A Randomized Controlled Trial Comparing Right Lateral Decubitus and Left Lateral Decubitus Starting Position on Outcomes in Colonoscopy

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Abstract

Patient positioning in colonoscopy has been proposed as a simple and inexpensive technique to increase luminal distention and improve navigation through the large bowel. We sought to determine if right lateral (RL) starting position compared to the standard left lateral (LL) starting position could improve outcomes in colonoscopy.

Patients presenting for their scheduled colonoscopy were consented for the trial and randomized to RL or LL starting position. Variables including age, sex, BMI, time to cecal intubation, adenoma detection rate (ADR), NAPCOMs pain score, amount of sedation administered, and quality of bowel preparation were collected during their colonoscopy. The primary outcome was time to cecal intubation. All colonoscopists who had successfully completed upskilling courses were included in the trial.

A total of 185 patients were included in the analysis - 94 patients were randomized to RL and 91 patients were randomized to LL. No difference was found in time to cecal intubation comparing the starting position of RL (542.6s) to LL (497.85s) (p=0.354). There was also no difference in cecal intubation rate (RL - 94.9%, LL – 94.8%, p=0.960), ADR (RL – 56.3%, LL – 64.8%, p=0.240), or patient comfort (p=0.078) comparing the starting position.

In conclusion, no difference was found for outcomes in colonoscopy comparing the RL and LL starting position.

Keywords: Colonoscopy, starting position, right lateral decubitus, cecal intubation time

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List of Abbreviations

ADR – Adenoma Detection Rate APC – Adenomatous Polyposis Coli **BBPS** – Boston Bowel Preparation Scale BMI – Body Mass Index CAG – Canadian Association of Gastroenterology CRC – Colorectal Cancer CSI - Colonoscopy Skills Improvement CT – Computed Tomography DNA - Deoxyribonucleic Acid EPIC – Endoscopic Polypectomy Improvement Course EQUIP – Endoscopy Quality Improvement Program FAP – Familial Adenomatous Polyposis FIT – Fecal Immunochemical Test FOBT – Fecal Occult Blood Test FUSE – Full Spectrum Endoscopy System gFOBT – Guaiac-Based Fecal Occult Blood Test HLA – Human Leukocyte Antigen HNPCC – Hereditary Non-Polyposis Colon Cancer HREB – Human Research Ethics Board IBD – Inflammatory Bowel Disease LL – Left Lateral MRI – Magnetic Resonance Imaging MSI – Microsatellite Instability NAPCOMS – Nurse-Assessed Patient Comfort Score PDR – Polyp Detection Rate PET – Positive Emission Tomography RCT – Randomized Controlled Trial RL – Right Lateral ROLCOL – Right or Left Colonoscopy RPAC – Research Proposals Approval Committee SEE – Skills Enhancement for Endoscopy TER – Third Eye Retroscope TET – Train the Endoscopy Trainer UC - Ulcerative Colitis

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Chapter 1: INTRODUCTION

1.1 Colonoscopy

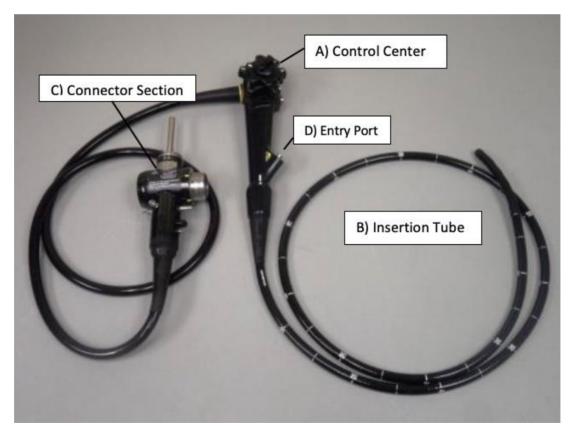
Colonoscopy is the endoscopic evaluation of the lumen of the large bowel and terminal small bowel. It is the preferred method to evaluate the colon in adult patients with large bowel symptoms, iron deficiency anemia, abnormal results from radiographic studies of the colon, positive results from colorectal screening tests, post polypectomy and post cancer resection surveillance, and in the diagnosis and surveillance of inflammatory bowel disease (IBD). In 2014, a total of 15 million colonoscopies took place in the United States ¹, making it the most commonly performed endoscopic procedure ^{2 3}.

In 1969, the first retrograde colonoscopy of the entire colon was performed. The pioneering work of Dr. Niwa, Dr. Yamagata, Dr. William Wolff, and Dr. Hiromi Shinya was initially done using an eyepiece attached to a fibreoptic scope. The procedure was an answer to polyps extending beyond the rectosigmoid junction which previously required laparotomy and bowel resection for removal. Polyps were identified and removed with minimal complications following 1600 procedures, establishing it as a standard of care for disease of the lower gastrointestinal (GI) tract. ⁴

Today, the procedure involves passing the device, a colonoscope, through the anus and maneuvering it around the large bowel to the cecum or terminal ileum. The basic design of a flexible endoscope consists of three main parts – a control section (A), the insertion tube (B), and the connector section (C) (Figure 1). The control section is held in the left hand and has

two stacked controls to deflect the tip up or down (one dial) and left or right (a separate dial). It also contains separate buttons for suction, air or water insufflation, and to capture images. Finally, an entry port for inserting accessories through the channel is found in this area of the instrument (D). The insertion tube is a flexible shaft attached to the control center that is maneuvered around the bowel. The tip of the insertion tube contains a camera for guidance, an illumination system, an opening for the air/water channel, and an objective lens (available in a variety of orientations). The connector section attaches the endoscope to an image processor, a light source, an electrical source, and an air/water source. ⁵

Figure 1: Standard Colonoscope depicting the Control Center (A), Insertion Tube (B), Connector Section (C) and Entry Port (D). (Original Photo taken by A. Greene)



The scope is maneuvered using the right hand for insertion and is manipulated using the control center in the left hand. Complete insertion is achieved when the cecum is reached and identified by three landmarks – the ileocecal valve, the appendiceal orifice, and the triradiate fold ⁶. Intubation of the ileocecal valve can be performed with luminal evaluation of the terminal ileum. Interventions are usually performed during withdrawal of the colonoscope. Instruments may be passed through the working port of the scope and maneuvered to perform biopsies, remove polyps, apply clips, etc. An endoscopy nurse is present to assist the endoscopist during the procedure.

Complications of colonoscopy range from patient discomfort, dehydration, and transient hypoxia to polypectomy bleeding and colonic perforation ⁷. The former symptoms are more common and can be related to bowel preparation and the use of sedation during the procedure. The latter, however, are more serious and may result in the need for transfusion or surgical intervention. Patients are monitored during and after the procedure for about 30 minutes and instructed to present to their local emergency department if severe abdominal pain or prolonged rectal bleeding occurs.

Although colonoscopy has seen vast improvement in its functionality and design since the 1960s, it is not a perfect procedure. Colonoscopy is very technically challenging and can be difficult for a number of reasons. In general, a difficult colonoscopy is one that is near impossible to reach the cecum. Difficulty may be measured based on the duration of time required to perform the colonoscopy, the amount of physical exertion required from the colonoscopist, or the amount of discomfort the patient experiences ⁸. Some believe that the scope is only as good as the operator who handles it. While some operators may be able to

manipulate the scope well and maintain good visualization, others experience difficulty that hinders the quality of the procedure. Today, all aspects of colonoscopy are being studied to improve the overall procedure. The colonoscope itself has seen many advances including the illumination system and camera, however multiple devices are being studied to improve the quality, definition, and view of the colonoscope. Quality improvement, education, and variations in the technical aspects of the procedure are also being studied to improve the procedure and patient acceptance of it.

Ultimately, colonoscopy provides direct visualization and access to endoluminal mucosa, allowing an opportunity to identify and remove or biopsy lesions. It is currently considered the gold standard in diagnosing diseases of the large intestine and is essential in screening and preventing colorectal cancer (CRC) today ⁹.

1.2 The Large Intestine

The gastrointestinal (GI) tract terminates with the large intestine, a highly absorptive organ consisting of the colon and the rectum. This anatomy can be complex due to unpredictable embryological development and multiple disease processes. For this reason, understanding the anatomy of the colon and rectum is important for imaging and performing colonoscopy.

The colon consists of the cecum, ascending colon, transverse colon, descending colon and the sigmoid colon (Figure 2). The rectosigmoid junction transitions the sigmoid colon into the rectum, which then transitions into the anal canal through the dentate line, or squamocolumnar junction.

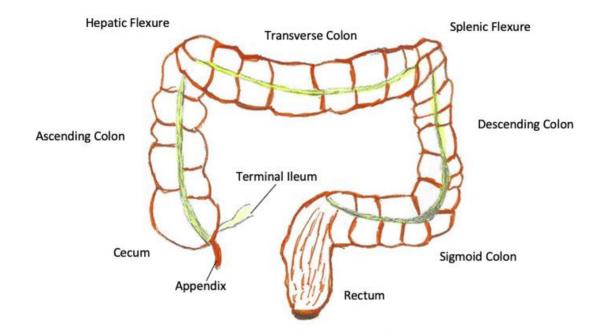
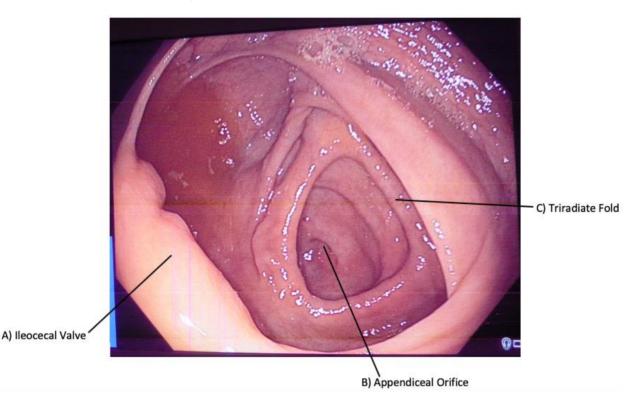


Figure 2: Anatomy of the Large Intestine. (Original Image drawn by A. Greene)

The cecum is located in the right iliac fossa and comprises the first part of the colon. It is a sac-like segment of the colon, averaging a diameter of 7.5 cm and a length of 10 cm. ⁶ The ileocecal valve connects the terminal ileum to the cecum, emptying through a thickened invagination. It is located on the prominent ileocecal fold encircling the cecum, between 3 and 5 cm distal to the cecal pole. The appendix extends from the cecum, approximately 3 cm below the ileocecal valve. It consists of a blind ending elongated tube, ~8-10 cm in length. Anatomically, the appendiceal orifice can be found at the convergence of taeniae coli. The appearance of the fusion of these three teniae coli around the appendix gives rise to the triradiate fold, commonly referred to as the "Mercedes Benz" sign. The most reliable colonoscopic landmarks of the cecum consist of these three things - the ileocecal valve (A),

appendiceal orifice (B), and triradiate fold (C). ¹⁰

Figure 3: Colonoscopic Landmarks for the Cecum - A) Ileocecal Valve, B) Appendiceal Orifice, and C) Triradiate Fold. (Original photo taken with permission by A. Greene showing healthy cecum and normal landmarks)



The ascending colon is retroperitoneally fixed and runs posteriorly from the cecum to the hepatic flexure. Between the hepatic flexure and the splenic flexure is the transverse colon, approximately 45 cm in length. It is enveloped in a double fold of peritoneum called the transverse mesocolon which comes down from the posterior stomach. This part of the colon often hangs down into the pelvis in females, contributing to a greater mean colon length in women. ¹¹ It can be a complicated area of the colon to navigate during colonoscopy. A redundant transverse colon, or transverse colon that "sags" into the pelvis, is prone to bowing

of the colonoscope and looping of the bowel, resulting in a longer and more painful procedure – particularly in females ¹². The hepatic and splenic flexures can be difficult to navigate as well due to the acuity of angulation seen with a redundant transverse colon and may limit a patient's tolerance of the procedure.

The splenic flexure is located beneath the left costal margin and is retroperitoneally fixed by the phrenocolic ligament. The descending colon is thin walled, lies ventral to the left kidney and extends from the splenic flexure for approximately 25 cm. It is retroperitoneal and fixed. At the level of the pelvic brim, an acute bend can occur when the relatively thin-walled, fixed descending colon transitions into the thicker, mobile sigmoid colon. The sigmoid colon can vary in length considerably, ranging from 15-50 cm. It is very mobile. The small diameter, muscular tube is suspended on a long floppy mesentery (the mesosigmoid) attached to the left pelvic sidewall. This area can also be particularly difficult to navigate during colonoscopy, producing the same bowing of the colonoscope and looping as seen in the redundant transverse colon. The application of loop resolution techniques are usually required here to ensure safe scope insertion and to minimize patient discomfort. ⁶

The rectosigmoid junction is located at the level of the sacral promontory and can be attached to the fixed rectum at an acute angulation. The rectum is ~12-15 cm in length and occupies the curve of the sacrum into the true pelvis. The anterior surface of the proximal third of the rectum is covered by visceral peritoneum. The posterior surface is almost completely extraperitoneal and adherent to the soft tissues. It is invested with a thick, closely applied mesorectum. The rectum also possesses three involutions or prominent semilunar folds known as the valves of Houston, which can act as potential blind spots for an endoscopist. Finally, the

anal canal is 3 cm long and extends up to the squamocolumnar junction, or dentate line, the embryological junction of the hindgut and proctodeum.⁶

Like the rest of the GI canal, the large intestine is made up of four tissue layers. The innermost layer is the mucosa, a simple columnar epithelial tissue. The mucosa is smooth and lacks the villi found in the small intestine. The crypts of Lieberkuhn are larger than in the small intestine. Mucous glands secrete mucous to lubricate and protect the surface. The submucosa surrounds the mucosa and is comprised of areolar connective tissue containing a rich supply of blood and lymphatic vessels, lymphoid follicles and nerve fibres to support the layers of the intestine. The muscularis propria possesses an inner circular muscle layer and a longitudinal outer muscular layer to produce the coordinated contractions of peristalsis, propelling material through the tract. Between these two layers is the myenteric plexus. Finally, the serosa is the outermost layer and is comprised of simple squamous epithelial tissue. ¹³

Depending on the anatomy and previous disease processes in a patient's abdomen, the technical difficulty of a colonoscopy can change drastically. Diverticular disease, abdominal or pelvic surgery, obesity, and sex differences can create angulation and tortuosity that are inherently more difficult to reach the cecum and complete the procedure ⁸. Emerging technologies and "tricks" are being utilized to handle the difficulty associated with this anatomy so that completion is possible.

1.3 Diseases of the Large Intestine

The large intestine is susceptible to a multitude of diseases with infectious, inflammatory, ischemic, and neoplastic etiologies. Common symptoms of disease include

diarrhea, constipation, weight loss, abdominal pain, and bleeding. Patients presenting with these symptoms often require bloodwork and imaging in addition to a history and physical assessment. A large portion of patients presenting with these symptoms will require a colonoscopy. While some diseases of the lower GI tract can be acute in nature, there are several diseases that portray chronicity and require close follow-up and screening or surveillance. Multiples colonoscopies are therefore needed for assessment over a patient's lifetime. Two such diseases requiring closer monitoring and follow up are IBD (*Section 1.3.1*) and CRC (*Section 1.3.2*).

1.3.1 Inflammatory Bowel Disease

Inflammatory bowel disease (IBD) is generally used to describe ulcerative colitis (UC) and Crohn's disease. Both diseases have similar general characteristics and unknown causes. The distinction between the two entities can usually be established on the basis of clinical and pathologic criteria, including history and physical examination, radiologic studies, gross appearance and histology. Colonoscopy is used to diagnose the disease, obtain biopsies of the colon, and to provide surveillance of the disease.

The prevalence of UC ranges from 40-100 cases per 100 000 people and commonly affects patients younger than 30 years of age. A small secondary peak of the disease occurs in the sixth decade. Both sexes are equally affected. The disease occurs more commonly in persons of northern European ancestry and Ashkenazi Jews. ⁶

The genetic predisposition for UC is not inherited in a classic Mendelian pattern suggesting environmental factors influences an individual's susceptibility. It is largely

multifactorial, with genome wide association studies having identified about 200 loci associated with IBD. While first degree relatives have four times the risk of developing the disease and 8-14% of patients with UC have a family history of it, only 7.5% of the disease variance can be explained by genetics ¹⁴. Genetic abnormalities found to be associated with UC are variation in DNA repair genes and class II major histocompatibility complex genes. Patients with UC display specific alleles of group HLA and DR2 with an association between certain alleles and expression of the disease. Family history also appears to be a risk factor. Further evidence that UC is influenced by environmental factors includes its higher prevalence in industrialized countries and increased incidence in individuals who migrate from low risk to high risk areas. Speculation on dietary factors and infectious factors have been questioned, although none of been confirmed. Smoking appears to confer a protective effect against the development of UC, as well as providing therapeutic improvement. ⁶

The major pathologic process for UC involves both the mucosa and submucosa of the colon, sparing the muscularis. Friable, granular mucosa is common in severe cases, with ulceration varying widely and potentially not being present in some cases. Small superficial erosions may be present or patchy, full-thickness ulceration of the mucosa. Rectal involvement (proctitis) is the hallmark of disease. Mucosal inflammation extends in a continuous, uninterrupted fashion for a variable distance into more proximal colon. Pseudopolyps, or inflammatory polyps, represent regeneration of inflamed mucosa and are composed of a variable mixture of non-neoplastic colonic mucosa and inflamed lamina propria. UC may include the entire colon, including the cecum and appendix, but does not affect any other part of the GI tract. The typical microscopic finding in UC is inflammation of the mucosa and submucosa with

characteristic crypt abscesses, in which collections of neutrophils fill and expand the lumina of individual crypts of Lieberkuhn. Hematochezia often results from marked vascular congestion.

In contrast, Crohn's disease also consists of inflammation but can have areas of normal segments interspersed, termed "skip lesions". Crohn's disease can affect any segment of the GI tract from the mouth to the anus. It is common for the terminal ileum to be involved in Crohn's disease, but is not crucial to the diagnosis. Crohn's disease varies between 1-10 per 100 000 people depending on geographic location. Again, there is a bimodal age distribution, with peaks between 15 and 30 years of age, and a second smaller peak between 55 and 80 years of age. It is more common in patients of Jewish descent and is frequently found in urban residents. Like UC, the disease is multifactorial with both environmental and genetic susceptibility. Children of parents with Crohn's disease have an increased risk of almost 8-fold for developing the disease. ¹⁵

Crohn's disease is transmural, predominantly submucosal inflammation characterized by a thickened colonic wall. It can give a cobblestone appearance endoscopically and may demonstrate long, deep linear ulcers that resemble railroad tracks or bear claws. In severe cases, creeping fat of the mesentery can encase the bowel wall, and strictures may develop in the small or large intestines. Microscopically, Crohn's disease consists of transmural inflammation, submucosal edema, lymphoid aggregation, and, ultimately, fibrosis. The pathognomonic histologic feature of Crohn's disease is the noncaseating granuloma – a localized, well-formed aggregate of epithelioid histocytes surrounded by lymphocytes and giant cells. A characteristic triad of symptoms exists for Crohn's – abdominal pain, diarrhea and

weight loss. Fever and recurrent oral aphthous ulcers may be involved. Fistulas and anal disease are also suggestive of Crohn's disease.

Medical management is the primary treatment modality of IBD. Medications are titrated and changed according to response, with some being used primarily in the acute setting and others for maintenance. Medications most commonly used include 5-aminosalicylates, corticosteroids, immunomodulators, and biologic therapies, with surgery being reserved for severe cases or complications.⁶

The most sensitive diagnostic modality for Crohn's disease and UC is colonoscopy. Biopsy samples are obtained during the procedure to aid with diagnosis. Most patients require periodic colonoscopic surveillance and biopsy about once every 1-2 years. This can be done to assess response to medical therapy. Additionally, the risk of developing colorectal carcinoma is higher in patients with IBD. UC carries a higher risk of CRC than Crohn's disease, with prolonged duration of the disease being the most important risk factor. Endoscopic evaluation is therefore done to help detect dysplastic lesions before they develop into invasive carcinoma. Ultimately, increased screening in these individuals can detect premalignant or malignant lesions for earlier intervention. ⁶

IBD commonly affects younger patients. With endoscopic surveillance and screening being a mainstay of the disease, these patients must undergo multiple colonoscopies in their lifetime to prevent severe symptoms and complications from the disease. Patient acceptance of undergoing these colonoscopies relies heavily on patient comfort during the procedure. Patient comfort is, therefore, a key component in colonoscopy and important area of investigation today.

1.3.2 Colorectal Cancer

Colorectal cancer (CRC) is the second most common cancer in Canada, accounting for 13% of all cancers. It is the second most common cancer in males (14.5%) and the third most common in females (11.5%). In 2017, approximately 26 800 cases of CRC were diagnosed in this country – 9 400 cases of new diagnosis will die from the disease each year. ¹⁶ Globally, 1-2 million patients are diagnosed with CRC each year, with over 600 000 people succumbing to the disease. ¹⁷

CRC often develops over more than 10 years, with dysplastic adenomas being the most common form of premalignant precursor lesions. Transformation of a polyp to a cancer occurs through a well-described adenoma-carcinoma sequence. The sequence is a stepwise pattern of mutational activation of oncogenes and inactivation of tumor suppressor genes that results in cancer formation (including *APC* gene mutations, *KRAS* oncogene, and *TP53* tumor suppressor gene). Given the slow development of these cancers, the disease is curable if detected and treated at an early stage. Moreover, removal of adenomas at early stages can prevent cancer development. The molecular pathogenesis of the disease is heterogenous. The interconnections between molecular pathogenesis, prognosis and therapy response have become increasingly apparent over the past two decades – including the molecular mechanisms and genetic changes that cause the hereditary forms of CRC. ¹⁷

Cancer of the large intestine occurs in sporadic, familial, and hereditary forms. Sporadic CRC are most common, comprising 60-80% of all colon cancers ¹⁷. They typically affect patients of an older population (60-80 years in the absence of family history). Genetic mutations associated with sporadic cancers are limited to the tumor itself, unlike in hereditary disease, in

which the specific mutation is present in all cells of the affected individual. Familial colon cancers account for 15-30% of all CRC cases.¹⁷ The risk for cancer increases as the number of family members with CRC rises. For example, individuals with a first-degree relative diagnosed with CRC prior to age 50 have an increased risk by 2-fold of developing colon cancer.

Hereditary CRC contributes about 3-5% of all CRC. It is characterized by a history of CRC in family members with onset at a young age, and with genetic defects that lead to cancer in multiple organ systems. The two most common forms of hereditary cancers are hereditary non-polyposis colon cancer (HNPCC or Lynch syndrome) and familial adenomatous polyposis coli (FAP). Both syndromes are autosomal dominant disorders and follow the molecular pathogenesis typical of CRC: Lynch syndrome-associated cancers show signs of mismatch repair deficiency and microsatellite instability (MSI), whereas FAP-associated cancers follow the classic adenoma-carcinoma sequence. ¹⁸

Mismatch repair-deficient CRCs, like those seen in patients with Lynch syndrome, are characterized by the accumulation of many insertion or deletion mutations spread along the genome. Clinically, MSI cancers follow these characteristics: localized to the proximal colon, manifests in people 50 years of age or younger, synchronous occurrence with additional tumors, and large local tumors with rare organ metastases. Lynch syndrome carries a 70-80% risk of developing colon cancer, along with an increased risk of developing other cancers. Once diagnosed, patients can enter into proper screening programs. Patients with MSI CRC have a better prognosis than patients with microsatellite stability. ¹⁷

FAP results from a mutant gatekeeper gene, *APC*, and displays profuse polyposis. ¹⁸ This cancer follows the model of Knudson's "two hit theory", with inactivation of one important

tumor suppressor or DNA repair gene, and the second gene receiving a somatic event (the second hit) that causes irregular function and tumor formation. ¹⁸ *APC* gene mutations are an early event in the multistep process of CRC formation and occur in more than 70% of colorectal adenomas. The adenoma-carcinoma sequence is thus activated and results in thousands of adenomatous polyps in the colon of affected individuals. These polyps can appear as early as teenage years and has a staggering lifetime cancer risk approaching 100% with varying penetrance. Following genetic testing, proctocolectomy is usually recommended.

Diagnosis of CRC is made histologically from biopsies taken during endoscopy. Complete colonoscopy or computed tomography (CT) colonography is mandatory to detect synchronous cancers. If this is not possible, visualization of the entire colon should be done within 6 months of curative resection. Staging of CRC is fundamental in management. For rectal cancer, exact local staging using magnetic resonance imaging (MRI) of the pelvis to look for local invasion and nodal disease, and CT of the abdomen and chest to look for metastases. Colon cancer proximal to the rectum requires only the CT scans of the abdomen and chest. Positive emission tomography (PET) scans are also becoming more common in CRC work up, however their exact role has not been identified. ¹⁷

CRC is linked to several modifiable risk factors including obesity, physical inactivity, consumption of processed meats, and smoking. Diabetes may also increase the risk of CRC ¹⁶. Diets low in fibre and IBD have also been linked to CRC.

Incidence of CRC has been declining among adults older than 50 years of age for several decades. However, a concurrent trend of increasing incidence among adults younger than 50 years of age has been reported in the United States and in Canada. Increasing incidence among

this low risk population prioritizes primary and secondary prevention to reduce the burden of this disease. ¹⁹ Secondary prevention in the form of early detection and screening are much better for slow growing CRCs than other types of cancer. ¹⁷

1.3.3 Screening in Colorectal Cancer

The slow development of CRC from an adenoma over many years lends itself well to secondary prevention. Current national guidelines in Canada aim to reduce deaths due to CRC by detecting and removing polyps and/or early-stage CRC. ¹⁷ The guideline recommends screening for CRC in asymptomatic adults aged 50 years and older who are *not* at high risk for CRC. Fecal occult blood tests (FOBT) are available in two forms, guaiac-based fecal occult blood test (gFOBT) or fecal immunochemical test (FIT) are currently recommended every two years. Otherwise, flexible sigmoidoscopy can be performed every 10 years. If the FOBT screening test or sigmoidoscopy screening is positive, a diagnostic colonoscopy is indicated. ⁹

Patients who are considered high risk for CRC have had previous CRC, IBD, signs or symptoms of CRC, a history of CRC in one or more first degree relatives, or adults with hereditary syndromes (FAP or Lynch syndrome). They have screening guidelines based on their risk factors and require periodic colonoscopy. ²⁰ Screening is not recommended in patients aged 75 years or older, and colonoscopy is not currently recommended as a primary screening test in CRC. CT Colonography, while used in patients where screening colonoscopy is not tolerated, has not made its way into current guidelines at this time. ⁹

During colonoscopy, colonic polyps can be diagnosed visually and immediately biopsied or resected. Because of the adenoma-cancer relationships and the mounting evidence that

resecting adenomas prevents cancer, most patients with polyps detected by flexible sigmoidoscopy, barium enema, or with a positive screening test, should undergo colonoscopy to excise the polyp and search for additional neoplasms. Most polyps can be completely and safely resected, termed a polypectomy, using snares or biopsy forceps inserted through the colonoscope. Scientific studies now conclusively show that resecting these adenomatous polyps prevents CRC. ²¹

Performing polypectomies in colonoscopy is the mainstay in preventing the development of CRC. Ensuring adequate resection and retrieval of the polyps, however, can be difficult. Various techniques have been developed to improve polypectomy success and reduce potential complications. Snares are available with varying shapes and the potential to use cautery (hot or cold snare) depending on their location in the bowel. Positioning the polyp in relation to the colonoscope is essential to ensure adequate removal and retrieval. Polyps should be positioned at the five or six o'clock position, as this is where snares and other accessories exit the scope. A critical point to ensure accuracy of polypectomy is to keep the shaft of the colonoscope straight during insertion. This enables transmission of torque to the tip and is easier for the endoscopist to maneuver. Otherwise, looping in the colonoscope shaft tends to absorb rotational motions making the snaring of polyps more difficult. Optimal insertion technique is required to ensure a straight scope. Applying techniques to counteract looping of the colonoscope and reducing loops when they develop are important for patient comfort and to enhance the success of polypectomy in colonoscopy.²²

In some cases, it is not possible to position a polyp adequately for snaring. Submucosal injection, which lifts a polyp off of the underlying muscularis propria, is often recommended in

cases removing larger polyps or polyps in difficult locations. This technique enables a more complete resection and reduces the risk of complications like perforation and bleeding. Polyps considered too large or too complicated to resect safely through the colonoscope are often removed surgically. ²²

1.4 Position Changes in Colonoscopy

Colonoscopy can be technically challenging. It is, ultimately, operator dependent and relies on adequate visualization of the colonic mucosa to detect abnormalities which may require intervention. This should be done with care to keep the patient comfortable throughout the procedure. A patient's colonic anatomy is highly variable which can impact one's ability to maneuver the scope through the bowel during the procedure. It can be further distorted by abnormalities including adhesions, colonic diseases, and abdominal wall hernias. To date there have been several interventions to improve luminal distention and patient comfort during colonoscopy. These include improving the device and field of view (High Definition, balloon assisted colonoscopy, Full Spectrum Endoscopy), water infusion techniques, insufflation with carbon dioxide, and bowel preparations. While multiple advancements have been made, the procedure is not perfect and continues to be studied for technical improvements.

Position changes were commonly used during barium enemas. Radiologists experienced improved luminal distention and better examination by altering position changes for different areas of the bowel ²³. This concept requires the area of interest being brought to the highest point by gas rising and fluid being displaced to a dependent area. Position change allows for

improved luminal distention and can open up areas of the colon with acute bends, specifically at the hepatic and splenic flexures ²⁴. Left lateral (LL) decubitus positioning opens up the hepatic flexure while right lateral (RL) positioning opens up the splenic flexure. Supine positioning provides the best views of the transverse colon ²⁵.

In the LL position, the sigmoid colon is in a dependent position, with air rising away from it and fluid collecting within it. With the use of air (or carbon dioxide), the sigmoid colon distends, increasing the likelihood of acute angulations forming. In addition, the right colon fills with air which may increase patient discomfort. Without air insufflation, the colon is collapsed which can hinder visualization. In the RL decubitus position, air rises and fills the left colon, allowing for good visualization and scope advancement. The right colon is dependent and does not distend. ²⁶. Ultimately, RL decubitus positioning may result in decreased cecal intubation times and improved patient comfort during the procedure.

The results of studies examining the effects of position changes during colonoscopy have been conflicting. Several randomized controlled trials (RCT) have been done comparing the effect of position changes on cecal intubation times. Only one trial compared starting positions in RL decubitus and LL decubitus – the ROLCOL (right or left colonoscopy) trial. They found that RL positioning resulted in decreased cecal intubation times (due mainly to decreased times to the transverse colon) and improved patient comfort scores compared to LL positioning. ²⁶ More recently, a study by Zhao et al. in 2019 compared the effect of a supine starting position to a left horizontal (lateral) starting position on cecal intubation times. They found that supine positioning also decreased cecal intubation times and improved patient comfort. ²⁷ Prone positioning has also been studied in comparison to LL positioning. Vergis et

al. conducted an RCT comparing cecal intubation times in prone position and LL decubitus position in obese patients. They found that cecal intubation times were longer and the procedure was more technically challenging with prone positioning. ²⁸ A similar trial had been conducted in 2013 by Uddin et al. who found that prone positioning in obese patients resulted in significantly shorter cecal intubation times and a decreased need for patient repositioning compared to the LL position. ²⁹

There have been five RCTs examining the use of position changes during colonoscope withdrawal and its effect on a number of variables including the adenoma detection rate (ADR). In 2007, East et al. conducted a randomized, blinded, crossover trial to compare videos of colonoscopy on withdrawal comparing prescribed position changes to the standard static LL decubitus position. The position changes were LL for the cecum to hepatic flexure, supine through the transverse colon, and RL for the left colon and sigmoid. They concluded that position changes improved luminal distention. ²⁵ In 2013, Yamaguchi et al. also showed that dynamic position changes during colonoscope withdrawal also decreased the sensation of abdominal fullness ²³. During that year, Koksal et al. showed an improvement in ADR with changing patient position on colonoscope withdrawal compared to LL decubitus positioning. They did not have pre-prescribed positions for areas of the colon. ³⁰ Prescribed position changes were studied by Ou et al. in 2014 and they concluded that position changes during colonoscope withdrawal did not affect the polyp/adenoma detection rate compared to the standard LL decubitus positioning. Their prescribed positions were: ascending colon/hepatic flexure in LL decubitus, transverse colon in supine position, splenic flexure to rectum in RL decubitus position. ³¹ Ball et al. found conflicting results in 2013. They found an increase in

ADR in the right colon with position change to the LL decubitus compared to other position changes, but found no difference in ADR in the left colon comparing different position changes. ³² (Figure 4).

Comparison Vergis et al, 2015 **RL and LL Starting Position Cecal Intubation Time** Decreased cecal intubation RCT time and improved patient comfort in RL position Zhao et al, 2019 RCT Supine and LL Starting Cecal Intubation Time Decreased cecal intubation Position time and improved patient comfort in supine starting position Vergis et al, 2016 RCT Prone and LL Starting Cecal Intubation Time Increased cecal intubation **Position in Obese Patients** time in prone position Uddin et al, 2013 RCT Prone and LL Starting **Cecal Intubation Time** Decreased cecal intubation **Position in Obese Patients** time and fewer position changes in the prone position East et al, 2007 Position changes and LL ADR RCT Position changes improved position on withdrawal of luminal distention the colonoscope Yamaguchi et al, RCT Dynamic position change vs Sensation of Dynamic position change 2013 LL position during abdominal fullness decreased the sensation of abdominal fullness colonoscope withdrawal Koksal et al, 2013 RCT Position changes and LL ADR Improvement in ADR with position during colonoscope position changes withdrawal Ou et al, 2014 RCT Position changes and LL ADR No difference in ADR position during colonoscope withdrawal Ball et al, 2013 RCT Right side of colon ADR Increase in ADR in the right comparing supine and LL colon in LL position, no position, left colon difference in ADR in the left comparing supine and RL colon in either position position

Figure 4: Summary	v of Literature	Comparing	Position Change	on Outcomes in Colonoscopy.

These conflicting reports have resulted in mixed opinions regarding the utility of including position change in everyday practice. Currently, the use of position changes as a technique to improve colonoscopic performance is routinely taught as part of colonoscopic skills improvement courses. Their impact on cecal intubation time, ADR and patient comfort is, however, uncertain.

1.5 Purpose

Given the equipoise found in the literature, we aimed to determine if RL decubitus starting position can decrease cecal intubation times and improve patient comfort compared to the standard LL decubitus starting position. This study is a randomized controlled trial comparing RL decubitus and LL decubitus starting position. The primary outcome is cecal intubation time. Secondary outcomes include cecal intubation rates, ADR, patient comfort during their colonoscopy, sedation dosage, number of position changes required, and amount of water used between the two starting positions.

1.6 Null Hypothesis

H₀: Starting position in colonoscopy has no effect on cecal intubation time.

Chapter 2: BACKGROUND

2.1 Quality Indicators

The quality of healthcare, in this case the procedure of colonoscopy, can be measured by comparing the performance of an individual or group of individuals with an ideal or benchmark. A quality indicator is a parameter used for this comparison. Quality indicators can be divided into three categories: 1) structural measures – assesses characteristics of the entire health care environment (e.g. systemic clinical database registry), 2) process measures – assesses performance during the delivery of care (e.g. ADR or biopsy sampling during colonoscopy), and 3) outcome measures – assesses the results of care that was provided (e.g. Prevention of cancer by colonoscopy and reduction of incidence of colonoscopic perforation).

These indicators can help ensure high-quality healthcare by facilitating analysis and comparison of the results of interventions. Common quality indicators in colonoscopy include adenoma/polyp detection rate, cecal intubation time/rate, withdrawal time, bowel preparation quality, sedation/medication use and patient comfort. Using these quality indicators to compare different colonoscopic techniques can demonstrate efficacy for everyday practice.

2.1.1 Adenoma Detection Rate (ADR)

The adenoma detection rate (ADR) is the fraction of patients undergoing screening colonoscopy who have had one or more adenomas detected. The recommended targets for

ADR are based on screening colonoscopy studies and were set at levels slightly below the mean detection rates of adenomas in those studies. The current performance target is >25% for the asymptomatic, average risk population, with a higher rate in men (\geq 30%) then women (\geq 20%).³³

Studies have found significant numbers of interval cancers due to missed lesions or incomplete polypectomies. An enormous amount of literature has identified failed detection of lesions by colonoscopists as the reason for interval cancer development ^{34 35 36}. In fact, each 1% increase in ADR has been associated with a 3% decrease in risk of interval cancer development ³⁷.

There is substantial interaction between ADR and recommended interval for screening and surveillance colonoscopy. In general, surveillance guidelines are based upon polyp size, histology, and the number of polyps detected. With fewer lesions identified, a longer time period is recommended before the next examination whereas more lesions prompt shorter interval examinations. Therefore, optimal patient safety cannot be correctly predicted without knowledge of both an adequate ADR and adherence to recommended intervals. Colonoscopists with high ADRs clear colons better and bring patients back at shorter intervals because the recommended intervals are shorter when precancerous lesions are detected. With low ADRs, colonoscopists fail to identify patients with precancerous lesions and find fewer patients with multiple lesions – putting patients at risk for cancer by failure to examine the entire colon and recommending inappropriately long intervals between examinations.

ADR is currently considered the primary measure of the quality of mucosal inspection and the single most important quality measure in colonoscopy. ³³ It is also the only quality indicator that has been shown to decrease the risk of interval cancer development. ³⁴

Polyp detection rate (PDR) is a surrogate measure for ADR. It is easier to measure because it does not require histological review. Although PDR correlates with ADR, it is a less desirable measure and is not currently endorsed as a quality indicator.

2.1.2 Cecal Intubation

Cecal intubation confers the completion of a colonoscopy. In order to visualize the entire colonic mucosa, intubation of the endoscope to the cecum is mandatory. ³⁷ It is defined as a passage of the colonoscope tip to a point proximal to the ileocecal valve, so that the entire cecal caput and it's three landmarks (ileocecal valve, the appendiceal orifice, and triradiate fold) are visible. Identification and visualization of this area is crucial due to the persistent finding that a substantial fraction of colorectal neoplasms are located in the proximal colon, i.e. the cecum. Without visualizing this area, the risk exists of missing a premalignant or malignant lesion. Low cecal intubation rates have therefore been associated with higher rates of interval proximal colon cancer. Colonoscopists should identify this area in all of their cases, and documentation with photography of the cecum is mandated. Effective colonoscopists should be able to intubate the cecum in \geq 90% of all cases and \geq 95% of cases when the indication is screening in a healthy adult. ³³

The amount of time it takes from identifying rectal mucosa (the very beginning of a colonoscopy) to identifying landmarks in the cecum is the insertion time in a colonoscopy. The mean time to reach the cecum has been reported as approximately 6.4 minutes. ²⁶

2.1.3 Withdrawal Time

Withdrawal time is the amount of time it takes an endoscopist to start removing the colonoscope from the cecum to the time it is fully out of the rectum ³⁸. The theory surrounding withdrawal time is that a longer withdrawal time confers a better and more thorough visualization of the colon. This should result in higher detection rates of lesions. Retrospective studies have clearly demonstrated an association between longer withdrawal time and higher detection rates. ³³ A mean withdrawal time of at least 6 minutes has been therefore formulated as a quality indicator in several endoscopic guidelines. ³⁷

Withdrawal time is, however, a secondary measure. The primary utility of withdrawal time may be correcting performance of colonoscopists with substandard ADRs. In a study comparing endoscopists before and after instituting a minimum eight-minute withdrawal protocol, ADR improved. Increases in ADR were found among all endoscopists with baseline lower rates of ADR, and ADR was highest in endoscopies with intermediate withdrawal times. ³⁹

2.1.4 Patient Comfort and Sedation/NAPCOMS

Patient comfort is an essential component of a high-quality colonoscopy. When colonoscopies induce a lot of pain, patient satisfaction decreases, and the procedure is often abandoned as the risk of perforation outweighs the benefit of continuing. Although a colonoscopy can be performed without sedation, most centers in North America use sedation. A combination of short-acting benzodiazepines and an opioid are typically administered by an endoscopy nurse upon instruction from the physician performing the scope. Recently, there has been a trend towards using more Propofol mediated sedation due to its rapid onset of action, short half-life and improved patient satisfaction over traditional sedatives. Propofol is usually administered by anesthesiologists but can be given by others provided they have the appropriate training. Its use requires someone other than the colonoscopist to be in the endoscopy suite providing sedation during the procedure. Recovery and discharge times have been reported as faster with use of Propofol compared to a benzodiazepine/opioid mix. ⁴⁰ Other studies contradict these findings with no association of shorter recovery with Propofol administration. ⁴¹

Cecal intubation rates and polyp detection rates are not affected by the type of sedation used. While some have suggested that Propofol administration may improve quality indicators ⁴⁰, others have found no difference between the sedative used and cecal intubation rate or detection of polyps.

Colonoscopy without sedation is also being adopted by some endoscopists. Studies have shown that the procedure can be done with no sedation, provided patients are agreeable and able to tolerate it. ⁴²

While the amount and type of sedative(s) used may differ between places, it should be noted that the level of sedation achieved can drastically change the procedure. Monitoring of vitals including oxygen saturation, respiration rate, heart rate and blood pressure are of utmost importance and can be impacted by the level of sedation. This is especially important in patients who are considered high risk for anesthetic procedures due to pre-existing medical conditions. ⁴² In addition to the increased anesthetic risks of propofol sedation, heavily sedated patients cannot turn themselves during the procedure, making the use of position changes during colonoscopy much more difficult.

NAPCOMS

Due to the subjective nature of pain and patient discomfort, several tools have been developed as "pain scales". One such scale is the Nurse-Assessed Patient Comfort Score, or NAPCOMS score by Rostom et al ⁴³. It was developed for nurses to assess and document pain scores during a colonoscopy using a score sheet. The scoring sheet has grading scales for three domains: pain – intensity, frequency, and duration; sedation – level of consciousness; and global – tolerability. The scale ranges from 0 (no pain) to 9 (severe pain). The NAPCOMS scale is a validated, reliable, and easy to use instrument to document patient comfort with good interobserver reliability.

2.1.5 Bowel Preparation

Inadequate preparation of the bowel can be costly in terms of mucosal visualization, scope maneuvering, missed lesions and complications ⁴⁴. Poor bowel preparation is a common

problem and is estimated to affect 4-17% of colonoscopies ⁴⁵. A variety of bowel preparations exist, however there is no single preparation that is widely accepted. Patient acceptance of bowel preparation is also crucial. ³³

The most important determinant of preparation quality is the interval between the end of ingestion and the start of procedure. Quality diminishes as the interval increases. Currently, the prescription of split-dose bowel preparation is gaining favor, with half of the preparation being taken on the day of the procedure. For afternoon colonoscopies, the entire preparation can be taken on the day of the procedure. ³³

Most centers will use a Likert scale when describing preparation quality, rating preparations as: excellent, good, fair, or poor ^{46 47}. This scale is at the discretion of the colonoscopist and rated by them following the procedure. Several other scoring systems, including the Boston Bowel Preparation Scale (BBPS) and the Ottawa Bowel Preparation Quality Scale are available for use. As a general rule, if the preparation is inadequate to identify polyps >5mm in size, then the procedure should be repeated ⁴⁵.

A preparation rated at Fair or Poor should be redone to ensure adequate luminal exposure. To date, there is no widely accepted bowel preparation regimen after failure to adequately cleanse the colon for repeat colonoscopy, though studies are ongoing ⁴⁵.

2.2 Specialty and Experience

Higher annual case volume has been shown to be associated with better quality outcomes. Specifically, an annual procedural volume of greater than 200 colonoscopies has been shown to improve the quality measures of ADR, polyp detection, and cecal intubation.

The specialty of gastroenterology has also been shown to be a better predictor of ADR when compared to other specialties including surgeons, internists and family physicians. Some studies have shown that specialty may be a better indicator than annual case volume. ⁴⁸

The amount of education and technical training varies by specialty. In gastroenterology, fellows undergo two years of dedicated training after completion of internal medicine training and typically get exposed to a higher case volume than their surgical counterparts. In Canada, general surgery residents typically receive three-five months of dedicated endoscopic training during their surgical residency.

It is currently recommended that trainees undergo a minimum of 140 colonoscopies to assess their competency. ⁴⁹ ADRs have been shown to be significantly lower when colonoscopy is performed by trainees. Trainees have also been shown to have shorter withdrawal times. It is therefore crucial that trainees are taught proper skills including withdrawal technique to achieve adequate ADRs. ⁵⁰

Although a body of knowledge around the proper skills and techniques required to be a competent colonoscopist does exist, it is unclear if all trainees achieve these skills. The Mayo Colonoscopy Skills Assessment Tool is a currently recommended tool for trainees to measure skill acquisition ⁴⁹. However, it remains uncertain if these skills are acquired in the same manner by trainees across different specialties and different training programs.

While there appears to be a relationship between colonoscopy quality and specialty, case volume is also a key factor. Although a specified number of colonoscopies does not necessarily imply competence, at last one study has shown that case volume and accreditation are more important than specialty in determining quality standards for the practice of

colonoscopy. ⁵¹ The ROLCOL trial also clearly showed that endoscopist experience, as measured by procedural volume, also had an impact on quality indicators ²⁶.

2.2.1 Training/Education

There are multiple educational strategies currently used to target quality improvement in colonoscopy. These opportunities may be directed at trainees or experienced endoscopists. Interventions may consist of didactic teaching, simulation and/or hands-on teaching.

In Canada, the Skills Enhancement for Endoscopy (SEE) program is an initiative of the Canadian Association of Gastroenterology (CAG) to ensure standards for quality markers in colonoscopy are met across the country. The program consists of three types of accredited programs – the Colonoscopy Skills Improvement (CSI) course, the Train the Endoscopy Trainer (TET) course, and the Endoscopic Polypectomy Improvement (EPIC) course. The CSI course is designed for all practicing endoscopists, providing up-skilling and improvement of colonoscopy skills and procedure conscious competence needed to teach endoscopy. The EPIC course is designed to improve skills related to the identification and management of colonic polyps. ⁵²

The CSI course has gained popularity across Canada. The course was developed based on a framework for effective, efficient delivery of training skills in endoscopy. It provides hands-on colonoscopy skills by two SEE certified faculty over one day, with a teacher to learner ratio of two teachers to three learners. The framework focuses on providing performance enhancing feedback to trainees using a structured approach and applying basic adult learning techniques. Educational goals are set early to align agendas between the trainers and specific

needs of the trainees. All feedback is provided in a non-judgemental fashion. Each learner performs two colonoscopies overseen by a certified SEE faculty, enabling them to practice techniques learned during the course and to outline performance-enhancing feedback specific to each trainee ⁵². In 2018, an increase in ADR was found among endoscopists who had successfully completed this course compared to their baseline ⁵³. Completion of this course is becoming a standard in centers across the country.

Incorporating programs designed to target quality improvement have been shown to improve ADR. A large multicenter RCT was published in 2015 that showed a sustained improvement in ADR by participants of approximately 4%. ⁵⁴ Two smaller RCTs at the Mayo Clinic also showed an improvement in ADR after the educational intervention "EQUIP" (endoscopy quality improvement program). ^{55 56}

2.3 Technical Considerations

Measuring and improving quality indicators in colonoscopy has emerged as a central focus in quality improvement. ADR, as previously mentioned, has become the most important quality measure, with cecal intubation, patient comfort, and bowel preparation also gaining recognition. Measurement of the ADR has, unfortunately, identified many colonoscopists who fall below the recommended minimum thresholds. While an adequate bowel prep is essential, there are several adjunctive tools or technical considerations that can help improve ADR. These include mucosal exposure devices, lesion highlighting techniques, and non-device methods such as double right colon examination, scope retroflexion, water exchange and patient position change.

The majority of mucosa is examined during withdrawal of the colonoscope. The components of effective mucosal exposure include: 1) a detailed effort to probe and expose the proximal sides of the bowels, haustral folds, and flexures; 2) wash and clean areas of residual debris, and 3) adequate luminal distention.

By using these techniques, improvement in ADR can reflect an improvement in the overall technical colonoscopic procedure.

2.3.1 Mucosal Exposure Tools

The Panoramic Third Eye Retroscope (TER) is a reusable device that clips on to a colonoscope of all manufacturers and provides lateral images to the side that are displayed adjacent to the forward viewing image of the colonoscope. This gives a "panoramic" view, seeing around folds that forward viewing scopes may not. ³⁶ Limitations of this device include interference with polypectomies and cost. There are no large trials examining the efficacy of this device.

The Full Spectrum Endoscopy (FUSE) system, which utilizes imaging clips on both sides of the colonoscope tip to create a 330-degree field of view in the horizontal direction and 120 degree in the vertical direction, produced a reduction in adenoma miss rates in a tandem study. ⁵⁷ Unfortunately, concerns regarding the lower image resolution have caused uncertainty about the future of the device. Other devices with wider angle views have undergone preliminary testing, but none are commercially available at this time.

Devices designed to fit on the tip of a colonoscope and flatten haustral folds to improve mucosal exposure are also being studied. These include the short cap or hood, a reusable

balloon called G-EYE, EndoRings, and the Endocuff. While all of these devices differ slightly in design, they have all been shown to be effective in increasing ADR. To date there have been no head to head trials showing a superior design. ³⁶

2.3.2 Lesion Highlighting Techniques

Modern colonoscopy is best performed with high definition instruments, proving essential to polyp differentiation and enhancing evaluation of a post polypectomy scar. High definition instruments produce a 2-4% gain in ADR.

Autofluorescence or electronic chromoendoscopy, including narrow band imaging and blue laser imaging, appear to be beneficial in differentiating hyperplastic from adenomatous polyps. They have not been shown to be effective in increasing ADR. Pancolonic spraying or chromoendoscopy may be effective in detection of adenomas or serrated lesions during routine colonoscopy, however it has not been adopted for routine colonoscopy. ³⁶

2.3.3 Non-Device Methods

Non-device methods infer lesser cost and are easier to implement compared to other devices or techniques. These methods include measuring ADR, double right colon examination, retroflexion in the right colon, water exchange, and position changes.

2.3.3.1 Measuring ADR

Simply measuring the ADR can improve ADR. It provides measurement and feedback to physicians, which may result in gains in performance due to the Hawthorne effect ⁵⁸.

2.3.3.2 Double Right Colon Examination and Retroflexion

The right colon (cecum and ascending colon) is more susceptible to missed lesions. This has been demonstrated in several case-control studies. ^{59 60} Colonoscopy is less protective for patients developing right-sided colon cancer (40-60% protective effect) than left-sided colon cancers (80% protective effect). ⁶¹ To reduce the risk of interval cancer growth, cecal intubation is imperative with photo documentation. Double right colon examination, in which the cecum is intubated twice after withdrawal to the hepatic flexure, has been introduced as a method to decrease missed lesions. Retroflexion of the colonoscope in the cecum has also been proposed. These measures allow for better mucosal inspection of the right colon. ³⁶

2.3.3.3 Water Exchange

Water exchange is the practice of filling the colon with water and exchanging the dirty water for clean water. Essentially, it improves visualization by improving bowel preparation. Water exchange has been shown to improve adenoma detection, particularly in the proximal colon. ³⁶

Patient comfort also appears to be improved with the use of water in insertion. The use of water (as opposed to air) could potentially cause less pain due to less luminal distention and less kinking of the bowel, which can be difficult to navigate the colonoscope through. ⁶² Use of

water on insertion of the colonoscope has also been shown to require fewer position changes than air insufflation ⁶³.

2.3.3.4 Position Change

Position change or patient rotation, as discussed previously, is built on the concept that increasing luminal distention will improve mucosal visualization. By changing positions, the colon can change from a dependent position to a non-dependent position, allowing it to fill with gas and become more distended. Thus, the right colon should be examined in the LL decubitus position, the transverse colon in the supine position, and the left colon in the RL decubitus position ²⁵. Patient rotation requires light to moderate sedation to allow patients to move themselves during the procedure.

The conflicting reports of position changes in colonoscopy has failed to change the standard practice of a LL decubitus starting position. The potential benefit of position changes and their incorporation into everyday practice requires further investigation.

Chapter 3: METHODS

3.1 Literature Search

PubMed, Embase, and Cochrane databases were searched to find relevant literature on the topic of position changes in colonoscopy. The keywords in the search were the MeSH terms "colonoscopy" and "position change". The search yielded a total of 81 results. Restrictions used in the search were patients aged 18 years or older and publications in English only. Papers were excluded if they included interventions other than position change, i.e. abdominal binders and pressure, type of colonoscope, and type of insufflation. All levels of research were included and there was no restriction on date. Relevant articles were selected after reviewing all abstracts and only full publications were included. A total of 18 studies were identified with reference to position changes in colonoscopy and consisted of one systematic review, one meta-analysis, ten RCTs comparing different position changes during insertion and withdrawal of the colonoscope, five review papers and one editorial on best practice in colonoscopy. Bibliographies of all selected studies were then screened to identify any additional resources missed in the original literature search.

3.2 Study Design

This study was a RCT comparing starting position in the RL decubitus position to the LL decubitus position on outcomes in colonoscopy. All endoscopists who had successfully completed the colonoscopy skills improvement course under the umbrella of the SEE program were included in the study – a total of eight general surgeons and five gastroenterologists.

Patients who were scheduled for a colonoscopy between the months of April 1, 2019 to September 30, 2019 received information regarding the trial in their appointment letters and were given an opportunity to contact the team with any questions or concerns they may have had with the study.

After arriving for their scheduled colonoscopy, patients were approached and consented to take part in the trial. During their consent, patients were asked their height, weight, and past medical history including previous abdominal surgeries. After consent, they were randomized to start their colonoscopy in either the LL decubitus or RL decubitus position. The randomization was performed using a random numbers generator to code either "Right" or "Left", these were then printed and sealed in opaque envelopes so that the randomization was masked prior to commencing the colonoscopy. Required information was collected by a trained individual who remained in the room during the colonoscopy.

The NAPCOMS score was taken directly from the nursing notes (this validated score was introduced and education of nursing staff was done prior to the study taking place). All patients undergoing colonoscopy at these sites are assigned a NAPCOMS score. The score for bowel preparation was taken from the colonoscopist's reports (rated as excellent, good, fair, or poor) and represented their assessment. The amount of water used was determined by measuring the amount in the infusion bottle at the start of the case and subtracting the amount remaining after the colonoscopy was completed to the cecum. The endoscopist's specialty (Gastroenterology and General Surgery) was collected, as was their experience – defined as being greater than five years in practice or less than five years. There was no follow up involved

in the study and patients were not required to answer any questions during or after the conclusion of their colonoscopy.

Full approval was obtained from the provincial Health Research Ethics Board (HREB) and from the Research Proposals Approval Committee (RPAC) at Eastern Health. This project was registered with ClinicalTrials.gov, approval number NCT03355495.

3.3 Inclusion/Exclusion Criteria

All patients aged 18 years and older who presented for their scheduled colonoscopy were considered for inclusion in the study. Patients were excluded if they had a previous large bowel resection, if they had a musculoskeletal problem preventing them from certain positioning (hip or back problems, recent surgeries, etc.), and if they refused to take part in the study.

All endoscopists performing colonoscopy at the Health Sciences Center and St. Clare's Mercy Hospital in St. John's, NL who had successfully completed the CSI course and were available at the time of the study were included. Trainees were excluded from the study.

3.4 Outcome Measurements

The primary quality outcome was time to cecal intubation comparing both the RL and LL decubitus starting positions. Secondary outcomes included cecal intubation rates, ADR, NAPCOMS score, sedation dosage, number of position changes on insertion and withdrawal time.

Data were collected on the patient's age, sex, body mass index (BMI), previous surgeries (especially abdominal surgeries), procedure indication, time to cecal intubation, time of withdrawal, ADR, number of position changes required to complete the colonoscopy, NAPCOMs pain score, amount of sedation administered, amount of water infused, quality of bowel preparation and the endoscopist performing the colonoscopy.

3.5 Statistical Analysis

Students T-test, chi-squared tests, Pearson's Correlation, ANOVA, linear and logistic regression models were used, when appropriate, to analyse the data. Univariate analysis was performed to identify factors associated with the following outcomes – cecal intubation time, cecal intubation rate, ADR, and patient comfort. A p-value of ≤ 0.10 was considered significant in the univariate analysis. Multivariate logistic regression and linear regression were used to assess variables identified in univariate analysis to identify those independently associated with outcomes of interest using a significance level of ≤ 0.05 . All other comparisons were done using a two-tailed significance level of ≤ 0.05 . All analyses were done using SPSS Statistics v25 (IBM Corporation, USA).

3.6 Sample Size Calculation

The sample size was calculated using a continuous endpoint with two independent samples model. A mean cecal intubation time of 384 seconds with a standard deviation of 180 seconds has been cited in the literature ²⁶ and was used in this calculation. A significant change

was defined as 20%. An alpha of 0.05 was used (two-tailed) with a power of 0.8. Using these terms, a sample size of 172 was calculated, 86 participants in each study arm.

An additional 12% of participants were included for possible dropout from the study that could not be identified prior to randomization. These were patients who had an incomplete colonoscopy for a variety of reasons. The final total was 192 participants.

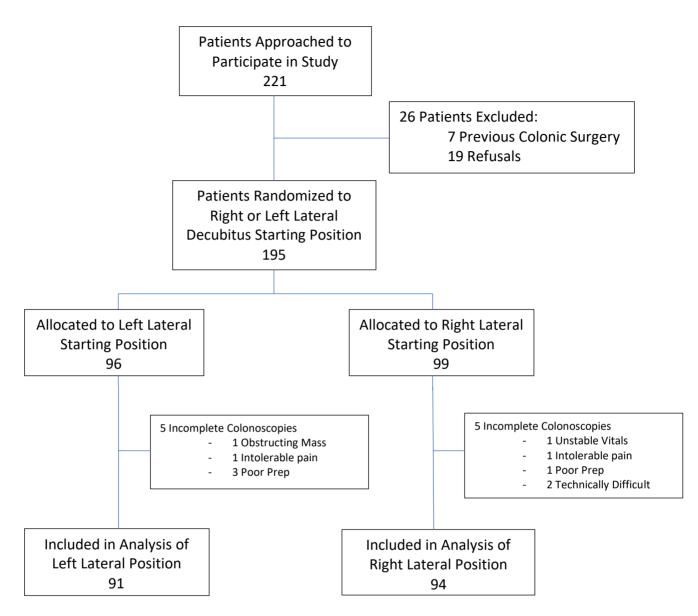
Chapter 4: RESULTS

4.1 Enrollment Process

A total of 221 patients were approached to take part in the study between March 12, 2019 and August 5, 2019. With 26 exclusions from the study, 195 participants were enrolled and consented to participate. The two main reasons for exclusion were previous colonic surgery (7) and refusal to participate (19). The 195 enrolled participants were randomized to either RL decubitus starting position (100) or LL decubitus starting position (95) immediately before the start of the procedure. There was one instance where, following randomization, a colonoscopist decided to start a patient on the opposite side than they had been randomized. This patient was therefore included in the intention to treat analysis.

There were 10 patients, five in each group, who had incomplete colonoscopies. This was due to poor bowel preparation (4), intolerable pain (2), technically difficult anatomy (2), obstructive masses (1), or unstable vitals (1). 185 patients were included in the analysis, 94 in the group starting in the RL decubitus position and 91 in the LL decubitus starting position (Figure 5).

Figure 5: Flowchart of enrollment process.



4.2 Patient Demographics

Patient demographics were comparable between groups (Table 1). There was no difference between the two groups in terms of age, sex, BMI, previous abdominal surgery, indication for procedure, or specialty of endoscopist. The most common indication for

performing a colonoscopy was screening or surveillance (51.9%). The mean BMI of the patients who took part in this study was 28.31, placing a large proportion of participants in this study in an overweight category.

<u>Variable</u>	<u>Total</u>	<u>RL (N=94)</u>	<u>LL (N=91)</u>
Age (years)	60.17	60.49	59.83
Sex (% Male, (N))	47.6 (88)	42.5 (40)	52.7 (48)
ВМІ	28.31	28.17	28.54
Previous Abdominal Surgery	46.5 (86)	47.9 (45)	45.1 (41)
Adequate Bowel Preparation	88.1 (163)	85.1 (80)	91.2 (83)
Indication			
Screening/Surveillance	51.9 (96)	52.1 (49)	51.6 (47)
Diagnostic	33.5 (62)	36.2 (34)	45.2 (28)
FIT Testing	14.6 (27)	11.7 (11)	17.6 (16)
Endoscopist Specialty			
Gastroenterologist	54.6 (101)	57.4 (54)	51.6 (47)
General Surgeon	45.4 (84)	42.6 (40)	48.3 (44)

Table 1: Demographic Information of Participants and Procedure Indication

4.3 Statistical Analysis on Outcomes

4.3.1 Bowel Preparation

The sites included in this study used a bowel preparation scale of "excellent, good, fair or poor". For the purposes of our analysis, bowel preparations were considered 'adequate' or 'inadequate'. An 'adequate' bowel preparation was rated as either "excellent" or "good" as per the procedural record by the attending endoscopist. 'Inadequate' bowel preparations were rated as "fair" or "poor". Analysis comparing bowel preparation between RL and LL position was done using ANOVA and chi square tests. There was no difference in the bowel preparation quality between the two groups (Table 2).

Variable	<u>Total (%)</u>	<u>RL (%) (N=94)</u>	<u>LL (%) (N=91)</u>
Bowel Preparation			
Excellent	60.5 (112)	58.5 (55)	62.6 (57)
Good	27.6 (51)	26.6 (25)	28.6 (26)
Fair	5.41 (10)	6.38 (6)	4.40 (4)
Poor	6.48 (12)	8.51 (8)	4.40 (4)
Adequate Bowel Preparation	88.1 (163)	85.1 (80)	91.2 (83)

Table 2: Bowel Preparation Scale and Adequate Preparation Comparing Right and Left Lateral Decubitus

4.3.2 Primary and Secondary Outcomes

In terms of the primary outcome, there was no difference in cecal intubation time in RL decubitus (542.6s \pm [360.7s]) or LL decubitus (497.9s \pm [288.3s]) starting position (p=0.354). Secondary outcomes also did not show a significant difference based on starting position. Cecal

intubation rates were high for both positions - 94.9% on the right and 94.8% on the left, with no difference between the two groups (p=0.960). The ADR between groups was also not significantly different (p=0.240). (Table 3).

Variable	<u>Total</u>	<u>RL (N=94)</u>	<u>LL (N=91)</u>	P-Value
Cecal Intubation Time (s)	520.57	542.56	497.85	0.354
Cecal Intubation Rate (%)	94.9 (185)	94.9 (94)	94.8 (91)	0.960
ADR (%)	60.5 (112)	56.3 (53)	64.8 (59)	0.240

Table 3: Primary and Secondary Outcomes

4.3.3 Analysis of Time to Cecal Intubation

Univariate and multivariate regression analysis was performed to identify variables associated with the time to cecal intubation. Univariate analysis was completed to identify variables independently associated with time to cecum. The analysis was done using Student t-tests, ANOVA, Pearson's correlation and univariate linear regression when appropriate with a cut-off of p=0.10. The data have been presented using mean time to cecum for categorical variables and correlation models for continuous variables. Univariate linear regression output for all variables may be found in the appendix (Table 17). Variables associated with time to cecum in the univariate analysis included sex, previous abdominal noncolonic surgery, indication, adequate bowel preparation, specialty of endoscopist, experience of endoscopist, NAPCOMS score, amount of Versed used, the amount of water used, and the number of position changes required to reach the cecum (Table 4).

Variable	Category	<u>Time (s)</u>	<u>95% Cl</u>	P-Value
Sex	Male	418.17	104.22 – 286.165	<0.001
	Female	613.46		
Prev Abd Surgery	Yes	591.29	38.774 – 225.545	0.006
	No	459.13		
Indication	Screening/Surveillance	464.86	473.14 - 568.00	0.048
	Diagnostic	592.42		
	FIT Testing	553.63		
Bowel Prep	Adequate	499.92	-318.35428.897	0.019
	Inadequate	673.55		
Position	RL	542.56	-50.190 – 139.625	0.354
	ш	497.85		
Specialty	General Surgery	651.94	-329.475 – 151.792	<0.001
	Gastroenterology	411.31		
Experience	<5 Years	673.71	50.394 – 310.525	0.007
	>5 Years	493.25		

Table 4: Univariate Analysis for Time to Cecum

Variable	Pearson's Correlation Coefficient	P-Value
Age	0.102	0.167
ВМІ	-0.081	0.274
NAPCOMS	0.455	<0.001

0.114	0.124
0.128	0.081
0.394	<0.001
0.705	<0.001
	0.128 0.394

Multivariate analysis was performed using linear regression. Variables independently associated with time to cecum included sex, specialty of the endoscopist, experience of the endoscopist, NAPCOMS score, amount of water used, and number of position changes required to reach the cecum (Table 5). The R Squared for the model was 0.708.

Variable	<u>B</u>	Standard Error	95% Confidence Interval	P-Value
Constant	-380.911	116.108	-610.046151.777	0.001
Sex (Ref: Male)	85.416	28.443	29.285 – 141.547	0.003
Specialty (Ref: GI)	197.984	30.101	138.581 – 257.388	<0.001
Experience (Ref:>5)	119.393	46.091	28.436 - 210.351	0.010
NAPCOMS	31.255	5.860	19.691 - 42.819	<0.001
Total Water Used	0.376	0.077	0.224 - 0.528	<0.001
Position Changes (#)	135.284	11.193	113.196 – 157.372	<0.001

Table 5: Multivariate Regression Model for Time to Cecum

The multivariate linear regression analysis indicates that NAPCOMS score is significantly associated with time to cecum. Further analysis was therefore done to understand this

relationship. This analysis used ANOVA to determine if there was a difference between NAPCOMS score and the average amount of time it took to reach the cecum (Table 6). This demonstrated that shorter insertion times were significantly associated with lower NAPCOMS Score (p<0.001).

NAPCOMS Score	Time to Cecum (s)	95% CI	P-Value
0 (N=59)	354.97	301.69 - 408.24	<0.001
1 (N=3)	475.67	-90.85 – 1042.19	
2 (N=3)	455.67	347.21 - 564.13	
3 (N=65)	502.12	432.89 – 571.36	
4 (N=13)	498.31	289.74 - 706.87	
5 (N=7)	967.43	405.69 – 1529.17	
6 (N=18)	741.17	588.39 - 893.94	
7 (N=7)	886.29	578.65 – 1193.92	
8 (N=5)	643.20	153.94 – 1132.46	
9 (N=5)	783.80	436.13 - 1131.47	

Table 6: Analysis of Time to Cecum and NAPCOMS Score

4.3.4 Analysis of Cecal Intubation Rate

The overall cecal intubation rate was 94.9%. There was no difference in cecal intubation rate based on starting position (right = 94.8%, left = 94.8%, p=0.960), (Table 2).

Univariate analysis was done specifically to identify variables associated with cecal intubation rates. The analysis was performed using chi square tests and t-tests with a cut off of p=0.10. Dichotomous variables are presented as rates of cecal intubation per subcategory; continuous variables are presented as means of the variable for complete or incomplete cecal intubation. Univariate analysis using binary logistic regression may be found in the appendix (Table 18). Variables associated with cecal intubation in univariate analysis included bowel preparation, patient age, indication, and position changes (Table 7).

Variable	Category	Cecal Intubation (%)	P-Value
Sex	Male	94.62	0.881
Jen			0.001
	Female	95.10	
Previous Surgery	Yes	94.50	0.828
	No	95.19	
Indication	Screening/Surveillance	Screening/Surveillance 97.96	
	Diagnostic	93.94	
	FIT Testing	87.10	
Bowel Preparation	Adequate	98.19	0.001
	Inadequate	84.62	
Position	RL	94.95	0.960
	LL	94.79	
Specialty	General Surgery	93.33	0.367

Table 7: Univariate Analysis for Cecal Intubation Rate

	Gastroenterology	96.19	
Experience	<5 years	90.32	0.211
	>5 years	95.73	

Variable	Cecal Intubation	Mean	<u>P-Value</u>
Mean Patient Age (yrs)	Complete	59.79	0.054
	Incomplete	67.10	
ВМІ	Complete	28.36	0.682
	Incomplete	27.56	
NAPCOMS Score	Complete	2.88	0.424
	Incomplete	3.63	
Fentanyl dose (mcg)	Complete	59.32	0.768
	Incomplete	56.25	
Versed dose (mg)	Complete	2.116	0.134
	Incomplete	2.556	
Amount of Water (mL)	Complete	209.8	0.120
	Incomplete	341.7	
Position Changes (#)	Complete	1.33	0.014
	Incomplete	2.80	

Multivariate analysis was conducted using binary logistic regression with a significance of p=0.05. The factors associated with cecal intubation rate were adequacy of bowel preparation

and the indication for the procedure. Patients were more likely to have a completed procedure if their colonoscopy was done for screening or surveillance. Patients presenting with positive FIT testing were less likely to complete the procedure. The R squared for this model was 0.066. (Table 8)

Variable		Odds Ratio	<u>SE</u>	<u>95% CI</u>	P-Value
Bowel Preparation	Inadequate	Reference			
	Adequate	9.879	0.797	2.072 – 47.093	0.004
Indication		3.409	0.558	1.143 - 10.169	0.028

Table 8: Multivariate Logistic Regression Model for Cecal Intubation Rate

4.3.5 Analysis of Adenoma Detection Rate

The overall ADR was 60.5%. Univariate and multivariate regression analysis were once again performed to identify variables associated with ADR. Univariate analysis was completed using chi square test, t-tests and ANOVA with the cut-off of p=0.10. The results are presented as rates for categorical variables, continuous variables are presented as means of the variable for adenomas that were detected or not detected. Univariate analysis using univariate logistic regression may be found in the appendix (Table 19). Variables associated with ADR in the univariate analysis were age, sex, previous surgery, experience of the endoscopist, amount of versed used and the amount of water used (Table 9).

Table 9: Univariate Analysis for Adenoma Detection Rate

Variable	Category	Adenomas Detected (%)	P-Value
Sex	Male	72.73	0.001
	Female	49.48	
Previous Surgery	Yes	52.33	0.033
	No	67.68	
Indication	Screening/Surveillance	62.50	0.286
	Diagnostic	53.25	
	FIT Testing	70.37	
Bowel Preparation	Adequate	59.51	0.435
	Inadequate	68.18	
Position	Right	56.38	0.240
	Left	61.54	
Specialty	General Surgery	61.90	0.729
	Gastroenterology	59.41	
Experience	<5 years	82.14	0.011
	>5 years	56.69	

Variable	Detection of Adenoma	Mean	P-Value
Age (in years)	Detected	62.88	<0.001
	Not Detected	55.05	
ВМІ	Detected	28.62	0.458
	Not Detected	27.95	

NAPCOMS Score	Detected	2.73	0.320
	Not Detected	3.11	
Fentanyl Dose (mcg)	Detected	57.81	0.381
	Not Detected	61.64	
Versed Dose (mg)	Detected	2.027	0.075
	Not Detected	2.253	
Amount of Water (mL)	Detected	230.86	0.075
	Not Detected	177.74	
Position Changes (#)	Detected	1.25	0.310
	Not Detected	1.45	

Multivariate analysis was performed using binary logistic regression. Variables associated with ADR in the multivariate analysis included age, previous surgery, and the amount of water used (Table 10). The R square value for this model was 0.159.

Table 10: Multivariate Logistic Regression for ADR

Variable		Odds Ratio	<u>SE</u>	<u>95% CI</u>	P-Value
Age		0.935	0.016	0.906 - 0.964	<0.001
Previous Surgery	Yes	Reference			
	No	2.604	0.340	1.337 – 5.072	0.005
Amount of Water		0.998	0.001	0.996 – 1.000	0.042

4.3.6 Patient Comfort

In terms of patient comfort, there was no difference in the NAPCOMS score comparing the positions of RL or LL decubitus (p=0.078). The amount of Fentanyl used also did not differ between the two groups (p=0.484). There was a significant difference in the amount of Versed used comparing the two positions, with more Versed used in the RL decubitus position (p=0.016). (Table 11)

Table 11: Patient Comfort comparing Right Lateral and Left Lateral Decubitus Position

<u>Variable</u>	<u>Total</u>	<u>RL (N=94)</u>	<u>LL (N=91)</u>	P-Value
NAPCOMS Score	2.93	3.20	2.55	0.078
Fentanyl (mcg)	59.41	60.90	57.69	0.484
Versed (mg)	2.14	2.20	2.03	0.016

Univariate and multivariate analyses were carried out to determine if any factors were associated with the pain scores (NAPCOMS score) during colonoscopy. Univariate analysis was performed to identify variables independently associated with the NAPCOMS score. The analysis was done using t-tests, ANOVA, Pearson's Correlation and linear regression with a cut off of p=0.10. The data has been presented using mean NAPCOMS score for categorical variables and correlation models for continuous variables. Analysis using univariate linear regression may be found in the appendix (Table 20). Variables associated with NAPCOMS score in univariate analysis included sex, BMI, position, amount of fentanyl used, amount of versed used, and number of position changes (Table 12).

Variable	Category	NAPCOMS Score	<u>95% CI</u>	P-Value
Sex	Male	1.93	0.990 - 2.371	<0.001
	Female	3.77		
Indication	Screening/Surveillance	2.70	5.110 – 7.716	0.824
	Diagnostic	3.44		
	FIT Testing	2.26		
Previous Surgery	Yes	3.10	-0.313 - 1.149	0.261
	No	2.69		
Bowel Prep	Adequate	2.90	-1.624 – 0.632	0.797
	Inadequate	3.04		
Position	Right	3.20	-0.073 – 1.378	0.078
	Left	2.55		
Specialty	General Surgery	3.32	-0.843 – 0.626	0.387
	Gastroenterology	2.82		
Experience	<5 years	2.43	-1.551 – 0.484	0.303
	>5 years	2.96		

Table 12: Univariate Analysis for NAPCOMS

Variable	Correlation Coefficient	P-Value
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Age	0.117	0.114
ВМІ	-0.128	0.082
Fentanyl Used	0.319	<0.001
Versed Used	0.326	<0.001
Amount of Water Used	-0.033	0.658
Position Changes (#)	0.297	<0.001

Multivariate analysis was conducted using linear regression. The three variables that were associated with the NAPCOMS score were sex, amount of fentanyl used, and the number of position changes required to reach the cecum. (Table 13). The R squared for this model was 0.234.

Table 13: Multivariate Analysis for NAPCOMS Score using Linear Regression

Variable	<u>B</u>	Standard Error	95% Confidence Interval	P-Value
Constant	0.858	0.398	0.073 - 1.644	0.032
Sex (Ref: M)	1.218	0.339	0.548 - 1.887	<0.001
Fentanyl	0.021	0.006	0.010 - 0.033	<0.001
# of Position Changes	0.475	0.125	0.229 – 0.722	<0.001

4.3.7 Position Changes

Position changes were defined as a change from one position to another in which maneuvering of the scope was attempted. Position changes included were RL, LL, supine, and prone. There was no difference in the number of position changes required to reach the cecum comparing the RL and LL decubitus starting positions. The mean number of position changes required per colonoscopy to reach the cecum was 1.37, with a range of position changes from 0 to 6. The LL starting position required an average of 1.43 position changes, the right side required 1.31 (p=0.559). (Table 14)

Table 14: Position Changes and Amount of Water Used Comparing Starting Position

Variable	<u>Total</u>	<u>RL (N=94)</u>	<u>LL (N=91)</u>	P-Value
Number of Position Changes	1.37	1.43	1.31	0.559
Amount of Water Used (mL)	212.8	191.2	234.74	0.140

4.3.8 Amount of Water Used

The amount of water used during each colonoscopy was recorded using the measurement scale (volume in mL) located on the side of each water reservoir. The mean amount of water used per colonoscopy was 212.8mL. There was no difference in the amount of water used comparing starting positions. Colonoscopies performed on the right side used 191.2mL, while the colonoscopies starting on the left required 234.7mL (p=0.140). (Table 13).

4.3.9 Experience and Comparison of Starting Positions

The experience of participating endoscopists was further broken down to determine if there was any difference in time to cecal intubation and starting position based on the number of cases performed by the endoscopist. The breakdown looked at colonoscopists who had performed less than 500 cases, 500-5000 cases, and more than 5000 cases. The analysis was done using Student's t-tests. Only the endoscopists who had performed 500-5000 cases were found to have a statistically significant difference in the time to cecum comparing the starting position, with longer times in the RL position (RL 747.92s, LL 504.92s, p=0.003). (Table 15)

Table 15: Time to Cecum in Right Lateral and Left Lateral Positions Comparing Experience of Endoscopist based on Number of Cases

Experience	<u>Total (s)</u>	<u>RL (s)</u>	<u>LL(s)</u>	P-Value
<500 Cases	693.00	637.78	738.18	0.476
500-5000 Cases	624.80	747.92	504.92	0.003
≥5000 Cases	395.39	366.42	428.50	0.228

4.3.10 Analysis of Time to Cecum and Starting Position in Females and Patients with Previous Abdominal Surgery

In previous studies, positioning was found to significantly alter the time to cecum in females with a history of abdominal noncolonic surgery. Further analysis into female sex and previous abdominal surgery was therefore done comparing the RL and LL positions. The analysis was done using Student t-tests. There was no difference found in time to cecum for females comparing the RL and LL starting position (RL 594.95s, LL 628.20s, p=0.662). There was also no difference found in time to cecum in patients who had previous abdominal noncolonic surgery comparing these two positions (RL 626.16s, LL 553.02s, p=0.354). (Table 16)

Table 16: Comparison of Positioning in Time to Cecum in Females and Patients with Previous Abdominal Noncolonic Surgery

<u>Variable</u>	<u>Total (s)</u>	<u>RL (s)</u>	<u>LL (s)</u>	P-Value
Female Sex	613.46	594.95	628.20	0.662
Previous Abdominal Surgery	591.29	626.16	553.02	0.354

Chapter 5: DISCUSSION

5.1 Starting Position and Cecal Intubation Time

The findings of this study do not support the previous study comparing RL and LL starting positions. The current study failed to show a difference in the time to cecal intubation comparing the starting positions of RL decubitus to the standard LL decubitus (Table 3). No difference was found in cecal intubation rates or ADRs based on these starting positions. Furthermore, no difference was demonstrated in patient comfort (Table 11), the amount of water required, or the number of position changes needed to complete a colonoscopy based on the starting position (Table 14).

These results differ from ROLCOL, the RCT comparing RL and LL decubitus positioning by Vergis et al. that found a 30% improvement in time to cecal intubation using a RL starting position. They noted a corresponding improvement of 187 seconds to the transverse colon starting in the RL position and concluded a large proportion of this improvement stemmed from negotiation of the sigmoid colon. ROLCOL also reported improved patient comfort in the RL position. ²⁶

While this trial has a very similar design to ROLCOL, the endoscopists included in the trials differed. ROLCOL included trainees and did not require completion of upskilling courses (like the CSI or equivalent) to take part in their study. We therefore speculate that the disparity in outcomes between the two studies could be due to these differences.

When examining the effect of endoscopist experience upon their primary outcome, the improvement in cecal intubation times with a RL starting position reported by ROLCOL was only

attributed to experienced endoscopists who had performed over 5000 cases prior to the study initiation. The ROLCOL authors speculated that experienced colonoscopists were able to adapt to the change in starting position and negotiate the colon more readily. Interestingly, our study failed to show an association between experience, RL starting position, and improved cecal intubation times (Table 15). Our study found that a less experienced group of endoscopists, those who had performed between 500-5000 cases, had longer cecal intubation times with a RL starting position.

Given that all endoscopists in the current study had completed the CSI course, it is possible that starting position appeared to have no impact on cecal intubation times due to the techniques taught in the course. Specifically, the course focused on early position change from the LL starting position and the use of water on insertion as opposed to air. These techniques may not help ease scope advancement with a patient in RL starting position. While it makes sense that air may help open up the left colon with a RL starting position due to gravity, the benefits of using water with a RL starting position are uncertain as this topic has not been studied. Studies that have shown the benefit of water infusion on insertion were based upon patients starting in a LL starting position ⁶³.

5.2 Technique in Right Lateral and Left Lateral Starting Position

Multiple techniques for colonoscopy starting in the LL decubitus position have been identified and developed for education. All endoscopists included in the current study have successfully completed the CSI course and would know these techniques. Techniques to ease scope advancement with a RL decubitus starting position, however, are not discussed. For this

reason, there may have been an unseen advantage to the LL decubitus position that was not obvious when designing this trial.

The CSI course taught the benefits of turning a patient early during colonoscopy from the standard LL decubitus position to supine and then possibly to the RL decubitus position. These maneuvers may help straighten the sigmoid colon and open up the splenic flexure while also applying clockwise torque. Clockwise torque, applied by twisting the body of the scope in a clockwise direction, straightens the colonoscope and is helpful in preventing and potentially reducing n-spiral loops and alpha loops which commonly occur in the sigmoid colon during colonoscopy ⁶⁴. A study by Shah et al. revealed that n-spiral loops occur in 79% of cases and alpha loops form in about 12% of cases ⁶⁵. If endoscopists usually turned their patients early when starting in the LL position, the benefit of a RL starting position may be nullified. While there may be some benefit from turning the patient from RL starting position to prone to produce clockwise torque, the endoscopists in this study were not familiar with this and rarely, if ever, did this.

The CSI course encourages judicial use of water during insertion of the colonoscope in the standard LL decubitus position in order to ease the passage of the colonoscope and improve patient comfort. There is no evidence to support the use of water when starting a patient in the RL decubitus starting position. In this position, water can be displaced to dependent areas of the sigmoid which may cause it to fall into the right side of the abdomen, making the sigmoid longer and more tortuous. It may be possible that using air in the RL position, a technique that is discouraged during the CSI course, may stay in the sigmoid and

straighten it. This may simplify advancement of the scope and improve cecal intubation times, as noted in the ROLCOL trial.

In conclusion, while no difference was found in cecal intubation times comparing the RL and LL decubitus starting position, it is worth noting that techniques utilized in the LL decubitus position may not necessarily work in the RL decubitus position and may actually make scope advancement more difficult.

5.3 Variables Associated with Cecal Intubation Times

While starting position had no effect on the time to cecal intubation, the model developed from this study accounted for a large amount of variation indicating that the most important variables were included (Table 5). Similar to previous trials, this model identified female sex as the only demographic factor associated with longer cecal intubation times. It also identified the NAPCOMS score, total water used, and the number of position changes as being associated with longer times. Specialty – specifically general surgeons - and being less experienced (less than five years in practice) were also associated with longer times to cecal intubation. Previous abdominal noncolonic surgery was significantly associated with increased time to cecal intubation in the ROLCOL trial, but it was not associated with time to cecum in the current study. The ROLCOL trial also found that the RL position was specifically efficacious for females and patients who had undergone previous abdominal noncolonic surgery. Neither of these variables were found to be more efficacious in the RL position in this study (Table 16).

Difficult colonoscopies are often labeled as those that take more time to reach the cecum ⁸. Several of the variables included in the model for time to cecal intubation are also

associated with more difficult colonoscopic procedures. Female sex has long been identified as a factor in difficult colonoscopies, potentially due to increased colon length ⁸. If a colonoscopy is inherently more difficult, more water is typically used to ease the passage of the colonoscope, and position changes are more frequently implemented. Both of these interventions take more time to perform, as well. In keeping with previous studies, gastroenterologists perform faster colonoscopies and more experienced colonoscopists take less time to intubate the cecum. This is in keeping with the idea that more experience and technical skill enables endoscopists to negotiate difficult bowels more readily. It is possible that these variables indicate the difficulty experienced in a colonoscopy and a causal relationship between these variables and time to cecal intubation does not actually exist.

Difficult colonoscopies can also be defined as those that cause the patient more discomfort ⁸. Higher NAPCOMS scores – indicating more pain – were also associated with increased time to the cecum (Table 6). Again, this likely signifies more difficult procedures and it is difficult to determine if a causal relationship exists here.

Of note, the mean time to cecal intubation in this study (520.57s [\pm 327.0]) is longer than the time reported in the literature and used for this sample size calculation (384s \pm 180s). There are a number of factors that could contribute to this increase in time. In comparison to other studies, the patients in this study were more obese (average BMI 28.3 compared to BMI 25.0 in ROLCOL ²⁶) and more participants had undergone previous abdominal surgery (41.4% in ROLCOL, 46.5% in the current study). It is possible that this could translate into more difficult colonoscopies and longer cecal intubation times. Additionally, there were more experienced endoscopists (>5000 cases) included in the ROLCOL trial compared to the present study (32

endoscopists vs. four endoscopists, respectively). As discussed, more experienced endoscopists often have faster cecal intubation times, and this could contribute to the difference observed in this trial.

5.4 Variables Associated with Patient Comfort

Previous studies, including the ROLCOL trial, identified improvement in patient comfort in the supine or RL starting position. The current study, however, did not find an association between patient comfort and starting position to support these findings.

This trial used the NAPCOMS score, a validated scale with nursing assessment, to score pain during colonoscopy. Nursing staff spent most of the procedure speaking directly to the patients and appeared to have a better idea of how much pain the patient was experiencing. We believe this score was an accurate reflection of the subjective measure of pain.

The multivariate analysis identified female sex, amount of fentanyl required, and the number of position changes needed to reach the cecum as being significantly associated with higher NAPCOMS score (Table 13). As outlined above, difficult colonoscopies are often labeled as procedures that cause more pain or require longer cecal intubation times. It is entirely possible that these associations may be a reflection of difficult colonoscopy rather than having direct causal affect with pain. The amount of fentanyl required, however, was not included in the time to cecal intubation model and may in fact be directly related to the NAPCOMS score.

The amount of water used on scope insertion was not associated with patient comfort. While a recent meta-analysis reported improved patient comfort using water infusion, the comparison group was air insufflation ⁶². In our study, water was used in preference to air

during insertion in the majority of cases. The amount of water used during insertion, however, has not been analysed to determine if there is an association with patient comfort.

5.5 Other Considerations Regarding Right Lateral Positioning

There are other considerations when using RL patient positioning. Aside from the benefits noted in the ROLCOL trial, it has been shown that RL positioning may optimize visualization of the left colon and may also lead to improved ADRs on withdrawal ²⁴²⁵. This is potentially due to the effect of air filling the left colon when the patient is in this position.

Another interesting area of discussion evolved with colonoscopists included in this study - the ergonomic challenges associated with RL decubitus positioning. This position has long been identified as less efficacious in performing a digital rectal exam which is the initial examination of every colonoscopy. It is also more difficult to insert the colonoscope with RL decubitus positioning as the anus is further away from the endoscopist. Multiple colonoscopists in this study described discomfort associated with keeping their right arm extended for long periods of time due to reaching further forward to hold the colonoscope with their right hand. To help reach the scope, the endoscopist may need to bend forward at the waist and extend their neck to see the screen. This may result in more fatigue and potentially could cause harm. This was especially difficult for colonoscopists who were pregnant at the time of the study. To avoid this discomfort, one could speculate that endoscopists in this study may have turned their patients away from this position or avoided this position in order to assume a more comfortable, familiar position. This may have biased the results.

Several review articles have discussed the "awkwardness" associated with the RL decubitus position, citing patient awkwardness with genitals facing towards the colonoscopist ⁶⁶. We note that regardless of starting position, position changes are taught in colonoscopic education courses and are frequently used to aid difficult colonoscopies. This "awkwardness" would therefore be present during the procedure regardless of starting position.

Recent literature has reported a high prevalence of endoscopy-related injury and highrisk biomechanical exposures during the performance of routine colonoscopy. To date, a large proportion of this literature has focused on what endoscopists can do to minimize their risk of injury ⁶⁷. Instead, a realistic goal could be to identify and implement workplace interventions and endoscopic design to improve endoscopic safety. Ergonomically designed endoscopy is an area that could improve and enhance the procedure for physicians and patients alike.

5.6 Future Work

While this study did not show a difference in starting position on time to cecal intubation or patient comfort, it remains unclear if starting position improves either of these variables. A larger trial comparing these two starting positions and including endoscopists who did and did not complete upskilling courses may help answer this question. Further investigation into the use of water on insertion in the RL starting position is also needed. Similarly, trials examining the effect of patient rotation on quality indicators such as patient comfort and satisfaction are also required.

Further investigation into the ergonomics of patient positioning for colonoscopists is currently underway. Ergonomics, specifically comparing the ergonomics during a colonoscopy

with a patient positioned in RL decubitus and LL decubitus, will be studied. Identifying specific ergonomic strategies will enable the implementation of workplace interventions and endoscopic design to ultimately improve endoscopic safety.

5.7 Limitations

There are several limitations in this trial. The first is the lack of blinding. It would be impossible to blind patients and endoscopists to the starting position of a colonoscopy, therefore it was not attempted. The data collector present in the endoscopy suite also was not blinded. It is possible that the inability to blind endoscopists to the patient position could have affected the results of this trial. Most endoscopists, however, do their best for their patients and try to complete the procedure safely with high quality - regardless of starting position.

Secondly, there are multiple confounding factors that could impact these results. It is difficult to decipher if variables outlined in these models independently affect outcomes of colonoscopy or if there are multiple associations taking place. In the ROLCOL study, colonoscopists were asked to rate the difficulty of each completed procedure. This gave them the ability to assess difficulty and include it in their models. Difficulty was not included as a variable and was not collected during the current trial. We were therefore unable to include it in our models and must speculate on its association. Randomization was the only method used to control for confounders. It should also be noted that using time as the variable of interest inadvertently included things external to the actual colonoscopic procedure. For example, refilling the water bottle, fixing a blocked suction channel, answering urgent pages, etc. may have impacted the time to insertion.

It appears this study may have been biased in terms of the technical education provided for the LL starting position. With all colonoscopists having successfully completed the CSI course, they likely used many of the techniques taught during the course. Their comfort level and willingness to adhere to their usual practice could have affected the results. For example, colonoscopists were allowed to turn their patients as needed after commencing the procedure in the randomized starting position. Colonoscopists may have turned their patients out of the RL position to be able to use what they learned in the CSI course. Several colonoscopists voiced concerns regarding the ergonomics of the RL position and may have avoided this position to feel more comfortable. Including as many endoscopists and allowing them to use their normal technique was thought to enhance the external validity of this trial. It is, however, quite possible that this study may have been biased due to the training course completed by all participants. Ideally, a trial period for the right lateral position could have been provided to participating endoscopists prior to study commencement.

5.8 Conclusion

In summary, we accept the null hypothesis that starting position in colonoscopy has no effect on time to cecal intubation. This RCT did not find a difference in cecal intubation time comparing the RL decubitus and LL decubitus starting positions. There was also no difference in cecal intubation rate, ADR, or patient comfort comparing these starting positions. This contradicts the previous study that found decreased cecal intubation time and improved comfort with the RL decubitus starting position.

References

- 1. Joseph, D. A. *et al.* Colorectal cancer screening: Estimated future colonoscopy need and current volume and capacity. *Cancer* **122**, 2479–2486 (2016).
- Lieberman, D. How good is your dentist? how good is your endoscopist? the quality imperative. *Gastroenterology* 142, 194–196 (2012).
- 3. Rastogi, A. & Wani, S. Best of Colonoscopy. *Gastrointest. Endosc.* **85**, 59–66 (2017).
- Wolff, W. I. & Shinya, H. Polypectomy via the Fibreoptic Colonoscope. *N. Engl. J. Med.* 288, 329–332 (1978).
- 5. Varadarajulu, S. *et al.* GI endoscopes. *Gastrointest. Endosc.* **74**, 1-6.e6 (2011).
- 6. Mahmoud, N. *et al.* Colon and Rectum. in *Sabiston Textbook of Surgery: The Biological Basis of Modern Surgical Practice* 1312–1391 (2016).
- Reumkens, A. *et al.* Post-colonoscopy complications: A systematic review, time trends, and meta-analysis of population-based studies. *Am. J. Gastroenterol.* **111**, 1092–1101 (2016).
- Witte, T. N. & Enns, R. The difficult colonoscopy. *Can. J. Gastroenterol.* **21**, 487–490 (2007).
- Bacchus, C. *et al.* Recommendations on screening for colorectal cancer in primary care.
 Can. Med. Assoc. J. 188, 1–9 (2016).
- Papathomas, A. *et al.* To print this document, select the Print. *Hist. Work. J.* **80**, 302 (2016).
- 11. Jayasekeran, V., Holt, B. & Bourke, M. Normal Adult Colonic Anatomy in Colonoscopy.

Video J. Encycl. GI Endosc. **1**, 390–392 (2013).

- Saunders, B. P. *et al.* Why is colonoscopy more difficult in women? *Gastrointest. Endosc.* 43, 124–126 (1996).
- Vadlamudi, H., Raju, P., R, Y. & J, V. Anatomical, Biochemical, and Physiological Considerations of the Colon in Design and Development of Novel Drug Delivery Systems. *Bentham Sci. Publ.* 5, (2012).
- Ungaro, R., Mehandru, S., Allen, P. B., Peyrin-Biroulet, L. & Colombel, J.-F. Seminar
 Ulcerative colitis. *Lancet* 389, 1756–1770 (2017).
- Friedman, S. & Nørgård, B. M. Confirming Complexity: Assessing Environmental and Genetic Risk Factors for Inflammatory Bowel Disease. *Gastroenterology* **156**, 2124–2125 (2019).
- 16. Canadian Cancer Society's Advisory Committee on Cancer Statistics. Canadian Cancer Statistics 2017, Special topic: Pancreatic cancer. *Can. Cancer Soc.* 1–141 (2017).
- 17. Brenner, H., Kloor, M. & Pox, C. P. Colorectal cancer. Lancet 383, 1490–1502 (2014).
- Peltomäki, P. Mutations and epimutations in the origin of cancer. *Exp. Cell Res.* **318**, 299–310 (2012).
- Brenner, D. R. *et al.* National Trends in Colorectal Cancer Incidence Among Older and Younger Adults in Canada. *JAMA Netw. Open* 2, e198090 (2019).
- 20. Risk factors for colorectal cancer Canadian Cancer Society.
- 21. Bond, J. H. Polyp guideline: Diagnosis, treatment, and surveillance for patients with colorectal polyps. *Am. J. Gastroenterol.* **95**, 3053–3063 (2000).
- 22. Vormbrock, K. Difficult colon polypectomy. World J. Gastrointest. Endosc. 4, 269 (2012).

- Yamaguchi, K., Mitsuhashi, K., Nakagawa, Y. & Hayashi, M. Dynamic position changes during the colonoscope withdrawal phase decrease abdominal fullness. *Chiba Med. J.* 89, 9–14 (2013).
- Lee, S. W. *et al.* Effect of Dynamic Position Changes on Adenoma Detection during Colonoscope Withdrawal: A Randomized Controlled Multicenter Trial. *Am. J. Gastroenterol.* **111**, 63–69 (2016).
- 25. East, J. E., Suzuki, N., Arebi, N., Bassett, P. & Saunders, B. P. Position changes improve visibility during colonoscope withdrawal: a randomized, blinded, crossover trial{A figure is presented}. *Gastrointest. Endosc.* **65**, 263–269 (2007).
- Vergis, N., McGrath, A. K., Stoddart, C. H. & Hoare, J. M. Right or left in COLonoscopy (ROLCOL)? A randomized controlled trial of right-versus left-sided starting position in colonoscopy. *Am. J. Gastroenterol.* **110**, 1576–1581 (2015).
- Zhao, S. *et al.* Impact of the supine position versus left horizontal position on colonoscopy insertion: a 2-center, randomized controlled trial. *Gastrointest. Endosc.* 89, 1193-1201.e1 (2019).
- Vergis, N., Scarborough, A. J., Morris, J. A. & Hoare, J. M. Prone or Left for Colonoscopy?
 A Randomized Controlled Trial of Prone versus Left-sided Starting Position for
 Colonoscopy. J. Clin. Gastroenterol. 52, 82–86 (2018).
- 29. Uddin, F. S. *et al.* Prone positioning of obese patients for colonoscopy results in shortened cecal intubation times: A randomized trial. *Dig. Dis. Sci.* **58**, 782–787 (2013).
- 30. Köksal, A. Ş. *et al.* A simple method to improve adenoma detection rate during colonoscopy: Altering patient position. *Can. J. Gastroenterol.* **27**, 509–512 (2013).

- Ou, G. *et al.* A randomized controlled trial assessing the effect of prescribed patient position changes during colonoscope withdrawal on adenoma detection. *Gastrointest. Endosc.* **80**, 277-283.e1 (2014).
- Ball, A. J., Johal, S. S. & Riley, S. A. Position change during colonoscope withdrawal increases polyp and adenoma detection in the right but not in the left side of the colon: Results of a randomized controlled trial. *Gastrointest. Endosc.* 82, 488–494 (2015).
- Rex, D. K. *et al.* Quality indicators for colonoscopy. *Am. J. Gastroenterol.* **110**, 72–90 (2015).
- Corley, D. A. *et al.* Adenoma Detection Rate and Risk of Colorectal Cancer and Death. *N. Engl. J. Med.* **370**, 1298–1306 (2014).
- Kim, Y. D. *et al.* Difference in Adenoma Detection Rates Acccording to Colonoscopic Withdrawal Times and the Level of Expertise. *Korean J. Gastroenterol.* 64, 278–283 (2014).
- Rex, D. K. Polyp detection at colonoscopy: Endoscopist and technical factors. *Best Pract. Res. Clin. Gastroenterol.* **31**, 425–433 (2017).
- Pullens, H. J. Quality indicators for colonoscopy: Current insights and caveats. World J. Gastrointest. Endosc. 6, 571 (2014).
- Shaukat, A. *et al.* Longer Withdrawal Time Is Associated With a Reduced Incidence of Interval Cancer After Screening Colonoscopy. *Gastroenterology* 149, 952–957 (2015).
- Barclay, R. L., Vicari, J. J. & Greenlaw, R. L. Effect of a Time-Dependent Colonoscopic Withdrawal Protocol on Adenoma Detection During Screening Colonoscopy. *Clin. Gastroenterol. Hepatol.* 6, 1091–1098 (2008).

- 40. Baker, F. A. *et al.* Propofol sedation in colonoscopy: From satisfied patients to improved quality indicators. *Clin. Exp. Gastroenterol.* **12**, 105–110 (2019).
- Lovett, P., Gómez, V., Hodge, D. O. & Ladlie, B. Propofol Versus Midazolam/Fentanyl Sedation for Colonoscopy in the Elderly Patient Population. *J. Perianesthesia Nurs.* 32, 210–214 (2017).
- 42. Iqbal, N., Ramcharan, S., Doughan, S. & Shaikh, I. Colonoscopy without sedation: Patient factors alone are less likely to influence its uptake. *Endosc. Int. Open* 04, E534–E537 (2016).
- 43. Rostom, A. *et al.* Development and validation of a nurse-assessed patient comfort score for colonoscopy. *Gastrointest. Endosc.* **77**, 255–261 (2013).
- 44. Rostom, A. & Jolicoeur, E. Validation of a new scale for the assessment of bowel preparation quality. *Gastrointest. Endosc.* **59**, 482–486 (2004).
- 45. Sey, M. S. L. *et al.* Multicentre endoscopist-blinded randomised clinical trial to compare two bowel preparations after a colonoscopy with inadequate cleansing: A study protocol. *BMJ Open* 9, 1–6 (2019).
- Sulz, M. C. *et al.* Meta-analysis of the effect of bowel preparation on adenoma detection:
 Early adenomas affected stronger than advanced adenomas. *PLoS One* **11**, 1–17 (2016).
- 47. Kastenberg, D., Bertiger, G. & Brogadir, S. Bowel preparation quality scales for colonoscopy. *World J. Gastroenterol.* **24**, 2833–2843 (2018).
- Pace, D. *et al.* Effect of Colonoscopy Volume on Quality Indicators. *Can. J. Gastroenterol. Hepatol.* (2016). doi:10.1155/2016/2580894
- 49. Sedlack, R. E. et al. Colonoscopy core curriculum. Gastrointest. Endosc. 76, 482–490

(2012).

- 50. Kim, Y. D. o. *et al.* Difference in adenoma detection rates according to colonoscopic withdrawal times and the level of expertise. *Korean J. Gastroenterol.* **64**, 278–283 (2014).
- 51. Bhangu, A. *et al.* Volume and accreditation, but not specialty, affect quality standards in colonoscopy. *Br. J. Surg.* **99**, 1436–1444 (2012).
- 52. Gastroenterology, C. A. of. SEE Program. (2019). Available at: https://www.cagacg.org/quality/see-program. (Accessed: 2nd September 2019)
- 53. Evans, B. *et al.* Effect of an Educational Intervention on Colonoscopy Quality Outcomes. *Surg. Endosc.* (2019).
- 54. Kaminski, M. F. *et al.* Leadership training to improve adenoma detection rate in screening colonoscopy: A randomised trial. *Gut* **65**, 616–624 (2016).
- 55. Coe, S., Crook, J., Diehl, N. & Wallace, M. An Endoscopic Quality Improvement Program Improves Detection of Colorectal Adenomas. *Am. J. Gastroenterol.* **103**, 219–226 (2013).
- Ussui, V. *et al.* Stability of Increased Adenoma Detection at Colonoscopy. Follow-Up of an Enoscopic Quality Improvement Program - EQUIP-II. *Am. J. Gastroenterol.* **110**, 489–496 (2015).
- Gralnek, I. M. *et al.* Standard forward-viewing colonoscopy versus full-spectrum endoscopy: An international, multicentre, randomised, tandem colonoscopy trial. *Lancet Oncol.* 15, 353–360 (2014).
- McCambridge, J., Witton, J. & Elbourne, D. R. Systematic review of the Hawthorne effect: New concepts are needed to study research participation effects. *J. Clin. Epidemiol.* 67, 267–277 (2014).

- 59. Brenner, H. *et al.* Protection from right-and left-sided colorectal neoplasms after colonoscopy: Population-based study. *J. Natl. Cancer Inst.* **102**, 89–95 (2010).
- 60. Singh, H. *et al.* The reduction in colorectal cancer mortality after colonoscopy varies by site of the cancer. *Gastroenterology* **139**, 1128–1137 (2010).
- 61. Lai, C. & Yuen, M. Annals of Internal Medicine. Ann. Intern. Med. (2007).
- 62. Liu, Y., Huang, Q., Dong, X. & Piao-Piao, J. Water Exchange vs Air Insufflation for colonoscopy: A Meta-Analysis. *Saudi J Gastroenterol* **24**, 311–316 (2018).
- 63. Hafner, S. *et al.* Water infusion versus air insufflation for colonoscopy. (2015).
- 64. Lee, S. *et al.* Colonoscopy procedural skills and training for new beginners. **20**, 16984–
 16995 (2014).
- Shah, S. G., Saunders, B. P., Brooker, J. C. & Williams, C. B. Magnetic imaging of colonoscopy: An audit of looping, accuracy and ancillary maneuvers. *Gastrointest. Endosc.* 52, 1–8 (2000).
- Kaif, M. & Peter, S. Position Change in Colonoscopy A Turn for the Better? *Am. J. Gastroenterol.* **111**, 1034–1035 (2016).
- 67. Shergill, A. K. & McQuaid, K. R. Ergonomic endoscopy: An oxymoron or realistic goal? *Gastrointest. Endosc.* **90**, 966–970 (2019).

Appendices

Variable	В	Standard Error	95% Confidence Interval	P-Value
Sex (Ref: M)	195.293	46.057	104.422 – 286.165	<0.001
Age	2.861	2.064	-1.211 - 6.934	0.167
ВМІ	-4.378	3.992	-12.254 - 3.498	0.274
Indication	64.156	32.904	-0.764 – 129.076	0.053
Previous Surgery	132.159	47.332	38.774 – 225.545	0.006
Adequate Bowel Prep	173.625	73.354	28.897 – 318.354	0.019
Position (Ref: LL)	44.718	48.103	-50.190 - 139.625	0.354
Specialty (Ref: GI)	240.634	45.028	151.792 – 329.475	<0.001
Experience (Ref: <5y)	-180.460	65.923	-310.525 – -50.394	0.007
NAPCOMS	59.187	8.559	42.300 - 76.074	<0.001
Fentanyl Used	1.281	0.829	-0.354 – 2.916	0.124
Versed Used	49.537	28.273	-6.247 – 105.321	0.081
Amt of Water	0.648	0.112	0.426 - 0.869	<0.001
Position Changes (#)	288.365	24.284	240.453- 149.023	<0.001

Appendix 1 - Table 17: Univariate Analysis of Time to Cecum using Linear Regression

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Variable		Odds Ratio	SE	95% CI	P-Value
Age		1.066	0.033	0.999 – 1.138	0.054
Sex	Male	Reference			
	Female	0.907	0.649	0.254 – 3.239	0.881
ВМІ		0.976	0.060	0.867 – 1.098	0.680
Previous Surgery	Νο	Reference			
	Yes	1.151	0.649	0.322 – 4.111	0.828
Bowel Prep	Inadequate	Reference			
	Adequate	7.409	0.743	1.728 – 31.765	0.007
Position	Left	Reference			
	Right	0.968	0.649	0.271 – 3.456	0.960
Specialty	Gen Surg	Reference			
	GI	1.804	0.662	0.493- 6.604	0.373
Experience	<5 Years	Reference			
	>5 Years	0.416	0.720	0.101-1.706	0.223
NAPCOMS		1.113	0.134	0.856 – 1.447	0.424
Fentanyl Used		0.996	0.014	0.970 – 1.023	0.765
Versed Used		1.659	0.334	0.861 – 3.195	0.130
Amount of Water		1.002	0.001	1.000 - 1.005	0.136
Position Changes (#)		1.785	0.259	1.075 – 2.964	0.025
Indication		2.623	0.428	1.135 – 6.063	0.024

Appendix 2 - Table 18: Univariate Analysis for Cecal Intubation Rate using Logistic Regression

Variable		Odds Ratio	SE	95% CI	P-Value
Age		0.938	0.015	0.910 – 0.966	<0.001
Sex	Male	Reference			
	Female	2.722	0.314	1.471 – 5.036	0.001
ВМІ		0.981	0.026	0.933 – 1.032	0.457
Previous Surgery	Νο	Reference			
	Yes	1.908	0.305	1.050 – 3.466	0.034
Bowel Preparation	Inadequate	Reference			
	Adequate	0.686	0.485	0.265 – 1.774	0.437
Position	Left	Reference			
	Right	1.426	0.302	0.788 – 2.580	0.240
Specialty	Gen Surgery	Reference			
	GI	0.901	0.303	0.498 – 1.629	0.729
Experience	>5 Years	Reference			
	<5 Years	3.515	0.519	1.271 – 9.721	0.015
NAPCOMS Score		1.062	0.060	0.944 – 1.194	0.318
Fentanyl Dose		1.005	0.005	0.994 – 1.015	0.382
Versed Dose		1.385	0.187	0.961 – 1.997	0.081
Amount of Water		0.998	0.001	0.997 – 1.000	0.081
Position Changes (#)		1.122	0.113	0.898 - 1.401	0.310
Indication		0.967	0.208	0.644 - 1.454	0.873

Appendix 3 -Table 19: Univariate Analysis for Adenoma Detection Rate using Logistic Regression

Variable	В	Standard Error	95% Confidence Interval	P-Value
Age	0.025	0.016	-0.006 - 0.056	0.114
Sex (Ref: Male)	1.680	0.350	0.990 – 2.371	<0.001
ВМІ	-0.053	0.031	-0.114 - 0.007	0.082
Previous Surgery	0.418	0.370	-0.313 - 1.149	0.261
Adequate Bowel Prep	0.496	0.572	-0.632 - 1.624	0.387
Position (Ref: LL)	0.653	0.368	-0.073 - 1.378	0.078
Specialty (Ref: GI)	0.109	0.372	-0.626 - 0.843	0.770
Experience (Ref: <5 yrs)	0.533	0.516	-0.484 - 1.551	0.303
Fentanyl Used	0.028	0.006	0.016 - 0.040	<0.001
Versed Used	0.968	0.207	0.559 – 1.377	<0.001
Amount of Water Used	0.000	0.001	-0.002 - 0.001	0.658
Position Changes (#)	0.565	0.134	0.300 - 0.830	<0.001
Indication	0.008	0.256	-0.496 - 0.513	0.975

Appendix 4 - Table 20: Univariate	e Analysis for NAPCOMS	Score using Linear Regression
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