The second European evidence-based consensus on the diagnosis and management of Crohn's disease: Definitions and diagnosis

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2. Clinical diagnosis and imaging

2.1. Clinical features of CD

ECCO statement 2A

Symptoms of CD are heterogeneous, but commonly include diarrhoea for more than 6weeks, abdominal pain and/or weight loss. These symptoms should raise the suspicion of CD, especially in patients at a young age. Systemic symptoms of malaise, anorexia, or fever are common [EL5, RG D].

2.2 Diagnosis

ECCO statement 2B

A single gold standard for the diagnosis of CD is not available. The diagnosis is confirmed by clinical evaluation and a combination of endoscopic, histological, radiological, and/or biochemical investigations. Genetic testing is currently not recommended for routine diagnosis or management of CD. [EL5, RG D].

2.2.1. History and examination

ECCO statement 2C

A full history should include detailed questioning about the onset of symptoms, recent travel, food intolerances, medication (including antibiotics and non-steroidal anti-inflammatory drugs), and history of appendicectomy [EL5, RG D]. Particular attention should be paid to well proven risk factors including smoking, family history, and recent infectious gastroenteritis [EL1b RGB].

ECCO statement 2D

Careful questioning about nocturnal symptoms, features of extraintestinal manifestations involving the mouth, skin, eye, or joints, episodes of perianal abscess, or anal fissure is appropriate. General examination includes general wellbeing, pulse rate, blood pressure, temperature, abdominal tenderness or distension, palpable masses, perineal and oral inspection, and rectal digital examination. Measurement of body weight and calculation of body mass index are recommended [EL5, RG D].

2.2.2. Initial laboratory investigations

ECCO statement 2E

Check for signs of acute and/or chronic inflammatory response, anaemia, fluid depletion, and signs of malnutrition or malabsorption [EL5, RG D]. Initial laboratory investigations should include CRP [EL2, RG B], and full blood count [EL5, RG D]. If C-reactive protein is not available, then measurement of the erythrocyte sedimentation rate (ESR) may be used [EL5, RG D]. Other biochemical markers may also be used to identify gut inflammation, in particular faecal calprotectin. [EL1b RG B] Microbiological testing for infectious diarrhoea including Clostridium difficile toxin is recommended [EL2, RG B]. Additional stool tests may be needed for patients who have travelled abroad [EL5, RG D].

2.2.3. Procedures recommended to establish the diagnosis

ECCO statement 2F

For suspected CD, ileocolonoscopy and biopsies from the terminal ileum as well as each colonic segment to look for microscopic evidence of CD are first line procedures to establish the diagnosis [EL1b, RG A]. Irrespective of the findings at ileocolonoscopy, further investigation is recommended to examine the location and extent of any CD in the upper gastrointestinal tract or small bowel [EL5, RG D].

2.3. Extent of disease

2.3.1. Procedures recommended for establishing the extent of CD

ECCO statement 2G

MR and CT enterography or enteroclysis is an imaging technique with the highest diagnostic accuracy for the detection of intestinal involvement and penetrating lesions in CD [EL1b, RGB]. Radiation exposure should be considered when selecting techniques. Because of the lower sensitivity of barium studies,

alternative techniques are preferred if available. Transabdominal ultrasonography is a useful additional technique for assessing bowel inflammation.

2.3.3. Procedures recommended for detecting extramural complications

ECCO statement 2H

CT and MR are the recommended techniques for detection of extramural complications of CD [EL1b, RGA]. Transabdominal ultrasonography may also be used, but diagnostic accuracy is lower [EL2b, RGB].

2.3.5. Role of small bowel capsule endoscopy (SBCE) and double balloon enteroscopy (DBE) in suspected or proven CD

ECCO statement 2I

Small bowel capsule endoscopy (SBCE) should be reserved for patients in whom the clinical suspicion for CD remains high despite negative evaluations with ileocolonoscopy and radiological examinations (SBE/SBFT or CTE or MRE) [EL2; RG B]. Double balloon enteroscopy (DBE) 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 [EL5, RG D].

2.3.6. Procedures recommended preoperatively

ECCO statement 2J

Pre-operative imaging should follow strategies employed for the primary diagnosis of CD [EL5, RG D].

3. The histological diagnosis of Crohn's disease

3.1. Procedures for the diagnosis with endoscopic biopsies

3.1.1. Number of biopsies

ECCO statement 3A

For a reliable diagnosis of Crohn's disease “multiple” biopsies from five sites around the colon (including the rectum) and the ileum should be obtained. Multiple biopsies imply a minimum of two samples from each site [EL2, RG B].

ECCO statement 3B

In patients with fulminant colitis, two samples from at least one site should be obtained [EL5, RG D].

3.1.2. Handling of biopsies

ECCO statement 3C

The biopsy samples should be accompanied by clinical information including the age of the patient, duration of disease and duration and type of treatment [EL5, RG D].

ECCO statement 3D

All tissue samples should be fixed immediately by immersion in buffered formalin or an equivalent solution prior to transport [EL5, RG D].

ECCO statement 3E

Since lesions may be mild or focal it is recommended that multiple sections from each sample are examined [EL2, RG B].

3.2. Diagnostic features

3.2.1. Combined microscopic features

ECCO statement 3F

Focal (discontinuous) chronic (lymphocytes and plasma cells) inflammation and patchy chronic inflammation, focal crypt irregularity (discontinuous crypt distortion) and granulomas (not related to crypt injury) are the generally accepted microscopic features which allow a diagnosis of Crohn's disease [EL2, RG B]. The same features and, in addition, an irregular villous architecture, can be used for analysis of endoscopic biopsy samples from the ileum. If the ileitis is in continuity with colitis, the diagnostic value of this feature should be used with caution [EL2, RG B].

3.3. Histology and dysplasia–intraepithelial neoplasia

ECCO statement 3G

The microscopic features for the diagnosis and grading of dysplasia–intraepithelial neoplasia of the colon in Crohn's disease are the same as those proposed for ulcerative colitis and, similarly, a second opinion is recommended for a firm diagnosis [EL2, RG B].

ECCO statement 3H
As for ulcerative colitis, sporadic adenomas may be difficult to distinguish from dysplasiaassociated lesions or masses (DALM). The distinction is however important, because the management of sporadic adenomas differs from that of colitis-associated dysplasia. The patient's age, the site and morphology of the lesion, along with biopsies of flat surrounding mucosal, may be helpful in this distinction [EL2, RG B].

3.4. Surgery and pathology

ECCO statement 3I
A surgical sample needs a complete gross examination, carried out in an orderly and systematic manner, including photographic documentation, preferably at the time when the specimen is removed [EL5, RG D]. Once gross observations are completed, the sample is opened along its longitudinal axis (along the antimesenteric or antimesocolic border, except perhaps at the sites of any carcinoma, where it may be preferable to leave that small segment unopened during fixation) and specimens for microscopy are collected, including the lymph nodes, terminal ileum and appendix [EL2, RG B].
ECCO statement 3J
The optimum number of samples from a colectomy specimen that should be obtained has not been established. However, multiple samples will improve the diagnostic yield. It is a mistake to sample only visible lesions. The samples can be processed routinely [EL5, RG D].

3.5. Histology and disease activity
ECCO statement 3K
The pathology report should give an indication of the activity of the disease. Inactivity in the biopsy may not reflect inactivity in the patient [EL5, RG D].

4. Classification of Crohn's disease

4.1. General recommendations
ECCO statement 4A
The use of Montréal classification of Crohn's disease is advocated. No evidence-based recommendation can be made at this time to implement the routine clinical use of genetic tests or serological markers to classify Crohn's disease.
ECCO statement 4B
The course of Crohn's disease may be predicted by clinical factors at diagnosis (including young age, ileocolonic location and perianal disease) which should be taken into account when determining the initial therapeutic strategy [EL2b RG C].
ECCO Statement 4C
Serum levels of CRP are useful for assessing a patient's risk of relapse [EL2b, RG B]. High CRP levels are indicative of active disease [EL2a, RG B] or a bacterial complication [EL3, RG C]. CRP levels can be used to guide therapy and follow up [EL2a, RG B].

The second European evidence-based consensus on the diagnosis and management of Crohn's disease: Current management

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5.0. Medical management of active Crohn's disease

5.2. Treatment according to site of disease and disease activity

5.2.1. Mildly active localised ileocaecal Crohn's disease

ECCO Statement 5A

Budesonide 9 mg daily is the preferred treatment [EL2a, RG B]. The benefit of mesalazine is limited [EL1a, RG B]. Antibiotics cannot be recommended [EL1b, RG A]. No treatment is an option for some patients with mild symptoms [EL5, RG D].

5.2.2. Moderately active localised ileocaecal Crohn's disease

ECCO Statement 5B

Moderately active, localised ileocaecal Crohn's disease should preferably be treated with budesonide 9 mg/day [EL1a, RG A], or with systemic corticosteroids [EL1a, RG A]. Antibiotics can be added if septic complications are suspected [EL5, RG D. Azathioprine/6-mercaptopurine or methotrexate in combination with steroids is also an appropriate option. Anti-TNF therapy should be considered as an alternative for patients with objective evidence of active disease, who have previously been steroid-refractory, -dependent, or -intolerant. Risks should be carefully considered and discussedwith patients [EL1b, RG B].

5.2.3. Severely active localised ileocaecal Crohn's disease

ECCO Statement 5C

Severely active localised ileocaecal Crohn's disease should initially be treated with systemic corticosteroids [EL1a, RG A]. For those who have relapsed, anti-TNF therapy with or without an immunomodulator is an appropriate option for patients with objective evidence of active disease [EL1a, RG B for infliximab]. For some patients who have infrequently relapsing disease, restarting steroids with an immunomodulator may be appropriate. Surgery is a reasonable alternative for some patients and should also be considered and discussed [EL5 RG D].

5.2.4. Colonic disease

ECCO Statement 5D

Active colonic CDmay be treated with sulfasalazine if only mildly active [EL1b, RG A], or with systemic corticosteroids [EL1a, RG A]. For those who have relapsed, anti-TNF therapy with or without an immunomodulator is an appropriate option for patients with objective evidence of moderate or severely active disease [EL1a, RG B for infliximab]. For some patients who have infrequently relapsing disease, restarting steroids with an immunomodulatori may be appropriate. Before initiating immunomodulatori or anti-TNF therapy, surgical options should also be considered and discussed [EL5, RG D].

5.2.5. Extensive small bowel disease

ECCO Statement 5E

Extensive small bowel Crohn's disease should be treated with systemic corticosteroids and thiopurines or methotrexate [EL5, RGD]. For patients who have relapsed, anti- TNF therapy with or without azathioprine is an appropriate option if there is objective evidence of moderate or severely active disease [EL5, RG D]. Adjunctive nutritional support is appropriate [EL4, RG C]. Surgical options should also be considered and discussed at an early stage.

ECCO Statement 5F

Patients who have clinical features that suggest a poor prognosis currently appear to be the most suitable patients for early introduction of thiopurines, methotrexate and or anti-TNF therapy [EL5 RG D].

5.2.6. Oesophageal and gastroduodenal disease

ECCO Statement 5G

Oesophageal or gastroduodenal Crohn's disease may best be treated with a proton pump inhibitor [EL5, RG D], if necessary together with systemic corticosteroids [EL4, RG C] and thiopurines or methotrexate [EL4, RG D]. Anti-TNF therapy is an alternative for severe or refractory disease [EL4, RG D]. Dilatation or surgery is appropriate for obstructive symptoms [EL4, RG C].

5.3. Treatment according to the course or behaviour of disease

5.3.3. Steroid-refractory Crohn's disease

ECCO Statement 5H

Patients with objective evidence of active disease refractory to corticosteroids should be treated with anti-TNF therapy, with or without thiopurines or methotrexate [EL1a, RG B for infliximab], although surgical options should also be considered and discussed at an early stage.

5.4. Therapy-specific considerations

5.4.4. Anti-TNF strategies

ECCO Statement 5I

All currently available anti-TNF therapies appear to have similar efficacy and adverse-event profiles, so the choice depends on availability, route of delivery, patient preference, cost and national guidance [EL5, RG D].

ECCO Statement 5J (new)

Loss of response to anti-TNF therapy should lead to reevaluation of disease activity, exclusion of complications and discussion of surgical options with the patient [EL5, RG D]. For active disease, reduction in interval between doses, or dose escalation are appropriate strategies before switching to another agent [EL5 RG D]. Switching is an effective strategy [EL1b, RG A], but reduces future therapeutic options. For intolerance, especially if severe, switching to an alternative anti-TNF agent is appropriate. Response to a third anti-TNF therapy occurs in some patients and may be an appropriate option [EL3 RG C], although surgical options should also be considered and discussed. Primary lack of response may be determined within 12 weeks and an alternative anti-TNF agent tried for active disease [EL3, RG C].

ECCO Statement 5K

Particular care should be taken to consider opportunistic infections as a complication of anti-TNF therapy [EL5, RG D]. Patients with fever, cough, systemic symptoms or other unexplained illness should be evaluated for opportunistic infection including tuberculosis or fungal infection, if possible with advice from an infectious diseases' specialist. The long-term combination of azathioprine/mercaptopurine and anti-TNF therapy is best avoided in young people because of the risk of hepatosplenic T-cell lymphoma [EL4, RG D].

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6.0. Management of medically induced remission

6.1. Medical management of patients in medically induced remission

6.1.2. First presentation of localised disease

ECCO Statement 6A

After the first presentation if remission has been achieved with systemic steroids, a thiopurine [EL1a, RG A] or methotrexate [EL1b, RG A] should be considered. There is no consistent evidence for efficacy of oral 5-aminosalicylic acid [EL1b, RG B]. No maintenance treatment is an option for some patients [EL5 RG D].

6.1.3. Relapse of localised disease

ECCO Statement 6B

If a patient has a relapse, escalation of the maintenance treatment can be considered [EL5, RG D]. Steroids should not be used to maintain remission [EL1a, RG A]. Surgery should always be considered as an option in localised disease [EL4, RG D].

6.1.4. Extensive disease

ECCO Statement 6C

For patients with extensive disease, azathioprine is recommended for maintenance of remission [E1b, RG A].

6.1.5. Steroid-dependent Crohn's disease

ECCO Statement 6D

Patients who are dependent on corticosteroids should be treated with thiopurines or methotrexate with or without anti-TNF therapy [EL1a, RG A for thiopurines and methotrexate], EL1a, RG B for infliximab and adalimumab], although surgical options should also be considered and discussed.

Relapse while on azathioprine

ECCO Statement 6E

Patients receiving azathioprine or mercaptopurine who relapse should be evaluated for adherence to therapy and have their dose optimised. Change of their maintenance therapy to methotrexate [EL1b RG B] or anti-TNF therapy [EL1a RGB] should be considered. Surgery should always be considered as an option in localised disease [EL4, RG D].

6.1.6. Maintenance after induction of remission with Anti-TNF therapy

ECCO Statement 6F

If remission has been achieved with an anti-TNF agent, maintenance with regular anti-TNF therapy should be considered [EL1b, RG B]. Azathioprinemay be considered in combination with anti-TNF therapy or is an option as monotherapy if naïve to thiopurines [EL2b, RG C].

6.1.7. Duration of maintenance treatment

ECCO Statement 6G

For patients in remission on azathioprine as maintenance treatment, cessation may be considered after four years of remission [EL2b, RG C]. Benefit and risks of continuing azathioprine should be discussed with individual patients.

ECCO Statement 6H

No recommendation can be given for the duration of treatment with methotrexate or anti-TNF agents, although prolonged use of these medications may be considered if needed [EL3, RG C]. Potential risks and benefits should be discussed on an individual basis.

7.0. Surgery for Crohn's disease

7.2. Small intestinal or ileocolonic disease

7.2.1. Localised ileal or ileocaecal disease

ECCO Statement 7A

Localised ileocaecal Crohn's disease with obstructive symptoms, but no significant evidence of active inflammation, should be treated by surgery [EL2b, RG C].

7.2.2. Concomitant abscess

ECCO Statement 7B

Active small bowel Crohn's disease with a concomitant abdominal abscess should preferably be managed with antibiotics, percutaneous or surgical drainage followed by delayed resection if necessary [EL3, RG C].

7.2.3. Stricturoplasty

ECCO Statement 7C

Stricturoplasty is a safe alternative to resection in jejuno-ileal Crohn's disease, including ileocolonic recurrence, with similar short-term and long-term results. Conventional stricturoplasty is advised when the length of the stricture is b10 cm. However, in extensive disease with long strictured bowel segments where resection would compromise the effective small bowel length, non-conventional stricturoplasties may be attempted [EL2a, RG C].

7.2.4. Anastomotic technique

ECCO Statement 7D

There is evidence that a wide lumen stapled side-to side (functional end-to-end) anastomosis is the preferred technique [EL2a, RG B].

7.2.5. ‘Coincidental’ ileitis

ECCO Statement 7E

Terminal ileitis resembling Crohn's disease found at a laparotomy for suspected appendicitis should not routinely be resected [EL5, RG D].

7.2.6. Laparoscopic resection

ECCO Statement 7F

A laparoscopic approach is to be preferred for ileocolonic resections in Crohn's disease [EL 2A, RG B] where appropriate expertise is available. In more complex cases or recurrent resection, there is insufficient evidence to recommended laparoscopic surgery as the technique of first choice [EL3, RG C].

7.3. Crohn's disease of the colon

7.3.1. Localised colonic disease

ECCO Statement 7G

If surgery is necessary for localised colonic disease (less than a third of the colon involved) then resection only of the affected part is preferable [EL3, RG C].

7.3.2. Multi-segment colonic disease

ECCO Statement 7H

Two segmental resections can be considered for a patient with an established indication for surgery when macroscopic disease affects both ends of the colon [EL3, RG C].

7.3.3. Dilatation of strictures

ECCO Statement 7I

Endoscopic dilatation of stenosis in Crohn's disease is a preferred technique for the management of accessible short strictures. It should only be attempted in institutions with surgical back-up [EL2a, RG B].

7.3.4. Colonic stricturoplasty

ECCO Statement 7J

Stricturoplasty in the colon is not recommended. [EL4, RG D]

7.3.5. Ileopouch-anal anastomosis

ECCO Statement 7K

All the available evidence suggests that in patients with an unsuspected diagnosis of Crohn's disease after IPAA there are higher complication and failure rates. At present an IPAA is not recommended in a patient with Crohn's colitis. [EL2a, RG B].

7.4. Surgery and medication

7.4.1. Surgery after anti-TNF therapy

ECCO Statement 7L

Whether there is a higher rate of post-operative complications from abdominal surgery during or after anti-TNF therapy remains controversial [EL3, RG D]. The safe interval remains to be determined.

7.4.2. Patients on steroids

ECCO Statement 7M

Prednisolone 20 mg daily or equivalent for more for more than six weeks is a risk factor for surgical complications [EL2b, RG B]. Therefore, corticosteroids should be weaned if possible [EL5, RG D].

7.4.3. Patients on thiopurines

ECCO Statement 7N

Azathioprine can safely be continued in the perioperative period and beyond [EL2b, RG B].

7.5. Surgical decision making

7.5.1. Surgery and medicine are complementary

ECCO Statement 7O

In complicated Crohn's disease, surgery at an early stage is a valid alternative to medical therapy [EL5 RG D].

ECCO Statement 7P

Multidisciplinary clinical conferences to discuss the treatment strategy of individual cases are recommended especially for the management of patients with complicated CD [EL5 RG D].

The second European evidence-based Consensus on the diagnosis and management of Crohn's disease: Special situations

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8 Risk factors, prophylaxis, diagnosis and management of post-operative recurrence of Crohn's disease

8.2. Predicting post-operative recurrence

ECCO Statement 8A

The following are considered predictors of early post-operative recurrence after ileocolonic resection: smoking, prior intestinal surgery [EL 1 and RG A], penetrating disease behaviour, perianal location and extensive small bowel resection [EL2b, RG B]. Absence of prophylactic treatment [EL1a, RG A] is associated with a higher risk of relapse.

8.3. Diagnosis of post-operative recurrence

ECCO Statement 8B

Clinical assessment, including measurements of disease activity and acute phase reactants are used during follow up, but their value remains to be determined [EL5, RG D].

ECCO Statement 8C

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 [EL2a, RG B]. Ileocolonoscopy is recommended within the first year after surgery where treatment decisions may be affected [EL2a, RG B].

ECCO Statement 8D

Trans-abdominal ultrasound, MR enterography, small bowel capsule endoscopy (SBCE) are less invasive diagnostic methods emerging as alternative tools for identifying post-operative recurrence [EL2b RG C].

8.4. Medical prophylaxis

ECCO Statement 8E

All patients should be encouraged to quit smoking after surgery for Crohn's disease [EL1b, RG B].

ECCO Statement 8F

Prophylactic treatment is recommended after small intestinal resection [EL1, RG A]. Thiopurines are more effective than mesalazine or imidazole antibiotics alone for preventing both clinical and endoscopic recurrence [EL1, RG A]. In patients with a risk factor for early postoperative recurrence the drug of choice is azathioprine/mercaptopurine [EL3, RG C]. High dose mesalazine is an option for patients with an isolated ileal resection [EL1b, RG B]. Imidazole antibiotics have been shown to be effective after ileocolic resection but are less well tolerated [EL1a, RG A].

ECCO Statement 8G

Prophylaxis is best started within two weeks of surgery, although an early start has not been proven superior to later treatment [EL5, RG D].

ECCO Statement 8H

The duration of prophylaxis should be at least 2 years [EL1a, RG B].

9. Diagnosis and management of fistulating Crohn's disease

9.4. Diagnosis of perianal fistulae

9.4.1. Initial diagnostic approach

ECCO Statement 9A

Pelvic MRI should be the initial procedure because it is accurate and non-invasive, although it is not needed routinely in simple fistulae [EL2b, RG B].

ECCO Statement 9B

Examination under anaesthetic is considered the gold standard only in the hands of an experienced surgeon. It may allow concomitant surgery, but care should be taken to obtain appropriate informed consent of the patient, since unexpected findings may preclude this [EL5, RG D].

ECCO Statement 9C

Anorectal ultrasound requires expertise, but can be equivalent to pelvic MRI in completing examination under anaesthesia if rectal stenosis has been excluded. [EL2b, RG B]. Fistulography is not recommended [EL3, RG C].

ECCO Statement 9D

Since the presence of concomitant rectosigmoid inflammation has prognostic and therapeutic relevance, proctosigmoidoscopy should be used routinely in the initial evaluation [EL2b, RG B].

9.4.2. Classification of perianal fistulae

ECCO Statement 9E

There is no consensus for classifying perianal fistulae in CD. In clinical practice most experts use a classification of simple or complex. From the surgical point of view Parks' classification is more descriptive and can influence surgical decisions, but it is complicated to use in routine practice [EL5, RG D].

9.5. Treatment of fistulating disease

9.5.1. Simple perianal fistulae

ECCO Statement 9F

The presence of a perianal abscess should beruled out and if present should be drained as a matter of urgency [EL5, RGD].

ECCO Statement 9G

For simple perianal fistulae it is important to know if they are symptomatic. If they are not, nothing has to be done. Only when simple fistulae are symptomatic are the options of non-cutting Seton or fistulotomy recommended [EL3, RG D]. Antibiotics, metronidazole (750–1500 mg/day) or ciprofloxacin (1000 mg/day), should be added [EL3, RG D].

9.5.2. Complex perianal disease

ECCO Statement 9H

Seton placement should be recommended [EL4, RGD] for complex fistulae. The timing of removal depends on subsequent therapy.

ECCO Statement 9I

Active luminal Crohn's disease should be treated if present, in conjunction with appropriate surgical management of fistulae [EL5, RGD].

ECCO Statement 9J

Antibiotics and azathioprine/mercaptopurine should be used as the first choice of therapy for complex perianal Crohn's disease in combination with surgical therapy, in spite of a lack of clinical trials [EL4, RG D].

ECCO Statement 9K

Infliximab [EL1b, RGA] or adalimumab [EL1b, RGB] should be used as a second line medical treatment [EL1b, RGB].

9.5.5. Monitoring the therapeutic response

ECCO Statement 9L

In evaluating the response to medical or surgical treatment in routine practice, clinical assessment (decreased drainage) is usually sufficient [EL2b, RG D]. To quantify treatment efficacy the Perianal Crohn's Disease Activity Index (PCDAI) should be used [EL5, RGD]. In the setting of clinical trials, MRI in combination with clinical assessment is now considered mandatory [EL2b, RG D].

9.6. Continuing therapy for perianal Crohn's disease

ECCO Statement 9M

Azathioprine/6-mercaptopurine [EL2B, RG C], infliximab [EL1b, RG A] or adalimumab [EL1b, RG B] or seton drainage, or a combination of drainage and medical therapy [EL3 RG C] should be used as maintenance therapy. All maintenance therapies should be used for at least one year [EL1b, RG A].

9.6.2. Therapeutic approach in the event of infliximab failure

ECCO Statement 9N

In the event of anti-TNF failure, the use of azathioprine/mercaptopurine or methotrexate, with antibiotics as adjunctive treatment, is the first therapeutic choice [EL5, RGD]. Depending on the severity of the disease, a diverting ostomy can be performed and can rapidly restore quality of life, or proctectomy as the last resort [EL5, RG D].

9.7. Management of non-perianal fistulating Crohn's disease

9.7.2. Enterogynaecological fistulae

ECCO Statement 9O

Low anal-introital fistula may not need surgical treatment [EL5, RG D] if asymptomatic.

ECCO Statement 9P

If the patient has a symptomatic fistula, surgery is usually necessary (including diverting ostomy) [EL5, RG D]. Active Crohn's disease especially with rectal inflammation should be treated medically prior to surgery [EL5, RG D].

10. Crohn's disease in children and adolescents: diagnosis and treatment

10.2. Diagnosis

ECCO Statement 10A

Children and adolescents with suspected IBD require a thorough history and examination, including assessment of growth velocity and pubertal stage [EL4, RGC]. Normal laboratory investigations do not exclude a diagnosis of IBD [EL 2b, RG B]. Normal levels of faecal surrogate markers for intestinal inflammation, such as calprotectin or lactoferrin, make active disease in the lower gastrointestinal tract unlikely and may guide the need for invasive investigation [EL 3b, RG B].

ECCO Statement 10B

Initial investigation should consist of colonoscopy (including terminal ileal intubation) with multiple biopsies [EL2b, RG B], upper GI endoscopy with multiple biopsies [EL2b, RGB], and small bowel imaging [EL2b, RGB]. The technique used to examine the small bowel will depend on local expertise; but dynamic contrast-enhanced magnetic resonance imaging can reliably show most lesions of Crohn's disease without exposure to ionizing radiation [EL 2b, RG C].

10.3. Treatment

10.3.2. Induction therapy

ECCO Statement 10C

Both exclusive enteral nutrition (EEN) and corticosteroids are effective for induction of remission irrespective of disease activity or location [EL1a, RGA]. However, EEN has fewer side effects and promotes growth [EL2b RGB]. Elemental enteral formula is not more effective compared to polymeric formula feeds [EL3, RG C].

ECCO Statement 10D

Budesonide is effective and favoured over prednisolone in mild to moderate active ileo-caecal CD because of significantly fewer side effects [EL1b, RG A]. The role of budesonide in the treatment of severe or extensive Crohn's disease is uncertain.

ECCO Statement 10E

The role of mesalazine [EL2b, RG B], antibiotics [EL4 RGD] and probiotics [EL4, RGC] for inducing remission in children with active CD is unclear.

10.3.3. Maintenance therapy

ECCO Statement 10F

Neither prednisolone/prednisone [EL5, RG D] nor budesonide [EL1a, RG B] should be used as maintenance treatment in paediatric Crohn's disease.

ECCO Statement 10G

The role of mesalazine in maintaining remission in paediatric Crohn's disease is unclear [EL2b, RG B].

ECCO Statement 10H

Azathioprine or mercaptopurine is effective for the maintenance of remission [EL1b, RG A]. Early introduction should be considered at the time of remission induction with either corticosteroids or exclusive enteral nutrition as a part of the treatment regimen in newly diagnosed paediatric patients with severe or extensive Crohn's disease [EL1b, RG A].

ECCO Statement 10I

Methotrexate is effective in maintaining remission in patients resistant or intolerant to azathioprine/ mercaptopurine [EL2b, RG B].

10.3.4. Refractory disease

ECCO Statement 10J

Infliximab is effective for induction of remission in paediatric Crohn's disease patients with moderate to severe disease who are refractory to or intolerant of standard induction therapy [EL2b, RGB]. Regular infliximab infusions can maintain remission for patients with an initial response [EL1b, RGA] and may be effective at closing fistulae [EL4, RGC], although a significant proportion will require dose modification [EL4, RG C].

ECCO Statement 10K

Elective surgery should be considered in children with disease resistant to medical therapies, especially in pre-pubertal or early pubertal children with growth failure and localized Crohn's disease [EL4 RGC].

10.4. Supportive management

ECCO Statement 10L

Psychosocial support should be given to patients and their families [EL4, RG C].

ECCO Statement 10M

Nutritional status, growth and pubertal development should be recorded at diagnosis and during the course of disease. Nutritional deficiencies should be vigorously treated [EL3, RG B].

ECCO Statement 10N

The care of children with CD should involve a multi-disciplinary team in a paediatric Gastroenterology centre [EL5, RGD]. Transition clinics for adolescents with Crohn's disease represent optimal care and are highly recommended [EL5, RG D].

11. The management of pregnancy in Crohn's disease

11.1. Fertility in Crohn's disease

ECCO Statement 11A

Crohn's disease does not seem to affect fertility when the disease is inactive [EL3b, RG B]; however active disease leads to reduced fertility [EL3b, RG B]. Female patients who undergo surgery are at risk for impaired tubal function [EL3b, RG B]. In male patients rectal excision may lead to impotence or ejaculatory problems; however there is no comparison with the general population [EL4, RG C]. Sulfasalazine therapy causes infertility (reversible) in male patients because of changes in semen quality [EL3b, RGB].

11.2. Influence of disease activity on the course and outcome of pregnancy

ECCO Statement 11B

It is advisable to strive for clinical remission before conception. Flares are best treated aggressively to prevent complications [EL3a, RG B]. Crohn's disease is a risk for preterm delivery and low birth weight [EL 1a, RG B]. Insufficient data exist about maternal morbidity and fetal mortality at surgery.

11.3. The influence of pregnancy on the course of CD

ECCO Statement 11C

If conception occurs at a time of quiescent disease the risk of relapse is the same as in non-pregnant women [EL5, RG D]. If conception occurs at a time of active disease, two thirds have persistent activity and of these two thirds deteriorate [EL3b, RG B]. Both clinical activity and surgical interventions decline with pregnancy and parity [EL4, RG C]. Nutritional status also influences parity [EL4, RG C].

11.4. Mode of delivery

ECCO Statement 11E

The mode of delivery should primarily be governed by obstetric necessity and indication, but also in conjunction with the gastroenterologist and/or the colorectal surgeon. Patients with uncomplicated Crohn's disease without perianal disease or rectal involvement can deliver vaginally after obstetric evaluation has been performed [EL4, RG C]. Caesarean section should be preferred in perianal disease or rectal involvement [EL4, RG C]. An ileoanal pouch is regarded as an indication for caesarean section [EL4, RG C]. Colostomy or ileostomy patients can deliver vaginally [EL4, RG C].

11.5. Surgery during pregnancy

ECCO Statement 11F

Indications for surgery in pregnant women with Crohn's disease are the same as for nonpregnant patients: obstruction, perforation, haemorrhage and abscess. In the severely ill patient, continued illness is a greater risk to the fetus than surgical intervention [EL5, RG D].

11.6. Medical treatment during pregnancy

ECCO Statement 11G

Medical treatment for Crohn's disease (except methotrexate) should generally continue during pregnancy, because the benefits outweigh the risk of medication.

12. Crohn's disease and psychosomatics

12.2. Psychosocial factors

ECCO Statement 12A

Psychological disturbances seem to be a consequence of the illness rather than the cause or specific to Crohn's disease. The degree of psychological distress correlates with the disease severity and predicts health related quality of life. Its influence upon the course of disease remains controversial [EL1b, 2b and 3b, RG B].

ECCO Statement 12B

An association between psychological factors and the aetiology of Crohn's disease is unproven [EL3b, 4, RG D] and the role of psychological factors on the disease course is controversial [EL1b, 2b, RG B].

12.3. Psychological factors influencing the course of Crohn's disease

ECCO Statement 12C

It remains unclear whether acute life events trigger relapses [EL1b,2b, RG B] Most patients consider stress to have an influence on their illness [EL2c,3, RG C].

12.4. Doctor–patient relationship, information and clinical care

ECCO Statement 12D

The psychosocial consequences and healthrelated quality of life of patients should be taken into account in clinical practice at regular visits. Individual information and explanation about the disease should be provided through a personal interview. The course of the disease can be improved by combining self-management and patient-centred consultations [EL1b,3b, RG B].

12.5. Assessment of health related quality of life, psychological distress and provision of integrated psychological support

ECCO Statement 12E

Physicians should assess the patient's psychosocial status and demand for additional psychological care and recommend psychotherapy if indicated. Integrated psychosomatic care should be provided in IBD centres [EL2b, RG B].

ECCO Statement 12F

Patients should be informed of the existence of patient associations [EL 5, RG D].

12.6. Psychotherapeutic interventions

ECCO Statement 12G

Psychotherapeutic interventions are indicated for psychological disorders, such as depression, anxiety, reduced quality of life with psychological distress, as well as maladaptive coping with the illness [EL1b,2b,3b, RG B].

12.6.2. Choice of psychotherapeutic methods and psycho-pharmaceuticals

ECCO Statement 12H

The choice of psychotherapeutic method depends on the psychological disturbance and should best be made by specialists (Psychotherapist, Specialist for Psychosomatic Medicine, Psychiatrist). Psycho-pharmaceuticals should be prescribed for defined indications [EL5, RG D].

13. Extraintestinal manifestations of Crohn's disease

ECCO Statement 13A

Arthropathy associated with CD belongs to the concept of spondylarthritis and includes axial arthropathy [EL2b, RG B]. Diagnosis of non-axial arthritis and arthropathy associated with IBD is made on clinical grounds based on characteristic features and exclusion of other specific forms of arthritis [EL3b, RG C]. Type I is pauci-articular and affects large joints acutely at times of IBD activity, while type II is polyarticular, affecting a larger number of peripheral joints independently of IBD activity [EL 2b, RG B]. Axial arthritis, including sacroiliitis and ankylosing spondylitis, is diagnosed on conventional rheumatological grounds, and is supported by characteristic radiological changes, magnetic resonance imaging being the most sensitive [EL2b, RG B]. Although HLA B-27 is over-represented in axial arthritis related to Crohn's disease it is without diagnostic value [EL2b, RG B].

13.2. Arthropathy

ECCO Statement 13B

In the case of peripheral arthritis there is general support for use of short term treatment with nonsteroidal anti-inflammatory agents, local steroid injections, and physiotherapy [EL4, RG D]. The emphasis should be on that of the underlying Crohn's disease [EL2c,RG C]. Sulfasalazine has a role in persistent peripheral arthritis [EL1a, RG B]. In axial arthropathy arguments in favour of intensive physiotherapy [EL2a, RG B], associated with NSAIDs are stronger, but safety concerns mean that long-term treatment with NSAIDs is best avoided if possible [EL1b, RG C]. Sulfasalazine [EL1a], methotrexate [EL1b] and azathioprine are generally ineffective, or only marginally effective. The efficacy of anti-TNF therapy for patients with ankylosing spondylitis and Crohn's disease intolerant or refractory to NSAIDs is well established [EL1b, RG B].

13.3. Metabolic bone disease

ECCO Statement 13C

Patients on steroid therapy or those with reduced bone density should receive calcium and vitamin D supplements [EL2b, RG B]. Isotonic exercise [EL2B, RG B] and cessation of smoking [EL2b, RG B] are beneficial. Patients with established fractures should be treated with bisphosphonates [EL2b, RGB]. The efficacy of primary prevention of fracture with bisphosphonates has not been demonstrated in patients with Crohn's disease. Routine hormone replacement in postmenopausal women in not warranted due to the risk of side effects. Men with low testosterone may benefit from its therapeutic administration [EL3b, RG C].

13.4. Cutaneous manifestations

ECCO Statement 13D

Diagnosis of the cutaneous manifestations of IBD is made on clinical grounds, based on their characteristic features and (to some extent) the exclusion of other specific skin disorders; biopsy can be helpful in atypical cases [EL3b, RG C].

ECCO Statement 13E

Treatment of erythema nodosum is usually based on that of the underlying Crohn's disease. Systemic steroids are usually required [EL4, RG D]. Pyoderma gangrenosum is initially treated with systemic steroids or calcineurin inhibitors [EL4, RG D] or infliximab [EL1b, RG C].

13.5. Ocular manifestations

ECCO Statement 13F

Diagnosis of simple episcleritis depends on the exclusion of the more sinister features of uveitis. When this is not possible referral to an ophthalmologist for expert opinion and slit-lamp examination is wise [EL4, RG D]. Episcleritis may

not require specific treatment, but will usually respond to topical steroids [EL4, RG D]. Uveitis is treated with steroids, and it may be necessary to use both topical and systemic routes [EL3b, RG C]. Immunomodulatory therapy has been thought helpful in resistant cases [EL4, RG D].

13.6. Hepatobiliary disease

ECCO Statement 13G

Diagnosis of hepatobiliary disorders in association with Crohn's disease follows the standard investigatory pathways prompted by abnormal liver function tests, with ultrasound scanning, and serology to identify specific auto-immune and infective causes [EL2a, RG B]. Magnetic resonance cholangiography is now established as the first-line diagnostic test for primary sclerosing cholangitis [EL2a, RG B]. Primary sclerosing cholangitis substantially increases the risk of both cholangiocarcinoma and colorectal carcinoma [EL1a, RG A].

ECCO Statement 13H

PSC appears to respond to ursodeoxycholic acid (ursodiol), which improves abnormal liver function tests [EL1b, RG B] may, at 20 mg/kg, improve prognosis [EL2a, RG C], and will perhaps reduce the risk of colonic cancer in these patients [EL2a, RG C]. ERCP may be used to treat dominant strictures by dilatation and/or stenting [EL4, RG C]. Advanced liver disease may necessitate transplantation [EL2a, RG B].

13.7. Venous thromboembolism

ECCO Statement 13I

Antithrombotic prophylaxis should be considered in all hospitalized patients with CD [EL5, RG D]. Treatment of venous thromboembolism in IBD should follow established antithrombotic therapy options [EL 1a, RG A] taking into account the potentially increased risk of bleeding [EL5, RG D].