindication to urinary tract reconstruction. However, pan-enteric disease is an absolute contraindication to the use of bowel in urinary tract reconstruction.

3.4.1.2 Crohn's disease is considered a high-risk disease in those potentially considering urinary tract reconstruction, even if the disease is in remission.

3.4.1.3 Active Crohn's disease, or an acute flare, is an absolute contraindication and all elective reconstructive surgery should be performed after a minimum of three months following resolution of the acute flare. This is to allow for correction of all abnormalities, including protein and electrolyte deficiencies, and appropriate weaning of steroids.

A specialist colorectal or gastroenterology opinion is advisable to confirm if the patient is fit to proceed with elective bowel surgery.

3.4.1.4 Crohn's disease can be a progressive disease and the anticipated course of the disease should be considered when planning surgery.

3.4.1.5 Disease progression patterns can be predicted in some cases, but specialist input is required to help assess the phenotype and subsequent likelihood of progression.

3.4.1.6 Risk factors for progression include early age of onset, multi-focal disease, multiple skip lesions, stricture disease and/or fistulating disease, and the presence of more proximal disease. These factors should all be taken into careful consideration, as urinary tract reconstruction may not be feasible or safe in this cohort.

3.4.1.7 Bowel conservation (where possible) should be a key priority to try and reduce the risk of short bowel syndrome, as these patients are likely to require further bowel resection for their Crohn's disease.

3.4.2 Selection of bowel segment in Crohn's disease

3.4.2.1 Reconstructive surgical options may be limited depending on the location and extent of gastrointestinal segment(s) affected and the phenotype of disease (mucosal vs muscular stricturing vs penetrative).

3.4.2.2 In disease limited to the colon, ileum may be used, but patients must be appropriately counselled about the risk of disease progression with subsequent ileal involvement which could affect their reconstructed urinary tract.

3.4.2.3 In those with pan-enteric disease in whom urinary tract reconstruction cannot be avoided, alternative reconstructive techniques should be considered, including cutaneous ureterostomy urinary diversion or gastric conduit.

3.4.2.4 In localised segmental disease, the segment of bowel chosen must not be in proximity to a site of current or previously active disease.

3.4.2.5 If small bowel needs to be harvested in an individual with terminal ileal disease, we recommend harvesting the most distal macroscopically-healthy segment of gut.

3.4.2.6 Gastric conduits are seldom performed. However, acknowledging the importance of bowel conservation, gastric and jejunal segments can be considered if necessary when there is extensive ileal disease precluding its use.

3.4.2.7 All patients with suspected Crohn's disease should undergo specialist investigation to determine the extent of their disease, including assessment of both the colon and small bowel, prior to planning reconstructive surgery (i.e. endoscopic evaluation + magnetic resonance enterography +/- capsule endoscopy).

#### 3.4.3 Pre-operative optimisation in Crohn's disease

3.4.3.1 Concurrent steroid use is an absolute contraindication to elective reconstructive surgery, due to an increased risk of poor tissue healing. Steroids should be stopped for at least six weeks prior to proceeding with reconstructive surgery.

This is particularly relevant to patients that are on 20mg once daily Prednisolone (or equivalent) for more than six months [6].

A plan from the IBD MDT should be sought pre-operatively regarding medical therapy and may require re-discussion should the clinical course change in the post-operative setting.

3.4.3.2 Biologics (e.g. anti-TNF-alpha drugs Infliximab and Adalimumab) and most immune modulators (e.g. Methotrexate and Azathioprine) can be continued pre-, intra- and post-operatively at their normal dose.

A plan from the IBD MDT should be sought pre-operatively regarding medical therapy and may require re-discussion should the clinical course change in the post-operative setting.

3.4.3.3 Electrolyte abnormalities, anaemia, diabetic control and renal insufficiency should be corrected pre-operatively.

3.4.3.4 Smoking cessation is paramount for Crohn's disease preoperative optimisation and strong consideration must be made for referral for further support to help achieve this. Cessation is recommended for at least four weeks prior to surgery.

3.4.3.5 A nutritional assessment should always be conducted. Where appropriate, dietetic input should be sought pre-operatively (i.e. extremes of BMI, recent history of rapid weight loss or gain).

The validated Malnutrition Universal Screening Tool (MUST; https:// www.bapen.org.uk/pdfs/must/must\_full.pdf) can be used to help identify malnutrition. However if there is any concern, an expert opinion should be obtained.

#### 3.4.4 Post-operative complications in Crohn's disease

3.4.4.1 The presence of bowel in a reconstructed urinary tract will often result in mucus production. Excessive mucus production can occur when larger segments of bowel are harvested, or when actively diseased bowel segments are used. In those with excessive mucus production and inadequate bladder emptying, there is a resultant increased risk of infection, stones and pyocystis. Any ISC regimen (e.g. number of catheterisations, type of catheter) may need to be reviewed to cope with mucus production and poor bladder emptying, and minimise risk of complications such as rupture of the reconstructed bladder.

3.4.4.2 Patients must be counselled about the increased risk of post-operative morbidity and sepsis whilst taking any form of immunosuppressive therapy. Clinicians must have a low threshold for suspecting sepsis in these patients.

3.4.4.3 The incidence and severity of urinary tract infections may be exacerbated by the use of immunosuppressive treatment for managing Crohn's.

3.4.4.4 Urinary tract infections (UTIs) can commonly occur in patients with penetrating fistulating disease +/- recurrent abscess formation. Due to the resulting frequent use of antibiotics (e.g. Ciprofloxacin and Metronidazole), there is a potential increased risk of multi-drug resistant bacteria.

3.4.4.5 Trimethoprim should be avoided for the treatment of UTIs in patients on Methotrexate, due to significant risk of increased myelosuppression and nephrotoxicity.

3.4.4.6 There is an increased risk of adhesions and subsequent adhesional bowel obstruction in those with a history of previous extensive colonic disease and/or prior abdominal surgery.

3.4.4.7 Stomal stenosis can occur in patients with a stricturing Crohn's phenotype and this should be considered when planning reconstruction. Parastomal pyoderma gangrenosum can occur in patients with more aggressive Crohn's disease and should also be considered when planning reconstruction.

3.4.4.8 The risk of post-operative fistula formation is modified by ensuring the reconstruction has not used any active diseased segments. The risk may be slightly higher in those with a penetrative disease phenotype, but this is mitigated by ensuring reconstruction is performed when the disease is in remission.

3.4.4.9 The risk of anastomotic complications is less severe if a disease-free segment has been harvested and the patient is not on concomitant steroid treatment. The presence of renal failure or liver derangement can increase the risk of anastomotic breakdown and therefore requires specialist input and optimisation pre-operatively. This risk is considerably higher in patients requiring dialysis.

It is important to note that both renal impairment (usually defined as a GFR  $<30mL/min/1.73m^2$ ) and hepatic dysfunction are relative contraindications to performing urinary tract reconstruction using bowel [14].

3.4.4.10 Abdominal wall hernias are more common in patients with a history of prolonged steroid use and those deconditioned pre-operatively. Hence, effort must be made to discontinue steroids and improve muscle mass pre-operatively through early involvement of physiotherapists.

3.4.5 Post-operative follow-up and management in Crohn's disease

3.4.5.1 Patients with Crohn's disease are often hypercoagulable. Although there is limited evidence in the literature, we recommend that all patients undergoing major pelvic surgery should be given extended pharmacological thromboprophylaxis (e.g. low molecular weight heparin for 28 days post-operatively), provided there are no contraindications.

Due to limited evidence, the working group recommends venous thromboembolism prophylaxis to reflect the practice of pelvic oncological surgery.

3.4.5.2 Bile salt malabsorption is likely to be encountered following reconstruction using bowel, especially when terminal ileum is harvested, resulting in chronic diarrhoea. Those with significant bowel disturbance after surgery need gastroenterology input, however terminal ileum should be spared in any reconstructive procedure where possible.

Bile salt diarrhoea becomes increasingly likely for longer extents of terminal ileum harvesting. Fat malabsorption is likely to be encountered additionally when more than 100 cm is harvested.

3.4.5.3 All patients with diarrhoea following their procedure persisting for more than six weeks should be referred for a gastroenterology review, with a view to commencing therapy.

This is often treated with bile acid sequestrants (e.g. cholestyramine), but is best managed by the gastroenterologists.

3.4.5.4 There is an increased risk of chronic diarrhoea if large lengths of bowel are harvested and/or the ileocaecal valve is resected.

3.4.5.5 Vitamin B12 deficiency is common following terminal ileum resection. B12 should be monitored with annual blood tests and replaced as necessary. Follow-up should be lifelong, as it can take several years for this to manifest.

Management needs to recognise the importance of early identification of vitamin deficiency to prevent serious complications, notably anaemia or neurological problems, and should be undertaken in accordance with applicable guidance, e.g. [15]. For those with no neurological involvement, 1mg intramuscular hydroxcobalamin is required three times a week for two weeks. This is usually continued every two to three months for life, but specialist haematology input should be sought [15]. If neurological involvement is evident, urgent specialist advice from a haematologist is needed.

3.4.5.6 Folate should be monitored and replaced as necessary in those who have had more extensive small bowel resection.

Management needs to recognise the importance of identifying vitamin deficiency to prevent serious complications, notably pancytopenia and megaloblastic anaemia in severe folate deficiency. Treatment should be undertaken in accordance with applicable guidance, e.g. [15]. Patients should be prescribed 5mg oral folic acid once daily and will often require this lifelong. Dietary advice can also be given and a specialist haematology opinion should be sought [15].

3.4.5.7 Patients who have undergone multiple previous resections for Crohn's disease are at higher risk of electrolyte disturbance and should be counselled and monitored appropriately. This risk is even higher in patients that already have an ileostomy, due to the possibility of a concurrent high stoma output.

3.4.5.8 A mild, subclinical hyperchloraemic metabolic acidosis is encountered in almost all patients undergoing urinary diversion using bowel segments. Monitoring of bicarbonate and chloride is recommended when there are concerns about clinical metabolic acidosis (e.g. those with resorptive bone disease).

3.4.5.9 Although small intestinal bacterial overgrowth (SIBO) is common in patients with Crohn's disease undergoing bowel surgery (especially following ileo-caecal valve resection), there is limited evidence to support routine antibiotic administration. This is because there is a high likelihood of persistent or recurrent bacterial overgrowth and a single course of antibiotics is unlikely to offer a definitive treatment. If the patient reports a change in bowel function (including abdominal distension, diarrhoea, steatorrhoea or weight loss), a referral to gastroenterology or an IBD specialist is recommended for appropriate assessment and treatment.

Hydrogen and methane breath tests are often used as non-invasive tests to help diagnose SIBO. However, there is a risk of false positive breath tests in this context, resulting in incorrect diagnosis of bacterial overgrowth and subsequent risk of antibiotic resistance if repeated antibiotics are used.

3.4.5.10 Although there is an increased risk of colorectal adenocarcinoma with Crohn's disease, especially in those with colonic involvement, robust evidence is lacking to support mandatory surveillance. We therefore recommend following local unit surveillance policies pertaining to method of urinary reconstruction, pending further research. Nonetheless, all patients must be counselled about the importance of seeking urgent medical advice if they were to develop any red flag symptoms.

There is no clear consensus on the frequency and duration of surveillance following urinary tract reconstruction with bowel but it is recommended, due to the small risk of developing adenocarcinoma. Common surveillance protocols involve lifelong annual cystoscopic surveillance of the reconstructed bladder after 10 years due to the small risk of adenocarcinoma [15].

All patients with Crohn's disease should undergo specialist investigation to determine the extent of their disease. This would also provide the opportunity to exclude any overt malignancy prior to reconstruction.

3.4.5.11 If the segment of bowel used for reconstruction becomes diseased at a later stage, an urgent specialist gastroenterology/colorectal and urological assessment is required.

#### 4. Discussion

The use of bowel for urinary tract reconstruction in IBD patients is a rare occurrence and there is a clear paucity of literature reporting outcomes. Indeed, it is a challenging area to study with prospective trials. Consequently, the majority of evidence is reliant on retrospective data and expert opinion. This limits the ability to develop evidencebased recommendations. The current consensus report, developed using rigorous qualitative methodology, provides a framework for clinicians potentially considering urinary tract reconstruction in this cohort. It is applicable to open surgery and, in appropriate cases and with sufficient experience, may also be appropriate for minimally invasive approaches (laparoscopic and robot-assisted laparoscopic surgery).

This consensus statement focusses on urinary tract reconstruction in patients with non-malignant urinary tract disease. Many such patients also have neurological disease, which potentially can affect gut function [16]; in these patients the multifactorial nature of gut dysfunction should also be considered when evaluating the potential implications of IBD.

The consensus opinion indicates that urinary tract reconstruction using bowel segments is feasible in carefully selected and optimised patients with IBD lacking alternative management options. Within IBD, UC is a relatively low risk disease for surgical procedures, although still greater than the risk of a patient without any co-morbidities. Crohn's is a higher risk condition, in which there is a considerably increased risk of morbidity. The potential risks of this type of surgery must be properly discussed with patients considering reconstructive urological procedures.

Patients must be discussed with a team of healthcare professionals with appropriate multidisciplinary skills. Specialist assessment of the IBD disease state (active vs quiescent) is needed, as it is crucial for establishing suitability of bowel use, and consensus on which bowel segment to use and the safe permissible length. Patients should be maximally optimised pre-operatively. In certain cases, input from a colorectal surgeon with IBD experience may be required intra-operatively, and input from an IBD specialist may also be required post-operatively if the patient has any unexplained gastrointestinal symptoms such as persistent diarrhoea. In order to optimise post-operative recovery, ERAS protocols are recommended for most patients, including avoidance of pre-operative fasting, avoiding bowel preparation products, and early removal of nasogastric tubes. However, this is not always suitable for all patients and care should be tailored accordingly.

The long-term effects of using bowel for urinary tract reconstruction in this cohort is not known, both in terms of efficacy of the reconstruction and subsequent gastrointestinal function. In addition, there is a risk of skip lesions developing in the bowel used for reconstruction, generally in Crohn's cases. The management and complications of this type of IBD activity is not yet established. Patients should therefore be carefully counselled about the uncertainties of long-term outcomes, and should undergo regular and thorough follow-up with both IBD and urological teams.

In conclusion, bowel use for urinary tract reconstruction in patients with IBD is feasible, provided the potential implications for serious adverse events are considered carefully. It should be carried out in specialist centres with access to expert multidisciplinary professionals in both urological reconstruction and IBD surgery. Outcomes should be carefully monitored and published to confirm the safety and efficacy of this procedure in the IBD cohort, including full description of the IBD status.

## Declaration of competing interest

The authors declare the following financial interests/personal relationships which may be considered as potential competing interests:

AS declares the following potential conflicts of interest; Boston Scientific (Grant), Allergan, Ferring and Boston Scientific (Speaker), Saluda Medical, Medtronic (Trials). MJD declares the following potential conflicts of interest; Ferring (Advisory Board member), Allergan, Astellas and Pfizer (Speaker).

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## Appendix A. Supplementary data

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