Research Article

Colonic stasis and chronic constipation: Demystifying proposed risk factors for colon polyp formation in a spinal cord injury veteran population

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Background and Aims: Patients with spinal cord injury (SCI) suffer significant morbidity from neurogenic bowel. Chronic constipation has long-been a proposed risk factor for polyp development. We performed a retrospective cohort study in veterans with SCI to assess polyp presence in the setting of colonic stasis.

Methods: All consecutive patients at the James A. Haley Veterans Affairs Hospital with SCI and neurogenic bowel who completed screening colonoscopy between January 1, 2004 to June 30, 2013 were included. Colonoscopies were excluded if they were aborted, not completed to the cecum, of less than adequate preparation, or if polypectomy was precluded. Patient data included level, duration, and completeness of SCI. Polyp data included number, location, and histology.

Results: 325 patients ultimately met inclusion criteria. Most were male (96%). The average age at screening colonoscopy was 62.8 years. The majority of patients had injury to the cervical spine (41.5%). Colon polyps were detected in 130 patients (40%). Adenomatous change was seen in 95 (73%) of these patients. The adenoma detection rate (ADR) across all patients was 29.2%. Polyp presence and ADR demonstrated no statistically significant correlation with level, degree, or duration of SCI. Only patient age at time of screening colonoscopy had a significant correlation with polyp and adenoma presence ($P < 0.05$).

Conclusions: SCI had no statistically significant correlation with polyp or adenoma presence. The ADR in our veteran SCI population with chronic constipation is comparable with that reported in the general population.

Keywords: Spinal cord injuries, Colon polyps, Neurogenic bowel

Introduction

Approximately 12,000 to 20,000 new individuals are affected by spinal cord injuries each year in the United States according to the Centers for Disease Control and Prevention; with an overall incidence of about 200,000 persons.¹⁻⁴ Bowel dysfunction has been reported to affect between 27% and 62% of SCI patients; with constipation being a predominant feature (42–81%).⁵ Both

upper motor neuron (UMN) and lower motor neuron (LMN) lesions can lead to neurogenic bowel and result in complications including diarrhea and/or constipation. UMN lesions will typically lead to bowel dysrhythmia, increased colonic wall tone, and stool retention. LMN lesions, while generally retaining a higher level of colonic activity, can similarly result in constipation through a loss in reflex arc-mediated colonic peristalsis.⁵⁻⁷

Such alterations in normal bowel function can have a tremendous impact on the quality of life in the SCI population and have also been associated with an

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increase in morbidity and mortality.⁸ Despite advancements in post-injury care, this chronic gastrointestinal (GI) manifestation of SCI plays a detrimental role in the care of these patients; especially when concerning colonoscopy for colon cancer screening. According to two self-reported studies, SCI patients are significantly less likely to undergo screening colonoscopies and other preventative services compared to the general population.^{9,10} In addition, colonoscopies performed on SCI patients are technically more difficult for the endoscopist due to the higher likelihood of redundancy and inadequate bowel preparation secondary to colonic inertia.¹¹

This delay in colonic transit, while having a definite impact on the morbidity and overall quality of life in the SCI population, has also been theorized to possibly predispose such patients to an increased risk of colorectal cancer (CRC).¹² One of the hypothesized mechanisms of CRC development in this population includes prolongation of contact between carcinogens in the stool and colonic mucosa.¹² CRC is currently the 3rd most common and deadly cancer in the United States.¹³ Presently, consensus guidelines on CRC screening do not recommend any alteration in screening parameters for patients with chronic constipation due to neurogenic bowel.

Based on our experiences with a large SCI veteran population, it anecdotally appeared that such patients exhibited a higher degree of colonic polyps compared to the general veteran population. It is the goal of this retrospective cohort study to review colonoscopies performed at our single-site SCI veteran population to investigate if chronic constipation and colonic stasis due to SCI yield an increased risk of polyp and specifically adenoma formation in the colon.

Materials and methods

Study design

We performed a retrospective cohort chart review of veterans who routinely seek their medical care at the James A. Haley Veterans Affairs (VA) hospital and dedicated SCI primary care unit. Data were collected from veteran patients who have already received routine screening colonoscopies from January 1st 2004 through June 30th 2013 by a team of staff gastroenterologists at our facility. Our analysis focused on the number and pathology of colon polyps in our SCI population as well as the level, degree of SCI completeness, and duration of injury. Results in our analysis were compared with the risk of polyp and adenoma development in the average-risk population.

Patient selection

At our single-site SCI veteran population 1296 patients were initially identified. 325 patients ultimately met inclusion criteria. This required all study participants to have documented neurogenic bowel with chronic constipation resulting from either traumatic or non-traumatic SCI. Each colonoscopy was to be of at least adequate bowel preparation, be conducted for routine CRC screening purposes, and be complete reaching the cecum. Polypectomy was not to be precluded.

Risk assessment

Demographic data assessed in our analysis included patient age, sex, level of SCI injury, completeness of SCI injury according to the American Spinal Injury Association (ASIA),¹⁴ duration of injury (years) at first screening colonoscopy, aspirin use, and presence of diabetes and associated therapy (metformin, insulin).

Statistical analysis

Data were analyzed using the SPSS 22.0 statistical software for Windows. Quantitative data were expressed as mean $\pm$ standard deviation. Categorical data were analyzed utilizing the chi-square test. Pearson chi-square test, Fisher's exact test, and odds ratio were used to examine significance of association between polyp and adenoma burden and level of SCI, completeness of SCI according to the ASIA criteria, aspirin use, presence of diabetes, and use of metformin and/or insulin therapy. Logistic regression analysis was utilized to examine the relationship between polyp and adenoma burden with patient age and duration of injury (years). Statistical significance was set at $P < 0.05$.

Results

Patient demographics

Of the total study participants, 325 met inclusion criteria and were included in the analysis out of a total population of 1296 subjects at our VA facility. The study group consisted of predominantly male patients (96%). The average age was 62.8 years. Level of SCI included 135 patients (41.5%) with injury to the cervical spine, 113 (34.8%) with injury to the thoracic spine, 26 (8.0%) with injury to the lumbar spine, 43 (13.2%) patients had multiple sclerosis (MS), and 8 patients (2.5%) had SCI due to amyotrophic lateral sclerosis (ALS).

SCI completeness scores according to the ASIA classification included 120 patients (37%) with a score of A, 20 (6.1%) had a score of B, 33 (10.3%) had a score of C, 100 (30.9%) had a score of D, and 51 (15.8%) were unclassified. The average duration of SCI from date of injury to date of 1st screening colonoscopy

was 18.2 years. Eighty patients had diabetes as a comorbidity. Twenty-two of these patients were on insulin as sole therapy in this regard, 25 patients were on metformin, 9 patients were on combination metformin and insulin, and 24 patients were not on any treatment for diabetes. Of the 325 study patients, 122 patients were taking 81mg of aspirin daily, 16 patients were taking 325mg of aspirin daily, and 187 patients were not on an aspirin regimen. Demographic data can be found listed in (Table 1).

Colonoscopy findings

For the 325 patients in our study, all colonoscopy studies completed between January 1st 2004 and June 30th 2013 were of either adequate or excellent bowel prep; with the majority being prepped with two gallons of Golytely® formulation. 130 patients (40%) had polyps present on colonoscopy. The majority of these patients (18.2%) had only 1 polyp, 7 patients (2.2%) had innumerable polyps. The frequency and overall percentage of adenomas detected in our cohort can be found in (Table 2). Adenomatous changes were found in 95 of these patients (73%). The adenoma detection rate for all patients was 29.2%. With advancing age adenomas were found more frequently in the right colon; however this did not reach statistical significance. Polyp pathology and number demonstrated no statistically significant difference with respect to the left and right colon. Other studies have found a significantly

Table 1 Demographic data.

Variable	Descriptive Statistic
Total Patients	325
Age	62.8 ± 9.7
Male	(96)
Female	(4)
Level of Injury	
Cervical Spine	(41.5)
Thoracic Spine	(34.8)
Lumbar Spine	(8.0)
MS [†]	(13.2)
ALS [‡]	(2.5)
ASIA§ Scale	
A	(37)
B	(6.1)
C	(10.3)
D	(30.9)
NA	(15.8)
Length of injury (years)	18.23 ± 15.1
Polyp Detection Rate (PDR)	(40)
Polyp count	2.9 ± 14.3
Adenoma Detection Rate (ADR)	(29.2)
Adenoma count	1.2 ± 7.8

[†]Multiple sclerosis; [‡]Amyotrophic lateral sclerosis; [§]American Spinal Injury Association. Descriptive statistic represented as mean ± SD or percentage (P).

Table 2 Adenoma detection chart.

Adenoma number (total colon)	Frequency [†]	Percent
0	230	70.8
1	53	16.3
2	19	5.8
3	6	1.8
4	4	1.2
5	4	1.2
6	2	0.6
7	3	0.9
8	1	0.3
9	1	0.3
Innumerable	2	0.6

[†]Frequency out of total cohort of 325 patients.

higher proportion of proximally located adenomas in patients with age greater than 60.¹⁵ There was no case of CRC diagnosed via screening colonoscopy.

Polyp risk assessment

With respect to patient demographic data, only age demonstrated a statistically significant association ($P < 0.05$) with both polyp and adenoma presence. Level, degree of completeness, and duration of SCI demonstrated no statistically significant correlation with polyp or adenoma presence as indicated in (Table 3). Such results were consistent when restricted to polyp and adenoma presence in the left and right colon, individually. The presence of diabetes and associated treatment were not significant factors in polyp or adenoma presence. Aspirin likewise demonstrated no statistical significance in the rate of polyp and adenoma presence in our study population.

Discussion

Colonic stasis secondary to neurogenic bowel is a serious medical condition with significant impact on quality of life in the SCI population. Studies indicate that the prevalence of chronic constipation in this cohort can reach between 48% and 81%.^{16,17} Other potential complications including chronic abdominal pain, hemorrhoids, colonic distention, and autonomic hyperreflexia are also all too common.⁵ The precise mechanism underlying the development of neurogenic bowel dysfunction following SCI is still an area of active research. One likely contributing factor is compromised colonic motility; a feature that has been well-documented following SCI.

In a study by Fajardo *et al.* of eight patients with SCI, it was discovered via the attachment of a manometric probe to the colonic splenic flexure that both the resting and post-prandial motility indices were significantly less than healthy age-matched controls.⁷ It has

Table 3 Risk factors for polyp and adenoma development.

Variable	Polyp Presence (P-value)	Adenoma Presence (P-value)
Age	0.025*	0.002*
Level of injury	0.58	0.68
ASIA Score	0.26	0.64
Duration of Injury	0.32	0.39
Aspirin Use	0.07	0.45
Diabetes	0.29	0.69
Metformin	0.55	0.44
Insulin	0.53	0.22

* $P < 0.05$ set as marker of statistical significance in our study.

been postulated that impaired sympathetic inhibitory input may contribute to such dysmotility.¹⁸ In the non-SCI general population, the development of chronic constipation can be secondary to colonic inertia resulting in a clinical picture very similar to that of the SCI cohort; however, it is often times multifactorial and commonly related to the effects of medications.¹⁹

The focus of our study was the potential predisposition toward polyp development in light of such chronic constipation due to colonic inertia. Several studies have proposed constipation to increase exposure time of potential stool carcinogens such as bile acids to the colonic mucosa; thus increasing the risk of developing CRC.^{12,20–23} Frisbie *et al.* in 1984 found that CRC was two to six times more common and more advanced at diagnosis in male patients with myelopathy than in non-paralyzed patients.²⁴ A meta-analysis by Sonnenberg *et al.* of 14 case-control studies further supported this hypothesis with a pooled odds ratio of 1.48 for CRC in patients with constipation.²⁵

A number of more recent studies, however, have been unable to replicate these results; finding no significant correlation between constipation and CRC.^{26,27} The concept was also reviewed in Brazilian patients with Chagas disease, whose motility disturbances led to megaesophagus and megacolon. Even though an increased prevalence of esophageal squamous cell carcinoma was seen in patients with Chagas disease, a higher incidence of CRC was not observed despite the existence of colonic dilation and fecal stasis.^{28,29}

More recently, a systematic review and meta-analysis by Powers *et al.* in 2013 also failed to demonstrate a correlation between constipation and CRC.³⁰ Stratton *et al.* likewise found that tumor distribution and stage of CRC were similar in SCI and neurally intact patients; however, they did not report on the overall incidence.³¹ Some studies, such as that by Obusez *et al.* interestingly discovered a decreased ADR and rate of CRC in

patients undergoing colonoscopy for constipation than for average risk individuals undergoing routine screening studies.³² For the purposes of our study, we elected to evaluate polyp presence and consequently CRC risk in a population with a notably high rate of chronic constipation. Our findings are similar to those of other recent studies reporting no increased CRC risk in chronic constipation. The ADR and polyp detection rate (PDR) of our SCI cohort were 29.2% and 40%, respectively; a result comparable to that documented from adequate colonoscopies in the average-risk population.^{33,34}

A similar retrospective study conducted by Meheroz *et al.* evaluated the presence of colonoscopic lesions in an SCI cohort of 71 patients. Their results indicated that the duration of SCI had a statistically significant correlation with total colonoscopic lesions (including polyps, hemorrhoids, and diverticula). In our study, neither the duration nor the level of injury correlated with polyp presence. Only age, an already well-established risk factor for polyp and CRC development, proved to correlate both with polyp and adenoma presence.³⁵ A Korean case-control study by Han *et al.* also evaluated for variations in colonoscopic lesions in 25 SCI patients. They found the same incidence of colonoscopic lesions between this and a control group of 41 healthy individuals.³⁶ This study, unfortunately, carries limited informative value in regards to constipation and CRC risk as the colonoscopic lesions included any abnormality seen during the endoscopy, such as hemorrhoids or melanosis coli, and were not specific to colon polyps as in our study.

It has recently been noted in a prospective study by Citronberg *et al.* that the use of non-fiber laxatives was associated with an increased risk of CRC; whereas fiber laxatives were inversely associated with such a risk.³⁷ Their findings were also similar with ours in the lack of establishing any association between constipation and CRC. This study does bring to light an important limitation in our investigation. The combined use of laxatives, stool softeners, or promotility agents in the SCI population is commonplace. Unfortunately, such management is frequently unsuccessful, and other more invasive measures including digital evacuation are often employed.⁸ As noted above, the frequent use of certain laxatives in this cohort may in itself predispose such patients to an increased CRC risk. Our study did not take into account the precise bowel regimens used by such patients. Further investigation taking into account such factors would help to further our understanding of both the management of neurogenic bowel and its potential inherent risks. Direct measurement of

colonic motility could also add our understanding of the effect SCI has on colonic motility in this population.

Our study has additional limitations including its male predominance, single-site analysis, and somewhat limited size given the prevalence of SCI in the general population. A larger, multi-center prospective study would help with some of the limitations from our study and help determine if our results can be applied to the general SCI population. Despite such limitations, our study helps to further the understanding of polyp and specifically adenoma detection rates in the SCI population. Our findings contribute to the growing body of literature demonstrating no increased risk of adenoma or CRC development in patients with chronic constipation.

Abbreviations

SCI: Spinal cord injury
ADR: Adenoma detection rate
UMN: Upper motor neuron
LMN: Lower motor neuron
GI: Gastrointestinal
CRC: Colorectal cancer
ASIA: American spinal injury association

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References

- 1 National Spinal Cord Injury Statistical Center (NSCISC). Volume 2014: University of Alabama at Birmingham, 2014.
- 2 Bernhard M, Gries A, Kremer P, Bottiger BW. Spinal cord injury (SCI)--prehospital management. *Resuscitation* 2005;66(2):127–39.
- 3 Burke DA, Linden RD, Zhang YP, Maiste AC, Shields CB. Incidence rates and populations at risk for spinal cord injury: A regional study. *Spinal Cord* 2001;39(5):274–8.
- 4 Sekhon LH, Fehlings MG. Epidemiology, demographics, and pathophysiology of acute spinal cord injury. *Spine (Phila Pa 1976)* 2001;26(24 Suppl):S2–12.
- 5 Ebert E. Gastrointestinal involvement in spinal cord injury: a clinical perspective. *J Gastrointest Liver Dis* 2012;21(1):75–82.
- 6 Connell AM, Frankel H, Guttmann L. The Motility of the Pelvic Colon Following Complete Lesions of the Spinal Cord. *Paraplegia* 1963;1:98–115.
- 7 Fajardo NR, Pasillao RV, Modeste-Duncan R, Creasey G, Bauman WA, Korsten MA. Decreased colonic motility in persons with chronic spinal cord injury. *Am J Gastroenterol* 2003;98(1):128–34.
- 8 Correa GI, Rotter KP. Clinical evaluation and management of neurogenic bowel after spinal cord injury. *Spinal Cord* 2000;38(5):301–8.
- 9 Johnston MV, Diab ME, Chu BC, Kirshblum S. Preventive services and health behaviors among people with spinal cord injury. *J Spinal Cord Med* 2005;28(1):43–54.
- 10 Lavelle SL, Weaver FM, Smith B, Chen K. Disease prevalence and use of preventive services: comparison of female veterans in general and those with spinal cord injuries and disorders. *J Womens Health (Larchmt)* 2006;15(3):301–11.
- 11 Ancha HR, Spungen AM, Bauman WA, Rosman AS, Shaw S, Hunt KK, et al. Clinical trial: the efficacy and safety of routine bowel cleansing agents for elective colonoscopy in persons with spinal cord injury - a randomized prospective single-blind study. *Aliment Pharmacol Ther* 2009;30(11–12):1110–7.
- 12 Burkitt DP. Epidemiology of cancer of the colon and rectum. *Cancer* 1971;28(1):3–13.
- 13 Siegel R, Desantis C, Jemal A. Colorectal cancer statistics, 2014. *CA Cancer J Clin* 2014;64(2):104–17.
- 14 Kirshblum SC, Waring W, Biering-Sorensen F, Burns SP, Johansen M, Schmidt-Read M, et al. Reference for the 2011 revision of the International Standards for Neurological Classification of Spinal Cord Injury. *J Spinal Cord Med* 2011;34(6):547–54.
- 15 Klein JL, Okcu M, Preisegger KH, Hammer HF. Distribution, size and shape of colorectal adenomas as determined by a colonoscopist with a high lesion detection rate: Influence of age, sex and colonoscopy indication. *United European gastroenterol J* 2016;4(3):438–48.
- 16 Naicker AS, Roohi SA, Naicker MS, Zaleha O. Bowel dysfunction in spinal cord injury. *Med J Malaysia* 2008;63(2):104–8.
- 17 Faaborg PM, Christensen P, Finnerup N, Laurberg S, Krogh K. The pattern of colorectal dysfunction changes with time since spinal cord injury. *Spinal Cord* 2008;46(3):234–8.
- 18 Lynch AC, Frizelle FA. Colorectal motility and defecation after spinal cord injury in humans. *Prog Brain Res* 2006;152:335–43.
- 19 Andrews CN, Storr M. The pathophysiology of chronic constipation. *Can J Gastroenterol* 2011;25 Suppl B:16B–21B.
- 20 Jacobs EJ, White E. Constipation, laxative use, and colon cancer among middle-aged adults. *Epidemiology* 1998;9(4):385–91.
- 21 Le Marchand L, Wilkens LR, Kolonel LN, Hankin JH, Lyu LC. Associations of sedentary lifestyle, obesity, smoking, alcohol use, and diabetes with the risk of colorectal cancer. *Cancer Res* 1997;57(21):4787–94.
- 22 Kotake K, Koyama Y, Nasu J, Fukutomi T, Yamaguchi N. Relation of family history of cancer and environmental factors to the risk of colorectal cancer: a case-control study. *Jpn J Clin Oncol* 1995;25(5):195–202.
- 23 Narisawa T, Magadia NE, Weisburger JH, Wynder EL. Promoting effect of bile acids on colon carcinogenesis after intrarectal instillation of N-methyl-N'-nitro-N-nitrosoguanidine in rats. *J Natl Cancer Inst* 1974;53(4):1093–7.
- 24 Frisbie JH, Chopra S, Foo D, Sarkarati M. Colorectal carcinoma and myelopathy. *J Am Paraplegia Soc* 1984;7(2):33–6.
- 25 Sonnenberg A, Muller AD. Constipation and cathartics as risk factors of colorectal cancer: a meta-analysis. *Pharmacology* 1993;47 Suppl 1:224–33.
- 26 Simons CC, Schouten LJ, Weijenberg MP, Goldbohm RA, van den Brandt PA. Bowel movement and constipation frequencies and the risk of colorectal cancer among men in the Netherlands Cohort Study on Diet and Cancer. *Am J Epidemiol* 2010;172(12):1404–14.
- 27 Otani T, Iwasaki M, Inoue M, Sasazuki S, Tsugane S, Japan Public Health Center-Based Prospective Study G. Bowel movement, state of stool, and subsequent risk for colorectal cancer: the Japan public health center-based prospective study. *Ann Epidemiol* 2006;16(12):888–94.
- 28 Garcia SB, Aranha AL, Garcia FR, Basile FV, Pinto AP, de Oliveira EC, et al. A retrospective study of histopathological findings in 894 cases of megacolon: what is the relationship between megacolon and colonic cancer? *Rev Inst Med Trop Sao Paulo* 2003;45(2):91–3.

- 29 Adad SJ, Etchebehere RM, Araujo JR, Madureira AB, Lima VG, Silva AA, *et al.* Association of chagasic megacolon and cancer of the colon: case report and review of the literature. *Rev Soc Bras Med Trop* [2002](#);35(1):63–8.
- 30 Power AM, Talley NJ, Ford AC. Association between constipation and colorectal cancer: systematic review and meta-analysis of observational studies. *Am J Gastroenterol* [2013](#);108(6):894–903.
- 31 Stratton MD, McKirgan LW, Wade TP, Vernava AM, Virgo KS, Johnson FE, *et al.* Colorectal cancer in patients with previous spinal cord injury. *Dis Colon Rectum* [1996](#);39(9):965–8.
- 32 Obusez EC, Lian L, Kariv R, Burke CA, Shen B. Diagnostic yield of colonoscopy for constipation as the sole indication. *Colorectal Dis* [2012](#);14(5):585–91.
- 33 Anderson JC, Shaw RD. Update on colon cancer screening: recent advances and observations in colorectal cancer screening. *Curr gastroenterol Rep* [2014](#);16(9):403.
- 34 Boroff ES, Gurudu SR, Hentz JG, Leighton JA, Ramirez FC. Polyp and adenoma detection rates in the proximal and distal colon. *Am J Gastroenterol* [2013](#);108(6):993–9.
- 35 Rex DK, Johnson DA, Anderson JC, Schoenfeld PS, Burke CA, Inadomi JM, *et al.* American College of Gastroenterology guidelines for colorectal cancer screening 2009 [corrected]. *Am J Gastroenterol* [2009](#);104(3):739–50.
- 36 Han SJ, Kim CM, Lee JE, Lee TH. Colonoscopic lesions in patients with spinal cord injury. *J Spinal Cord Med* [2009](#);32(4):404–7.
- 37 Citronberg J, Kantor ED, Potter JD, White E. A prospective study of the effect of bowel movement frequency, constipation, and laxative use on colorectal cancer risk. *Am J Gastroenterol* [2014](#);109(10):1640–9.