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MINIREVIEW

The large intestine from fetal period to adulthood and its impact on the course of colonoscopy

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ABSTRACT

The human large intestine in the living adult has a total length of about 1300 mm, ranging from 1100 to 2108 mm. The development of the gut continues after birth, up to the age 4–5. The large intestine ascends at the beginning in the right abdominal quadrant, then it traverses the abdominal cavity, and finally it descends to the anus. The left and right colic flexures are the basic flexions between the transverse, ascending and descending colon, respectively. Additionally, there are secondary bendings between intestinal segments. The angles between the neighbouring parts can vary between examined subjects. Most of the angulations can be found in the transverse (range 2–9) and sigmoid colon (range 1–9), making them the most troublesome parts to pass with a colonoscope.

Colonoscopy (usually performed in the left lateral or supine position) is one of the most important examination of the large intestine mucus membrane. During this procedure the endoscope is passed through the colon into the cecum or terminal ilium. The individual anatomical features (tortuosity, supernumerary loops and elongation) may slow down or interfere with the progress of the scope.

We summarize current knowledge on the human large intestine from the fetal period to adulthood and carve out some aspects that are currently less known to colonoscopists.

1. Introduction

Large intestine (LI) extends from the distal ileum to the anus. Colonoscopy is one of the most important examinations of the LI. Its aim is to identify diseases of the colon, both in children and adults. Endoscopy in children should be conducted by an endoscopist who deals with young patients only, as the examination differs form that performed in adults (Lightdale et al., 2014; Thakkar et al., 2016; Tringali et al., 2016). Video-assisted colonoscopy is the main method for screening for colorectal cancer (Baxter, 2009; Rees et al., 2014; Smith et al., 2017).

Other methods used in the LI diagnostics are computed tomographic (CT) colonography, computer assisted colonoscopy and endoscopic capsules (Eickhoff et al., 2007; Rösch et al., 2008; Tortora et al., 2009; Valdastri et al., 2008).

During colonoscopy, the endoscopist tries to reach the cecum, visualize the ileo-cecal valve and pass the tip of endoscope into the terminal ileum. The quality of a colonoscopy exam depends on professional skills of the endoscopist, quality of available equipment, but also on individual anatomical features of the colon. The most important anatomy-related factors are: tortuosity (increased number of flexures), elongation of the LI (increased colonic length) and supernumerary loops of the intestine. Other anatomical features that could make the procedure problematic or incomplete are: mobility of the bowel (which depends on the anatomy of the mesentery) and intestinal wall resilience. The length, flexures, haustra, teniae, and mesenteries of the LI develop in the prenatal period, and continue to grow after birth. Morphological features of the bowel remain a controversial matter, as seen in literature. The

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aim of this review is to analyse the basic anatomical features of the LI from the fetal period to adulthood.

2. Large intestine

In the living adult it has a total length (LIL) of about 1300 mm, but this ranges from 1100 to 2108 mm (Alazmani et al., 2016; Hanson et al., 2007; Hounnou et al., 2002; Khashab et al., 2009; Marnerides et al., 2012; Minko et al., 2014; Phillips et al., 2015; Punwani et al., 2009; Sadahiro et al., 1992; Saunders et al., 1996, 1995). The LIL in prenatal period ranges from 80 mm in fetuses aged 14 weeks of pregnancy (wks), through 250 mm at 23 wks to 327 mm at 40 wks (Shanklin and Cooke, 1993; Struijs et al., 2009). Proportionally, the longest parts of the intestine are the transverse (TC) and the sigmoid colon (SC) (30% and 27%, respectively). The remaining parts are relatively shorter and constitute: cecum 3%, ascending colon 12%, descending 14%, and rectum 14% (anal canal circa 3%) (Sadahiro et al., 1992). Its segments bend at different angles (if the bending is very sharp – below 90°, it is called acute flexure). The number of acute flexures of the intestine varies from 5 to 19 in various papers (Eickhoff et al., 2010; Hanson et al., 2007; Khashab et al., 2009).

3. Colonoscopy

The aim of this examination is to study the mucous membrane of the LI from the rectum to the cecum. The cecum intubation rate depends on the endoscopist's skills, but also on anatomical conditions (Arcovedo et al., 2007; Hsieh et al., 2008; Kaminski, 2010; Krishnan et al., 2012.). In their guidance document, Rex et al. suggest cecum intubation should be achieved in ≥90% of all procedures and in ≥95% of screening examinatios (Rex et al., 2006).

Research papers on exam quality reporte rates of incomplete colonoscopies of 13.1–14.0% (Antipova et al., 2017; Rex, 2008; Shah et al., 2007). The procedure is usually performed with the patient in the supine or left lateral decubitus positions. When difficulties in advancing the colonoscope occur, additional maneuvers are required, among them: rotation of the patient or compression on the abdominal wall (Shah et al., 2000). These maneuvers are used to change the angles between two neighboring parts of the intestine or to dislodge bowel segments. Some authors studied the correlation between body rotations and morphological differences in the intestine. In a CT colonography study of 10 male and 10 female subjects, Punwani et al. found minimal changes in the LIL between prone and supine position (in prone 1842 ± 269 mm vs. supine 1839 ± 226 mm in males, $p = 0.98$; 1757 ± 333 mm vs. 1736 ± 327 mm in females, $p = 0.87$, student's t-test) (Punwani et al., 2009). Additional maneuvers during colonoscopy are time-consuming and result in prolonged colonoscopy time (PCT). Some authors suggested that PCT correlated with obesity (both general and visceral) (Chung et al., 2014; Nagata et al., 2014). Others described differences between genders. Saunders et al. who reported on 2194 endoscopies suggested that endoscopy in women is more difficult to perform than in males (31% of exams in women were technically difficult compared to 16% in men; 183 female and 162 male barium enema series). The authors stated, that the female LIL was greater than in men (1550 mm vs. 1450 mm, $p = 0.005$, Mann–Whitney test). That elongation was caused by lengthening of the TC (Saunders et al., 1996; Shah et al., 2000). Rex suggested that a more complicated course of colonoscopy in women was caused by morphology of the pelvis and/or acute rectosigmoid angle in lean women (Rex, 2008).

4. Changes in large intestine caused by death or fixation

Scientific investigations are conducted either in living individuals (for example during laparotomy or X-ray studies) or cadavers (fresh or fixed). The data obtained by different methods differ, so corrections of measured parameters are required, because formalin fixation is responsible for shrinkage of the bowel. Despite its great importance, very little information is available on human bowel formalin-related or post-mortem contraction. This issue appears very rarely in literature. Bhatnagar et al. (research method used in study (meth): 19 cadavers and 51 live individuals undergoing laparotomy for a disease not involving the colon) confirmed considerable shrinkage of the SC length of 25–40%. That authors established its mean length in living subjects to be 46.6 ± 11.2 cm, and in cadavers 28.0 ± 7.6 cm ($p > 0.05$) and the mean for mesocolon width 8.8 ± 2.1 cm vs. 6.5 ± 2.0 cm, respectively ($p = 0.007$, Mann Whitney test) (Bhatnagar et al., 2004). In contrast, Alatise et al. (meth: 50 subjects undergoing surgery and 50 fresh cadavers) concluded that the lengths of SC in living and cadaver subjects are not significantly different (living, 48.9 ± 1.3 cm vs. cadaver, 50.1 ± 1.6 cm; $p > 0.05$, student t test) (Alatise et al., 2013).

Goldstein established this loss of the LIL to be 57%. He used 26 sigmoid and rectum specimens (a 5.0 cm segment). The bowel shrank by 40% of the initial length during 10–20 min after removal and the remaining 17% after formalin fixation, so only 30% of the total shrinkage can be attributed to formalin fixation (Goldstein et al., 1999). Clarke et al. (meth: 12 canine small intestinal specimens) established a significant decrease in length after resection and fixation. The mean shrinkage was 28.3% immediately after excision ($p < 0.0001$, t-test) and 26.3% after 24 h of fixation in 10% formalin ($p < 0.0001$, t-test) (Clarke et al., 2014).

Wang et al. (meth: 25 LI specimens obtained after surgical resection) established the contraction to be 15.6% before any fixation, and 36.6% after 6–8 h, and 38% after 48–72 h in 10% formalin solution (Wang et al., 2004). The new fixation techniques (among them glycerine-ethanol embalming solution, the nitrite pickling salt embalming, tannic acid in glutaraldehyde or glyoxal acid-free fixative) change the LI analysed parameters, but no applicable data can be found in the literature yet.

The detailed data are showed in Table 1.

5. Rediscovery of the intestine

We witness a growing interest in intestine anatomy. The greatest attention is paid to mesenteries and peritoneum. Van Baal et al. concentrated on peritoneal anatomy and postulated its key role in the inflammatory response. That author suggested that the peritoneum was essential to generate new hypotheses for future research (for example resolve questions regarding the preferred location of peritoneal metastases on the peritoneum or new immune therapy-based treatments for peritoneal metastases) (Van Baal et al., 2017).

Coffey et al. postulated the contiguity of the mesentery from the mesoesophagus to the mesorectum. The mesentery merits the same attention that is applied to other abdominal systems, because distinctive and functional features (contiguity of lymphatic, neurological, vascular and connective tissue) have been revealed that justify the mesentery as an organ (Coffey and O'Leary, 2016). Culligan et al. disclosed that contiguous mesocolon and retroperitoneum were separated by mesothelial and connective tissue layers, which played a key role in colonic and mesocolonic mobilization (Culligan et al., 2014). Gao et al. studied the fasciae posterior to the colon and its associated mesocolon and concluded that they were composed of two independent layers: the visceral and parietal fasciae (Gao et al., 2013). Rigoard et al. supported the

Table 1
Changes in large intestine caused by death or fixation.

Author, publication year	Material	Range of shrinkage	Remarks
Bhatnagar et al. (2004)	Human SC	25–40%	Fixed cadavers vs. live individuals (undergoing laparotomy)
Alatise et al. (2013)	Human SC	not significantly different	Fresh cadavers vs. live individuals
Goldstein et al. (1999)	Human sigmoid and rectum specimens	57%	40% during 10–20 min. after removal; 17% after formalin fixation
Clarke et al. (2014)	Canine small intestine specimens	54%	28.3% immediately after excision and 26.3% after 24 h of fixation in 10% formalin
Wang et al. (2004)	LI specimens	54%	15.6% before any fixation, and 36.6% after 6–8 h, and 38% after 48–72 h in 10% formalin

peritoneal fusion theory (the intestine and its mesentery merge with the primitive posterior peritoneum and the mesothelium that leans up during the fetal period, disappears and is replaced by a fibro-connective tissue) (Rigoard et al., 2009). Soffers et al. investigated the key role of the mesentery in “intestinal rotation” and hypothesized that malrotation resulted from stunted development of secondary loops (distal jejunum) (Soffers et al., 2015).

6. Fetal period

We recently have witnessed the development of methods used to examine living fetuses – and now ultrasonography is supported by magnetic resonance imaging (Bach-Ségura and Droullé, 2008; Colombani et al., 2010; Rubesova, 2012). During this period, the alimentary tract lengthens gradually and“ rotates” (Soffers et al., 2015). Shanklin et al. (meth: 100 infants ranged from 12 to 42 wks; autopsy within 24 h of demise) reported that LIL increases positively linearly with gestation and crown-heel length (CHL), but curvilinearly with birth weight (Shanklin and Cooke, 1993). Harris et al. (meth: 64 human fetuses aged 11–20 wks, radiological study) distinguished two parts of the bowel: proximal (presplenic) and distal (postsplenic), with border located in the highest point of the splenic flexure. In the presplenic part 3 types of colon were identified: type 1 — essentially transverse in position in younger fetuses (14–18 wks), type 2 — oblique and type 3 — advanced in development with colon showing ascending and transverse components, present in older individuals (28–40 wks). According to this author, LIL increased slightly curvilinear in relation to crown-rump length (CRL). The distal part of the bowel lengthened at a higher rate than the proximal. It may be caused by traction of the phrenico-colic ligament or fusion of the descending colon mesentery with the retroperitoneal space (so it starts to grow like the abdominal wall) (Harris et al., 1976). Malas et al. (meth: 131 fetuses between 10 and 40 wks, postmortem examination) divided the colon into two parts — the first portion, which extended from the ileal orifice to the end of the descending colon, and the second one composed of the SC. In the first part, the adult type of colon (ascending, transverse and descending colon) was present in 60% of fetuses aged 38–40 wks, but only in 24% individuals in age 13–25 wks. The mean macroscopic colon diameters were measured as an average between 0.75 and 15.44 mm during the fetal period (from 10 to 40 wks, respectively) (Malas et al., 2004). Marnerides et al. (meth: 201 fetuses and 2 prematurely born infants, ages ranging from 14 to 27 wks, autopsy) compared the parameters of fetuses appropriate for gestational age (AGA), and intrauterine growth restricted (IUGR), stated that the decrease in length in IUGR could be observed after 24 wks, because of the time needed to reveal anomalies in morphology (Marnerides et al., 2012). The mentioned authors did not find any differences in colonic features between the genders. Some studies analysed other typical features of the large intestine - haustra and teniae. Malas et al. described the development of the colon haustra and teniae as a gradually progressive process (quite slow at the beginning of fetal development), which occured earlier in the ascending colon and proceeded to the SC. In 10–12 wks (n = 10) the haustra were not developed in 70% of examined subjects in both ascending and TC, in 60% in descending and in 100% of SC. In full term fetuses (38–40 wks) well developed haustra were observed in 60% of analysed individuals in ascending colon, 54% of TC, 44% of descending, and only 26% of SC. The teniae were not developed in fetuses aged 10–12 wks in 90% of subjects in ascending, transverse and descending colon and in all examined SC specimens. When compared to 38–40 wks fetuses, the teniae were well developed in 60% of subjects in ascending, transverse and descending colon, respectively, and only in 46% of SC (Malas et al., 2004). Madiba et al (meth: 296 Black African foetuses and 37 non-African) disclosed that Black African had elongated colon in utero, a broad shape of the mesentery was more common in females and the long-narrow shape was more common in males (p = 0.038) (Madiba et al., 2015).

After birth, the process of LI development and differentiation continue.

7. Postnatal period

A limited number of authors analyzed the LIL. Struijs et al. (meth: 108 patients, aged 24 hbd up to 5 years of age; laparotomy; measured the bowel from the ileocecal valve to the proximal rectum) stated that LIL ranged from 568 ± 27 mm in children under 6 months of life to 1224 ± 57 mm in individuals aged 49–60 months, and recommended the body height as proper parameter to predict the LIL. The extremely rapid elongation of the LI stoped at age 5, and from that moment, the length resembled that found in adults. The same LIL was observed in children who weighed near 20 kg and measured 120 cm (Struijs et al., 2009). Others papers analyzed LIL differences between genders.

Hounnou et al. (meth: 100 female and 100 male; cadavers, student’s t-test or Kruskal–Wallis test) stated that the male bowel was significantly (p = 0.03) longer than female. The strength of the correlation M vs. F was significant (p = 0.003) in the left colon (from a point situated between 2/3 right and 1/3 left of TC to the anus), but not (p = 0.364) for the right colon (from cecum to border point). The authors also demonstrated correlations between LIL and weight of studied individuals (p = 0.018) and no statistically important correlation with age (p = 0.618) and height (p = 0.510; Student’s t-test in all comparisons) (Hounnou et al., 2002). This statement is in contrast to the others authors — we suppose that LIL can be related to the defecations or/and diet habits — but we do not have any evidence for this theory in the literature. Khashab et al. (meth: 266 women, 239 men, CT colonography) revealed differences in LIL: insignificant between persons older and younger than 60 years: (1929 ± 269 mm vs. 1886 ± 261 mm, p = 0.22, respectively), but significant between women and men (1933 ± 256 mm vs. 1854 ± 265, p = 0.02). That authors reported significant variations between overweight adults (BMI > 25) and those with BMI ≤ 25 (1872 ± 249 vs. 1945 ± 284, p = 0.005 Kruskal–Wallis tests) (Khashab et al., 2009). Sadahiro et al. (meth: 86 female, 434 male; double contrast barium enema) revealed no correlations between body weight and LIL in males. According to them, the differences in LIL were found between females whose body weight was 60–70 kg vs. less than 50 kg ($p < 0.05$, Student's t-test). They stated that the female LI is longer than the male (1328.3 ± 156.9 mm vs. 1258.7 ± 154.2 mm respectively, $p < 0.01$, Student's t-test) (Sadahiro et al., 1992). One of the key factors for mobility of the colon segments inside the abdominal cavity is intestinal length. Another one is flexures and mesenteries. Mesenteries of the TC and SC cause them to be the most mobile parts of the colon. The left colic flexure (LCF) and right colic flexure (RCF) are very important endoscopic landmarks used to identify the location of the colonoscope inside the colon. Additionally, there are secondary flexures between intestinal segments. The angles between the intestinal parts can vary between examined subjects. Very few papers addressed these issues. Bourgouin et al. (meth: 50 female, 50 men; three-dimensional coordinates for each point recorded on tomography scans) measured the changes in relations between LI flexures and fixed points in the abdominal cavity. This study identified the RCF as the most variable point, and the colosigmoid junction (CS) as the least variable of all assessed points (Bourgouin et al., 2012). Saunders et al. (meth: 229 patients, 115 Caucasian, 114 Oriental; laparotomy) analyzed the movement ranges of bowel segments in Western vs. Oriental patients. These authors found a mobile LCF in 20% of studied Western compared to 9% in Oriental patients ($p = 0.016$), and more mobile TC in Western patients. In 29% of Western vs. 10% Oriental patients the mid-TC reached the pubic symphysis or lower ($p < 0.001$) (Saunders et al., 1995). Philips et al. (meth: 48 fixed cadavers) found a mobile proximal portion of ascending colon in 66% of subjects, but also a mobile portion of the descending colon (rudimentary mesentery) in 31% individuals. The heights of TC and SC mesenteries were 7.4 ± 3.6 cm and 6.3 ± 2.6 cm, respectively (Phillips et al., 2015). According Michael et al. (31 fixed cadavers) the height of SC mesentery was 7.3 ± 3 cm (Michael and Rabi, 2015). Anatomical text books and atlases state that the "normal" number of flexures is from 4 to 5 (Drake et al., 2005; Waschke and Paulsen, 2011). Hanson et al. (meth: 200 patients after incomplete and complete colonoscopy; CT colonography) established the amount of acute flexures (<90°) in patients after incomplete vs. complete colonoscopy as 11.9 ± 2.7 vs. 9.6 ± 2.4, respectively ($p < 0.001$, Chi-square test). They stated that the number of flexures correlated with the difficulty of the endoscopic procedure (Hanson et al., 2007). Eickhoff et al. (meth: 200 patients, CT colonography performed after colonoscopy) reported the mean of acute angulations to be 9.6 ± 2.4 (Eickhoff et al., 2010). Khashab et al. stated this number as 10.9 ± 2.4 (range 5–19), most of them were found in the TC - 4.7 ± 1.2 (range 2–9), and a little less in the SC 4.4 ± 1.2 (range 1–9) (Khashab et al., 2009).

The LI data presented above differed significantly, because of the methods applied in studies. Wasserman et al. (71 patients, intraoperative measurements) stated that the anthropometric definition of the rectum was not precise and highly variable. They suggested there is a need for amending the nomenclature of large intestine segments (Wasserman et al., 2016). The lack of precision in these matters could lead to misunderstandings. Most of the inaccuracies are connected with measurements of specimen lengths and widths (both intestine and mesentery). The creation of development curves of changes in LIL from fetal to adult period requires corrections of some parameters. Struits et al. studied the length of intestine in children aged up to 5 years (weight <20 kg, height <120 cm). Their LILs did not include the lengths of the cecum and anal canal (these parts constitute together about 6% of LIL) – so using them for comparisons requires a 6% surplus correction. Sadahiro et al. measured the LIL in adults whose age ranged from 14 to 92 years; weight from 40 kg to 80 kg; and height from 140 cm to 180 cm (Sadahiro et al., 1992; Struijs et al., 2009).

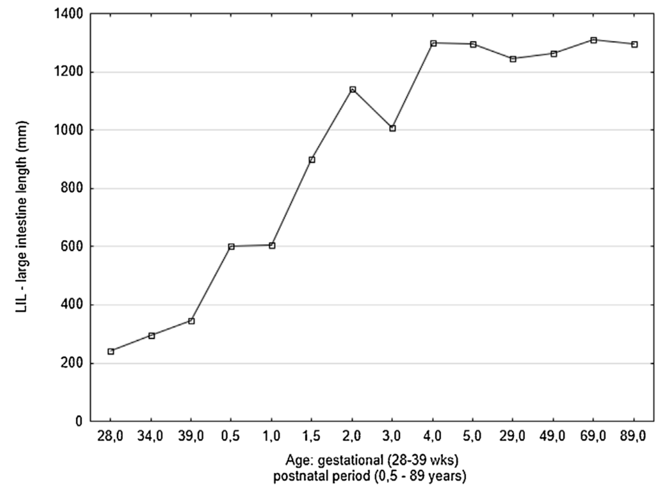

Fig. 1. Relation between LIL and prenatal (in wks; 28*–39*) and post-natal age (in years; 0.5–89).

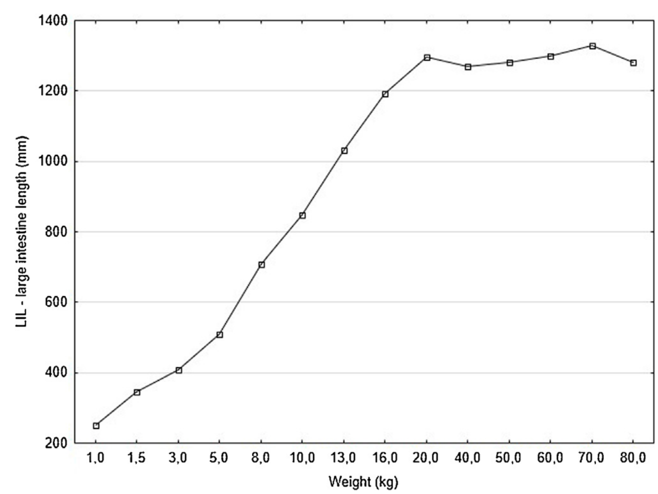

Fig. 2. Relation between LIL and weight (pre- and post-natal period).

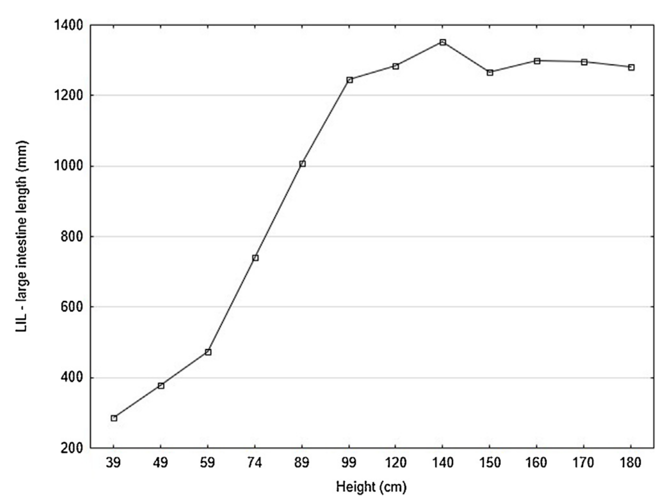

Fig. 3. Relation between LIL and height (pre- and post-natal period).

The so "established" LIL curves (corrected parameters measured in fetuses, children and adults) in relation to age, weight and height, based on data given by Struits and Sadahiro are shown in Figs. 1–3.

8. Conclusions

It can be conclude that the LI lengthens till age 4–5 (when the child achieves 130–140 cm body length or weighs 25–30 kg) to 1224 ± 57 mm, and remains “constant” in length. There are usually 10–11 acute colonic flexures (<90 degrees; RCF, LCF, descendosigmoid, sigmoidorectal and supernumerary: in the TC and SC); therefore these parts are the most troublesome to pass through with an endoscope. When patients change position (prone vs. supine) - the change in LIL is subtle (prone: F - 1757 ± 333 mm, M - 1842 ± 269 mm; supine F - 1736 ± 327 mm, M – 1839 ± 226 mm, respectively).

Ethical statement

The authors declare: the study was performed in accordance with the provisions of the WMA Declaration of Helsinki 1964 (with later revisions) and Good Clinical Practice.

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