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THE CECOCOLONIC JUNCTION: AN ANATOMIC, HISTOLOGIC, MORPHOMETRIC, RADIOLOGIC AND ENDOSCOPIC STUDY OF ITS STRUCTURE IN HUMANS WITH IDENTIFICATION OF AN ANATOMIC CECOCOLONIC SPHINCTER

(Research article)

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Abstract: *Aim*. We have recently demonstrated that the cecocolonic junction is a high-pressure zone of a mean length of 1.6 ± 0.6 cm. It reacts to cecal or colonic distension by dilatation or narrowing, respectively. These findings presumably indicate the existence of a physiologic sphincter at the cecocolonic junction. We hypothesized the presence of an anatomical cecocolonic sphincter and investigated this hypothesis in the current communication.

Methods. Histomorphologic and morphometric studies were carried out in 14 cadavers and radiologic studies in 20; endoscopic studies were done in 16 healthy volunteers. Longitudinal sections along the cecum, cecocolonic junction and ascending colon were stained with H & E and Masson's trichrome stain. The morphometric studies measured the muscle thickness of the cecum, cecocolonic junction and ascending colon using image analyzer computer equipment. The cecocolonic junction was examined radiologically by the method of small bowel barium meal administration and endoscopically by pancolonoscopy.

Results. A cecocolonic fold was identified 2-2.5 cm distal to the ileocecal nipple. It extended along the gut circumference, shelf-like, and was marked by a shallow groove on the outer aspect of the colon. Microscopically, the cecocolonic fold consisted of mucosa, sulmucosa and muscularis externa, all of which were a continuation of those of the cecal wall. The circular muscle layer was thicker than that of the cecum or ascending colon. Branching cells with ovoid nuclei representing probably intestinal cells of Cajal were identified in the muscularis externa. Also the morphometric study showed that the circular muscle layer was significantly thicker than that of the cecum or ascending colon ($p<0.0001$, $p<0.0001$, respectively), while the longitudinal muscle exhibited no significant difference ($p>0.05$, $p>0.05$, respectively). Radiologic studies demonstrated narrowing at the cecocolonic junction, which became wider on cecal contraction and narrower or closed on colonic contraction. Endoscopically, the cecocolonic junction was narrow due to the presence of the cecocolonic fold, which exhibited spontaneous contractions.

Conclusion. Our findings suggest the presence of an "anatomic" sphincter at the cecocolonic junction as evidenced histomorphometrically, radiologically and endoscopically. The sphincter showed spasmodic contractions on endoscopic examination as well as dilatation and contraction on cecal and ascending colon contraction, respectively. The detection of interstitial cells of Cajal in the cecocolonic fold postulates the possible existence of a pacemaker in the cecocolonic fold, a point that needs further study.

. **Key words:** cecocolonic fold, ileocecal nipple; interstitial cells of Cajal, pacemaker.

INTRODUCTION

The ileum joins the large intestine end to sides, marking the beginning of the ascending colon (AC) distally and the cecum (C) proximally to the junction (Faussone-Pellegrini et al., 1995). The area between the C and AC is called the cecocolonic junction (CCJ). In herbivorous and carnivorous animals, a sphincter could be identified at the CCJ (Pelckmans, 1998). In humans, radiologists and endoscopists have reported a circumferential contraction and a prominent ileocecal fold at the junction between the C and AC (Hickel and Bernard, 1963; Torsoli et al., 1968; Schiller et al., 1986; Cotton and Williams, 1990). Furthermore, microscopic studies showed the existence of muscular and innervational patterns different from those of the adjacent areas (Faussone-Pellegrini et al., 1993a; 1993b; 1994). Pellegrini et al found, endoscopically, spontaneous or evoked spasms in an ileocecal fold (Faussone-Pellegrini et al., 1995). In surgical specimens, a thick circular fold containing muscle fibers could be seen at the level of the CCJ (Faussone-Pellegrini et al., 1995).

Recent studies have shown that the CCJ is a high-pressure zone of a mean length of 1.6 ± 0.6 cm (Shafik et al., 2002a). It reacts to cecal or colonic distension by dilatation or narrowing, respectively, and this reaction was suggested to be reflex in nature (Shafik et al., 2002a). These data presumably denote the existence of a physiologic sphincter at the CCJ. However, the existence of a cecocolonic sphincter in humans appears to be poorly addressed in the literature. The current communication studied the histomorhologic and morphometric structure of the CCJ, aiming at elucidating its function in the light of its anatomical structure. Knowledge of the structural-functional relationship of the CCJ might be of importance in the assessment of functional and pathological disorders of this area.

MATERIAL and METHODS

Material. Histomorphologic and morphometric studies were carried out in 14 cadavers, and radiologic studies in 20; endoscopic studies were performed in 16 healthy volunteers. The cadaveric specimens consisted of the terminal ileum, C and AC.

Histomorphologic and morphometric studies. The 14 cadavers (10 male, 6 female; mean age 34.4 ± 12.3 SD years, range 8-50) had a normal gastrointestinal tract. They were studied after being fixed in 10% formalin. The AC was cut transversely, 5 cm above the ileocecal junction, allowing an overview of the CCJ, similar to that of the endoscopist; a magnifying loupe was used when necessary. The specimen was then opened by a cut along the tenia coli starting from the C and extending towards the AC for morphologic examination of its interior. The examination was performed with the help of a magnifying loupe, fine surgical instruments and bright light. After naked eye examination, the findings were photographed.

Histologic study. The 14 cadaveric specimens were cut longitudinally along the colon, CCJ and C at 4 sites: antimesenteric, mesenteric and laterally between the 2 sites. The specimens were fixed in buffered formalin, processed for paraffin sections of 5-µm thickness, and stained with hematoxylin and eosin and Masson's trichome stain. The cecocolonic fold (CCF) was examined microscopically. Other folds in the specimen distal to the CCF were examined as well.

Morphometric study. The data were obtained by using

image analyzer computer equipment (Leica Qwin 500, London, UK). The image analyzer consists of a colored video camera, colored monitor and a computer connected to the microscope and controlled by Leica Qwin 500 software. Prior to the test, the image analyzer was calibrated to automatically convert the measurement units produced by image analyzer program into actual micrometer units with all objective lenses of the microscope. The data measured were the muscle thickness of both the circular and longitudinal layers of the wall of various segments in serial longitudinal sections of the C, CCJ and AC. Ten fields were measured in each specimen and the mean was calculated. The data of the CCJ were compared with those of the C and AC for both the inner circular and the outer longitudinal muscle layers.

Radiologic study. The CCJ was studied radiologically in 20 healthy volunteers (12 men, 8 women; mean age 40.2 ± 13.9 SD years, range 21-52) after giving an informed consent. The subjects had no gastrointestinal complaints in the past or at the time of enrolment. They had a mean stool frequency of 8.7 ± 1.6 / week, (range 7-10) which matched the normal frequency in our laboratory. Our Faculty Review Board and Ethics Committee approved the study. The CCJ was studied by giving barium sulfate by mouth using the method of small bowel meal described by Sutton (1990).

Endoscopic study. Colonoscopic examination was performed in 16 healthy volunteers who had no gastrointestinal complaint. Ten were men and 6 women with a mean age of 38.6 ± 7.9 years (range 29–52). The subjects gave an informed consent. The endoscope used was the video-endoscope EC–200–LR (Fujinon, Osaka, Japan). After colonic preparation, the C, AC and CCJ were examined. The colonoscopy was performed under no pharmacologic treatment nor sedatives, analgesics or antispasmodics. The pancolonoscopy showed a normal colon.

The results of the study were analyzed statistically using the Student's t test. Differences assumed significance at $p<0.05$ and values were given as the mean ± standard deviation (SD).

RESULTS

Anatomical findings. An overview of the CCJ through the AC has revealed circumferential narrowing of the colonic lumen 2-3 cm distal to the ileocecal junction. When the colon was cut along the anterior tenia coli, a thick circular fold causing narrowing of the colonic lumen could be seen . The fold apparently defined the border area between the C and AC. This "cecocolonic fold" (CCF) was located 2-3 cm distal to the suspensory ligament of the ileocecal nipple. The suspensory ligament started at the ileocecal stoma and extended circumferentially around the cecal wall (Shafik et al., 2002b). No folds could be identified between the CCF and the suspensory sling.

The CCF extended along the gut circumference, protruded shelf-like into the lumen of the CCJ, measured 0.75-1.5 cm in breadth and had a smooth surface. The colonic lumen was partially occluded at the level of the CCF, which we recognized as the cause of the narrowing of the gut lumen when we viewed the gut through the open end of the transversely cut AC. A shallow groove, which was lying opposite to the CCF, could be identified on the outer aspect of CCJ; it was located 2-2.5 cm proximal to the ileocecal junction.

Microscopic structure of the CCJ. Microscopic examination showed the CCF to consist of all layers of the cecocolonic wall: mucosa, submucosa and muscularis externa. These microscopic layers of the CCF were a continuation of those in the cecal wall. The muscularis externa consisted of circular and longitudinal muscle layers. The latter passed from the cecal wall to the CCF and continued with the same thickness as that of the cecal wall. Meanwhile, the circular muscle was much thicker in the CCJ than in the C and the AC.

The muscle arrangement in the C and AC was in the form of an outer longitudinal and inner circular muscle; this arrangement was reversed when the cecal muscle entered the CCF: the muscularis externa in the fold consisted of an outer circular and inner longitudinal muscle. The CCF had a mucosal covering of intestinal crypts. It enclosed well-formed nerve plexuses which showed branching cells with an ovoid nucleus that were similar to those described as interstitial cells of Cajal. In some specimens, the mucosa was thrown into multiple folds. At the base of the CCF, the mucosa was rich in aggregated lymph follicles. The lamina propria contained fat cells and many blood vessels. In some specimens, the CCF showed excess adipose connective tissue which was condensed near the tip region of the fold. The CCJ core contained areolar connective tissue with many blood vessels. The serosa extended uninterruptedly from the C to the AC across the base of the CCF; it did not follow the curve of the muscularis externa inside the CCF.

Microscopic examination of the folds distal to the CCF showed them to consist of covering mucosa and to contain connective tissue and blood vessels in their core; we could not identify muscle fibers in any of these folds. We did not find folds existing between the ileocecal nipple and CCF.

Morphometric findings. The morphometric findings of the outer longitudinal and inner circular muscle layers of the C, CCJ and AC are depicted in table 1. The inner circular muscle layer of the CCJ was significantly thicker than that of the C and AC ($p<0.0001$, $p<0.0001$, respectively). Meanwhile, the thickness of the outer longitudinal muscle layer showed no significant difference from that of the C and AC ($p>0.05$, $p>0.05$, respectively).

Radiologic findings. When the C and AC were filled with barium, a constriction was identified 1–2 cm distal to the ileocecal junction. This narrowing corresponded to the site of the CCJ as identified by the current cadaveric and endoscopic studies. At rest, the cecocolonic opening was narrow and had a mean diameter of 2.2 ± 1.2 cm (range 1.5-3). The ileocecal junction appeared as a nipple-like filling defect in the barium-filled C. When the terminal ileum became full with barium while the ileocecal nipple was closed, ileal contraction effected opening of the ileocecal nipple, thus allowing barium to pass to the C . The C was full with barium while the CCJ appeared narrow or closed. On cecal contraction, the CCJ became wider and full with barium which passed to the AC. AC contraction was associated with narrowing of the CCJ.

During our fluoroscopic follow-through-meal study we found that the C, when it became full with barium, contracted and evacuated its contents into the AC. We did not observe in any of the studied subjects synchronous contraction of the AC with the C. When the AC became full, usually with more than one cecal contraction, it contracted. During colonic contraction, we did not observe colocecal reflux. The CCJ during colonic contraction became narrow but was not closed except in only 3 subjects.

Endoscopic findings. Proceeding from the cecal pole,

Table 1.

Mean values (μm) of thickness of muscularis externa of the cecum, cecocolonic junction and ascending colon.

	Cecum		**Junction**		**Colon**	
	IC	**OL**	**IC**	**OL**	**IC**	**OL**
Mean	473.62	357.95	1420.86	626.41	501.18	362.95
SD	24.12	17.30	125.39	90.54	9.7	11.42
P_1	0.000***				0.000***	
P_2		0.270				0.235

IC = inner circular OL = outer longitudinal
SD = standard deviation
p_1 vs junction IC
p_2 vs junction OL
*** very highly significant ($p<0.0001$)

the first prominent fold encountered was that attached to the stoma of the ileocecal nipple which is called the "suspensory ligament" (Shafik et al., 2002b). This fold stretched along the whole cecal circumference in 10 subjects and occupied part of the circumference in 6. It was preceded by 2–3 small and less prominent folds. Another prominent fold, 2–3 cm aborally and encircling the whole circumference of the colon, could be identified in all of the examined subjects and was easily distinguished from the proximally lying fold which is the suspensory ligament. Distally to this CCF there were multiple colonic folds which differed from the CCF by being smaller, less prominent, and incomplete i.e. not encircling the whole colonic circumference.

The colonic lumen at the CCF was narrower than that of the C or AC. Spontaneous spasm of the fold occurred in 12/16 subjects and caused narrowing of the colonic lumen to the extent of its complete closure in 2 subjects. The fold spasm lasted a mean of 96.6 ± 21.6 seconds (range 50-140).

DISCUSSION

The C and colon contained many mucosal folds. Those folds, however, were small, had no fixed location, did not encircle the colonic lumen completely and, most important, contained no muscle fibers (Faussone-Pellegrini, 1994). Meanwhile, a perpetual mucosal fold has been described to exist at the ileocecal nipple (Shafik et al., 2002b). This fold, named "suspensory ligament", is attached to the ileocecal nipple and is suggested to serve 2 functions: a) it suspends the ileocecal nipple and b) it assists in closing the ileocecal stoma on cecal distension (Shafik et al., 2002b).

In the current study, we could identify another mucosal fold which encircled the colonic lumen completely and had a fixed location. The fold existed in all the studied cadaveric specimens and in the endoscopically examined subjects. It was located 2-3 cm distally to the suspensory ligament of the ileocecal nipple; no further folds could be detected between the 2 folds. This fold which we termed "cecocolonic fold" (CCF) seems to represent the junctional area between the C and AC. Endoscopically, the 2 folds could be easily differentiated: the suspensory ligament was attached to the ileocecal stoma while the CCF lay 2-3 cm distally.

Cecocolonic anatomic sphincter. The CCF contained muscularis externa, which was a continuation of that of the C. However, the circular muscle layer of the muscularis externa was significantly thicker than that of the C or AC as evidenced histomorphometrically. These findings presumably indicate the presence of an "anatomic" sphincter at the CCJ. Physiologically, the contractile nature of this sphincter was evident from the spontaneous contractions at the CCJ observed during colonoscopy. Moreover, a recent study (Shafik et al., 2002a) has shown that the CCJ responds to cecal or colonic distension by relaxation or contraction, respectively. This response was reflex and mediated through the cecocolonic inhibitory and colocecal excitatory reflexes (Shafik et al., 2002a).

Endoscopic and radiologic findings seem to support the presence of a sphincter at the CCJ. This is evident from the narrow colonic lumen at the CCJ, its dilatation during cecal evacuation of barium into the AC and its narrowing after termination of evacuation.

Role of cecocolonic fold in the colocecal antireflux mechanism. In the current study we observed that the AC did not contract synchronously with the cecal contraction. The C contracted at first and was followed by AC contraction. The absence of colocecal reflux during AC contraction appears to be due to CCF contraction synchronously with the AC contraction. Although we did not achieve complete closure of the CCJ in most of the cases, we believe that the colocecal antireflux mechanism depends on two factors: a) the high pressure zone at the CCJ (Shafik et al., 2002a), and b) the increase of the intraluminal pressure at the CCJ as a result of narrowing of the CCJ upon AC contraction.

Role of interstitial cells of Cajal. The localization and morphology of the branching cells with ovoid nucleus related to the myenteric plexus suggest that they are interstitial cells of Cajal. The detection of these cells in the CCF probably adds new functional significance to the CCF. Several investigators presented studies supporting the role of the interstitial cells of Cajal in generating spontaneous pacemaker activity (Sanders, 1996; Vanderwinden et al., 2000; Ward, 2000). The slow wave frequency has been associated with interstitial cells of Cajal function. With the detection of the interstitial cells of Cajal in the CCF, we hypothesize that a pacemaker exists in the CCF which delivers slow waves to the AC. This hypothesis, when verified, might explain the non-synchronous contraction of the C and AC and the presence of a pacemaker for each of them.

In conclusion, our findings suggest the presence of an "anatomic" sphincter at the CCJ as evident histomorphometrically, radiologically, and endoscopically. The muscularis externa was significantly thicker than that of the C and AC. Spasmodic contractions of the CCF were observed on endoscopic examination. Radiologic studies showed dilatation and narrowing of the CCJ on cecal and AC contraction, respectively. Absence of colocecal reflux on colonic contraction is probably due to the high-pressure zone at the CCJ and to contraction of the CCF. The detection of interstitial cells of Cajal in the CCF postulates the possible existence of a pacemaker in the CCF, a point that needs further investigation.

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REFERENCES

1. Cotton PB, Williams CB. 1990. Practical gastrointestinal endoscopy. Blackwell, Oxford, pp 209-211.
2. Faussone-Pellegrini MS, Pantalone D, Cortesini C.1993a. Morphological evidence for a cecocolonic junction in man and functional implications. Acta Anat 146: 22-30.
3. Faussone-Pellegrini MS, Bacci S, Pantalone D, Cortesini C. 1993b. Distribution of VIP-immunoreactive nerve cells and fibers in the human ileocecal region. Neurosci Lett 157: 135-139.
4. Faussone-Pellegrini MS, Bacci S, Pantalone D, Cortesini C, Mayer B. 1994. Nitric oxide synthase immunoreactivity in the human ileocecal region. Neurosci Lett 170: 261-265.
5. Faussone-Pellegrini MS, Manneschi LI, Manneschi L. 1995. The cecocolonic junction in humans has a sphincteric anatomy and function. Gut 37: 493-498.
6. Hickel L, Bernard JM. 1963. Anatomo-physiologie radiologique du gros intestin normal. Semaines Hôpitalières 39:139-150.
7. Pelckmans PA. 1998. Study on the sphincteric nature of the ileocecal junction: a morphological and pharmacological approach (thesis). Antwerp: University of Antwerp
8. Sanders KM. 1996. A case for interstitial cells of Cajal as pacemakers and mediators of neurotransmission in the gastrointestinal tract. Gastroenterology 111: 492-515.
9. Schiller KFR, Cockel R, Hunt RH. 1986. A colour atlas of gastrointestinal endoscopy. Chapman, London, pp 181-182.
10. Shafik A, Mostafa RM, Shafik AA, Ahmed I. 2002a. Study of the functional activity of the cecocolonic junction with identification of a 'physiologic sphincter' and 'cecocolonic inhibitory and colocecal excitatory reflex'. Under publication
11. Shafik A, Wahdan M, Asaad S, Shafik AA, El-Neizamy E. 2002b. Ileocecal junction: anatomic, histologic, radiologic, and endoscopic studies with special reference to its antireflux mechanism. Under publication.
12. Sutton D. 1990. The small bowel. In: Sutton D (ed) A textbook of radiology and imaging. 4th edn, Churchill Livingstone, Edinburgh, pp 863-903.
13. Torsoli A, Ramorino ML, Crucioli V. 1968. The relationships between anatomy and motor activity of the colon. Am J Dig Dis 13: 462-467.
14. Vanderwinden JM, Rumessen JJ, Bernex F, Schiffmann SN. 2000. Distribution and ulltrastructure of interstitial cells of Cajal in colon, using antibodies to Kit and Kit (W-lac Z) mice. Cell Tissue Res 302: 155-170.
15. Ward SM. 2000. Interstitial cells of Cajal in enteric neurotransmission. Gut 47 (Supplement IV): 40-43.

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