COLONOSCOPE 'LOOPING' DURING ILEO-COLONOSCOPY IN CHILDREN IS SIGNIFICANTLY DIFFERENT TO THAT OBSERVED IN ADULT PRACTICE

Keywords: Paediatric; Child; Ileo-colonoscopy; Colonoscopy; Bayesian Analysis

ABSTRACT

Objectives

Ileo-colonoscopy (IC) can be technically challenging because of unpredictable colonoscope loop formation. Aims of this study were to assess the risk of loop formation and to attempt to understand which factors were likely to predispose to which subtype of loop.

Methods

Prospective study conducted on children referred for an IC at Sheffield Children's Hospital. Presence and type of loop was objectively assessed using the magnetic endoscope imaging tool.

Results

300 procedures were prospectively evaluated. Only 9% of paediatric ICs were loop-free. Alpha loops were the most common loop in children older than 5, while reverse alpha loops and a wider variety of complex and repetitive loops were observed in younger patients. Once a specific type of loop has formed, the risk of re-looping in a different way or in a different position of the colon is reduced. Left lateral starting position was found to increase the risk of reverse alpha loops and re-looping. Challenging loops, such as reverse alpha, were more frequent in males. Higher BMI was associated with an increased risk of alpha and deep transverse loops formation, while lower BMI with a higher incidence of reverse alpha and N loop. Loop formation did not prevent 100% ileal intubation.

Conclusions

This study represents the first attempt to describe loop formation according to patient characteristics in a large paediatric series. Further studies are needed in order to establish if these findings could be helpful in simplifying the execution of IC procedures in children and facilitate the learning curve

during endoscopy training programs.

What is known:

- In adult ileo-colonoscopy (IC) N and alpha are predominant types of loop;
- Incidence and relative occurrence of loops in IC in children has not yet been studied.

What is new:

- Loop formation occurs in 91% of childhood IC, with alpha loop accounting for 65%. In children <5 years of age, reverse alpha loops are predominant;
- Once a specific type of loop has formed, the risk of re-looping in a different way is reduced;
- Initial left lateral positioning of the patient increased the risk of reverse alpha loops and re-looping;
- Lower BMI is associated with a higher incidence challenging loops.

INTRODUCTION

Paediatric ileo-colonoscopy (IC) can be technically challenging because of unpredictable colonoscope loop formation mainly in the sigmoid and transverse colon. The magnetic endoscope imaging (MEI) tool (ScopeGuide®, Olympus, America, Inc., Allentown, PA) (1,2) is a non-radiographical technique for picturing the colonoscope shaft in real time (3-5) and it represents a useful tool for training purposes (6). Studies on loop formation have been published in adults (7-9) but no studies so far have been conducted in paediatric IC.

The aims of our study were to assess the risk of loop formation during IC in children, to identify the type of loops formed, and to attempt to understand which factors (patient demographics, anthropometry and positioning of patient) were likely to predispose to which subtype of loop and in which part of the colon.

METHODS

Patient enrolment and procedure description

Children referred for an IC at Sheffield Children's Hospital NHS Foundation Trust, a large centre for paediatric endoscopy, from December 2017 to January 2019, were consecutively prospectively enrolled. Patients with previous colonic resections or those who was known to have extensive adhesions or malrotation were excluded from the study. All IC procedures were performed using variable stiffness colonoscopes in conjunction with the MEI tool (ScopeGuide®, Olympus, America, Inc., Allentown, PA). The 'paediatric' variable stiffness colonoscope (Olympus PCF-H290DL, shaft width 11.8mm, tip width 11.7mm, length 1680mm) was employed for children <12kg and the standard 'adult' colonoscope (Olympus CF-HQ290L, shaft width 12.8mm, tip width 13.2mm, length 1680mm) for those >12kg. All procedures occurred, as is standard practice in this institution, under general anaesthesia, by five experienced paediatric endoscopists (>1000 ICs performed in career prior to this study). Examinations were commenced with the patient in the left lateral (LLi) or supine (Si)

position, according to operator choice.

Data recorded included age, sex, weight, height, Body Mass Index (BMI), BMI decile, BMI z score, decubitus starting position, number and type of loops and patient position when loops occurred, and the manoeuvre/patient position used to resolve the loop.

Hospital board approval for a service evaluation and audit study was obtained.

Statistical analysis

Continuous data were described as mean ± standard deviation (SD), median and range of values to have a better appreciation of the observed distribution; for categorical data, numerosity and percentage over the total of each class was reported. To reach our goals we used a non-parametric causal inference approach, founded in the potential outcome framework (10), to model the relationship between the outcome and the risk factors jointly through machine learning, which can automatically pick up complex, non-linear relationships. A machine learning algorithm called Bayesian Additive Regression Trees (BART) with 50 trees, 250 burn-in and 5000 post burn-in iterations, a strongly regularizing parameter k = 5, and automatic missing data imputation, was used to this purpose (11, 12). The model predictive performance was evaluated through the posterior Area Under the Curve (AUC), with values above 85% indicating a reliable model. The effect of the individual risk factor is estimated by predicting the impact at the patient level (Individual Treatment Effect, ITE) by using the model to simulate a change in a risk factor while keeping the other fixed and then averaging the effect along the entire dataset. This estimator is called the Average Treatment Effect (ATE) (10, 13). In addition to the ATE we tried to investigate how the average effect of one variable would change in the presence of other variables, the Heterogeneous Treatment Effect (HTE) (14 - 16). The statistical significance of the findings was summarised by the probability of direction (pD) (17) and by the probability of the region of practical equivalence (pROPE) for both ATEs and HTEs (16). A pD > 90% was considered indicative of a possible effect, > 95% for a probable effect, > 99% for strong evidence of effect; conversely, a pROPE lower than 10%, 5%, 1% indicated growing

evidence against a non-relevant/null effect, while a pROPE above 70% strongly suggested it.

The detailed description of the methods and the results included in the manuscript are reported in Supplemental Digital Content file 1 (SDC 1), while the full analysis and the code to reproduce it is described in the file SDC 2. The code is also available online at https://github.com/AD-Papers-Material/Colonoscopy-Loops.

All analyses and figures were computed in R v4.0.5 (18).

RESULTS

300 procedures were prospectively evaluated. Patient characteristics are summarized in **Table 1.** Procedure completion rate, including terminal ileum intubation, was 100%.

Loop formation

Table 2 and **Table SDC 1.1** describe the number and type of loops observed among patients. Loops were generally negatively associated with one another.

Seventy-one patients (23.7%) presented with multiple loop formations of varying combinations, with especially deep transverse (RR: 8.86 [5.8, 15.7]) and alpha loops (RR: 4.15 [2.02, 10.5]) having a strong probability of happening more than once and followed by gamma (RR: 3.71 [2.17, 6.47]) and reverse alpha loops (RR: 3.36 [1.92, 6.21]) (**Table SDC 1.4)**; all these associations showed strong certainty (pD: 100%, pROPE: 0%). The association was slightly weaker for N loop (RR: 1.71 [0.92, 3.24], pD: 91%, pROPE: 4.12%) due to the limited number of events.

Position of the patient and loop formation

The patient starting position was Si in 216 patients (72.2%) and LLi in 57 (19.1%). There was no compelling evidence of initial position influencing general loop formation during the procedure (RR LLi vs Si: 0.94 [0.85, 1.02], pD: 87.7%, pROPE: 44%). **Table 3** shows that LLi position was found

to strongly increase the risk of reverse alpha and, less markedly, gamma loops and N loops, with less compelling evidence in the last two cases. Conversely, there is only weak evidence of a negative association between LLi position and deep transverse loops and almost no evidence of association with alpha loops. Effect heterogeneity analysis showed that the increase in risk of reverse alpha loops in LLi position was 55% [-4.34%, 171%] higher in female kids aged more than 4 years old (**Table SDC 1.9**). A lack of a relationships between the characteristics of the patients and the chosen initial starting position suggests no residual confounding related to these parameters (**Table SDC 1.2)**. The LLi position tended to increase the risk of repeated loop formation (**Table SDC 1.4** and **SDC 1.6**) with an RR, considering the loop types in the model equal to 1.64 [CrI 0.97, 2.84], pD: 94%, pROPE: 3.7%, and, not considering the loops equal to 1.43 [0.91, 2.13], pD: 91.1%, pROPE: 5.64%). Repeated loops were more commonly associated with deep transverse loops (RR: 8.86 [5.8, 15.7]), followed by alpha (RR: 4.15 [2.02, 10.5]), gamma (RR: 3.71 [2.17, 6.47]), and reverse alpha loops (RR: 3.36 [1.92, 6.21]), all with pD ~ 100% and pROPE ~ 0% (**Table SDC 1.4**), with an increase in the relative risks related to alpha, DT and gamma loops when a Si position was used and a weakly increased risk related to reverse alpha loops in males (**Table SDC 1.5**). The association of N loops with repeated loop formation was instead relatively weaker (RR: 1.71 [0.92, 3.24], pD: 91.6%, pROPE: 4.12%, **Table SDC 1.4**).

Age of children and loop formation

Children less than 5 years tended to have more diverse looping, such that reverse alpha loops were recorded in 120 (40%), alpha loops in 99 (33%), N loop in 21 (7%), gamma in 93 (31%), deep transverse in 21 (7%) and multiple loops in 99 (33%). This compared to older children in whom alpha loops tended to be the most frequent (180 patients, 60%), followed by deep transverse (48, 16%), reverse alpha loop (47, 15.7% each), N loop (24, 8%) and gamma loop (22, 7.3%). The age of the patient has probably no influence on the incidence of overall loop formation (pROPE > 70%, **Table SDC 1.3**), but may show a more complex pattern depending on the specific loop type. Specifically,

alpha loops showed a positive association with age (**Table SDC 1.7)**, peaking at 12 years of age. A negative association with increasing age instead could be observed for reverse alpha loops (**Table SDC 1.8**). Deep transverse (**Table SDC 1.11**) and gamma (**Table SDC 1.12**) loops also showed a weak negative association. There were not enough N loops to infer a negative or positive association with age (both pD and pROPE were low, Table S29).

Sex of children and loop formation

The sex of the child did not seem to influence the incidence of loops overall (**Table SDC 1.3**). However, we found that male sex was positively associated with reverse alpha loops (RR: 1.5 [0.97, 2.46], pD: 93.4%, pROPE: 4.72%) and negatively with gamma loops (RR: 0.62 [0.35, 1.08], pD: 91.8%, pROPE: 4.84%). The positive association of male sex and reverse alpha loops was stronger if the initial position was supine (**Table SDC 1.9**). Furthermore, a weak negative association of male sex and DT loops was observed, while suggestive evidence of no association with alpha loop and lack of enough data for clear results for N loops. Interestingly, male sex was associated with a lower risk of a second loop (RR: 0.74 [0.53, 1.02], pD: 93.6%, pROPE: 6.12%) (**Table SDC 1.6**).

BMI and loop formation

Risk of general loop formation was not associated with BMI (**Table SDC 1.3)**. An indication of non-linear effect was found between standardized BMI (in deciles and Z-score) and the risk of alpha loops (RR: 1.2 [0.97, 1.57], pD: 91.8%, pROPE: 12.1%) (**Table SDC 1.7**). A somewhat opposite effect could be observed for reverse alpha loops, with a decrease in risk (**Table SDC 1.8)**, and a similar negative trend was observed for N loops, but with weaker evidence due to the smaller number of affected patients. Conversely, a more linear positive association was observed between the standardized BMI and the risk of deep transverse loops (**Table SDC 1.10**) while no clear relationship could be described for gamma loops (**Table SDC 1.12**). No clear relationship was evident between BMI and re-looping risk (**Table SDC 1.6**).

Loop resolution

Alpha loops were resolved via clockwise (CW) rotation, whilst reverse alpha loops were resolved by anti-clockwise (anti-CW) rotation, as is standard practice. Only 4% of loops were not resolved and pushed through during the IC. Regarding N loops, the resolution manoeuvres were CW in 15 cases (60% of N loops), anti-CW in 4 cases (16%) and pushed through in 6 cases (24%). There was some evidence of relationship between the resolutive N loop manoeuvres and an LLi procedure position (**Tables SDC 1.13 A, B, C**): specifically, a weak negative association with CW resolution (RR: 0.75 [0.43, 1.17], pD: 85.4%, pROPE: 8.7%), a stronger positive one with anti-CW (RR: 1.88 [0.85, 4.49], pD: 90.7%, pROPE: 3.34%) and an uncertain association with pushed through resolution (RR: 1.33 [0.59, 2.98], pD: 73.1%, pROPE: 6.5%). The N loops resolution manoeuvres was also correlated with the presence of repeated loops: this association was strong and negative with CW resolutions (RR: 0.62 [0.35, 0.95], pD: 96.8%, pROPE: 2.88%), weak and positive with anti-CW ones (RR: 1.38 [0.57, 3.46], pD: 74%, pROPE: 6.5%) and strong and positive with a push-through resolution (RR: 2.18 [1.09, 5.2], pD: 96.5%, pROPE: 1.64%). No clear associations were found between the manoeuvres and other patient characteristics. For deep transverse loops, the distribution of resolution manoeuvres was: 29 (33.7%) CW, 25 (29.1%) anti-CW, and 32 (37.2%) pushed through. For these loops, the only clear association that could be found was a positive one between repeated loops and a pushed through resolution (RR: 1.38 [0.95, 2.22], pD: 92.3%, pROPE: 6.06%) (**Table SDC 1.15 C**). Other weak trends and associations which need more investigation are described in **Table SDC 1.15 A, B, C** and **Table SDC 1.14 A, B, C**.

Predictive model performance evaluation

Most of the models do not show strong predictive performance (AUC < 90%) unless the specific loop type is included, and this means that the collected morphological characteristics by themselves are

not enough to describe the phenomenon of looping and that residual confounding may be present in the analysis.

DISCUSSION

This study shows that loop formation is frequent during IC in children, occurring in about 90% of our sample, with alpha loops predominant (65%), followed by deep transverse loops (21%), reverse alpha loops (15%), N loops (8%) and gamma loops (8%). However, loop formation did not affect the procedure completion rate, which was 100% to the terminal ileum. The stronger finding of this study was that once a specific type of loop has formed, the risk of re-looping in a different way or in a different position of the colon is reduced. Moreover, some loops (especially alpha and deep transverse loops) had a strong tendency to re-looping, which occurred in about 24% of our patients. Regarding the patient starting position, LLi starting position strongly increased the risk of reverse alpha loops and repeated loops. By stratifying the type of loop recorded for age, we found more variability in children less then 5 years old, compared to those over the age of 5. Interestingly, younger children had a much higher incidence of reverse alpha loops than older ones (40% vs 16%, respectively), in whom alpha loops were predominant (33% in younger children compared to 60% in older ones). Challenging loops, such as reverse alpha loops, were positively associated to male sex, although the sex of the child did not seem to influence the incidence of loops in general. In our series we found a non-linear increase of alpha loop risk with BMI, while a more linear increase was observed for deep transverse loops with BMI. Conversely, the risk of reverse alpha loops and N loops decreased with BMI. As expected, the effective resolution manoeuvre was clockwise rotation of the scope for alpha loops and anti-CW rotation for reverse alpha loops, with a resolution rate of 96%. Only 4% of loops were not resolved and pushed through during the IC. N loops, indeed, were resolved more frequently with anti-clockwise rotation only in patients in the LLi position with no preferential choice identified among Si patients. Contrary to the ‘received wisdom’ that N loops normally allow the operator to

'push through', we reported a CW resolution manoeuvre of N loops in 60% of cases, anti-CW in 16% and push-through in 24%. A significantly higher probability of pushing through the loop was recorded in patients with a repeated N and repeated deep transverse loops.

According to previous literature, paediatric IC may be more challenging and therefore by inference time-consuming than those performed in adults (19,22-28). Several factors have been hypothesized to be associated with a longer procedural time in children, such as less adipose tissue with diminished potential stabilisation of the colon, the increased colonic elasticity in children, and their less developed abdominal musculature, that all might potentially lead to more frequent looping during IC (26,29). Indeed, most difficulties during IC in either age group arise as a result of recurrent, often unpredictable looping of the instrument shaft within the variable colonic anatomy (26,30,31). Available in vivo studies reported a mean colon length at birth of about 50-57 cm, which doubles in length at around two years of life and reaches adult length at around 5 years of life (32-39). It can be deduced that the large bowel is therefore relatively longer in children, for their relative body size, compared to adults. This might suggest that it may be easier to loop during IC in children.

Many adult gastroenterologists begin the procedure in the LLi position and change only when difficulty is encountered (25). In our series the Si position was preferred as the starting point and this, compared to other initial patient positions, was associated with a lower risk of repeated loops. In contrast, an initial LLi position was found to increase the risk of reverse alpha loops and re-looping. It might be that in the Si position, loops are possibly better palpated, and pressure might be applied to prevent the regeneration of further loops (40,41).

Adult literature reports slightly lower rates of looping during IC, occurring in about 70-80% of cases (9,42), especially in females (9), with a relative preponderance of N-loops (30-79%) and alpha loops (11-15%) (42-44). Female sex is associated with a higher risk of difficult IC in adults (27,31,45-49). The fact that the sex of the child didn't seem to influence the presence of loop could be due to the similarities in body shape before the onset of puberty, although reverse alpha loops, that are generally considered more challenging, were positively associated to males.

Reflecting adult IC, in which it has been demonstrated that lower BMI was associated with a prolonged insertion time and greater patient discomfort (27,45,50), in our series we found that children with low BMI presented a higher risk of challenging loops formation, such as reverse alpha and N loops. This suggests that poorer nutrition leads to a higher degree of difficulty in paediatric IC, possibly allowing a more mobile mesentery and with less abdominal wall rigidity to prevent loop formation than would be encountered in more muscular, or indeed more obese, children.

Our study is the first of its kind to investigate the type of colonoscope loop formation in children. However, several limitations need to be acknowledged: no randomization on starting position decubitus was applied. Also, there are multiple confounding factors that could impact these results, such as the use of external compressions and the variable use between operators of the variable stiffness function of the colonoscopes during the procedures. Moreover, data on bowel preparation were not recorded, and this could have affected the number of loops formed. Unfortunately, data about duration of the procedures were not documented, therefore we couldn't make practical conclusion about which kind of loop might be more time-consuming and therefore require more anesthesia.

Nonetheless, this study presents also several strengths: patients were consecutively enrolled, potentially reducing the effect of bias from confounding variables. Moreover, the endoscopists involved were all experienced, minimizing the operator dependence of procedure performance. Loop formation was assessed using ScopeGuide®, thus an objective recognition of the loop and its successful resolution was possible. Another strength of this study is the use of a formal analytical framework, based on modern machine learning techniques, grounded in causal inference theory and with a Bayesian approach to inference.

Conclusion

This study represents the first attempt to describe loop formation according to patient characteristics in a large paediatric series.

Further studies are necessary in order to establish stronger predictors of loop risk (e.g. colon anatomy characteristics) in order to simplify the execution of IC procedures in children, reducing procedure length, and consequently anaesthesia exposure and procedure-related complications, and as a natural knock-on effect the facilitation of endoscopy training.

References

1. Olympus ScopeGuide®, https://www.olympus.co.uk/medical/en/Products-and-solutions/Medical-solutions/ScopeGuide-Platform

2. Franciosi JP, Mascarenhas M, Semeao E, et al. Randomised controlled trial of paediatric magnetic positioning device assisted colonoscopy: a pilot and feasibility study. Dig Liver Dis 2009;41(2):123-6.

3. Shah SG, Brooker JC, Williams CB, et al. Effect of magnetic endoscope imaging on colonoscopy performance: a randomised controlled trial. Lancet 2000;356:1718–1722.

4. Mark-Christensen A, Brandsborg S, Iversen LH. Magnetic endoscopic imaging as an adjuvant to elective colonoscopy: a systematic review and meta-analysis of randomized controlled trials. Endoscopy 2015;47(3):251-61.

5. Klare P, Hartrampf B, Haller B, et al. Magnetic endoscope imaging for routine colonoscopy: impact on propofol dosage and patient safety - a randomized trial. Endoscopy 2016;48(10):916-22.

6. Broekaert I, Tzivinikos C, Narula P, et al. European Society for Paediatric Gastroenterology, Hepatology and Nutrition Position Paper on Training in Paediatric Endoscopy. J Pediatr Gastroenterol Nutr 2020;70(1):127-140.

7. Shah SG, Brooker JC, Williams CB, et al. The variable stiffness colonoscope: assessment of efficacy by magnetic endoscope imaging. Gastrointest Endosc 2002;56:195–201

8. Hawari R, Pasricha PJ. Going for the loop: a unique overtube for the difficult colonoscopy. J Clin Gastroenterol 2007;41(2):138-40.

9. Rowland RS, Bell GD, Dogramadzi S, et al. Colonoscopy aided by magnetic 3D imaging: is the technique sufficiently sensitive to detect differences between men and women? Med Biol Eng Comput. 1999;37(6):673-9.

10. Hill, Jennifer L. "Bayesian nonparametric modeling for causal inference. J Comput Graph Stat 2011; 217-240.

11. Chipman HA, George EI, McCulloch RE. BART: Bayesian additive regression trees. Ann Appl Stat 2010; 4(1):266-98

12. Kruschke, John K. What to believe: Bayesian methods for data analysis. TiCS 2010. 14.7: 293-300.

13. Alberto C, Manolopoulou I, Baio G. Estimating individual treatment effects using non-parametric regression models: a review. arXiv preprint arXiv 2020:2009.06472.

14. Kwonsang L, Bargagli-Stoffi FJ, Dominici F. Causal rule ensemble: Interpretable inference of heterogeneous treatment effects. arXiv preprint arXiv 2020;2009.09036.

15. Torsten H, Zeileis A. Partykit: A modular toolkit for recursive partytioning in R. J Mach Lear Res 2015;16.1: 3905-3909

16. Kruschke, JK. (Rejecting or accepting parameter values in Bayesian estimation. AMPPS 2018;1(2), 270-280.

17. Makowski D, Ben-Shachar MS, Chen SHA, et al. Indices of Effect Existence and Significance in the Bayesian Framework. Front Psychol 2019;10:2767.

18. R Core Team (2021). R: A language and environment for statistical computing. R Foundation for Statistical Computing, Vienna, Austria. URL https://www.R-project.org/

19. Cole TJ, Flegal KM, Nicholls D, Jackson AA. Body mass index cut offs to define thinness in children and adolescents: international survey. BMJ 2007;335(7612):194)

20. Barlow SE, Expert C. Expert committee recommendations regarding the prevention, assessment, and treatment of child and adolescent overweight and obesity: summary report. Pediatrics 2007;120(Suppl 4):S164–92.

21. Chipman HA, George EI, McCulloch RE. BART: Bayesian additive regression trees. Ann Appl Stat 2010;4(1):266-98.

22. Thakkar K, Holub JL, Gilger MA, et al. Quality indicators for pediatric colonoscopy: results from a multicenter consortium. Gastrointest Endosc 2016;83(3):533-41.

23. Overholt BF, Brooks-Belli L, Grace M, et al. Withdrawal times and associated factors in colonoscopy: a quality assurance multicenter assessment. J Clin Gastroenterol 2010;44: e80-6.

24. Saunders BP, Macrae FA, Williams CB. What makes colonoscopy difficult? Gut 1993; 34: T179.

25. Rex DK. Achieving cecal intubation in the very difficult colon. Gastrointest Endosc 2008;67: 938-44.

26. Thomson M, Eltumi M, Singh C, Eyles M, et al. Sub-10-minute High-quality Diagnostic Colonoscopy With Terminal Ileum Intubation in Children Is Feasible and Safe. J Pediatr Gastroenterol Nutr 2019;69(1):6-12.

27. Bernstein C, Thorn M, Monsees K, et al. A prospective study of factors that determine cecal intubation time at colonoscopy. Gastrointest Endosc 2005;61:72–5.

28. Isoldi S, Cucchiara S, Repici A, et al. Gastrointestinal endoscopy in children and adults: How do they differ? Dig Liver Dis 2021; 7:S1590-8658(21)00084-0.

29. Williams CB, Laage NJ, Campbell CA, et al. Total colonoscopy in children. Arch Dis Child 1982;57:49–53.

30. Brahmania M, Park J, Svarta S, et al. Incomplete colonoscopy: maximizing completion rates of gastroenterologists. Can J Gastroenterol 2012;26(9):589-92.

31. Shah SG, Brooker JC, Thapar C, et al. Patient pain during colonoscopy: an analysis using real-time magnetic endoscope imaging. Endoscopy 2002;34(6):435-40.

32. Struijs MC, Diamond IR, de Silva N, et al. Establishing norms for intestinal length in children. J Pediatr Surg 2009;44(5):933-8.

33. Saunders BP, Phillips RK, Williams CB. Intraoperative measurement of colonic anatomy and attachments with relevance to colonoscopy. Br J Surg 1995;82(11):1491-3.

34. Sadahiro S, Ohmura T, Saito T, et al. Relationship between length and surface area of each segment of the large intestine and the incidence of colorectal cancer. Cancer 1991;68(1):84-7.

35. Mirjalili SA, Tarr G, Stringer MD. The length of the large intestine in children determined by computed tomography scan. Clin Anat 2017 ;30(7):887-893. doi: 10.1002/ca.22941.

36. Hounnou G, Destrieux C, Desmé J, et al. Anatomical study of the length of the human intestine. Surg Radiol Anat 2002;24:290-4.

37. Hirsch J, Ahrens EH, Blankenhorn DH. Measurement of the human intestinal length in vivo and some causes of variation. Gastroenterology 1956;31:274-84.

38. Underhill BML. Intestinal length in man. BMJ 1955;19:1243-6.

39. Duncan JE, McNally MP, Sweeney WB, et al. CT colonography predictably overestimates colonic length and distance to polyps compared with optical colonoscopy. AJR Am J Roentgenol 2009;193(5):1291-5.

40. Waye JD, Yessayan SA, Lewis BS, et al. The technique of abdominal pressure in total colonoscopy. Gastrointest Endosc 1991;37(2):147-51.

41. Gershman G, Thomson M. Practical pediatric gastrointestinal endoscopy, 3rd edition. Wiley-Blackwell publishing, 2021. ISBN: 978-1-119-42345-4

42. Painter J, Saunders DB, Bell GD, et al. Depth of insertion at flexible sigmoidoscopy: implications for colorectal cancer screening and instrument design. Endoscopy 1999;31(3):227-31.

43. Shah SG, Saunders BP, Brooker JC, et al. Magnetic imaging of colonoscopy: an audit of looping, accuracy and ancillary maneuvers. Gastrointest. Endosc 2000; 52: 1–8. 26

44. Sato K, Hirahata K, Fujinuma S, et al. Evaluation of patient pain during colonoscopy for types of looping between hood attached group and non-hood attached group: an analysis using magnetic endoscope imaging (MEI). Gastrointest. Endosc 2008; 67: AB77.

45. Anderson JC, Messina CR, Cohn W, et al. Factors predictive of difficult colonoscopy. Gastrointest Endosc 2001;54:558–562.

46. Saunders BP, Fukumoto M, Halligan S, et al. Why is colonoscopy more difficult in women?

Gastrointest Endosc 1996;43:124–126.

47. Chutkan R. Colonoscopy issues related to women. Gastrointest Endosc Clin N Am 2006;16:153–63.

48. Aslinia F, Uradomo L, Steele A, et al. Quality assessment of colonoscopic cecal intubation: an analysis of 6 years of continuous practice at a university hospital. Am J Gastroenterol 2006;101:721–31.

49. Hsu CM, Lin WP, Su MY, et al. Factors that influence cecal intubation rate during colonoscopy in deeply sedated patients. J Gastroenterol Hepatol 2012;27:76–80

50. Anderson JC, Gonzalez JD, Messina CR, et al. Factors that predict incomplete colonoscopy: thinner is not always better. Am J Gastroenterol 2000;95:2784-7.