# SAFETY AND EFFECTIVENESS OF CECAL RETROFLEXION IN EVALUATING PROXIMAL COLON – A CASE SERIES

By

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ABSTRACT

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**Background**: *Cecal retroflexion is a maneuver used by colonoscopists to evaluate the proximal sides of the colonic folds in the right-sided colon. Knowledge is limited regarding cecal retroflexion-associated risk and its effectiveness for increasing neoplasia detection rates in proximal colon. Recently, we encountered a contained perforation caused by cecal retroflexion. To our knowledge, there has been no report on cecal retroflexion-associated complications in the existing literature.*

**Objective**: *We aim to 1) report the case in detail, and characterize cecal retroflexion-related complication rates, and 2) assess whether there is improved neoplasia detection with cecal retroflexion.*

**Methods**: *We performed retrospective cohort study of all patients age 18 to 85 years who received colonoscopy by one endoscopist at UT Southwestern Medical Center from 9/1/2006 to 7/31/2012.We excluded patients who received colonoscopies prior to the initiation of cecal retroflexion, had missing colonoscopy reports, or were not found in the electronic medical record system. Our primary outcome is cecal-retroflexion-associated complication rates within 30 days after the procedure; the secondary outcome is cecal-retroflexion-associated neoplasia detection rates.*

**Results**: *A total of 1,247 patients were included in final analysis. Mean patient age was 57 years; 58.6% of patients were women. Among these patients, 624 (50.0%) received cecal retroflexion during colonoscopy. 1(Case) out of the 624 patients had a cecal retroflexion-related complication, with a complication rate of 1.6 per 1000 cecal retroflexion (95% Cl: 0 to 4.7 per 1000 cecal retroflexion). Of 459 patients underwent screening colonoscopy, 261 (56.9%) had cecal retroflexion. No cecal retroflexion-associated complications were observed with screening colonoscopy. We observed no statistically significant improvement in neoplasia detection rates among individuals who underwent colonoscopy with vs. without documented cecal retroflexion (P>0.05 for all comparisons).*

**Conclusion**: *Cecal retroflexion may be associated with rare but significant complications. Further, the practice does not clearly increase neoplasia detection rates. We postulate that routine implementation of this practice is unlikely to increase neoplasia detection rates substantially, and further, given the small non-significant differences observed in our study, that randomized trials of the practice are unlikely to show clinically significant superiority. We recommend future research explore alternate strategies to improve proximal neoplasia detection.*

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## PRIOR PUBLICATIONS & PRESENTATIONS

PUBLICATIONS:

Gupta S, Sussman DA, Doubeni CA, Anderson DS, Day L, Deshpande A, Elmunzer BJ, O.Laiyemo A, Mendez J, Somsouk M, Allison J, Bhuket T, **Geng Z**, Green B, Itzkowitz SH, Martinez ME. "Challenges and Possible Solutions to Colorectal Cancer Screening for the Underserved." Journal of National Cancer Institute. (2014) 106(4): dju032. At Press

Marquez E*, **Geng Z***, Pass S, Summerour P, Robinson L, Sarode V, Gupta S. "Implementation of routine screening for Lynch syndrome in university and safety-net health system settings: successes and challenges." Genetics in Medicine. 2013 Dec;15(12):925-32.
*Ms. Geng and Dr Marquez contributed equally to this work and shared credit as first authors

Gupta S, Halm EA, Rockey DC, Hammons M, Koch M, Carter E, Valdez L, Tong L, Ahn C, Kashner M, Argenbright K, Tiro J, **Geng Z**, Pruitt S, Sugg Skinner C. "Comparative Effectiveness of Fecal Immunochemical Test Outreach, Colonoscopy Outreach, and Usual Care for Boosting Colorectal Cancer Screening Among the Underserved: A Randomized Clinical Trial." JAMA Internal Medicine. 2013 Oct 14;173(18):1725-32.

Jung BC, Choi SI, Du AX, Cuzzocreo JL, **Geng ZZ**, Ying HS, Perlman SL, Toga AW, Prince JL, Ying SH. "Principal Component Analysis of Cerebellar Shape on MRI Separates SCA Types 2 and 6 into Two Archetypal Modes of Degeneration." Cerebellum. 2012 Dec;11(4):887-95.

PRESENTATIONS AND POSTERS:

**Geng Z**, Tong L, Ahn C, Halm E, Rockey D, Koch M, Carter E, Pruitt S, Skinner C, Gupta S. *Influence of Race and Ethnicity on Response to Fecal Immunochemical Test Outreach, Colonoscopy Outreach, and Usual Care As Part of a Randomized Controlled Trial in A Safety-Net Setting*. Digestive Disease Week 2013, Orlando, FL, May 18-21, 2013.

**Geng Z**, Gupta S. *Interventions to Increase Colorectal Cancer Screening Among Underserved Populations: A Systematic Review*. Digestive Disease Week 2013, Orlando, FL, May 18-21, 2013.

Gupta S, Halm E, Rockey D, Hammons M, Koch M, Carter E, Yong L, Ahn C, Kashner T, Argenbright K, Tiro J, **Geng Z**, Pruitt S, Skinner C. *Comparative Effectiveness of Fecal Immunochemical Test Outreach, Colonoscopy Outreach, and Usual Care for Boosting Colorectal Cancer Screening Among the Underserved: Primary Final Results of a Randomized Trial*. Oral Presentation presented at: Digestive Disease Week 2013; Orlando, FL.

Cuzzocreo JL, Du AX, Jung CH, **Geng Z,** Ying SH. *Visuospatial deficits correlate with regional cerebellar atrophy in SCA6*. Society for Neuroscience, San Diego, California, November 13-17, 2010.

## CHAPTER ONE: AN INTRODUCTION

Colorectal cancer (CRC) is the 2nd leading cause of cancer-related mortality in the United States. Approximately 140,000 individuals develop CRC, and over 50,000 die of the disease annually[1].

CRC incidence and mortality can be prevented through early detection and removal of colorectal polyps[2-5]. Colonoscopy is the most commonly used modality for CRC prevention used in the United States[6]. Observational studies on colonoscopy with polypectomy have demonstrated significant risk reduction in CRC incidence and mortality[7-9].

However, despite the evidenced risk reduction of CRC by colonoscopy, available data have suggested that CRC risk reduction associated with colonoscopy is suboptimal, and that colonoscopy is less effective in preventing right- versus left-sided CRC[2,4,5,7,10]. A large observational study from Ontario comparing individuals with (n=10,292) versus without (n=51,460) CRC mortality found that colonoscopy prevented deaths from left-sided CRC (adjusted conditional OR, 0.33 [Cl, 0.28 to 0.39]) but not from right-sided CRC (adjusted conditional OR, 0.99 [Cl, 0.86 to 1.14])[4]. A large cohort study (n=57,359) from Manitoba also reported colonoscopy reduced CRC mortality by 47% in the distal colon (SMR, 0.53; 95% CI, 0.42-0.67) but not in the proximal colon (SMR, 0.94; 95% CI, 0.77-1.17)[5]. In addition, a recent report from the Health professionals follow up study and Nurses health study comparing individuals with (n=2,740) versus without (n=45,710) exposure to lower endoscopy with polypectomy found that polypectomy was associated with a much more modestly reduced CRC incidence (HR=0.57, 95% Cl: 0.45-0.72) and no reduction in post polypectomy incidence of proximal CRC (HR=0.83, 95% Cl: 0.59-1.18)[2].

Possible explanations for this discrepancy of CRC risk reduction between left- and right-sided colons include at least 3 factors factors: 1) Quality factors, such as incomplete examinations, tendency for worse bowel preparation in the right-sided colon[11], and variation in polyp detection rates among colonoscopists[12]. 2) Different biological features between colonic lesions found in the right- versus left-sided colons. For example, cancers after colonoscopy are disproportionally right-sided and have features of hypermethylation and microsatellite instability[2,13,14]. 3) Lesions that are both difficult to detect and resect from a quality perspective, and that carry high risk biological features for progression if missed (e.g., sessile serrated adenomas), tend to occur in the right colon. These lesions tend to be flat and difficult to detect and remove, and have prevalence of hypermethylation and microsatellite instability, which may predispose these lesions to rapid progression to cancer if missed[2,15].

Cecal retroflexion is a maneuver used by the colonoscopists that may potentially reduce CRC risk by improving neoplasia detection in the proximal colon. This hypothesis is based on the assumption that some polyps may be missed because they are located on the proximal sides of the colonic folds and are therefore not seen on a forward view. In this technique, the bending section of the colonoscope is made a U-turn to form a hairpin shape during scope withdrawal, so the viewing lens is looking backward and the insertion tube is visible to the colonoscopists. This retroflexed view improves polyp detection by increasing visualization of the proximal sides of the right-sided colonic folds, and facilitates the removal of polyps located behind the colonic folds.

Prior studies have been inconclusive regarding the benefit of cecal retroflexion in increasing neoplasia detection[16,17], and additional studies may be hampered by concerns

regarding potential complications from this maneuver, though none have been reported[16-20]. Two studies were found in current literature reporting cecal retroflexion-associated neoplasia detection: one is a pilot randomized controlled trial (n=98) from Indiana University Hospital that showed no statistically significant differences between cecal retroflexion versus forward view in detecting neoplasia (p=0.31)[16]. The other one is a cohort study (n=1,000) that was conducted by the same group and found an additional 9.7% polyps and 9.8% adenoma were detected by cecal retroflexion versus forward view. In both studies, no cecal retroflexion-associated complications, such as perforation, bleeding or significant mucosal tear, were encountered during procedures[17].

Recently, one of the investigator (SG)'s patients had a contained colonic perforation after a procedure in which cecal retroflexion was performed. This is the first complication the principle investigator (PI) encountered in the past 5 years of using this technique. To our knowledge, there has been no report on cecal retroflexion-associated complications in existing medical literature.

Our objective is to create a case series on the occurrence of a contained colonic perforation associated with the use of cecal retroflexion. As part of this series, we aim to 1) describe in detail the complication encountered, 2) report rates of complication associated with cecal retroflexion, and 3) report rates of neoplasia detection with use of the technique. Our primary outcome is the rates of cecal retroflexion-associated complication within 30 days after the procedure; and secondary outcome is rates of neoplasia detection associated with this technique.

## CHAPTER TWO: CASE REPORT

A 76 year old Caucasian female with a history of coronary artery disease, hypertension, and osteoarthritis on NSAIDs, presented to GI clinic with one isolated episode of painless rectal bleeding. Diagnostic colonoscopy with cecal retroflexion was performed. Four polyps were detected and excised during the procedure, and details are summarized in **Table 1**. Notably, a 3mm polyp in ascending colon was found on the proximal side of a colonic fold via retroflexion, and could only be removed in the retroflexed position (**Figure 2**). All polyps were excised by either cold biopsy forceps or cold snare, and notably, the ascending colonic polyp was removed by cold biopsy forceps. No electrocautery was used. No active bleeding was noted during the procedure.

Approximately 4 hours after the procedure, the patient presented to emergency room with acute onset of sharp, crampy right lower quadrant abdominal pain, which was exacerbated by movement, and associated with nausea. She was unable to relieve gas and had no bowel movement since the procedure. On exam, she was alert, afebrile, and normotensive. Her abdomen was non-distended, with localized tenderness and guarding in right lower quadrant. No rebound tenderness was noted. Rectal exam was normal. Guaiac was negative. Laboratory data was significant for leukocytosis with WBC 15.5. CT abdomen/pelvis with contrast revealed fluid attenuation along the posterior half of the cecum and ascending colon over a 6 cm extent, beginning at the level of the ileocecal valve. No free air was noted (**Figure 3**). Her symptoms and imaging findings were most consistent with contained colonic perforation related to post-colonoscopy injury.

The patient was admitted to GI inpatient service. Colorectal surgery service was consulted.

Due to patient's stable hemodynamics, absence of peritoneal signs and no free air, it was decided to treat patient conservatively with bowel rest, intravenous fluids and intravenous antibiotics (meropenem). On hospitalization day 3, she reported significant improvement in her abdominal pain. She was discharged home on a 14-day course of per oral Ciprofloxacin and Metronidazole. At 1-week follow-up, the patient reported feeling well. Her abdominal pain had resolved. She was tolerating oral intake without any difficulties, and had normal bowel movements. Her presentation prompted us to embark on the case series reported herein.

## CHAPTER THREE: CASE SERIES METHODS

### *Study Setting and Population:*

We conducted a retrospective cohort study of all patients undergoing colonoscopies by one endoscopist (SG) at UT Southwestern Medical Center in Dallas, Texas. UT Southwestern is a 270-bed tertiary care university health system that mainly cares for insured patients.

### *Patient Selection:*

We identified all patients underwent colonoscopies by one investigator (SG) from 09/01/2006 through 07/31/2012 by querying colonoscopy procedure records at the institution. All colonoscopy procedure records were reviewed from 09/01/2006 onwards to identify the first date the endoscopist initiated cecal retroflexion. We included all patients aged 18-85 years. Patients who received colonoscopies prior to the initiation of cecal retroflexion, had missing colonoscopy reports, or were not found in the University Hospital electronic medical record system, were excluded from final analysis.

### *Data Collection:*

UT Southwestern University Hospital uses the EPIC electronic medical record system to store all patient-care activities, including procedure reports, pathology reports, and clinical progress notes. For each patient, both colonoscopy and pathology reports were reviewed, and data abstracted included age, sex, colonoscopy indication, cecal retroflexion performed (yes/no), right(splenic flexure and proximal)/left-sided adenoma detected (yes/no), right/left-sided colorectal adenocarcinoma detected (yes/no), right/left-sided sessile serrated adenoma

detected(yes/no), right/left-sided hyperplastic polyp >1cm detected (yes/no), and complications within 30 days after procedure.

***Data Analysis and Outcomes:***

Our primary outcome was rates of cecal retroflexion-associated complication defined as bleeding and/or perforation within 30 days of the procedure. Our secondary outcome measured rates of cecal retroflexion-related neoplasia detection. The neoplasia detection rates were stratified by pathologic diagnosis and size (adenoma, sessile serrated adenoma, colorectal adenocarcinoma, and large hyperplastic polyp >1cm); these results were further stratified by location (left- versus right-sided, using the splenic flexure and proximal to define right colon).

Categorical variable comparisons were performed with $\chi 2$ or Fisher exact tests. For all comparisons, $P < .05$ was considered statistically significant. All analyses were performed using Microsoft Excel and GraphPad. The study was approved by the UT Southwestern institutional review board.

## CHAPTER FOUR: RESULTS

### *Study Population*

Of 1,516 patients identified, 29 had missing colonoscopy reports, and 10 were not found in the electronic medical record system; the PI's first date of initiating cecal retroflexion was 08/2007, and 214 patients underwent colonoscopies prior to this date. A total of 1,247 (82.3%) patients age 18 to 85 were included for final analysis (**Figure 1**). The sample was 58.6% female, and the mean age was 57 years. The indication of the procedure was screening or surveillance colonoscopy in 36.8% patients. Demographic characteristics of patients were summarized in **Table 2**.

### *Primary Outcome: cecal retroflexion-associated complication rates*

Among the 1,247 patients included in final analysis, 624 (50.0%) had cecal retroflexion performed during colonoscopy. One (**Case**) out of the 624 patients had a cecal retroflexion-related complication (see Chapter Two). The complication rate was 1.6 per 1000 cecal retroflexion (95% Cl: 0 to 4.7 per 1000 cecal retroflexion) (**Table 3**).

Of the 459 patients at average risk underwent screening colonoscopy, 261 (56.9%) had cecal retroflexion performed. No cecal retroflexion-associated complications were observed.

### *Secondary Outcome: cecal retroflexion-associated neoplasia detection rates*

Overall, rates of neoplasia detection were 46.0% for any adenoma, 3.3% for sessile serrated adenoma, 0.9% for colorectal adenocarcinoma, and 1.4% for hyperplastic polyps $\geq$1cm. Cecal retroflexion-associated detection rates were 48.2% for any adenoma, 3.4% for sessile

serrated adenoma, 0.3% for colorectal adenocarcinoma, and 1.3% for hyperplastic polyps ≥1cm. There was no statistically significant improvement in neoplasia detection rates with versus without cecal retroflexion ($P > 0.05$ for all comparisons) **(Table 4)**.

Among those undergoing screening colonoscopy, rates of cecal retroflexion-related detection were 47.1% for adenoma, 2.7% for sessile serrated adenoma, 0.4% for colorectal adenocarcinoma, and 1.1% for hyperplastic polyps >1cm. No statistically significant improvement in neoplasia detection rates with cecal retroflexion was noted ($P> 0.05$ for all comparisons) **(Table 4)**.

## CHAPTER FIVE: DISCUSSION

In this retrospective cohort study of 1,247 patients undergoing colonoscopy, we encountered 1 complication associated with cecal retroflexion out of 624 patients receiving this maneuver. The complication rate was 1.6 per 1000 cecal retroflexion (95% Cl: 0 to 4.7 per 1000 maneuvers). We found no statistically significant improvement in neoplasia detection with cecal retroflexion for all patients, and for those at average risk undergoing screening colonoscopy ($P>0.05$ for all comparisons).

Prior studies on cecal retroflexion had not encountered any associated serious complications, such as perforation, mucosal tears or bleeding requiring overnight hospitalizations, including one large study that reported a series of 1,000 patients who underwent the maneuver[16,17,19,20]. Our finding of an infrequent complication incidence of 1 complication out of 624 maneuvers, with a 95% confidence interval ranging from 0 to 4.7 incidents per 1,000 maneuvers, is consistent with prior data, though we cannot estimate with certainty the expected rate in the general population. A large cohort study (n=16,318) from Kaiser Permanente of North California addressing the complication rates associated with standard colonoscopy found that perforation rates were 1.1 per 1000 colonoscopies with biopsy (95% Cl: 0.6 to 1.8 per 1000 with biopsy)[21]. Our measured complication rate falls in between the 95% confidence interval of their findings. Thus, the occurrence of our colonoscopy complication falls within reported rates, though in this case we uniquely attribute the complication to the use of retroflexion for inspection of the proximal colon.

There are 2 possible explanations for the occurrence of complication in our **Case**. One is that the tip of the colonoscope may have torn the cecum wall when the endoscopist straightened

the scope from the hairpin-shaped position. The other explanation is that the bending section of the colonoscope may have been pushed deep into the cecum wall while the endoscopist was trying to remove the adenoma located on the proximal side of the ascending colonic fold. We postulate that increased attention to careful control of the scope tip when straightening the scope after the retroflexion maneuver, and care in avoiding pushing the blunt end of the retroflexed scope into the cecal base might reduce future chances of retroflexion associated complications.

In addition to finding a rare complication of the maneuver, our study found no clinically significant improvement in proximal neoplasia detection with cecal retroflexion, consistent with prior work, and raising the possibility that routine use may not result in clinically significant improvements in outcomes after colonoscopy[16,17,22]. The only study of cecal retroflexion for polyp detection with positive findings was a prospective observational study performed at Indiana University Hospital. In that study, patients initially underwent careful examination of the proximal colon in forward view, and then underwent a second inspection in retroflexed view, with additional 9.8% right-sided adenoma detected[17]. Their approach was clinically significant but still inconclusive regarding the benefit of the technique because the study was not controlled. The percentage of patients with additional adenoma detected in the Indiana study was 4.4%, which is similar to our finding of 3.8%, calculated from the difference between percentages of patients with adenomas detected on retroflexion versus on forward view.

There is only 1 randomized controlled trial assessing polyp detection rates with cecal retroflexion, which was performed by the same group, with negative findings ($p=0.31$)[16]. Based on our study, even if we believe that a 3.8% improvement in proximal adenoma detection is clinically significant, we would have to randomize over 5,000 patients into

cecal retroflexion versus forward view, to detect a statistically significant difference of 3.8% or greater in proximal adenoma detection, assuming $\alpha$=0.05 and power to detect the difference of 80%. This suggests that additional randomized controlled trials on cecal retroflexion may not be feasible due to large sample size requirement, even if a 4% improvement in adenoma detection were to be considered clinically significant.

A few limitations may be considered in interpreting our report and findings. First, with regards to the estimated complication rate, our estimated confidence interval includes both 0 and 4; we are unable to provide a more precise estimate given our sample size (n=1,247). Second, our review is based on the experience of one colonoscopist – the complication could be specific to this colonoscopist alone. Further, the colonoscopist had a very high adenoma detection rate; colonoscopists with a lower detection rate might still be hypothesized to be able to increase their detection rate with use of the retroflexion technique. Third, this was not a controlled trial and we cannot rule out bias with respect to differences in patients for whom retroflexion was chosen versus not chosen.

We conclude that cecal retroflexion does not appear to result in clinically significant improvement in neoplasia detection, and may expose patients to rare but serious complications.. Randomized controlled studies of retroflexion technique for improving adenoma detection may not be feasible due to large sample size required, and, more importantly, may not be indicated given that current estimates suggest improvements in adenoma detection that are unlikely to be clinically significant. Future studies should focus on other approaches to improve right-sided colonic lesion detection, such as split dose bowel preparation[23,24], training in subtle polyp recognition, and advancing scope technology.

## LIST OF FIGURES

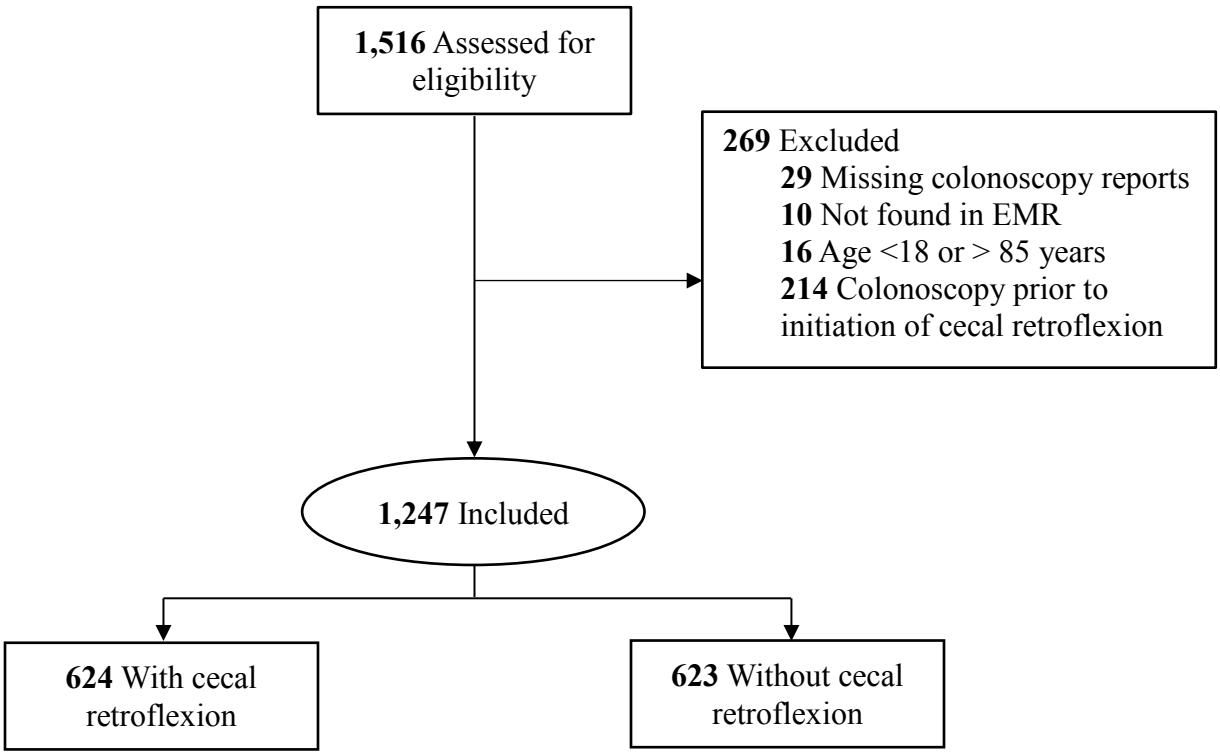


**Figure 1. Consort Diagram**
Patient identification and exclusion/inclusion criteria are depicted. EMR indicates electronic medical record.

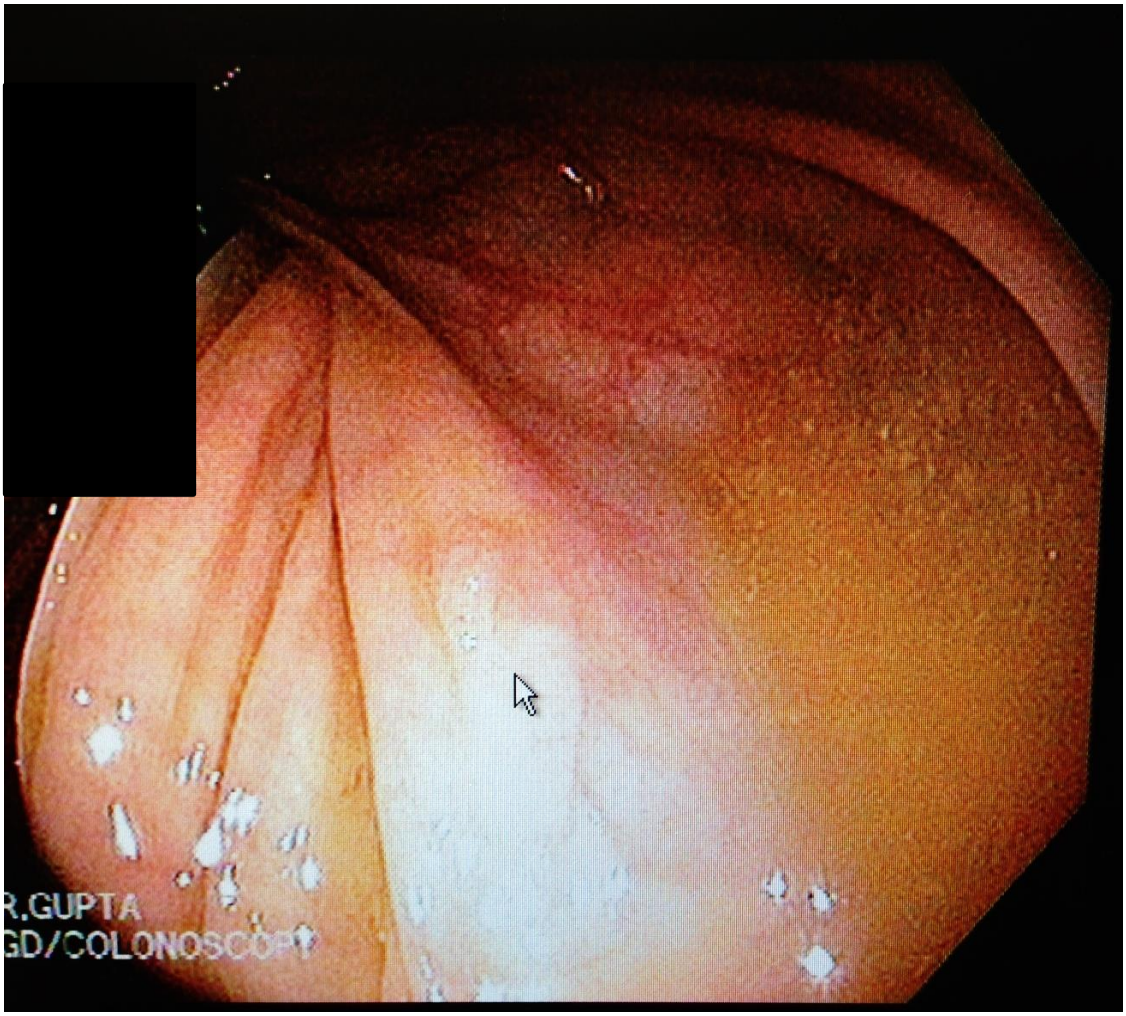


**Figure 2. Tubular Adenoma Detected and Removed on Cecal Retroflexed View**
Arrow points at tubular adenoma

**Figure 3. Circumferential Fluid Collection around Cecum**

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**Table 1. Characteristics of Polyps Detected and Removed for Case Patient**

| Location | Size | Removal Technique | Pathology |
|---|---|---|---|
| Ascending colon | 3mm | Cold biopsy forceps | Tubular adenoma * |
| Transverse colon | 4mm | Cold biopsy forceps | Hyperplastic polyp |
| Transverse colon | 5mm | Cold snare | Hyperplastic polyp |
| Rectum | 15mm | Cold snare | Tubulovillous adenoma w focal high grade dysplasia |

* detected and removed by cecal retroflexion

**Table 2. Demographic Characteristics of Patients**

| Patient Characteristics | All Patients (N=1,247) |
|---|---|
| Age, years | |
| Mean, years (SE) | 57.1 (0.35) |
| Median, years | 57 |
| Gender, n (%) | |
| Male | 516 (41.4) |
| Female | 731 (58.6) |
| Indication, n (%) | |
| Screening | 459 (36.8) |
| Other indications | 788 (63.2) |

SE indicates standard error of mean.

**Table 3. Cecal Retroflection-Associated Complication Rates**

| | Total Cecal Retroflexion Performed (N=624) | Cecal Retroflexion in Screening Colonoscopy (N=261) |
|---|---|---|
| Complication, n | 1 | 0 |
| Complication Rates, y per 1000 Cecal Retro (95% Cl) | 1.6 per 1000 Cecal Retro (Cl: 0 to 4.6 per 1000 Cecal Retro) | n/a |

Cl indicates confidence interval; Cecal Retro indicates cecal retroflexion.

**Table 4. Neoplasia Detection Rates Stratified by Adenoma, SSA, CRC, and Hyperplastic Polyps >1cm for All Patients, and Patients Underwent Screening Colonoscopy**

| | All Patients (N=1,247) | | | Patients with Screening Colonoscopy (N=459) | | |
|---|---|---|---|---|---|---|
| ***Detection, n (%)*** | ***Cecal Retro (N=624)*** | ***Forward (N=623)*** | ***P-value*** | ***Cecal Retro (N=261)*** | ***Forward (N=198)*** | ***P-value*** |
| Adenoma | 301 (48.2) | 272 (43.7) | 0.1117 | 123 (47.1) | 87 (43.9) | 0.5093 |
| *Right side* | 189 (30.3) | 165 (26.5) | 0.1486 | 77 (29.5) | 55 (27.8) | 0.7549 |
| SSA | 21 (3.4) | 20 (3.2) | 1.0000 | 7 (2.7) | 4 (2.0) | 0.7639 |
| *Right side* | 15 (2.4) | 14 (2.2) | 1.0000 | 9 (3.4) | 5 (2.5) | 0.7852 |
| CRC | 2 (0.3) | 6 (1.0) | 0.1781 | 1 (0.4) | 1 (0.5) | 1.0000 |
| *Right side* | 0 | 3 (0.5) | 0.1244 | 0 | 1 (0.5) | 0.4314 |
| Hyperplastic Polyps >1cm | 8 (1.3) | 10 (1.6) | 0.6450 | 3 (1.1) | 4 (2.0) | 0.4712 |
| *Right side* | 4 (0.6) | 3 (0.5) | 1.0000 | 2 (0.8) | 1 (0.5) | 1.0000 |

Abbreviation: Cecal Retro, cecal retroflexion; SSA, sessile serrated adenoma; CRC, colorectal adenocarcinoma.

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## REFERENCES


1. Siegel R, Naishadham D, Jemal A. Cancer statistics, 2013. *CA: a cancer journal for clinicians.* Jan 2013;63(1):11-30.
2. Nishihara R, Wu K, Lochhead P, et al. Long-term colorectal-cancer incidence and mortality after lower endoscopy. *The New England journal of medicine.* Sep 19 2013;369(12):1095-1105.
3. Baxter NN, Warren JL, Barrett MJ, Stukel TA, Doria-Rose VP. Association between colonoscopy and colorectal cancer mortality in a US cohort according to site of cancer and colonoscopist specialty. *Journal of clinical oncology : official journal of the American Society of Clinical Oncology.* Jul 20 2012;30(21):2664-2669.
4. Baxter NN, Goldwasser MA, Paszat LF, Saskin R, Urbach DR, Rabeneck L. Association of colonoscopy and death from colorectal cancer. *Annals of internal medicine.* Jan 6 2009;150(1):1-8.
5. Singh H, Nugent Z, Demers AA, Kliewer EV, Mahmud SM, Bernstein CN. The reduction in colorectal cancer mortality after colonoscopy varies by site of the cancer. *Gastroenterology.* Oct 2010;139(4):1128-1137.
6. Klabunde CN, Lanier D, Nadel MR, McLeod C, Yuan G, Vernon SW. Colorectal cancer screening by primary care physicians: recommendations and practices, 2006-2007. *American journal of preventive medicine.* Jul 2009;37(1):8-16.
7. Brenner H, Chang-Claude J, Seiler CM, Rickert A, Hoffmeister M. Protection from colorectal cancer after colonoscopy: a population-based, case-control study. *Annals of internal medicine.* Jan 4 2011;154(1):22-30.

8. Winawer SJ, Zauber AG, Ho MN, et al. Prevention of colorectal cancer by colonoscopic polypectomy. The National Polyp Study Workgroup. *The New England journal of medicine.* Dec 30 1993;329(27):1977-1981.

9. Citarda F, Tomaselli G, Capocaccia R, Barcherini S, Crespi M, Italian Multicentre Study G. Efficacy in standard clinical practice of colonoscopic polypectomy in reducing colorectal cancer incidence. *Gut.* Jun 2001;48(6):812-815.

10. Lakoff J, Paszat LF, Saskin R, Rabeneck L. Risk of developing proximal versus distal colorectal cancer after a negative colonoscopy: a population-based study. *Clinical gastroenterology and hepatology : the official clinical practice journal of the American Gastroenterological Association.* Oct 2008;6(10):1117-1121; quiz 1064.

11. Brenner H, Hoffmeister M, Arndt V, Stegmaier C, Altenhofen L, Haug U. Protection from right- and left-sided colorectal neoplasms after colonoscopy: population-based study. *Journal of the National Cancer Institute.* Jan 20 2010;102(2):89-95.

12. Kahi CJ, Hewett DG, Norton DL, Eckert GJ, Rex DK. Prevalence and variable detection of proximal colon serrated polyps during screening colonoscopy. *Clinical gastroenterology and hepatology : the official clinical practice journal of the American Gastroenterological Association.* Jan 2011;9(1):42-46.

13. Sawhney MS, Farrar WD, Gudiseva S, et al. Microsatellite instability in interval colon cancers. *Gastroenterology.* Dec 2006;131(6):1700-1705.

14. Arain MA, Sawhney M, Sheikh S, et al. CIMP status of interval colon cancers: another piece to the puzzle. *The American journal of gastroenterology.* May 2010;105(5):1189-1195.

15. Burnett-Hartman AN, Newcomb PA, Potter JD, et al. Genomic aberrations occurring in subsets of serrated colorectal lesions but not conventional adenomas. *Cancer research.* May 1 2013;73(9):2863-2872.

16. Harrison M, Singh N, Rex DK. Impact of proximal colon retroflexion on adenoma miss rates. *The American journal of gastroenterology.* Mar 2004;99(3):519-522.

17. Hewett DG, Rex DK. Miss rate of right-sided colon examination during colonoscopy defined by retroflexion: an observational study. *Gastrointestinal endoscopy.* Aug 2011;74(2):246-252.

18. Pishvaian AC, Al-Kawas FH. Retroflexion in the colon: a useful and safe technique in the evaluation and resection of sessile polyps during colonoscopy. *The American journal of gastroenterology.* Jul 2006;101(7):1479-1483.

19. Kessler WR, Rex DK. Impact of bending section length on insertion and retroflexion properties of pediatric and adult colonoscopes. *The American journal of gastroenterology.* Jun 2005;100(6):1290-1295.

20. Rex DK. Accessing proximal aspects of folds and flexures during colonoscopy: impact of a pediatric colonoscope with a short bending section. *The American journal of gastroenterology.* Jul 2003;98(7):1504-1507.

21. Levin TR, Zhao W, Conell C, et al. Complications of colonoscopy in an integrated health care delivery system. *Annals of internal medicine.* Dec 19 2006;145(12):880-886.

22. Dik VK, Moons LM, Siersema PD. Endoscopic innovations to increase the adenoma detection rate during colonoscopy. *World journal of gastroenterology : WJG.* Mar 7 2014;20(9):2200-2211.

23. Kilgore TW, Abdinoor AA, Szary NM, et al. Bowel preparation with split-dose polyethylene glycol before colonoscopy: a meta-analysis of randomized controlled trials. *Gastrointestinal endoscopy.* Jun 2011;73(6):1240-1245.

24. Gurudu SR, Ramirez FC, Harrison ME, Leighton JA, Crowell MD. Increased adenoma detection rate with system-wide implementation of a split-dose preparation for colonoscopy. *Gastrointestinal endoscopy.* Sep 2012;76(3):603-608 e601.