

Risk factors for colonoscopic perforation: A population-based study of 80118 cases

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Abstract

AIM: To assess the incidence and risk factors associated with colonic perforation due to colonoscopy.

METHODS: This was a retrospective cross-sectional study. Patients were retrospectively eligible for inclusion if they were 18 years and older and had an inpatient or outpatient colonoscopy procedure code in any facility within the Geisinger Health System during the period from January 1, 2002 to August 25, 2010. Data are presented as median and inter-quartile range, for continuous variables, and as frequency and percentage for categorical variables. Baseline comparisons across those with and without a perforation were made using the two-sample *t*-test and Pearson's χ^2 test, as appropriate.

RESULTS: A total of 50 perforations were diagnosed out of 80118 colonoscopies, which corresponded to an incidence of 0.06% (95%CI: 0.05-0.08) or a rate of 6.2 per 10000 colonoscopies. All possible risk factors associated with colonic perforation with a *P*-value < 0.1 were checked for inclusion in a multivariable log-binomial regression model predicting 7-d colonic perforation. The final model resulted in the following risk factors which were significantly associated with risk of colonic perforation: age, gender, body mass index, albumin level, intensive care unit (ICU) patients, inpatient setting, and abdominal pain and Crohn's disease as indications for colonoscopy.

CONCLUSION: The cumulative 7 d incidence of colonic perforation in this cohort was 0.06%. Advanced age and female gender were significantly more likely to have perforation. Increasing albumin and BMI resulted in decreased risk of colonic perforation. Having a colonoscopy indication of abdominal pain or Crohn's disease resulted in a higher risk of colonic perforation. Colonoscopies performed in inpatients and particularly the ICU setting had substantially greater odds of perforation. Biopsy and polypectomy did not increase the risk of perforation and only three perforations occurred with screening colonoscopy.

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Key words: Colonoscopic perforation; Colon cancer; Endoscopy

Core tip: This study is unique because we have used state of the art electronic medical records to collect information about risk factors which can predispose patient to a high risk of perforation. We have looked into multiple risk factors including but not limited to serum albumin, serum creatinine, body mass index (BMI), inpatient and outpatient colonoscopy and intensive care unit (ICU) patients. Limited literature is available about the above mentioned risk factors and there propensity

to cause perforation. The important findings deduced from this research can have important implication in day to day practice of colonoscopy. The findings of Albumin, BMI, and Inpatient and out patient colonoscopy particularly performing colonoscopy in ICU setting predisposing to higher risk of perforation are crucial piece of information that can help physician in considering available alternatives which in turn may help to reduce the number of colonoscopic perforations.

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INTRODUCTION

Colorectal cancer is the third most commonly diagnosed cancer and the second leading cause of cancer-related death in the United States^[1]. Early detection benefits patients and increases their quality of life, but also reduces health care expenditures. The ability of colonoscopy to detect polyps and colorectal cancer has been shown to reduce mortality and morbidity associated with this cancer^[2,3]. In July 2001, Medicare began covering screening colonoscopy for individuals over the age of 50 at average risk for colorectal cancer and depending on the detection of polyps, at variable intervals thereafter. Since that time, the use of colonoscopy has been increasing^[4-6].

Colonoscopy is generally regarded as a safe procedure; potential complications include perforation, post-polypectomy bleeding and post-polypectomy syndrome^[7]. The incidence of colonic perforation ranges from 0.005% and 0.63% with the majority of patients requiring laparotomy for repair^[8-12]. Colonoscopic perforation occurs due to one of three mechanisms; mechanical forces from the endoscope, barotrauma from air insufflation, or as a direct result of a therapeutic procedure (*e.g.*, polypectomy). To better understand the risk factors associated with colonoscopic perforation, we conducted a large cross-sectional study to estimate the incidence of this serious complication, and to examine potential contributing effects of demographic and medical characteristics of patients.

MATERIALS AND METHODS

Study cohort, design, and setting

This was a retrospective cross-sectional study. Patients were retrospectively eligible for inclusion if they were 18 years and older and had an inpatient or outpatient colonoscopy procedure code in any facility within the Geisinger Health System (GHS) during the period from January 1, 2002 to August 25, 2010. GHS is a primary care and multispecialty medical practice located in central and northeast Pennsylvania and is the largest rural not-

for-profit health system in the nation. GHS uses health information technology infrastructure for managing and using patient data. Colonoscopy procedures were identified by the presence of current procedural terminology (CPT) 2005 codes 45378-45387, 45391, and 45392.

The study outcome was the diagnosis of colonic perforation using International Classification of Disease, 9th revision (ICD-9) codes 569.83 and 998.2, defined as perforation of intestine and accidental puncture or laceration during a procedure, 7 d after the day of colonoscopy. We specifically looked at the 7 d post colonoscopy for perforation since previous studies have shown that almost all post-colonoscopy perforations were detected within this time frame^[13,14]. Both inpatient and outpatient procedures were included.

Variables obtained from the electronic health record included age at colonoscopy, gender, body mass index (BMI), albumin, serum creatinine, operator specialty (surgeon or gastroenterologist), and indications for the colonoscopy (identified by procedure codes in the colonoscopy report). Race was not assessed for analysis since the primary care population seen in Geisinger Health System is > 95% Caucasian.

Data on comorbid health conditions were also collected including history of coronary artery disease, congestive heart failure, peripheral arterial disease, cerebrovascular disease, dementia, chronic obstructive pulmonary disease, connective tissue disease, peptic ulcer disease, liver disease, diabetes mellitus, hemiplegia, chronic kidney disease, leukemia, lymphoma, metastatic cancer, and acquired immune deficiency syndrome.

Statistical analysis

Data are presented as median and inter-quartile range, for continuous variables, and as frequency and percentage for categorical variables. Baseline comparisons across those with and without a perforation were made using the two-sample *t*-test and Pearson's χ^2 test, as appropriate. The incidence of 7-d post-colonoscopy perforations was calculated as the number of colonic perforations divided by the total number of colonoscopies, and expressed as both percentage and as an incidence rate (*e.g.*, number of perforations per 10000 colonoscopies). The count of comorbid conditions was summarized as a general indicator of health.

The log-binomial model was used to estimate the incident rate ratios (IRR) for risk factors found to vary across the two groups. A fully adjusted model was then developed to identify those risk factors predictive of perforation. Variables were considered for inclusion in the model if they were found to vary between groups at a significance level of $P < 0.10$. Backward elimination was performed to obtain a final model that retained clinically meaningful predictors. Results are presented as RR and corresponding 95%CI. The analysis was performed using SAS v9.2 (SAS Institute, Inc., Cary, NC, United States) and R v2.13 (R Development Core Team, www.r-project.org)^[15].

Table 1 Potential risk factors stratified by colonic perforation *n* (%)

	No perforation (<i>n</i> = 80068)	Perforation (<i>n</i> = 50)	<i>P</i> -value
Age category (yr)			< 0.0001
18-50	13698 (17.11)	5 (10.00)	
50-65	38695 (48.33)	10 (20.00)	
65-80	22954 (28.67)	20 (40.00)	
80+	4271 (5.90)	15 (30.00)	
Gender	<i>n</i> = 80059	<i>n</i> = 50	0.0183
Male	38972 (46.68)	16 (32.00)	
Female	41087 (51.32)	34 (68.00)	
BMI (median, IQR) (5.35% unknown) ³	28.66 (25.14, 32.92) <i>n</i> = 79615	26.27 (20.70, 28.55) <i>n</i> = 48	0.0002
Operator specialty ⁴	<i>n</i> = 78421	<i>n</i> = 46	0.2290
Surgery	13826 (17.63)	5 (10.87)	
Gastroenterology	64595 (82.37)	41 (89.13)	
Type of colonoscopy ²			< 0.0001
Therapeutic	37867 (47.29)	13 (26.53)	
Polypectomy	16367 (20.44)	6 (12.42)	
Dilation	97 (0.12)	2 (4.08)	
Biopsy	18807 (23.49)	2 (4.08)	
Other ¹	2596 (3.2)	3 (6.1)	
Screening	29898 (37.34)	3 (6.12)	
Diagnostic	12303 (15.37)	33 (67.35)	
Number of Interventions performed ⁵			0.0342
1	73919 (92.32)	45 (90.00)	
2	5527 (6.90)	3 (6.00)	
3	622 (0.78)	2 (4.00)	
Count of morbidities			0.2004
0	55601 (69.4)	31 (62.0)	
1	17330 (21.6)	11 (22.0)	
2+	7137 (8.9)	8 (16.0)	
Setting			< 0.0001
Inpatient	4132 (5.2)	23 (46.0)	
Outpatient	75936 (94.8)	27 (54.0)	
ICU	85 (0.1)	9 (18.0)	< 0.0001
Indications for CP			
Abdominal pain	3623 (4.52)	7 (14.00)	0.0070
Anemia	1875 (2.34)	5 (10.00)	0.0063
Bleeding	3615 (4.51)	7 (14.00)	0.0070
Crohn's disease	329 (0.41)	2 (4.00)	0.0183
Diarrhea	2565 (3.20)	0 (0)	0.4115
Diverticulosis of colon	15635 (19.53)	10 (20.00)	0.9328
Obstruction	416 (0.52)	0 (0)	0.9999
Ulcerative colitis	920 (1.15)	1 (2.00)	0.4391
Weight loss	464 (0.58)	1 (2.00)	0.2526
Creatinine (median, IQR) (12% unknown)	0.9 (0.7, 1.0)	0.9 (0.7, 1.1)	0.9824

¹Includes foreign body removal, hemostasis; ²Info to ascertain type of colonoscopy in one perforation not available; ³Two body mass index (BMI) in perforation group not available; ⁴Operator specialty of 4 perforations are other than gastroenterology and general surgery; ⁵Number of interventions includes biopsy, polypectomy, dilations and hemostasis. ICU: Intensive care unit; CP: Cerebral palsy; IQR: Interquartile range.

RESULTS

A total of 50 perforations were diagnosed out of 80118 colonoscopies, which corresponded to an incidence of 0.06% (95%CI: 0.05-0.08) or a rate of 6.2 per 10000 colonoscopies. Thirty-nine patients underwent emergent exploratory laparotomy and 11 were managed conservatively.

Patients that had a perforation within 7 d of their procedures were more likely to be older, female gender,

lower BMI, have more comorbidities, and a lower albumin value (Table 1). Indications for colonoscopy including abdominal pain, anemia, and bleeding were reported more in those with a perforation as compared to the non-perforation group. Operator specialty and creatinine values were not found to vary between groups. The presence of end stage renal disease (ESRD) and prior abdominal surgeries also were not associated with colonic perforations in our cohort.

Based on the findings in Table 1, those risk factors meeting the criteria of a *P* < 0.1 were further described. Table 2 reports the number of perforations and the incidence rate per 10000 patients stratified by these important factors. For every year increase in age, the risk of a perforation increased by 7% (95%CI: 5-9) with the incidence of perforation increasing from 2.6 cases per 10000 in the 50-64 year old age group to 31.7 cases per 10000 in the 80+ year old age group. Females were twice as likely to have a perforation compared to males. Lower BMI resulted in a higher risk of perforation. Decreased albumin levels (≤ 4.0) (closest prior to colonoscopy) were associated with an increased risk of colonic perforation (IRR = 7.8, 95%CI: 4.1-14.6). There was also a significant difference of perforation rate between colonoscopy performed in an inpatient and outpatient setting. Inpatients were much more likely to have perforation compared with outpatients (55.4 and 3.6 cases per 10000, respectively). Similarly, the risk of perforation increased in intensive care unit (ICU)-patients compared to non-ICU patients.

All possible risk factors associated with colonic perforation with a *P*-value < 0.1 were checked for inclusion in a multivariable log-binomial regression model predicting 7-d colonic perforation. The final model resulted in the following risk factors which were significantly associated with risk of colonic perforation: age, gender, BMI, albumin level, ICU patients, inpatient setting, and abdominal pain and Crohn's disease as indications for colonoscopy. Approximately 21% of the patients did not have an albumin laboratory result available for analysis. Therefore, a model was fit with and without including albumin. Also, based on the descriptive results albumin was categorized at 4.0. The estimates from the final models are displayed in Table 3.

DISCUSSION

In reviewing literature from 1975 onward, we observed that the incidence rate of colonic perforation ranges between 0.005% to 0.63%. We noticed a gradual decline in the incidence of colonic perforation which has reached a plateau in the last 10 years. The differences in the incidence rates in this study compared to those in the literature can possibly be attributed to the way the studies were conducted. For example Sieg *et al.*¹⁶ and Rathgeber *et al.*¹⁷ both reported low incidence rate of perforation (0.005 and 0.01 respectively). Sieg *et al.*¹⁶ looked prospectively at 82, 16 colonoscopies but there was a selection

Table 2 Incidence of 7-d colonic perforation risk by important risk factors

Patient variable	Frequency	Perforations	Incidence per 10000	Incident rate ratio (95%CI)
Total	80118	50	6.2	-
Age (yr)				1.07 ¹ (1.05, 1.09)
18-49	13703	5	3.6	
50-64	38705	10	2.6	
65-79	22974	20	8.7	
80+	4736	15	31.7	
Gender				
Female	41121	34	8.3	-
Male	38988	16	4.1	0.50 (0.27, 0.90)
BMI (kg/m ²)				0.91 ¹ (0.86, 0.96)
< 24 (normal weight)	18019	21	11.7	
25-29 (overweight)	26873	17	6.3	
30+ (obese)	30873	10	3.2	
Type of Colonoscopy				
Therapeutic	37880	13	3.4	-
Screening	29901	3	1.0	0.29 (0.08, 1.03)
Diagnostic	12336	33	26.8	7.79 (4.10, 14.80)
Albumin result (percentile cut-offs)				0.15 ¹ (0.12, 0.20)
≤ 4.0	16537	36	21.8	7.76 (4.12, 14.64)
> 4.1	46366	13	2.8	-
ICU patients	94	9	957.4	186.9 (93.5, 373.5)
Non-ICU patients	80024	41	5.1	-
Inpatients	4155	23	55.4	15.6 (8.9, 27.1)
Outpatients	75963	27	3.6	-
Indications for CP				
Abdominal pain				3.4
Yes	3630	7	19.3	(1.5, 7.6)
No	76488	43	5.6	-
Anemia				4.6
Yes	1880	5	26.6	(1.8, 11.6)
No	78238	45	5.8	-
Bleeding				3.4
Yes	3622	7	19.3	(1.5, 7.6)
No	76496	43	5.6	-
Crohn's disease				
Yes	331	2	60.4	10.0
No	79787	48	6	(2.5, 41.2)

¹Variable was treated as continuous in the estimation of the incident rate ratio. ICU: Intensive care unit; CP: Cerebral palsy; BMI: Body mass index.

bias since only perforations that required surgical intervention were included in the study. Similarly, Rathgaber and Wick's study of 12407 colonoscopies, complications were gathered by monthly retrospective review of all hospitalizations and patient phone calls. Anderson *et al*^[18] reported an incidence 0.19% in 10486 colonoscopies and Gatto *et al*^[13] found 0.196% in 39286 colonoscopies. Both studies primarily looked at an older patient population which may have contributed to the higher rate of colonoscopic perforations.

This study looked at patients 18 years or older. By

Table 3 Multivariate log-binomial regression results predicting 7-d post colonoscopic perforation

Risk factor	Model without albumin	Model with albumin
Age	1.04 (1.01, 1.06)	1.03 (1.01, 1.05)
BMI	0.96 (0.91, 1.00)	0.94 (0.90, 0.99)
ICU	9.37 (4.42, 19.88)	5.83 (2.80, 12.14)
Inpatient	18.08 (8.58, 38.17)	11.05 (5.14, 23.75)
Type of colonoscopy		
Therapeutic	-	-
Screening	0.25 (0.07, 0.87)	0.17 (0.04, 0.76)
Diagnostic	12.93 (6.65, 25.13)	15.33 (7.79, 30.18)
Abdominal pain	5.32 (2.40, 11.82)	5.79 (2.64, 12.74)
Crohn's disease	11.26 (3.88, 32.70)	5.16 (1.79, 14.88)
Albumin (≤ 4.0)	-	3.58 (1.72, 7.47)

BMI: Body mass index; ICU: Intensive care unit.

including a wider range of patients, the current findings are likely to be more representative of the true incidence of perforation. We found that age greater than 65 years was a significant predictor for risk of perforation. This finding is in congruence with other studies^[12-14,19] that found increased age as an independent risk factor for perforation.

We found that the female gender is predisposed to a higher risk of perforation as compared to the male gender. Anderson *et al*^[18] and Korman *et al*^[12] also found female gender to be an independent risk factor for perforation. In contrast, Arora *et al*^[19] did not find female gender as a significant risk factor for perforation in 277434 colonoscopies.

We found lower BMI to be another statistically significant predictor of perforation. Literature on the relation between BMI and risk of colonic perforation is sparse. Takahashi *et al*^[20] postulated lower BMI as a predictor of pain and difficult colonic intubation during colonoscopy. Patients with low BMI may have sharper angulation of the sigmoid colon which theoretically can predispose these patients to a higher chance of mechanical injury during colonoscopy.

Increasing number of comorbidities resulted in increased risk of colonic perforation. Our findings are in congruence with other studies Gatto *et al*^[13] and Arora *et al*^[19] that demonstrated an increased risk of perforation with two or more co-morbidities.

Imai *et al*^[21] studied the risk of perforation in patients with ESRD on hemodialysis (HD) undergoing colonoscopy. The study looked at 1106 HD patients and 13992 controls, and the authors found a higher risk of perforation among HD patients. Our study looked at patients with ESRD on hemodialysis, and also at patients with chronic kidney disease who were not on HD. There were no perforations among the 321 patients with ESRD in our cohort. We did not find any statistically significant relationship with increasing creatinine level and risk of perforation.

Low albumin has been shown to be a predictor for failure to complete colonoscopy^[22]. Hypoalbuminemia is

a well-documented marker of morbidity and is a strong predictor of mortality in elderly patients^[22,23]. We found low albumin level to be associated with a higher risk for perforation. It is possible that a low albumin may decrease the tensile strength of the colonic wall and also generally indicates poor health status that can theoretically predispose to higher risk for perforation.

We did not find any significant difference in the rate of perforation between colonoscopies performed by gastroenterologists or surgeons. This is in congruence with a prospective study of 13580 colonoscopies done by surgeons Wexner *et al.*^[24], which found that colonoscopy performed by surgeons are safe with low morbidity and mortality.

We did not find performance of biopsy or polypectomy as significant risk factors for perforation. Similar findings were noted by Arora *et al.*^[19], but are in contrast to Levin *et al.*^[4] and Misra *et al.*^[25] who found increased risk of perforation after polypectomy. We found that the performance of invasive procedures such as foreign body removal, hemostasis increase the risk of perforation, similar findings were noted by Arora *et al.*^[19]. We also found dilation as a significant risk factor for perforation in our cohort.

A potential limitation of this study is the validity of coding and capturing of all perforations. We used ICD-9 and CPT codes to capture perforations and co-morbidities. It is possible that we may have missed perforations due to incorrect coding. Also, if a patient went outside of our health care system, then some perforations would not have been reported and thus, not identified. Therefore, underestimation of the incidence of perforation is possible in this study.

In conclusion, the cumulative 7 d incidence of colonic perforation in this cohort was 0.06%. Advanced age and female gender were significantly more likely to have perforation. Increasing albumin and BMI resulted in decreased risk of colonic perforation. Having a colonoscopy indication of abdominal pain or Crohn's disease resulted in a higher risk of colonic perforation. Colonoscopies performed in inpatients and particularly the ICU setting had substantially greater odds of perforation. Biopsy and polypectomy did not increase the risk of perforation and only three perforations occurred with screening colonoscopy.

The increased risk of perforation during inpatient colonoscopy among the elderly and very elderly (> 80 years), and ICU patients is not inconsequential. On the basis of this data, we have restricted inexperienced operators (such as first year gastroenterology fellows) from performing these types of cases. Additionally those over 80 years referred for diagnostic colonoscopy should also be advised of their increased risk of perforation. By understanding which patient populations are at greatest risk for colonoscopic perforation, considering available alternatives, and adjusting patient selection criteria balancing for those at highest risk, may help to reduce the number of colonoscopic perforations.

COMMENTS

Background

This study is unique because we have used state of the art electronic medical records to collect information about risk factors which can predispose patient to a high risk of perforation. The authors have looked into multiple risk factors including but not limited to serum albumin, serum creatinine, body mass index (BMI), inpatient and outpatient colonoscopy and intensive care unit patients. Limited literature is available about the above mentioned risk factors and there propensity to cause perforation. The important findings deduced from this research can have important implication in day to day practice of colonoscopy.

Research frontiers

Authors found lower BMI to be another statistically significant predictor of perforation. Literature on the relation between BMI and risk of colonic perforation is sparse. Yuuichi postulated lower BMI as a predictor of pain and difficult colonic intubation during colonoscopy. Patients with low BMI may have sharper angulation of the sigmoid colon which theoretically can predispose these patients to a higher chance of mechanical injury during colonoscopy.

Innovations and breakthroughs

This was a retrospective cross-sectional study. Patients were retrospectively eligible for inclusion if they were 18 years and older and had an inpatient or outpatient colonoscopy procedure code in any facility within the Geisinger Health System during the period from January 1, 2002 to August 25, 2010. Data are presented as median and inter-quartile range, for continuous variables, and as frequency and percentage for categorical variables.

Peer review

This is an interesting paper on a clinically important topic and with good numbers. By understanding which patient populations are at greatest risk for colonoscopic perforation, considering available alternatives, and adjusting patient selection criteria balancing for those at highest risk, may help to reduce the number of colonoscopic perforations.

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