Risk of perforation from a colonoscopy in adults: a large population-based study

Gaurav Arora, MD, Ajitha Mannalithara, PhD, Gurkirpal Singh, MD, Lauren B. Gerson, MD, MS, George Triadafilopoulos, MD

Stanford, California, USA

Background: Previous studies that reported the incidence of perforation from a colonoscopy are limited by small sample sizes, restricted age groups, or single-center data.

Objective: To determine the incidence and risk factors of colonic perforation from a colonoscopy in a large population cohort.

Design: Retrospective, population-based, cohort study, followed by a nested case-control study.

Setting: California Medicaid program claims database.

Patients: A total of 277,434 patients (aged 18 years and older) who underwent a colonoscopy during 1995 to 2005, age, sex, and time matched to 4 unique general-population controls.

Main Outcome Measurements: Perforation incidence in the 7 days after colonoscopy (or matched index date for controls) with odds ratio (OR); multivariate logistic regression to calculate adjusted ORs for subsequent analysis of risk factors.

Results: A total of 228 perforations were diagnosed after 277,434 colonoscopies, which corresponded to a cumulative 7-day incidence of 0.082%. The OR of getting a perforation from a colonoscopy compared with matched controls (n = 1,072,723) who did not undergo a colonoscopy was 27.6 (95% CI, 19.04-39.92), $P < .001$. On multivariate analysis, when comparing the group that had a perforation after a colonoscopy (n = 216) with those who did not (n = 269,496), increasing age, significant comorbidity, obstruction as an indication for the colonoscopy, and performance of invasive interventions during colonoscopy were significant positive predictors. Performance of biopsy or polypectomy did not affect the perforation risk. The rate of perforation did not change significantly over time.

Limitations: Validity of coding and capturing of all perforation diagnoses may possibly be deficient.

Conclusion: The risk of perforation from a colonoscopy is low, but, despite increased experience with the procedure, it remains unchanged over time. (Gastrointest Endosc 2009;69:654-64.)

Abbreviations: CPT, Current Procedural Terminology; FFS, Fee-For-Service; ICD-9, International Classification of Diseases, 9th revision; Medi-Cal, California Medicaid; OR, odds ratio.

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Ever since its introduction 4 decades ago, colonoscopy has played an important role as a diagnostic, therapeutic, and screening tool. One of its major roles is in the detection of colorectal carcinoma, currently the third most commonly diagnosed cancer in men and women, and the second leading cause of death attributable to cancer in the United States.[1] Screening has been shown to reduce the incidence of, and mortality from, colorectal cancer, and colonoscopy is being increasingly recommended by many experts as the initial screening method.[2] Beginning in July 2001, Medicare covered screening colonoscopy for individuals over age 50 years at average risk for colorectal

cancer and, when depending on the detection of polyps, at variable intervals thereafter, and, ever since, the use of colonoscopy has been increasing.[3-5] However, screening rates still remain low, and it is estimated that only half of the eligible population actually get screened.[4] It, therefore, is likely that the number of colonoscopies performed annually will continue to increase.

In general, colonoscopy is regarded as a safe procedure, but complications may occur. The most dreaded of these is colonic perforation. An estimated 50% to 100% of patients with a colonic perforation after colonoscopy require a laparotomy for closure of the perforation, with associated major postoperative morbidity and mortality reaching 39% and 25%, respectively.[6-10] The associated hospitalization and health care utilization costs are a significant additional burden on the health care system. In the past 3 decades, many studies have been done to ascertain the risk of colonic perforation from a colonoscopy. However, most of these studies were limited by small sample sizes, single center and/or practice data, or restricted age groups' analysis, not to mention strict inclusion criteria used in many, thus limiting their generalizability. Not surprisingly then, the rates of perforation varied widely, from 0.005% to 0.63% (Table 1).[6-45] Although currently low, the incidence of perforation has the potential to become a significant public health problem given the large and increasing absolute number of colonoscopies performed every year. In this study, we analyzed a large general population cohort to assess the risk magnitude and to characterize the associated risk factors of screening, diagnostic, or therapeutic colonoscopy.

Capsule Summary

What is already known on this topic

- Colonic perforation during colonoscopy increases morbidity and mortality, as well as hospitalization and health care utilization costs.

What this study adds to our knowledge

- In a retrospective, Medicaid population-based cohort study of 277,434 patients who underwent colonoscopy, the risk of colonic perforation was low and unaffected by performance of biopsy or polypectomy.
- Positive predictors for perforation were increasing age, comorbidity, obstruction as indication for colonoscopy, and performance of invasive interventions.

PATIENTS AND METHODS

Database

The present study is based on longitudinal data derived from Medi-Cal, the Medicaid program for the state of California.[46] The Medi-Cal program serves more than 6.5 million beneficiaries, of whom approximately 3.1 million (48%) are in the Fee-For-Service (FFS) system, whereas the remainder are enrolled in managed care plans.[47] In 1994, 86% of the Medi-Cal beneficiaries received their care via the FFS program; this decreased to just over 50% in 2001 and has continued at that level thereafter.[47,48] Medi-Cal provides comprehensive health care coverage for ethnically diverse, low-income, and disabled individuals who lack health insurance. The Medi-Cal database contains computerized records of eligibility status of all beneficiaries and detailed information on all medical services provided, including outpatient visits, hospital admissions, medical procedures, emergency department visits, laboratory and radiologic testing, and outpatient drug prescriptions, including many over-the-counter drugs, eg, aspirin.[47] Because there is no requirement for premiums or copayments, participation in the program is virtually 100%. All physicians contracted with Medi-Cal who perform colonoscopy are paid on a FFS basis. Hence, reporting of colonoscopy is expected to be comprehensive and complete, because physicians would not be paid unless the claim for the colonoscopy visit is submitted. In addition, because of the presence of a fiscal intermediary, FFS data were shown to be complete and valid.[47] We, therefore, limited our study to the FFS claims only. Because of the completeness of reporting, we believe it is highly unlikely that a significant postprocedural complication, such as a colonic perforation, would be missed. A recently published audit of Medi-Cal claims found that 96.4% were medically necessary, were billed appropriately, and were in concordance with the data in the claims files.[47]

Study cohort, design, and setting

We identified all patients 18 years or older enrolled in the Medi-Cal program during the period from January 1, 1995, to June 30, 2005. Colonoscopy procedures were identified by the presence of Current Procedural Terminology 2005 (CPT) codes (45378-45387, 45391, and 45392) (Table 2). There were 2 parts to our study. The first part consisted of assessing the incidence of perforation in the 7-day period after a colonoscopy and comparing the odds of this outcome with a control cohort from the same study population that did not undergo a colonoscopy. This was done to evaluate the comparative risk of getting a perforation from a colonoscopy as factors other than a colonoscopy, eg, inflammatory bowel disease and collagen vascular diseases have been reported in the literature to have caused spontaneous colonic perforation. The exposed cohort was composed of patients who had at least one colonoscopy. Only one colonoscopy (the first) was studied per patient. Potential patients were excluded if they were not enrolled in Medi-Cal continuously for the 7 days after their date of first colonoscopy (index date). For every case, we randomly selected 4 unique controls from individuals under observation in the database on

TABLE 1. Published perforation rates from a colonoscopy

Study	Publication year	No. colonoscopies	Perforation rate (%)
Smith and Nivatvongs[38]	1975	7959	0.264
Rogers et al[35]	1975	31,512	0.054
Smith[37]	1976	20,139	0.358
Fruhmorgen and Demling[20]	1979	35,892	0.217
Macrae et al[29]	1983	5000	0.12
Vincent and Smith[42]	1983	1547	0.388
Brynitz et al[14]	1986	1748	0.629
Reiertsen et al[34]	1987	4593	0.152
Carpio et al[15]	1989	5424	0.258
Soon et al[39]	1990	1832	0.38
Christie and Marrazzo[16]	1991	4784	0.15
Hall et al[24]	1991	17,500	0.086
Luchette et al[28]	1992	4593	0.588
Reed et al[33]	1992	1025	0.1
Waye et al[43]	1992	2097	0.095
Mandel et al[30]	1993	12,246	0.033
Jentschura et al[8]	1994	8390	0.191
Lo and Beaton[7]	1994	26,708	0.045
Foliente et al[19]	1996	6684	0.22
Gedebou et al[23]	1996	9106	0.2
Farley et al[6]	1997	57,028	0.075
Basson et al[12]	1998	5163	0.058
Wexner et al[44]	1998	2069	0.145
Anderson et al[11]	2000	10,486	0.19
Wexner et al[45]	2001	13,580	0.074
Araghizadeh et al[9]	2001	34,620	0.089
Dafnis et al[18]	2001	6066	0.1
Tran et al[40]	2001	26,162	0.08
Sieg et al[36]	2001	82,416	0.005
Kirchgatterer et al[25]	2002	781	0.128
Korman et al[26]	2003	116,000	0.032
Gatto et al[22]	2003	39,286	0.196
Biandrate et al[13]	2003	7358	0.081
Misra et al[31]	2004	7425	0.13
Cobb et al[17]	2004	43,609	0.032
Iqbal et al[10]	2005	78,702	0.084
Tulchinsky et al[41]	2006	12,067	0.058
Levin et al[27]	2006	16,318	0.09
Rathgaber and Wick[32]	2006	12,407	0.016
Garcia Martinez et al[21]	2007	16,285	0.092

(*continued on next page*)

TABLE 1 (*continued*)

the index date and matched them for age and sex to form the control cohort. All controls were required to be enrolled in Medi-Cal continuously for at least 7 days before and after the index date. The study outcome was the incident diagnosis of colonic perforation (physician diagnosis with 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), during the 7 days after the date of colonoscopy or the index date for matched controls. We restricted the follow-up time to 7 days, because it was shown that almost all the perforations that occur secondary to a colonoscopy are detected within 7 days.[22,27]

The second part of our analysis consisted of assessing risk factors within the above-exposed cohort for colonic perforation from a colonoscopy. These were patients who had at least one colonoscopy and had continuous eligibility in Medi-Cal for at least 3 months before and 7 days after the date of their first colonoscopy. The group that had a colonoscopy and a perforation was compared

TABLE 2. ICD-9 CM and CPT (2005) codes used for identifying indication for colonoscopy and the type of colonoscopy performed

Indication	ICD-9 CM codes
Abdominal pain	789.0, 787.9, 787.99, 789.00, 789.01, 789.02, 789.03, 789.04, 789.05, 789.06, 789.07, 789.09, 789.60, 789.61, 789.62, 789.63, 789.64, 789.65, 789.66, 789.67, 789.69
Anemia	280, 280.0, 280.1, 280.8, 280.9, V78.0, 285.9, 281, 281.9, 285, 285.1, 285.8
Bleeding (hemorrhage)	578, 578.0, 578.1, 578.9, 792.1
Crohn's disease	555, 555.0, 555.1, 555.2, 555.9
Diarrhea	787.91, 558.9
Diverticulosis of colon	562.10, 562.12, 562, 562.1, 562.11, 562.13
Obstruction	560, 560.0, 560.1, 560.2, 560.30, 560.9, 560.3, 560.39, 560.8, 560.81, 560.89
Ulcerative colitis	556, 556.1, 556.2, 556.3, 556.4, 556.5, 556.6, 556.8, 556.9, 556.0, 558.1, 558.2, 558.9
Weight loss	783.21, 783.2
Screening/ other	None of the above codes
Type of colonoscopy	**CPT codes**
Screening/ diagnostic	45378
With biopsy	45380
With polypectomy	45383, 45384, 45385
With dilation	45386, 45387
With "other" procedures*	45379, 45381, 45382, 45391, 45392

*Includes foreign-body removal, submucosal injection, hemostasis, EUS, and transmural or intramural aspiration and/or biopsy.

with the group that had a colonoscopy but no perforation during the study period. We classified the reason for colonoscopy by identification of the ICD-9 codes shown in Table 2 in the 3-month period immediately preceding the date of colonoscopy. The performance of any procedure, eg, biopsy, polypectomy, dilation, hemostasis, during the colonoscopy was identified by the presence of appropriate CPT codes (Table 2). A modified Charlson's comorbidity score[49] was calculated for each patient based on a 3-month observation period before the date of the colonoscopy. The outcome of interest was colonic perforation in the 0-day to 7-day period after the colonoscopy date.

Statistical analysis

All incidence rates were calculated per 100,000 colonoscopies. CIs for the incidence rates were calculated by using exact Poisson distributions. Odds ratios (OR) were calculated to estimate the risk for perforation from a colonoscopy in the exposed versus the unexposed group. Initial univariate analyses were followed by a multivariate logistic regression to study the effect of covariates: age, sex, race or ethnicity, year of colonoscopy, specialty of the operator, procedures performed during colonoscopy, indication for the colonoscopy, and the Charlson comorbidity score. These were selected based on prior published literature. Because several patients had more than one diagnosis as an indication for colonoscopy, we used the following hierarchy to assign one diagnosis per colonoscopy: obstruction, inflammatory bowel disease, hemorrhage, diverticulosis of the colon, diarrhea, anemia, abdominal pain, weight loss, and screening. Only variables that were statistically significant in the initial multivariate model were included in the final model. Adjusted ORs were calculated in each instance, and their CIs were derived by using the modified Wald method. Because the number of strata from matching was small relative to the overall sample size, it was not necessary to analyze those data with conditional logistic regression analysis techniques. Rather, unconditional logistic regression was used throughout. All calculated *P* values were 2 sided. Statistical significance was set at an alpha level of less than or equal to .05. Trend analysis was done by using the Cochran-Armitage test.[50] No correction of *P* values for multiple statistical testing performed on data arising from individual patients was made. This is because the *P* values and ORs from the final multivariate logistic regression analysis were considered definitive, because they described factors independently associated with perforation after adjusting for the contributions of the other variables. Other *P* values and statistical results should be taken as descriptive. All the above analyses were performed by using Statistical Analysis Software version 9.1.3 (SAS Institute, Cary, NC).

RESULTS

Perforation rate and analysis of risk compared with general population controls

A total of 277,434 individuals (exposed cohort) met the 7-day continuous eligibility criterion (after excluding 241 patients who did not). The corresponding number in the control cohort was 1,072,723. The mean (SD) age was comparable in the exposed and control cohorts, at 64.20 ± 14.80 years (range 18-107.8 years) and 63.97 ± 14.99 years (range 18-107.9 years), respectively. Among the respective demographic groups (Table 3), women, people aged 65 to 80 years, and whites accounted for the majority of colonoscopies performed. The number

TABLE 3. Incidence and risk of perforations from a colonoscopy compared with matched controls in the 7-day eligibility cohort

	Exposed cohort			Control cohort			Estimate of relative risk	
Group	Frequency	No. perforations	Incidence per 100,000	Frequency	No. perforations	Incidence per 100,000	Odds Ratio (95% CI)	*P* value
Total	277,434	228	82	1072,723	32	3	27.57 (19.04-39.92)	<.001
Age								
18-50 y	49,678	33	66	198,711	5	3	26.42 (10.31-67.67)	<.001
50-65 y	74,235	53	71	293,784	10	3	20.99 (10.68-41.26)	<.001
65-80 y	118,294	100	85	439,727	15	3	24.80 (14.41-42.68)	<.001
≥80 y	35,227	42	119	140,501	2	1	83.86 (20.30-346.43)	<.001
Sex								
Women	175,816	138	78	671,143	25	4	21.09 (13.77-32.29)	<.001
Men	101,618	90	89	401,580	7	2	50.85 (23.57-109.73)	<.001
Race								
White	108,946	105	96	392,713	11	3	34.44 (18.51-64.10)	<.001
African American	26,824	15	56	102,008	2	2	28.54 (6.53-124.79)	<.001
Hispanic	48,365	34	70	235,071	5	2	33.07 (12.93-84.57)	<.001
Other*	93,299	74	79	342,931	14	4	19.44 (10.98-34.42)	<.001

*Includes Asian, Native American, other, and unknown.

of colonoscopies performed annually increased during the study period (Table 4). A total of 228 perforations were diagnosed in the exposed cohort, which corresponded to a 7-day cumulative incidence of 0.082% or 82 (95% CI, 65-102) per 100,000 colonoscopies. In the control cohort, 32 (3/100,000) perforations were diagnosed, with an incidence of 0.003%, which yielded an OR of 27.6 (95% CI, 19.04-39.92). Patients aged 80 years or older had a much higher incidence (119/100,000 [95% CI, 99-142]) of a perforation from a colonoscopy compared with younger age groups. When patients aged 65 years or older were compared with those younger than 65 years, the former were found to have a higher incidence (92 vs 69 per 100,000) and risk (unadjusted OR 1.33 [95% CI, 1.02-1.74], $P = .03$) of a perforation. Among the 32 subjects in the control cohort who experienced a ''spontaneous'' perforation, the mean (SD) age was 64.90 ± 11.22 years and 25 (78%) were women. Most of these subjects were in the 50 to 80 years old age group (78%). The following diagnoses were apparent in the 7 days before their index date: abdominal pain (5), obstruction (2), and ulcerative colitis (1). However, the diagnosis was missing in most of these subjects (75%) because of the short period assessed for this. Based on the demographics, these controls are as equally likely to undergo a colonoscopy, if indicated, as are the exposed cohort.

Analysis of risk factors associated with perforation from a colonoscopy

A total of 269,712 individuals fulfilled the 3-month continuous eligibility criterion for this analysis after excluding 7722 who did not. The incidence rates in the various demographic and clinical subgroups from the univariate analysis are shown in Table 4. The incidence of perforation increased after age 65 years, with a significant overall trend between the various subgroups ($P_{trend} = .016$). Men had a slightly higher incidence of perforation compared with women. Whites had a higher incidence of perforation compared with African Americans. The perforation rate remained the same during the study period, from 1995 to mid 2005 ($P_{trend} < .213$) (Fig. 1), even though the number of colonoscopies performed annually increased during the same period (Table 4). Performance of a biopsy or polypectomy did not significantly alter the incidence of a perforation compared with no intervention. However, as expected, performance of invasive procedures, such as foreign-body removal, submucosal injection, hemostasis, EUS, and transmural or intramural aspiration or biopsy collectively resulted in a significantly higher incidence of perforation. We did not find any perforations in the much smaller group that underwent a colonic dilation.

When the specialty of the practitioner performing the colonoscopy was considered, surgeons had a higher and

TABLE 4. Incidence of perforation from a colonoscopy in the 3-month eligibility cohort

	No. colonoscopies (%) (N = 269,712)	No. perforations (N = 216)	Incidence per 100,000 colonoscopies (95% CI) (overall = 80 [95% CI 63-100])*
Age			
18-50 y	47,254 (17.5)	32	68 (53-86)
50-65 y	72,152 (26.7)	49	68 (53-86)
65-80 y	115,565 (42.8)	95	82 (65-102)
≥80 y	34,741 (12.9)	40	115 (95-138)
			P_{trend} = .016
Sex			
Women	171,733 (63.7)	132	77 (61-96)
Men	97,979 (36.3)	84	86 (69-106)
Race			
White	105,910 (39.3)	100	94 (76-115)
African American	26,314 (9.7)	15	57 (43-74)
Hispanic	46,603 (17.3)	31	67 (52-85)
Other†	90,885 (33.7)	70	77 (61-96)
Year			
1995	16,589 (6.1)	15	90 (72-111)
1996	22,444 (8.3)	18	80 (63-100)
1997	24,256 (9.0)	30	124 (103-148)
1998	19,037 (7.0)	13	68 (53-86)
1999	22,293 (8.3)	16	72 (56-91)
2000	24,946 (9.2)	21	84 (67-104)
2001	28,272 (10.5)	14	50 (37-66)
2002	33,033 (12.2)	29	88 (71-108)
2003	34,687 (12.9)	27	78 (62-97)
2004	30,663 (11.4)	27	88 (71-108)
2005‡	13,492 (5.0)	6	44 (40-59)
			P_{trend} = .213
Procedure during colonoscopy			
None	122,533 (45.4)	88	72 (56-91)
Biopsy	66,007 (24.3)	57	86 (69-106)
Polypectomy	79,063 (29.3)	61	77 (61-96)
Dilation	33 (0.01)	0	–
Other§	2076 (0.8)	10	482 (440-527)
Operator specialty			
Gastroenterologist	121,653 (45.1)	115	95 (77-116)

(*continued on next page*)

TABLE 4 (*continued*)

	No. colonoscopies (%) (N = 269,712)	No. perforations (N = 216)	Incidence per 100,000 colonoscopies (95% CI) (overall = 80 [95% CI 63-100])*
Surgeon‖	12,785 (4.7)	16	125 (104-149)
Primary care¶	72,228 (26.8)	49	68 (53-86)
Other#	63,046 (23.4)	36	57 (43-74)
Charlson comorbidity score			
0	142,195 (52.7)	95	67 (52-85)
1	62,367 (23.1)	44	71 (55-90)
≥2	65,150 (24.2)	77	118 (98-141)
Indication**			
Obstruction	9095 (3.4)	34	374 (337-414)
Inflammatory bowel disease	38,184 (14.2)	23	60 (46-77)
Bleeding (hemorrhage)	56,693 (21.0)	41	72 (56-91)
Diverticulosis of colon (+/−hemorrhage)	49,366 (18.3)	36	73 (57-92)
Diarrhea	6749 (2.5)	7	104 (85-126)
Anemia	18,698 (6.9)	18	96 (78-117)
Abdominal pain	31,321 (11.6)	17	54 (41-70)
Weight loss	1149 (0.4)	1	87 (70-107)
Screening	58,457 (21.7)	39	67 (52-85)

*Incidence, no. perforations per 100,000 colonoscopies.
†Includes Asian, Native American, other, and unknown.
‡Data are for half the year of 2005.
§Includes foreign-body removal, submucosal injection, hemostasis, EUS, and transmural or intramural aspiration or biopsy.
‖Includes general surgeons and colorectal surgeons.
¶Includes primary care, family practice, and preventive medicine.
#Includes other and unknown subspecialty.
**The indications are arranged according to the hierarchical order described in the Patients and Methods section.

primary care and ''other'' physicians had a lower incidence of perforation when compared with a gastroenterologist. A Charlson comorbidity score of 2 or more was associated with a significantly higher perforation rate. The distribution of patients in each Charlson score category was similar when considered according to the operator specialty (a score of ≥2 in 25% of gastroenterologists' patients, 21% of surgeons, 25% of primary care, and 22% of other physicians). Likewise, the distribution of indication for colonoscopy was similar across the different specialties of colonoscopy operators (data available but not included), except that ''other'' physicians performed more screening colonoscopies than gastroenterologists (31% vs 18%).

When classified on the basis of predefined criteria for finding the indication for the colonoscopy, almost 22% of all colonoscopies were found to be for screening (or other). Other common indications for the procedure were hemorrhage (21%), diverticulosis (18%), inflammatory bowel disease (14%), abdominal pain (12%), and anemia (7%). Obstruction, diarrhea, and weight loss accounted for the remainder. The identification of obstruction as an indication for a colonoscopy was associated with a much higher incidence of perforation (374 per 100,000) when compared with screening (67 per 100,000) or all causes other than screening and obstruction (71 per 100,000).

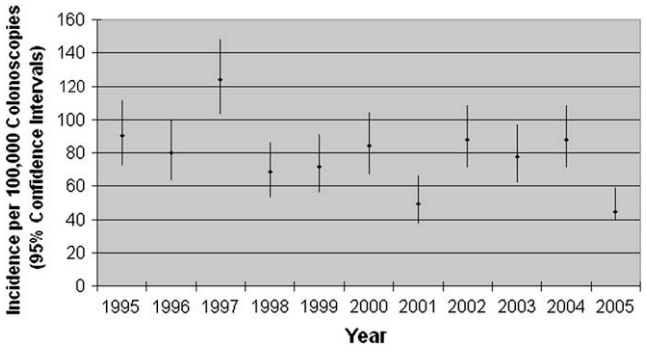

Figure 1. Secular trend in incidence of perforation from a colonoscopy.

The risk of perforation after adjusting for all other covariates, as determined by the multivariate analysis, is described in Table 5. Race and year of colonoscopy were excluded from the final model, because they were found not to affect the outcome in the initial multivariate model. Diarrhea and anemia, although associated with a higher incidence of a perforation in the univariate analysis, were not found to be significant in the multivariate analysis and were thus included only in the category of ''nonobstruction'' in the final model. Age, modeled as a continuous variable, was found to be a significant predictor of perforation from a colonoscopy, with the risk increasing 1% per year increase in age (OR 1.01 [95% CI, 1.00-1.02], $P = .007$). Men were not found to be at a higher risk of perforation compared with women. A Charlson score of 2 or more was found to increase the risk of perforation by more than 50% (OR 1.52; 95% CI, 1.12-2.06; $P = .007$) compared with those with a score of 0 (ie, no significant comorbidity). The adjusted OR for obstruction was 5.09 (95% CI, 3.17-8.20; $P < .001$), thus indicating a more than 5-fold associated risk when compared with that of a screening colonoscopy. None of the other indications were associated with an increased risk when collectively compared with screening ($P = .830$). After adjusting for all other confounding variables, the risk of perforation was more than 6 times higher with invasive procedures (''other'') compared with no procedure. No increased risk of a perforation was found with performance of a biopsy or polypectomy during the colonoscopy. The adjusted risk of perforation was not significantly different for surgeons when compared with gastroenterologists (OR 1.47 [95% CI, 0.87-2.49]), but, when compared with the latter, colonoscopy performed by primary care physicians (OR 0.71; 95% CI, 0.51-0.99) and ''other physicians'' (OR 0.64; 95% CI, 0.44-0.93) revealed a lower risk of perforation.

TABLE 5. Multivariate analysis of risk factors for a perforation from a colonoscopy

	Adjusted OR (95% CI)*	*P* value
Age at colonoscopy	1.01 (1.00-1.02)†	.007
Sex		
Women	1 (referent)	
Men	1.09 (0.83-1.44)	.533
Charlson comorbidity score		
0	1 (referent)	–
1	0.99 (0.69-1.42)	0.959
≥2	1.52 (1.12-2.06)	.007
Indication		
Screening	1 (referent)	–
Nonobstruction	1.04 (0.72-1.50)	.830
Obstruction	5.09 (3.17-8.20)	<.001
Procedure during colonoscopy		
None	1 (referent)	–
Biopsy	1.20 (0.86-1.68)	.285
Polypectomy	1.10 (0.79-1.54)	.562
Dilation	n/a	n/a
Other‡	6.12 (3.16-11.83)	<.001
Operator specialty		
Gastroenterologist	1 (referent)	–
Surgeon§	1.47 (0.87-2.49)	.149
Primary care‖	0.71 (0.51-0.99)	.049
Other¶	0.64 (0.44-0.93)	.019

n/a, Not available.
*Adjusted for all other covariates in this table.
†ORs for age indicate the multiplicative factor per year of increasing age.
‡Includes foreign-body removal, submucosal injection, hemostasis, EUS, transmural or intramural aspiration or biopsy.
§Includes general surgeons and colorectal surgeons.
‖Includes primary care, family practice, and preventive medicine.
¶Includes other and unknown subspecialty.

DISCUSSION

Recent large studies showed perforation rates between 0.016% and 0.090%, depending on the center and the data source. Of note, 3 studies found perforation rates outside of this range. By using a mailed questionnaire, Sieg et al,[36] prospectively evaluated 82,416 colonoscopies and found a low incidence of 0.005%. This could likely be explained by a selection bias because the physicians' self reported the perforations; also, only those perforations that required a surgical intervention were included in the study. Anderson et al[11] and Gatto et al[22] reported higher perforation rates of 0.190% and 0.196% in 10,486 and 39,286 colonoscopies, respectively. It is likely that such rates were driven by the older age of their study

populations (mean age 72 years and 74 years, respectively), especially given our finding that increasing age is a significant predictor of this outcome.

Age was shown as a risk factor for perforation in people over 60 years of age (5 times higher risk) by Levin et al,[27] in a series of more than 16,000 colonoscopies. Gatto et al,[22] also reported that there was a significant trend in the incidence of perforation with increasing age and that people aged 75 years or older were 4 times more likely than those aged 65 to 69 years to have a perforation. A study by Arora and Singh[51] did not find a difference in the risk between patients aged over 80 years old versus less than 80 years; however, that study involved a small sample size (924 colonoscopies). Our finding of a substantially higher risk of a perforation in the very elderly (aged $\geq$80 years) merits attention, especially given the finding from a recent study that showed that screening colonoscopy in this age group results in only 15% of the expected gain in life expectancy for those patients.[52] Female sex was not found to be a risk factor in our study. This is in contrast to the findings of Anderson et al,[11] who, in a series of 10,486 colonoscopies, reported that sex was an independent risk factor for colonoscopic perforation. However, their sample size was much smaller than ours, and they did not control for many confounding variables, as we did. Korman et al[26] found an increased incidence of perforation in women. However, adjusted risk was not calculated in that study.

Three large studies addressed secular trends of the rate of perforation after colonoscopy. Gatto et al[22] found a trend for a decreasing rate during 1991 to 1998 in 39,286 colonoscopies performed in a Medicare population. However, in 2 different studies from the Mayo Clinic, the rate of perforation did not change significantly over 2 decades (0.075% in 57,028 colonoscopies during 1980 to 1995 and 0.084% in 78,702 colonoscopies during 1994 to 2000).[6,10] The latter 2 studies included a wider age range and showed a similar perforation rate to ours (0.082% when calculated for 1980-2000). In our large population-based study of more than 277,000 individuals, we were unable to demonstrate a significant lowering of perforation rate from a colonoscopy over a decade (1995-2005). Overall, this trend is disturbing, because the complication rate of a procedure should decrease with time as cumulative experience increases. More studies are needed to evaluate this phenomenon, because it is not easily explainable by the presence of a learning curve, performance of a colonoscopy by trainees, or performance by inadequately trained endoscopists.

Comorbidity was shown by Gatto et al,[22] to significantly increase the adjusted risk of perforation from a colonoscopy. Instead of using the number of comorbidities as they did, we chose to use the comorbidity score, so that it would more accurately reflect the relative weight of the different comorbidities and found that a score of 2 or more increases the risk by 52%. Our study's finding, that performance of biopsy or polypectomy does not influence the adjusted risk of a perforation, is in contrast to some of the earlier studies with large sample sizes.[27,36] Levin et al[27] found a 90% higher risk in this context; however, they did not adjust for the presence of a comorbidity and less than 1% of their 16,318 colonoscopies were for screening, thereby making a true comparison difficult. Even though it makes biological sense, the notion that biopsy or polypectomy increases the risk of a perforation was not borne out in our study, which contains a sample size of more than a quarter of a million colonoscopies. As expected, invasive interventions during the colonoscopy imparted a much higher risk of perforation.

We found a slightly higher rate of perforation (0.125%) for surgeons than the one estimated by Wexner et al[45] (0.074%) in a series of 13,580 colonoscopies. However, when we adjusted for all significant confounding variables, there was no increased risk. The reasons for a lower rate and risk of perforation when a colonoscopy is performed by physicians other than gastroenterologists or surgeons are not entirely clear. It is possible that there exists a residual channeling bias whereby gastroenterologists or surgeons get the more technically demanding procedures and the relatively easier ones are performed by other practitioners. Miscoding of operator specialty is unlikely, because Medi-Cal claims data were found to have a high concordance rate.[47] Except for underlying colonic obstruction, which increased the risk of a perforation more than 5-fold, we did not find any other indication for colonoscopy as a risk predictor for perforation. Diverticulosis and abdominal pain were reported in prior studies as risk factors, but we did not find these to be significant.[22,26]

Spontaneous perforation of the colon was described in the literature in a variety of conditions, eg, Crohn's disease,[53,54] Ehlers-Danlos syndrome,[55] non-Hodgkin's lymphoma,[56] nonspecific colonic ulcers,[57] diverticulitis, and colorectal carcinoma. These reports were limited to either case reports and/or series or single center data. We showed the prevalence of this condition to be 3 per 100,000 at a population level, although the small absolute numbers preclude any definitive conclusions. Nevertheless, physicians who perform colonoscopies need to be aware of this potential pitfall.

There are several limitations to our study. Because our sample was derived from a Medicaid population, it represents data from people who typically are sicker and less affluent than their counterparts in the same geographical area. Consequently, there is a likelihood that our findings may overestimate the risk of perforation compared with the overall U.S. population. As with the use of any administrative database, the diagnosis of perforation and identification of comorbidity and indication for the procedure are dependent on the accuracy of coding procedures. Also, perforations that result from incomplete colonoscopies or colonoscopies billed as sigmoidoscopies would not be captured in our study, which possibly underestimated the perforation rate. However, as mentioned

earlier, Medi-Cal claims were found to have high accuracy.[47] It is possible that the controls (for the first part of our study) may not have been truly well matched, because the patients at highest risk for iatrogenic perforation were those with obstructive symptoms or those undergoing invasive interventions for colonic disease; however, we believe that the use of unconditional logistic regression to analyze those results may, at least in part, rectify that. We did not analyze prior surgery (abdominal, pelvic, or groin) as a risk factor for a perforation from a colonoscopy, which may increase the risk.[26] We could not determine with absolute confidence that the perforations were a consequence of the colonoscopy, and, thus, we limited the follow-up duration for the diagnosis of a perforation to 7 days. There is a possibility, albeit very small, that we could have missed some perforations as a consequence and, therefore, underestimated the perforation risk. The fraction of screening colonoscopies in our study was about 22% and may not be representative of many clinical settings where they account for a higher percentage of all colonoscopies performed.

Overall, our data reflect the largest population-based study to date on the incidence and risk of colonoscopic perforation. With broad inclusion criteria, these results are more likely to be representative of the current colonoscopic practices among the Medicaid patient population. In addition, because of no evidence that Medicaid status per se may be a risk factor for perforation from a colonoscopy and after adjustment for age, race, and comorbidity as we did, our findings may have good external validity to be generalizable to the U.S. population. Also, our study results should help physicians in making decisions regarding better selection of patients for colonoscopy and help public health officials in making policy decisions to hopefully reduce the incidence of perforation, the dreaded outcome of this increasingly used procedure.

In summary, our study showed the risk of perforation from a colonoscopy to be 82 per 100,000 (0.082%) and the odds of getting a perforation after colonoscopy compared with the general population not undergoing the procedure to be almost 28-fold. After adjusting for confounding variables, age at colonoscopy, significant comorbidity, obstruction as an indication for the colonoscopy and performance of invasive intervention during the colonoscopy were all significant positive predictors of the perforation risk. Patients' sex or race did not increase the risk. Other variables that did not lead to an increased risk of perforation were the year the colonoscopy was performed and the performance of a biopsy or polypectomy.

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Current affiliations: Division of Gastroenterology and Hepatology (G.A., G.S., L.B.G., G.T.), Stanford University School of Medicine, Stanford, Institute of Clinical Outcomes Research and Education (A.M., G.S.), Palo Alto, California, USA.

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Reprint requests: George Triadafilopoulos, MD, Division of Gastroenterology and Hepatology, Stanford University School of Medicine, Alway Bldg, Rm M-211, 300 Pasteur Dr, MC: 5187, Stanford, CA 94305-5187.

If you want to chat with an author of this article, you may contact him at vagt@stanford.edu.