Expert Forum

IBD Ahead 2011: National Meeting

Making Education Easy

5th Annual Exchange on Advances in IBD – July 2011

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About Expert Forums

Expert Forum publications are designed to encapsulate the essence of a local meeting of health professionals who have a keen interest in a condition or disease state. These meetings are typically a day in duration, and will include presentations of local research and discussion of guidelines and management strategies.

Even for local events it is not always possible for everyone with a similar therapeutic interest to attend. Expert Forum publications capture what was said and allows it to be made available to a wider audience through the Research Review membership or through physical distribution.

Welcome to this review of the recent New Zealand Meeting of IBD Ahead 2011, the 5th Annual Exchange on Advances in Inflammatory Bowel Disease, which was held in Wellington. This educational summary reports the discussions and views of the group in the context of evidence presented at the IBD Ahead National Meeting.

The IBD Ahead process

is an initiative intended to stimulate national and international discussion of evidence-based practice in inflammatory bowel disease (IBD), to generate guidance and resources. The 5th annual cycle of this process considers assessment methods and investigation of Crohn's Disease (CD) in four common clinical scenarios; baseline assessment, monitoring of symptomatic patients, monitoring asymptomatic patients, and post-surgical resection. The methods reviewed in each scenario were clinical symptom assessment, laboratory markers, endoscopy and imaging modalities.

The overall objectives of the 2011 IBD Ahead programme included reviewing evidence-based literature, exchanging ideas and generating guidance and resources to optimise daily practice. An international consultation process (see **Figure 1**) identified four key situations and four methods of assessment. Literature was reviewed and draft answers prepared by bibliographic fellows in conjunction with the International Steering Committee (ISC). Members of the New Zealand Society of Gastroenterology were invited to discuss these statements at the New Zealand IBD Ahead meeting, which included 25 gastroenterologists and a colorectal surgeon, all with expertise in IBD.

Figure 1: Overview of IBD Ahead 2011 programme.

The New Zealand IBD Ahead meeting was conducted in the following manner: For each assessment method, the proposed draft answers and evidence from the literature were presented by a member of the National Steering Committee. Where limited evidence was available, an opinion was drafted. The statements were then discussed by the group and draft answers challenged and modified where necessary to reflect local experience and expert opinion for best practice within New Zealand. After discussion and modification of the answer, delegates individually assigned an agreement score (1-9; strongly disagree – strongly agree) using electronic key pads. Consensus was reached if >75% of delegates voted to agree (agreement score 7-9) or disagree (agreement score 1-3). The level of endorsement is indicated by the mean score. If no consensus was reached (either for or

against) then the draft answer was further modified and the vote repeated until consensus was reached. The modified answers will be submitted to the ISC for integration with those from other participating countries for the purpose of generating educational case studies.

To minimise repetition in the national meeting, speakers presented evidence for each assessment modality across all four scenarios. However, this review has been restructured according to clinical scenario using all assessment modalities to be consistent with the original ISC format.

As none of the delegates were paediatric gastroenterologists, the discussion considered adult CD only. The level of evidence for each answer has been determined using the University of Oxford Centre for Evidence-Based Medicine system (see **Figure 2**).

Evidence level	Definition
A	Consistent randomised controlled clinical trial, cohort study, all or none, clinical decision rule validated in different populations
B	Consistent retrospective cohort, exploratory cohort, ecological study, outcomes research, case-control study; or extrapolations from level A studies
C	Case-series study or extrapolations from level B studies
D	Expert opinion without explicit critical appraisal, or based on physiology, bench research or first principles

Criteria are from the University of Oxford (UK) Centre for Evidence Based Medicine. Further details available from http://www.cebm.net/index.aspx?o=1025

Figure 2: Levels of evidence supporting answers.

Scenario 1 Baseline Assessment

Clinical Assessment

1.a.1 The CDAI and HBI, as well as the IBDQ are accepted tools for evaluating patients before entering clinical trials.
Level of Evidence: A

1.a.2 In everyday clinical practice most gastroenterologists rely on their global clinical judgment, which is less reproducible but simpler and readily available for decision-making.
Level of Evidence: D

When CDAI or HBI should be done at diagnosis of Crohn's Disease.
Level of Evidence: D

How Often CDAI or HBI should be obtained at all clinical visits.
Level of Evidence: D

Mean Vote: 7.1 Agreement Achieved: 84%

Commentary
The presentation of CD varies significantly, with diarrhoea in 85%[1], abdominal pain in 70%, bloody stools present in a variable percentage and extra-intestinal manifestations in up to a third of patients.

The CD Activity Index (CDAI) was developed in 1976[2] to compare the degree of illness across this broad range of symptoms. Symptoms are scored over 7 days, including liquid stools, abdominal pain and 'general well being', with objective markers of complications, treatment, haematocrit and weight. It is commonly used in modern trials and is the measure Pharmac chose for therapy eligibility. However, the 7 day prospective nature of the tool makes it cumbersome in daily practice. Both the Harvey-Bradshaw Index (HBI) and the IBD Questionnaire (IBDQ) are simpler bedside tools, with validation studies showing positive correlation to the CDAI both originally[3] and in the biological era[4]. The HBI is freely available and can be done in the clinic room. There are limitations to all clinical tools, as symptom-predominance is vulnerable to compounding when functional symptoms coexist, yet these tools are the best available.

In practice, a global clinical judgement is often based on the same dimensions as the HBI. Though no evidence exists that clinical judgement is inferior to structured scores, delegates felt that objective scoring provides an important baseline reference for disease response, and is useful for inter-observer comparisons over time. Therefore a formal assessment is recommended regularly, to contribute to clinical judgement at each clinical visit.

Endoscopy

1.b.1 For suspected CD, ileocolonoscopy and biopsies from the terminal ileum (if macroscopically abnormal) as well as each colonic segment, to look for microscopic evidence of CD are first-line procedures to establish diagnosis.
Level of Evidence: A

1.b.2 Patients with upper gastrointestinal (GI) symptoms should be investigated with upper GI endoscopy and biopsies.
Level of Evidence: D

1.b.3 Where there is a suspicion of small bowel disease, investigation of the small intestine can be performed radiologically or by use of small bowel capsule endoscopy (SBCE). Where there is suspicion of penetrating or extraluminal manifestations, cross sectional imaging is preferred.
Level of Evidence: B

1.b.4 Enteroscopy should be reserved for specific situations in which biopsy samples from suspected involved areas are important for diagnosis or in which a dilatation of strictures is reasonable.
Level of Evidence: D

When Diagnostic endoscopy should be performed as soon as possible (but within a maximum of 6 weeks) after patient presentation to allow instigation of appropriate therapy.
Level of Evidence: D

How Often The appropriate endoscopic modality/ies should be performed once at diagnosis by an appropriately trained endoscopist.
Level of Evidence: D

Mean Vote: 8.3 Agreement Achieved: 96%

Commentary
Endoscopy plays a major role in the baseline diagnosis of CD and also provides important prognostic information deduced from disease extent and severity. While ileocolonoscopy is clearly the most widely used endoscopic investigation to provide a means of endoscopic and histological confirmation of CD, in the 10% of predominantly younger patients with symptoms it is important to diagnose upper gastrointestinal CD.

Delegates debated the value of obtaining biopsies from normal appearing mucosa in terminal ileum and/or colonic segments during ileocolonoscopy.

Current literature[5] and delegates agree that terminal ileal biopsies are of greatest value when mucosa appears abnormal or if patient symptoms are highly suspicious of small bowel CD. Otherwise, terminal ileal biopsies of normal appearing mucosa are not routinely required.

Colonic biopsies of normal mucosa may not alter initial management of CD if disease distribution is clearly evident endoscopically. However, the presence of intervening normal mucosa assists histopathological differentiation of CD and ulcerative colitis. Furthermore, biopsies of endoscopically normal colonic mucosa allows exploration of differential diagnoses such as microscopic colitis.

Visualisation of small bowel can be achieved by small bowel capsule endoscopy or by radiological means (see section 1d) in the setting of high pre-test probability of CD based on clinical assessment +/- laboratory markers despite negative ileocolonoscopy.

The preferred initial mode of small bowel visualisation depends upon the clinical suspicion of small bowel strictures to avoid precipitating small bowel obstruction due to capsule retention. While many delegates perform cross-sectional imaging of the small bowel first, anecdotally the absence of radiologically visualised small bowel strictures does not guarantee prevention of capsule obstruction and a capsule patency study may still need to be considered prior to capsule endoscopy. Capsule endoscopy is the preferred initial mode if the patient is being investigated for iron deficiency anaemia.

Enteroscopy allows the additional advantage of endoscopic interventions to small bowel strictures or histological sampling from abnormal mucosa which may be otherwise inaccessible. Within New Zealand, access to double balloon enteroscopy is limited and therefore the original statement was adjusted to encompass all forms of enteroscopy including standard or single balloon enteroscopy.

Ileocolonoscopy should be performed as soon as possible to allow appropriate treatment to be instigated once the diagnosis is confirmed. The time frame of within 6 weeks was chosen based on the New Zealand-wide endoscopy grading criteria that places this as a semi-urgent procedure. Note that instigation of treatment prior to ileocolonoscopy can alter endoscopic and histological appearances and thus affect the strength of diagnosis. However, specific situations such as prior visualisation and biopsies by rigid or flexible sigmoidoscopy can allow initial treatment to be started prior to formal ileocolonoscopy.

Laboratory Markers

1.c.i.1 There is evidence for calprotectin and lactoferrin

Level of Evidence: A

When Calprotectin can be useful for excluding inflammatory bowel disease in young symptomatic patients at initial assessment in whom IBD is suspected.

Level of Evidence: D

How Often *Not applicable*

Mean Vote: 8.3 Agreement Achieved: 92%

1.c.ii.1 There is evidence for CRP, but a normal CRP does not exclude presence of Crohn's Disease.

Level of Evidence: A

When Initial evaluation of the patient as part of the clinical approach.

Level of Evidence: B

How Often *Not applicable*

Mean Vote: 8.2 Agreement Achieved: 97%

Commentary

There is a wide range of serum and faecal biomarkers intended to act as less invasive surrogates for colonoscopic monitoring. A perfect marker with high disease specificity and activity sensitivity does not exist, but of the faecal markers calprotectin has the best evidence and has been available in New Zealand since 2003. It is a neutrophil-derived protein of 36 kDa, stable at room temperature, requiring only 5 g of faeces for testing. It discriminates irritable bowel syndrome (IBS) from IBD[6] with a sensitivity and specificity of 0.93 and 0.98. In an analysis of index referrals, it decreased adult colonoscopy by 65%, with a cost of delayed diagnosis from false negatives of 6%.

When compared to mucosal appearance, calprotectin correlates significantly better (r=0.75) than CDAI (r=0.38) or C-reactive protein (CRP) (r=0.53).[7] However, there is a significant overlap between disease severities.

Delegate's practice has been to use calprotectin to screen for active mucosal inflammation, remembering a negative result does not necessarily exclude disease. It can also help differentiate co-existent IBS from IBD recurrence. However, there was discussion around the additional benefit of adding faecal calprotectin to clinical diagnostic criteria in diagnosing IBS, given its false positive rates from factors such as NSAID use.

CRP is a non-specific marker of inflammation, where significant rises occur in bacterial infections and IBD. Levels are proportional to disease extent in UC but do not correlate well with CD location or behaviour. Delegates found CRP to be a useful addition to disease assessment and management, however a normal CRP does not exclude active CD.

Imaging: Conventional Radiography & CT

1.d.i.1 A sole plain radiograph is a poor screening test at initial CD presentation, but it can serve for detecting free air, toxic megacolon, ischaemia and obstruction.

Level of Evidence: B

1.d.i.2 Abdominal multidetector-row computed tomography (MDCT) scanning is the modality of choice for an acutely ill patient that is admitted with a suspicion of CD.

Level of Evidence: C

1.d.i.3 MDCT and magnetic resonance (MR) techniques are used for the diagnosis of small bowel CD in cases where video capsule endoscopy is contraindicated.

Level of Evidence: B (CT), D (MRI)

1.d.i.4 MDCT or MR techniques are considered more sensitive than their conventional barium counterparts in detecting CD.

Level of Evidence: B (CT), D (MRI)

1.d.i.5 MDCT or MR modalities are superior to barium studies for detection of small bowel stenotic lesions proximal to the endoscopically accessible segment in patients presenting with symptoms suggestive of stricturing CD.

Level of Evidence: B (CT), D (MRI)

1.d.i.6 CT enteroclysis was superior to CT enterography in bowel distension, but diagnostic accuracy was similar for detection of stenotic lesions.

Level of Evidence: B

1.d.i.7 CT colonography can be used for the evaluation of colonic inflammatory lesions in the segments not explored by endoscopy in cases of incomplete colonoscopy due to an impassable colonic stricture.

Level of Evidence: C

1.d.i.8 MDCT techniques are highly accurate for the detection of extra-intestinal manifestations and especially abscesses and fistulae.

Level of Evidence: A

1.d.i.9 Positron emission tomography (PET) scan using fluorodeoxyglucose (FDG) is not considered first line modality for the evaluation of suspected CD.

Level of Evidence: C

Mean Vote: 8.0 Agreement Achieved: 96%

When Imaging can be used if the result is likely to influence management.

Level of Evidence: D

How Often Depending on symptoms, CT or CTE should be used in the acutely ill patient with known or suspected Crohn's disease. Diagnostic medical radiation exposure should be a limiting factor.

Level of Evidence: D

Mean Vote: 7.5 Agreement Achieved: 88%

Commentary

Gastrointestinal radiology has been identified by delegates as a potentially challenging topic to discuss within a group of non-radiologists. In a practical setting, specialist opinions from radiologists are often sought to choose an appropriate radiological modality based on the patient scenario. Additionally the total exposure to ionising medical radiation should be kept in mind. CT and radiographs should only be used when results alter immediate management.

Due to limited availability and familiarity with PET-scanning within New Zealand, recommendations have not been made.

Plain abdominal radiography is commonly performed as an initial investigation in acutely unwell CD patients to exclude perforation or bowel obstruction. It can also used to localise a small bowel patency capsule if spontaneous passage has not occurred. Barium studies were felt to be outdated and were not recommended.

CT imaging not only detects complicated CD including abscess, fistula and perforation, but with small bowel protocols can also be used to define mucosal involvement. CT/MR enteroclysis studies differ from CT/MR enterographic studies in that bowel contrast is delivered via a nasojejunal tube as opposed to oral administration in the latter case. Nasojejunal delivery of contrast permits better proximal small bowel distension for better visualisation of superficial mucosal appearances, but otherwise provides similar information in assessing small bowel CD extent and stricturing.

CT colonography can be considered in cases of incomplete ileocolonoscopy due to a colonic stricture. Alternatively, endoscopic dilatation of short strictures may be considered to allow endoscopic passage proximal to this stricture with the additional advantage of further histological sampling. However endoscopy is still preferred as the initial investigation.

MR was added as an alternative modality to CT for cross-sectional imaging of the abdominal or small bowel to acknowledge the need to minimise CT-related radiation exposure where possible.

Imaging: Ultrasound & MRI

1.d.ii.1 In patients with symptoms suggestive of small bowel disease MR enterography can be considered as a staging method to evaluate involvement of the small bowel. CT has the same diagnostic accuracy, but radiation should be avoided.
Level of Evidence: A

1.d.ii.2 Contrast enhanced ultrasonography (CEUS) and small intestine contrast ultrasonography (SICUS) have a limited role in baseline assessment due to their unstandardised methods and poor accessibility.
Level of Evidence: B

1.d.ii.4 MRI is a gold standard to image the perianal lesions of patients with suspicion of CD. Anorectal ultrasound (US) is helpful to evaluate the perianal abscesses. Transdermal perianal US might be helpful to evaluate the exact anatomy of the perianal complications.
Level of Evidence: A (MRI); B (Anorectal US); C (Transdermal perianal US)

1.d.ii.5 US is a useful imaging modality. Unfortunately it is not available in New Zealand due to lack of expertise.
Level of Evidence: D

Mean Vote: 8.0 Agreement Achieved: 100%

When 1.d.ii.6 Evaluation of the small bowel should be performed at diagnosis, where there is clinical suspicion of small bowel disease. Most accurate methods are SBCE, MR or CT enteroclysis/enterography
Level of Evidence: A (CT), D (SBCE)

How Often A single investigation of the small bowel at diagnosis is usually sufficient to define the presence and extent of small bowel disease. If concerns persist regarding undetected disease a further modality (including capsule endoscopy) should be used.
Level of Evidence: D

Mean Vote: 8.0 Agreement Achieved: 100%

Commentary

Discussion among delegates surrounding the choice of radiological modality depends upon radiological expertise and availability. In the absence of clinical suspicion of small bowel CD (i.e. in patients with symptoms limited to perianal or colonic CD), MR or CT imaging of the small bowel may not be required.

While small bowel US is proven a useful modality, worldwide regional differences exist, and New Zealand has limited access to expertise in this area. Furthermore, cross-sectional imaging is less time consuming and is less operator-dependent.

Perianal imaging by MR is indicated to exclude collections if biological agents and/or Seton drain removal are being considered.

The use of MR enteroclysis as a screening test was removed from the original statement as nasojejunal tube insertion was felt to be unnecessarily invasive for a screening test when modern enterography protocols give adequate information.

Scenario 2 Monitoring in Symptomatic Patients

Clinical Assessment

2.a.1 The CDAI and HBI, as well as the IBDQ, are commonly used in the clinical trials setting and especially for establishing the efficacy of the pharmaceutical agent under investigation. Measurement takes place at pre-determined time points.
Level of Evidence: A

2.a.2 In everyday clinical practice, these indices are sometimes used for therapeutic decision-making in patients under immunosuppressive or biological therapy.
Level of Evidence: D

When 2.a.3 In general, physicians should wait 3-6 months before judging immunosuppressive therapy and 8-12 weeks before judging biological efficacy.
Level of Evidence: D

2.a.4 Persisting symptoms must be evaluated clinically.
Level of Evidence: C

How Often CDAI or HBI should be performed at each clinic visit.
Level of Evidence: D

Mean Vote: 7.1 Agreement Achieved: 79%

Commentary

The frequency and significance of symptom response after initiating treatment varies significantly between patients, depending on baseline severity, disease extent and individual case characteristics. Additionally, different therapies, as reviewed in the 2010 IBD Ahead meeting, have different literature precedents of response assessment; for example, mesalazine has been assessed at 16 weeks, corticosteroids at 18 weeks, and biologicals as early as 4 weeks, but as late as 12 months.[8] Consequently an encompassing statement was made, to include adequate time-frames without inappropriately delaying the recognition of non-response.

Delegates recognised that any clinical assessment incorporates investigations as outlined below.

Endoscopy

2.b.1 Endoscopic confirmation of disease activity is appropriate before starting or escalating immunomodulator/biological therapy unless there is other objective evidence of active disease.
Level of Evidence: D

When 2.b.2 There is insufficient evidence to recommend routine endoscopy to assess mucosal healing in all patients, but it could be useful in symptomatic patients and is best performed before stopping biological therapy.
Level of Evidence: D

How Often Endoscopy is recommended for re-evaluation of symptomatic patients to assess the state of gut inflammation when there is a specific clinical or management decision dependent on the result.
Level of Evidence: D

Mean Vote: 8.0 Agreement Achieved: 92%

Commentary
Immunomodulators and biological agents used in management of CD are associated with risks of infection or adverse drug reactions and greater financial costs. Therefore endoscopic confirmation of active disease is required to warrant starting or escalating treatment. Statement 2.b.2 was reworded because endoscopy is not mandatory where symptomatic improvement has occurred.

The frequency of endoscopic assessment of symptomatic patients is situation-specific, but most useful in patients who are poorly-responsive to treatment or who have suspected disease recurrence due to loss of response to treatment. In these two situations, endoscopic staging of active disease informs management decisions.

Laboratory Markers

2.c.i.1 Faecal calprotectin and lactoferrin have the most robust data.
Level of Evidence: B

When Faecal calprotectin correlates strongly with mucosal appearances and could provide an alternative where colonoscopy is not performed for whatever reason.
Level of Evidence: D

How Often Where available faecal calprotectin could be performed to non-invasively assess inflammation when clinically appropriate.
Level of Evidence: D

Mean Vote: 7.6 Agreement Achieved: 87%

2.c.ii.1 CRP is recommended, but results may be misleading.
Level of Evidence: B

When If elevated when symptoms are present, CRP changes may provide a guide to treatment responses.
Level of Evidence: D

How Often
2.c.ii.2 In active colonic or ileocolonic CD, CRP may be performed at a frequency dependent on the clinical status of the patient.
Level of Evidence: D

Mean Vote: 7.4 Agreement Achieved: 80%

Commentary
See comments 1.c.i. Faecal calprotectin correlates more closely with endoscopic appearance than CRP or CDAI,[7] and in studies can distinguish between inactive, mild, moderate and severe disease, although there is significant variability within each group making interpretation for an individual difficult. There is no data available to support its use as a determinant for treatment changes, though this is currently under investigation. Colonoscopy therefore remains the best modality for assessing response to therapy.

There is limited evidence accumulated for lactoferrin.

The evidence for CRP is limited. It has been shown to differentiate severe from moderate disease, however both false positive and false negatives occur. Results can therefore be misleading, which delegates emphasised.

Imaging: Conventional Radiography & CT

2.d.i.1 A plain radiograph is useful in patients with fulminant symptoms for the detection of bowel obstruction, perforation or toxic colon distension.
Level of Evidence: B

2.d.i.2 Abdominal MDCT is the modality of choice for an acutely ill CD patient and its findings correlate well with disease activity.
Level of Evidence: B

2.d.i.3 Small bowel MDCT imaging techniques can detect disease activity at a stricture, thus differentiating an inflammatory from a fibrostenotic stricture, but their diagnostic value for making this distinction has not been adequately evaluated.
Level of Evidence: B

2.d.i.4 CT and/or MR enterography is also suitable for evaluating CD preoperatively. MRE is the preferred modality.
Level of Evidence: B (CT), D (MR)

2.d.1.5 Barium and MDCT techniques should not be used frequently due to ionising radiation hazard of malignancy. Alternative imaging modalities are available, especially for young patients and those with complicated or unfavourable disease course.
Level of Evidence: D

Mean Vote: 8.1 Agreement Achieved: 100%

When AXR should be used to monitor suspected toxic megacolon. MDCT should be used only if the situation deteriorates and a change in management is necessary.
Level of Evidence: D

How Often As little as possible and as often as necessary.
Level of Evidence: D

Mean Vote: 8.3 Agreement Achieved: 100%

Commentary
Bowel enhancement/mural attenuation and wall thickness seen in CT enterography correlates well with endoscopic and histological inflammation found on ileoscopy.[9,10]

The issue of radiation exposure was rediscussed as this was particularly an issue in younger patients with complicated CD who are likely to require repeated imaging. Attempts to decrease radiation exposure include minimising or avoiding use of CT and using MR imaging instead.[11,12]

Access to MR enterography varies between centres in New Zealand so may not be a realistic choice for acute imaging. CT therefore remains an appropriate modality if results alter the immediate management of an acutely unwell CD patient. Nevertheless MR remains the modality of choice in a semi-acute setting.

Anecdotally, delegates have described cases of CT-detected thickened bowel but with normal mucosa visualised endoscopically, concluding the CT finding a false positive result. However, these case descriptions conflict with clinical evidence mentioned in the previous paragraphs and therefore the statements remained unchanged.

Imaging: Ultrasound & MRI

2.d.ii.1 Disease activity and extent in the small bowel should be assessed by CT or MR-enterography. Both techniques are accurate in imaging of the extraluminal alterations also. MR seems to have greater accuracy regarding strictures.
Level of Evidence: A (CT or MRE), B (MR)

2.d.ii.2 US has limited sensitivity and negative predictive value to evaluate disease activity in CD. CEUS and SICUS have a comparable accuracy to MRI for evaluation of disease activity, but MRI, and particularly CT have a greater accessibility.
Level of Evidence: B (US), C (CEUS, SICUS)

2.d.ii.3 Existence and activity of perianal complications should be examined by MRI. Anorectal US might be an alternative. Transdermal perianal US might enhance the diagnostic accuracy regarding perianal fistulas and abscesses
Level of Evidence: A (MRI), B (Anorectal US), C (Transdermal perianal US)

Mean Vote: 8.4 Agreement Achieved: 100%

When
2.d.ii.4 Acute complications, like abscess, ileus or perforation should be diagnosed immediately.
Level of Evidence: D

How Often Because of the relative safety profile, MRI might be considered when decisions regarding changes in management or concerns over undetected disease require re-assessment of disease activity and endoscopy is unwarranted or unsuited to the situation.
Level of Evidence: D

Mean Vote: 8.1 Agreement Achieved: 100%

Commentary
Most statements pertaining to small bowel ultrasound were truncated or deleted due to the general lack of availability and expertise in this modality within New Zealand. Otherwise other statements have remained unaltered.

Scenario 3 Monitoring in Asymptomatic Patients

Clinical Assessment

3.a.1 The CDAI and HBI, as well as the IBDQ, are used for monitoring patients participating in clinical trials who achieve remission.
Level of Evidence: A

3.a.2 It is not common clinical practice to measure these indices in asymptomatic patients, although evidence exists that there is a continued impact on quality of life by the disease, even when it is inactive.
Level of Evidence: B

3.a.3 The CDAI and IBDQ have been used as tools for verifying remission in CD patients that are candidates for immunosuppressive or biological treatment discontinuation.
Level of Evidence: B

When CDAI or HBI should be performed when new treatment is initiated or existing treatment is changed, but should not be used in isolation.
Level of Evidence: D

How Often CDAI or HBI should be performed at each clinic visit.
Level of Evidence: D

Mean Vote: 7.2 Agreement Achieved: 84%

Commentary
During asymptomatic periods, there is benefit in objectively documenting symptom scores, both to confirm clinical remission and to monitor for recurrence. Delegates believe it to be an important part of routine clinic assessment.

Other factors impacting on quality of life other than disease activity, such as fatigue, should be additionally considered during clinical assessment. Absence of symptoms does not imply mucosal healing. Other investigations are required for assessment prior to de-escalating treatment.

Endoscopy

3.b.1 Mode of endoscopy should be determined by the previous sites of disease.
Level of Evidence: D

When
3.b.2 There is insufficient evidence to recommend routine endoscopy to assess mucosal healing in all patients, but it could be performed before stopping biological therapy.
Level of Evidence: C

3.b.3 Surveillance colonoscopy should be commenced as per local guidelines.
Level of Evidence: D

How Often
3.b.4 Endoscopy should not be performed unless it is likely to lead to a change in patient management.
Level of Evidence: D

3.b.5 Surveillance colonoscopy should performed as per local guidelines.
Level of Evidence: D

Mean Vote: 8.1 Agreement Achieved: 100%

Commentary
Two main clinical situations were identified by delegates where endoscopy in asymptomatic patients was felt to be beneficial; when de-escalation of maintenance medications is considered and when surveillance is indicated for bowel malignancy. In the former situation, there is evidence for repeating endoscopy to assess mucosal healing before stopping infliximab, but the use of endoscopy before stopping azathioprine is evidence free.
Colorectal malignancy guidelines for patients with long-standing Crohn's colitis were not rediscussed in this forum as this should be performed in accordance with the New Zealand Guidelines Group[13] and any future updates of this.

Laboratory Markers

3.c.i.1 There is evidence for the use of calprotectin and lactoferrin.
Level of Evidence: B (Calprotectin); C (Lactoferrin)

When In asymptomatic patients in whom treatment reduction is being considered, faecal calprotectin may be useful.
Level of Evidence: D

How Often Insufficient evidence

Mean Vote: 7.4 Agreement Achieved: 83%

3.c.ii.1 There is evidence for the use of CRP, but elevation may not be specific to Crohn's disease.
Level of Evidence: A

When
3.c.ii.2 CRP may help risk stratify CD patients if elevated.
Level of Evidence: D

How Often
3.c.ii.3 Repeating CRP regularly in asymptomatic patients is unlikely to be helpful.
Level of Evidence: D

Mean Vote: 7.2 Agreement Achieved: 83%

Commentary
In retrospective analyses of patients in remission, higher calprotectin levels predicted relapse, but another study found it to be more sensitive in UC than CD.[6]
Many asymptomatic patients are in disease control rather than in remission. Even when disease is controlled, there remains a risk of relapse and therefore biomarkers are of limited benefit predicting relapse and so are not advocated routinely. Equally there is no evidence that markers of disease activity guide treatment reduction, although basic principles would suggest that mucosal healing is a prerequisite. Clinical trials on faecal calprotectin-guided management are ongoing.
An elevated CRP correlates with a more severe clinical course, and therefore CRP is used at regular intervals by some delegates to monitor disease activity. The discussion consensus was that unless patients became symptomatic, it would however be unlikely to change management decisions.

Imaging: Conventional Radiography & CT

3.d.i.1 Barium and MDCT modalities are used for the determination of the extent and severity of lesions in the small bowel as well as the evaluation of mucosal healing and treatment efficacy.
Level of Evidence: D

3.d.i.2 FDG-PET scan has also been used for monitoring therapeutic efficacy.
Level of Evidence: C

When Diagnostic medical radiation modalities should NOT be used to monitor asymptomatic patients.
Level of Evidence: D

How Often Diagnostic medical radiation modalities should NOT be used to monitor asymptomatic patients.
Level of Evidence: D

Mean Vote: 8.7 Agreement Achieved: 100%

Commentary
Whilst Barium and CT modalities may help in assessing small bowel CD locations that are not otherwise accessible by standard gastroscopy or ileocolonoscopy, delegates felt that the risks associated with radiation exposure[14] exceeded the benefits of repeated monitoring using these modalities.

Imaging: Ultrasound & MRI

3.d.ii.1 There is no indication for routine screening in asymptomatic patients with Crohn's disease.
Level of Evidence: D

When and How Often
Because of their relative safety profiles, MRI might be considered when decisions regarding changes in management or concerns over undetected disease require re-assessment of disease activity and endoscopy is unwarranted or unsuited to the situation.
Level of Evidence: D

Mean Vote: 8.2 Agreement Achieved: 100%

Commentary
MRI has been identified as a way of assessing small bowel without the radiation risks that MDCT and barium studies pose. Given that US detects bowel thickening and dilatation in a patient with active disease, small bowel US is less likely to provide any yield in an asymptomatic patient.

Scenario 4 Monitoring in Post-Operative Patients

Clinical Assessment

4.a.1 A combination of symptom assessment plus endoscopic evidence of recurrence is currently the standard of care for assessing outcomes in post-operative CD.
Level of Evidence: B

When Following recovery from surgery, CDAI or HBI should be performed at clinic visits.
Level of Evidence: D

How Often Following recovery from surgery, CDAI or HBI should be performed at clinic visits.
Level of Evidence: D

Mean Vote: 8.0 Agreement Achieved: 95%

Commentary
The post-operative period is a difficult time to assess CD symptoms because of confounding factors such as post-operative complications, scars and surgical recovery, which is variable but can take months to stabilise. Formal symptom scores were therefore felt only to be of benefit when patients are considered to have recovered from surgery, which is often at the time when care is transferred from surgeons to gastroenterologists.
It is generally believed that recurrent mucosal damage precedes symptom development. Studies looking at this correlation have been contradictory, with one group demonstrating a close correlation between symptoms and early endoscopic ulceration[15], but subsequently no correlation at 1 year[16]. Ileocolonoscopic appearance must therefore be assessed in the context of clinical symptoms.
In a clinical trial setting, disease relapse has been defined using different CDAI or HBI thresholds, the need for surgery or physicians' global assessment.

Endoscopy

4.b.1 Ileocolonoscopy is the gold standard in the diagnosis of post-operative recurrence by defining the presence and severity of morphologic recurrence and predicting the clinical course.
Level of Evidence: B

When 4.b.2 Ileocolonoscopy should be performed 6-12 months after ileocolic resection and primary anastomosis in CD where treatment decisions may be affected.
Level of Evidence: D

How Often 4.b.3 Further ileocolonoscopy is recommended after surgery where treatment decisions may be affected.
Level of Evidence: B

Mean Vote: 8.4 Agreement Achieved: 96%

Commentary
The most common post-operative scenario in a CD patient is post ileocolic resection with primary anastomosis. In this context, severe endoscopic recurrence indicates poor prognosis.

Rutgeert's scoring system has been devised to predict symptom-free survival based on endoscopic mucosal findings at 1 year[17].

Ileocolonoscopy is recommended within 12 months[18] with the aim of assessing for disease recurrence requiring escalation of therapy.

Laboratory Markers

4.c.i.1 There is evidence for calprotectin and lactoferrin.
Level of Evidence: C

When Faecal calprotectin correlates strongly with mucosal appearances and could provide an alternative where colonoscopy is not performed. Colonoscopy is the preferred method of assessment.
Level of Evidence: D

How Often Where available, faecal calprotectin could be performed to non-invasively assess inflammation when clinically appropriate. Colonoscopy is the preferred modality.
Level of Evidence: D

Mean Vote: 8.0 Agreement Achieved: 95%

4.c.ii.1 There is evidence for the use of CRP, but results may be misleading.

Level of Evidence: C

When 4.c.ii.2 In symptomatic patients, an elevated CRP could suggest active inflammation.

Level of Evidence: D

How Often 4.c.ii.3 Not established in the literature; clinical routine each 2-3 months.

Level of Evidence: D

Mean Vote: 7.5 Agreement Achieved: 96%

Commentary

Post-operatively faecal calprotectin and lactoferrin levels are increased in symptomatic patients and may reflect mucosal activity more accurately than CRP, however there is no correlation with symptomatic disease recurrence demonstrated to date. Trials are ongoing in this area.

Few studies examined CRP in this context, and it is potentially compounded by surgical issues, however it could suggest gut inflammation, as has been shown post ileorectal pouch anastomoses. As has been reiterated above, ileocolonoscopy is the preferred assessment modality rather than lab markers.

Imaging: Conventional Radiography & CT

4.d.i.1 CT enterography has been proposed as an alternative to endoscopy for assessing post-operative disease activity. Colonoscopy is the preferred modality.

Level of Evidence: B

4.d.i.2 CT or MR enterography can be used for the diagnosis of inflammatory or fibrostenotic CD of the pouch, in those who experience symptoms suggestive of pouchitis. Transmural inflammation of the pouch detected on imaging is not necessarily CD, as it can also be seen in chronic pouchitis.

Level of Evidence: D

Mean Vote: 8.2 Agreement Achieved: 92%

When Diagnostic medical radiation should not be used to monitor post-resection.

Level of Evidence: D

How Often Diagnostic medical radiation should not be used to monitor post-resection.

Level of Evidence: D

Mean Vote: 8.8 Agreement Achieved: 100%

Commentary

While clinical evidence exists that CT enterography can provide information in assessment of post-operative disease[19] delegates agreed that colonoscopy is the preferred modality of assessing post-operative disease activity for numerous reasons including avoidance of radiation exposure, endoscopic visualisation and histological sampling of disease.

In investigating patients with symptoms of pouchitis with possible inflammatory or fibrostenotic CD of the pouch, MR is the preferred modality over CT, as this group of patients is likely to have had prior CT imaging. Barium enema studies were felt to be redundant given that most centres had access to CT or MR.

See previous sections for discussions on radiation exposure.

Imaging: Ultrasound & MRI

4.e.ii.1 While endoscopy is the preferred technique for assessing endoscopic recurrence, sophisticated US modalities, like oral contrast enhanced, may play a role in this indication in special circumstances.

Level of Evidence: B

When and How Often

Insufficient evidence.

Level of Evidence: -

Mean Vote: 8.2 Agreement Achieved: 100%

Commentary

See previous sections on limited access to US within New Zealand.

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