CT enterography in Crohn’s disease

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Abstract

CT enterography in Crohn’s disease.
Learning Objectives. To define the contribution of CT enterography (CTE) to the diagnosis, follow-up and prognosis of Crohn’s disease, and to detail image acquisition. To compare CT enterography with other diagnostic methods used for the study of the small bowel, defining advantages and disadvantages.

Topic Review. Crohn’s disease is a chronic inflammatory bowel disease that affects the entire gastrointestinal tract with a discontinuous and transmural compromise. The objectives are to determine small bowel involvement, diagnosis of active disease and its response to treatment. The course of disease, its complications (bleeding, obstruction, strangulation, abscesses and fistulas) and the severity of symptoms are variable. Initial diagnosis is based on a combination of clinical, endoscopic, biochemical and radiological findings.

Image Findings. The characteristic features in CTE are increased mural enhancement and enhanced lymph nodes after the administration of IV contrast (both signs of activity), wall thickening and halo sign (low attenuation ring in bowel due to deposit of submucosal fat), proliferation of mesenteric fat, prominence of the vasa recta, areas of stenosis, fistulas and abscesses.

Conclusion. CTE is readily available and easy to perform, being possible to determine the extent and stage of disease progression, extraintestinal involvement and potential complications. The combination of a short examination time, a single breath hold, accessibility and availability has made CTE an important tool in the diagnosis and follow-up of patients with Crohn’s disease.


TOPIC REVIEW

Crohn’s Disease (CD) is a common inflammatory bowel disease (IBD) that affects more than half a million patients in North America. In our country, the number of cases is increasing. As regards the incidence of CD, statistics suggest that in many developed countries, this condition occurs more frequently in individuals of Caucasian ethnicity and high social class. While in the United States incidence ranges from 7 to 13 cases per 100,000 inhabitants, in Latin America, rates are lower, with 0.5 cases per 100,000 people.

The estimated prevalence of IBD in Europe and the United States is approximately 100 to 300 per 100,000 for ulcerative colitis (UC) and 50 to 100 per 100,000 for CD. In Argentina, there are no national
registries for IBD.

The Gastroenterology Department of Hospital Italiano de Buenos Aires conducted in 2009 a retrospective, descriptive and cross-sectional study based on clinical suspicion data, confirmed by complementary studies, collected from electronic medical records. The estimated prevalence of IBD in Argentina is lower than that previously reported for the USA and Northern Europe and similar to that reported for Southern Europe and Puerto Rico. However, it should be noted that the sample evaluated is not representative of the overall population, as it is limited to a small percentage of Argentine inhabitants (Table 1).

Crohn’s disease has a bimodal distribution in age of onset, with the first peak occurring between the ages of 15 an 30 years and the second occurring late, between the ages of 60 and 80 years.

CD affects only the small bowel in 30% of cases and classic symptoms include abdominal pain, diarrhea and weight loss.

The disease usually follows a chronic course, with differences in the type and severity of symptoms. Complications include bleeding, obstruction, strictures, abscesses and fistula formation.

Initial diagnosis is based on a combination of clinical, endoscopic, biochemical and radiological findings (2).

Historically, CD has been difficult to diagnose, partly because symptoms of CD are similar to those of other bowel disorders, such as UC and irritable bowel syndrome. However, the main problem is that the small bowel is difficult to investigate using traditional methods (3).

PATHOLOGICAL FINDINGS

Even if CD may affect any segment of the gastrointestinal tract or a combination of segments, from the mouth to the anus, it most commonly affects the terminal ileum and the right colon. When only the colon is affected, lesions are segmental, unlike in UC, frequently sparing the rectum (Table 2). However, perianal disease is a prominent data in CD.

Histological changes consist in crypt inflammation, forming neutrophilic microabscesses, with consequent ulceration, but, unlike in UC, inflammation is deeper with involvement of the lamina propria by macrophages and lymphoid aggregates, leading to nonspecific transmural inflammation. In 50% of cases, these changes lead to the formation of non-caseating granulomas in any layer of the wall, the mesentery or the lymph nodes (characteristic of this disease). The inflammation may spread through the bowel wall (fistula). Collagen deposition is common, which may contribute to stenosis.

The small bowel in patients with CD is significantly shorter than in the general population. Furthermore, these patients have increased bowel permeability and higher antibody levels.

The presence of non-caseating granulomas is a typical feature of this disease. Half of them are close to lymphatic vessels, while mucus occurs in ulceration sites and is the consequence of ileal crypts.

Linear ulcers in CD generally have a predominant longitudinal orientation along the mesenteric side. The small vessels irrigating such region could generate ischemia, originating ulcers (4).

Clinical presentation determines disease course and complications. In both CD and UC, the clinical and demographic characteristics most constantly associated with disease course are age at diagnosis, disease location and smoking. Younger age at onset is associated with a more severe course in both diseases.

In CD, proximal small bowel and upper gastrointestinal

Table 1: Prevalence of patients with IBD in the Hospital Italiano de Buenos Aires health plan (2).

<table>
<thead>
<tr>
<th>IBD</th>
<th>UC</th>
<th>CD</th>
<th>IBS*</th>
</tr>
</thead>
<tbody>
<tr>
<td>N (%)</td>
<td>143</td>
<td>112</td>
<td>22</td>
</tr>
<tr>
<td>M/F</td>
<td>68/75</td>
<td>52/60</td>
<td>13/9</td>
</tr>
<tr>
<td>Age at diagnosis (median - range)</td>
<td>39 (3-83)</td>
<td>37.5 (3-78)</td>
<td>37 (11-81)</td>
</tr>
<tr>
<td>Prevalence in 100,000 (95% CI)</td>
<td>97.2 (82-114)</td>
<td>76.1 (63-91)</td>
<td>14.9 (10-23)</td>
</tr>
</tbody>
</table>

* IBS: Irritable Bowel Syndrome

Table 2: Main differences between inflammatory bowel diseases.

<table>
<thead>
<tr>
<th>Inflammatory bowel disease</th>
<th>Distribution in the gastrointestinal tract</th>
<th>Rectal involvement</th>
<th>Mucous membrane involvement</th>
<th>Mural involvement</th>
</tr>
</thead>
<tbody>
<tr>
<td>Crohn’s Disease</td>
<td>Segmental</td>
<td>Preserved rectum</td>
<td>Ulcerated or cobblestone mucosa submucosa</td>
<td>Fissures and fistulæ - from transmural to serosa</td>
</tr>
<tr>
<td>Ulcerative Colitis</td>
<td>Continuous</td>
<td>Rectal involvement</td>
<td>Granular mucosa</td>
<td>No fissures or fistulæ Normal serosa</td>
</tr>
</tbody>
</table>
nal tract location is associated with risk of recurrence and surgery. Small bowel disease with risk of surgery, and colonic disease, and particularly rectal disease, is associated with increased risk of perianal lesions. In UC, extensive colitis is associated with increased risk of colorectal cancer and colectomy.

Inflammatory bowel disease is a multifactorial disease with highly varied genetic determinants. In 2001, Hugot and Omura, separately published their discoveries that the NOD2 gene within the IBD1 locus on chromosome 16 is a marker for susceptibility to CD. Afterwards the gene’s pathogenic role was discovered.

More recently at least four new genes have been identified as potential generators of susceptibility to CD: DLG5, SCL, MDR1 and TLR. Several environmental risk factors, such as diet, smoking, or appendectomy contribute to its pathogenesis.

In 2005, the Montreal revision of the Vienna classification system was introduced. Using this classification system, it has been shown in a cohort-based clinical trial that there can be a significant change in disease time depending on disease location. The use of immunomodulators as early treatment and/or of biological modulators justified a decrease in the risk for disease progression. Therefore, it is important to identify patients at risk for disease progression as soon as possible for an early diagnosis and timely therapy.

In recent years, emphasis has been placed on the determination of the importance of predictive factors, with endoscopic findings and biomarkers being evaluated as relevant factors in the prediction of disease course. Disease progression may be divided into three stages, according to imaging presentation: early, intermediate and advanced.

**IMAGING FINDINGS**

Traditional methods for the diagnosis of CD in the small bowel have been endoscopy and barium follow-through, but at present there are new methods for the diagnosis of this disease. The advantages and disadvantages of these methods are discussed below.

**Small bowel follow-through**

The small bowel follow-through is performed with single barium contrast. It may be performed with 400 to 600 ml of barium sulfate suspension and intermittent fluoroscopy for, approximately 20 to 30 minutes until visualization of the terminal ileum.

Even if the small bowel follow-through may effectively diagnose transmural disease, it may be inaccurate for establishing mild diseases, such as aphthous ulcers, ulcers or any other mucosal abnormalities (Fig. 1).

**Capsule Endoscopy**

Capsule endoscopy is a noninvasive procedure for evaluating the small bowel. The test is performed using a capsule, a device that is the size of a large pill. The endoscope consists of a strong light source, a tiny camera and a transmitter. Once swallowed, the capsule travels through the digestive tract and the camera obtains several images that are transmitted to a data recorder.

Capsule endoscopy views several meters of the small bowel, helping to find abnormalities that are beyond the reach of traditional endoscopic procedures. In addition, the clarity of the images may also help physicians detect changes missed by other diagnostic methods.

In a retrospective study, 733 consecutive examinations performed at 4 large referral centers were analyzed.

In 8.46% of patients, technical limitations including gaps in the recordings, short duration of capsule batteries and failure of downloading occurred in the early phase of capsule use in 8.6% of examinations. Clinical problems, such as difficulty swallowing the capsule or incomplete small-bowel examination occurred in 16.4% of examinations, while capsule retention that required surgical or endoscopic retrieval occurred in 1.9% of cases.

Capsule endoscopy may be used for the study of CD in patients with a high clinical suspicion of this disease and with absence of abnormalities on colonoscopy and small-bowel follow-through (since these abnormalities may hinder passage of the capsule).
Colonoscopy

Colonoscopy is a direct examination of the colon, sometimes including the terminal portion of the small bowel. During the endoscopic procedures, the surgeon may obtain biopsy specimens for histopathological diagnosis. The disadvantage of colonoscopy is that it is an invasive method incapable of diagnosing extraluminal lesions.

Magnetic Resonance Enterography

Magnetic resonance enterography (MRE) has several advantages over computed tomography enterography (CTE) because it does not use ionizing radiation, using gadolinium as contrast agent (which, unlike iodine, does not cause major allergic reactions). The main limitations of MRE are its high cost, the claustrophobic effect, the longer duration of the study (difficulty for breath holding) and its lower availability, whereas CTE is more widely available, cheaper and faster (20 s) [5].

MRE allows identification of extraluminal complications, disease distribution and disease activity, as well as evaluation of proximal small bowel segments which are inaccessible by colonoscopy (Fig. 2).

Because of limited spatial resolution, it is difficult to see the earliest changes of CD, namely, mucosal nodularity, erythema, and superficial aphthous ulceration. Suboptimal distention of the loops makes evaluation of wall thickness difficult. However, MRE enteroclysis enables optimal distention of the loops, and thus helps to identify the early signs of disease.

Typical changes of CD include ileal involvement, adipose tissue proliferation, wall thickening, linear and aphthous ulcers, fistulization, skip lesions and cobblestoning. MRE findings associated with disease activity include wall thickening greater than 4 mm,
intramural and mesenteric edema, mucosal hyperemia, wall enhancement, transmural ulceration and fistula formation, vascular engorgement and inflammatory mesenteric lymph nodes. Enhancement of the latter is the most characteristic finding.

Indications for MRE include disease relapse, suspected obstructive disease, extraluminal complications, treatment failure, and planned surgical resection. It is more sensitive for the detection of fistulas and it might help to identify fibrous tissue resulting from chronic inflammatory changes in acute disease.

Nicholas Gourtsoyiannis et al, based on their findings, suggested performing MRE in patients with active disease and no correlation of imaging, clinical and laboratory findings. Anyway, these data should be interpreted with caution because a small sample size has been used. Authors found that patients with normal laboratory findings had changes representative of active disease on MRE images. The parameters used were: changes in signal intensity on post-gadolinium T1 images, signal intensity characteristics and wall thickness measurement on T2-weighted images, and perienteric changes. Specific findings indicative of active CD included the presence of deep ulcers, increased wall thickness and enhanced mesenteric lymph nodes.
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Doppler Ultrasound

The study of IBD, and particularly of CD, by Doppler ultrasound is of special interest for assessing disease activity and response to treatment, as this technique is useful for evaluating the superior mesenteric artery and the bowel wall.

CD is associated with hypervascularity of the bowel wall during active disease, which implies an increase in regional and local blood flow. Thus, color Doppler studies show an increase in blood flow and mean velocity, associated with a decrease in the resistance index (RI) in the superior mesenteric artery (related to disease activity). Some studies looking at the difference in blood flow, pulsatility index and RI before and after a meal have found a significant association. The measurements in the superior mesenteric artery may also be influenced by age, presence of atherosclerosis, and the length of the intestinal segment that is affected. Knowledge of normal bowel anatomy and pathological findings, as discussed below, should be evaluated together with data obtained from Doppler ultrasound.

Scanning is initiated with a curved 3 MHz transducer. This achieves greater depth and provides a better overview, enabling a rapid identification of the area of suspected activity; then, with higher frequency linear transducers (5 MHz), better image characterization is achieved, with visualization of bowel layers.

The normal small bowel (Fig. 3) consists of 5 layers corresponding, from the lumen outward, to the mucosal interface (hyperechoic), deep mucosa and muscularis mucosae (hypoechoic), submucosa (hyperechoic), muscularis propria (hypoechoic) and serosa interface (hypoechoic). Once the affected segment(s) has/have been detected, wall thickness has been measured and the pre-
sence of complications (fistulae, collections, etc.) has been identified on B-mode, Doppler examination of the loop with the maximum wall thickness is initiated, with special settings for evaluation of low flow velocity. Disease lies mainly in the submucosa, which appears hypoechoic because of edema, with loss of stratification and thickening of the wall of the affected bowel segment.

Fraquelli et al. (14) showed in a meta-analysis that when a bowel wall thickness threshold greater than 3 mm was used, sensitivity was 88% and specificity was 93% for suspected diagnosis of CD from wall thickening, while when a threshold greater than 4 mm was used, sensitivity and specificity were 75% and 97%, respectively. Thus, for primary diagnosis a threshold of 4 mm should be used because it is more representative of active disease.

Wall thickening is associated with the need for surgery and the risk of recurrence, but it is not a finding specific to CD. The established diagnosis is made by endoscopy and histological study. Wall thickening leads to a narrowing of the lumen of the affected loop, with resulting areas of stenosis and dilation of the previous loop (15).

Fig. 11: Sketch showing mural stratification replacement. Halo sign. (a) “Aqueous halo” representing aqueous infiltration, indicating an acute-subacute inflammatory process. (b) “Fat halo” representing infiltration of the submucosa with fat, a sequel of the chronic inflammatory process.

Fig. 12: Sketch showing vasa recta and enlarged vessels. Engorgement of the vasa recta of gastrointestinal loops. (a) Doppler ultrasound, (b) CTE and (c) MRE, showing hypervascularity at that level in the area of active disease. Doppler US shows evidence of active disease: increased wall thickness with submucosal edema and loss of wall stratification (arrow), low-resistance wall hyperflow, increased echogenicity of the adjacent adipose tissue, comb sign, enlarged caliber and greater visualization of the vasa recta in the mesenteric border of the loop (a finding consistent with active disease).

Fig. 13: Solid, heterogeneous material mixed with bubbles in the small bowel (normally seen in the colon). When seen in the small bowel, it is an indirect sign of poor transit time through that bowel segment (obstruction). Feces sign.

Fig. 14: Sketch and example. Interloop extraluminal fluid.
Enteroclysis

This method, considered as the gold standard imaging method for evaluation of small bowel disease was overcome by CT enteroclysis. Although there is no significant difference in characterizing mucosal and mural abnormalities between these two methods, CT enteroclysis provides important information about the extraintestinal extension of the disease (in particular, fistulas and abscesses). A comparative study evaluated the detection rate of skip lesions (17 with CT enteroclysis vs. 3 with conventional enteroclysis) and the detection rate of conglomeration of bowel loops (13 vs. 3, respectively), concluding that CT enteroclysis has a higher diagnostic accuracy (16).

An early detection of these two complications is crucial for an early treatment. Patients who develop abscesses and conglomeration of strangled bowel loops, as well as skip lesions, require surgical treatment (Fig. 4).

In experienced hands, enteroclysis has been considered superior to conventional small-bowel follow-through (16), producing better delineation of the small-bowel loops. Not only does enteroclysis produce better distention of individual loops, but the double contrast allows the distal ileum to be detected and appropriately separated.

CT enteroclysis combines the advantages and benefits of both techniques (enteroclysis and CT).

Computed tomographic enterography

At several institutions, CTE is the imaging method of choice for evaluating the extension and severity of small bowel disease in patients with IBD. Recent studies have shown a significant correlation of active disease with elevation of C reactive protein and CTE findings of mural enhancement, enhancement of wall thickening or of mesenteric fat density (Fig. 5) (19).

DETAILS OF THE CT ENTEROGRAPHY PROCEDURE

Patients are instructed to drink 1500 ml of negative contrast: 500 ml are given at 45 minutes, at 30 minutes and at 15 minutes before the procedure. When scanning begins, 150 ml of nonionic IV contrast medium is administered at a rate of 3 ml/s, and the imaging is conducted 40 seconds after the administration of the IV contrast medium is started. A Multidetector scanner must be used with 2-mm slices and 1-mm section thickness, 200 mA and 120 kVp (17). Reconstructions must be performed in 3 planes, with coronal reconstructions being the most relevant (at 3-mm intervals).

At our institution, scans are performed using 64- and 16-row multislice scanners. Except for some availability issues, most scans are performed using the former, with an average of 7 scans per week.

As negative oral contrast material, we use polyethylene glycol and mannitol. When polyethylene glycol is used, 750 ml are administered in 40 minutes (one glass every 10 minutes), and 750 ml are administered in less than 30 minutes (one glass every 5 minutes). When the negative oral contrast used is mannitol, the 1500-ml jug must be administered in 30 to 40 minutes.

Patients are placed in the ventral decubitus position to obtain distension and redistribution of the loops, and an intramuscular injection of Buscapina (N-butyl hyoscine bromide) is administered to avoid spasms in the gastrointestinal tract. Iodinated contrast

Fig. 16: (a) Sketch representing hyperdensity and (b) hypodensity. (a) Fat abnormality and increased density of mesenteric fat. (b) Fibroadipose proliferation and increase in adipose tissue of the mesentery separating vessels.
material is administered intravenously at a rate of 3 ml/s with an approximate volume of 120 ml and three contrast-enhanced images are obtained in the arterial phase (at 40 seconds) and one in the portal phase (at 70 seconds after the administration of contrast). If there is a non-characterized lesion in the hepatic parenchyma or associated with the excretory system (or related to this system), a delayed phase is performed: at 3 minutes for the former, and after 10 minutes for the latter. Thus, we avoid unnecessary phases that imply further exposure of patients to radiation.

**DIAGNOSIS**

The most sensitive imaging marker of CD is, in the first place, mural hyperenhancement, followed by increased mural thickness. Other authors suggest that a combination of mural thickening (Fig. 6) and increased attenuation of the perienteric fat (Fig. 7) are the most specific signs of active CD (17). Jejunal attenuation is significantly higher than ileal attenuation when examining distended small bowel loops at enteric phase CTE. Evaluating small bowel attenuation in patients with active disease is essential because segmental mural hyperenhancement at CT and magnetic resonance (MR) imaging is indicative of active inflammation (18).

Furthermore, in order to avoid overdiagnosing CD, it is important to know that collapsed bowel segments have greater attenuation than distended bowel segments and that the jejunum has greater attenuation than the ileum.

Terminal ileal attenuation is higher in patients with active CD than in patients without active CD. Voderholzer (17) found that, for terminal ileal inflammation due to CD, CTE had a sensitivity of 67%, while capsule endoscopy had a sensitivity of 80%. In a recent study comparing portal phase CTE, capsule endoscopy, small-bowel follow through, and ileocolonoscopy, sensitivities of 82%, 83%, 65%, and 74% were reported, respectively, for active CD, showing that CTE was more specific than capsule endoscopy (18).

Mural thickening above 3 mm with a relative attenuation cutoff of 50% can distinguish normal terminal ileum from active CD (18).
TYPICAL CTE FINDINGS IN CD

CT findings include: mucosal enhancement, mucosal vascularity, mural thickening, fat abnormalities, free fluid adjacent to the affected loop, fat proliferation, extraluminal gas, enlarged lymph nodes and interloop fistulas (Figs. 8-17).

An additional benefit of CTE is its ability to detect penetrating complications of CD and extraintestinal IBD manifestations. The presence of fistulas, abscesses or phlegmons may determine or alter management plans (Figs. 18 and 19). The finding of extraintestinal manifestations (such as nephrolithiasis, cholelithiasis, sacroiliitis, avascular necrosis, deep vein thrombosis, or primary sclerosing cholangitis) can influence patient care, in spite of the absence of luminal disease of the small bowel, and explain symptoms not related to this disease (17, 19, 20).

An agreement of 80% was shown between clinical symptoms and CTE findings, as regards disease progression or regression, in a retrospective study where 20 patients were evaluated (21). The study compared CTE, capsule endoscopy, ileoscopy and small-bowel follow-through in the same patients suspected of having CD. Results were as follows: CTE, capsule endoscopy and ileoscopy have a greater ability for depicting CD findings than small-bowel follow-through. Capsule endoscopy has better diagnostic ability for assessing proximal or early mucosal disease (6), whereas CTE is the best method for detecting transmural and extraluminal abnormalities (17). Both capsule endoscopy and CTE may depict nonobstructive CD, when ileoscopy or small-bowel follow-through produce negative or inconclusive findings (20).

CONCLUSION

CTE is readily available and easy to perform. It makes it possible to determine the extent and stage of progression of inflammatory bowel disease, extraintestinal involvement and potential complications. The combination of a short examination time, a single breath hold, accessibility and availability has made CTE an important tool in the diagnosis and follow-up of patients with Crohn’s disease.

However, we should bear in mind that each method provides different data on CD, therefore they complement each other. Confirmation by different methods increases diagnostic accuracy when findings are not categorical.

References


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