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Risk factors for severe complications of colonoscopy in screening programs

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ABSTRACT

Severe complications (SC) in colonoscopy represent the most important adverse effect of colorectal cancer screening programs (CRCSP). The objective is to evaluate the risk factors for SC in colonoscopy indicated after a positive fecal occult blood test in population-based CRCSP. The SC (n = 161) identified from 48,730 diagnostic colonoscopies performed in a cohort of all the women and men invited from 2000 to 2012 in 6 CRCSP in Spain. A total of 318 controls were selected, matched for age, sex and period when the colonoscopy was performed. Conditional logistic regression models were estimated. The analysis was performed separately in groups: immediate-SC (same day of the colonoscopy); late-SC (between 1 and 30 days after); perforation; and bleeding events. SC occurred in 3.30‰ of colonoscopies. Prior colon disease showed a higher risk of SC (OR = 4.87). Regular antiplatelet treatment conferred a higher risk of overall SC (OR = 2.80) and late-SC (OR = 9.26), as did regular anticoagulant therapy (OR = 3.47, OR = 7.36). A history of pelvic-surgery or abdominal-radiotherapy was a risk factor for overall SC (OR = 5.03), immediate-SC (OR = 8.49), late-SC (OR = 4.65) and perforation (OR = 21.59). A finding of adenoma or cancer also showed a higher risk of overall SC (OR = 8.71), immediate-SC (OR = 12.67), late-SC (OR = 4.08), perforation (OR = 4.69) and bleeding (OR = 17.02). The risk of SC doesn't vary depending on the type of preparation or type of anesthesia. Knowing the clinical history of patients such as regular previous medication and history of surgery or radiotherapy, as well as the severity of the findings during the colonoscopy process could help to focus prevention measures in order to minimize SC in CRCSP.

1. Introduction

Colorectal cancer (CRC) is the second cause of mortality from cancer in developed countries in both men and women (Ferlay et al., 2015). The World Health Organization and the European Union recommend population-based colorectal cancer screening programs (CRCSP) (Ferlay et al., 2015; Council Recommendation, 2003). The aim of these programs is to reduce mortality and the incidence of CRC through early detection of these tumors and elimination of adenomatous polyps (Pan et al., 2016; Hardcastle et al., 1996). There is evidence of the effectiveness of various screening tests, such as the fecal occult blood test (FOBT), sigmoidoscopy, colonoscopy and the combination of FOBT and colonoscopy (Segnan et al., 2010). In view of the recommendations of the World Health Organization and the European Union (Ferlay et al., 2015; Council Recommendation, 2003), CRCSP have been implemented since 2000 in various autonomous communities of Spain (Salas Trejo et al., 2017). These CRCSP use the FOBT as the screening test and colonoscopy for diagnostic confirmation (Salas Trejo et al., 2017).

Abbreviations: SC, Severe complication; CRC, Colorectal Cancer; CRCSP, Colorectal cancer screening programs

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Colonoscopy is considered a safe and effective technique in the detection and treatment of colorectal lesions (Pignone et al., 2002; Walsh and Terdiman, 2003), but carries a risk of severe complications (SC), any complication requiring hospital admission or causing death, due to perforation, bleeding requiring transfusion, vagal syndrome or peritonitis, and occurring between 0 and 30 days after colonoscopy, which represent an adverse effect of CRCSP (Segnan et al., 2010). In population-based CRCSP with guaiac FOBT, the estimated rate of perforation and serious hemorrhagic is between 0.5% and 1.6% of subjects undergoing colonoscopy (Segnan et al., 2010). The large-scale implementation of CRCSP has created the need to evaluate the benefits and possible harms of these programs. Specifically, one type of adverse effect is the complications of diagnostic colonoscopy, which is sometimes carried out for therapeutic purposes (resection of polyps and cancer) in these programs.

Previous studies have demonstrated that the risk of an SC is higher after colonoscopy with polypepctomy (Rutter et al., 2012; Levin et al., 2006; Ko et al., 2010). Some polyp characteristics have also been studied, such as size, type and localization, and patient characteristics, such as body mass index and sex, are risk factors for bleeding complications after polypectomy (Kim et al., 2007; Zhang et al., 2014; Blanks et al., 2015; Kwon et al., 2015) and perforation or death during and after colonoscopy (Heldwein et al., 2005). Several studies have related the quality of colonoscopy to the risk of complications; specifically, one study reported that inadequate bowel preparation increased the risk of complications (Chan et al., 2015), while others have associated the endoscopist's experience with the quality of the process (Jover et al., 2016; Rajasekhar et al., 2016; Cardin et al., 2012). The occurrence of post-colonoscopy bleeding is more common in patients taking anticoagulants (Tong et al., 2015; Hui et al., 2004).

Given that it is important to determine risk factors for SC to minimize the adverse effects of CRCSP and that the complications of colonoscopy can be associated with patients' personal history and characteristics of the procedure, the aim of this study was to evaluate the risk factors for SC in colonoscopy through a case-control study to estimate the risks of SC depending on personal history, procedural characteristics and colonoscopy findings.

2. Methods

2.1. CRIBEA project

The CRIBEA project is a retrospective study of a cohort of all the men and women invited to screening between 2000 and 2012 in 6 CRCSP implemented in the autonomous communities of the Canary Islands, Cantabria, Catalonia, Murcia, the Basque Country, and the Valencian Community in Spain. The project aims to identify the factors that can influence the balance between the benefits and harms of CRCSP. Participating CRCSP are population-based screening programs targeting men and women aged 50 to 69 years. The screening test is biennial FOBT and diagnostic confirmation is through colonoscopy. This study was approved by the Ethics Committee for Clinical Research. The study was performed in accordance with the principles of the declaration of Helsinki and the Spanish legal requirements of confidentiality.

The CRIBEA study designed a common database for the CRCSP containing information on 1,995,719 invitations sent to 1,320,300 people (Vanaclocha-Espi et al., 2017; Portillo et al., 2017). Within this project, a case-control study was designed to study the adverse effects of CRCSP related to the complications of colonoscopy. Cases and controls were selected from the cohort participating in the CRIBEA study, specifically among participants with a positive FOBT and diagnostic colonoscopies. Follow-up colonoscopies were not included. The total number of diagnostic colonoscopies conducted was 48,730. All patients provided informed consent to undergo colonoscopy and received an information sheet on preparation for the procedure indicating the need to discontinue antiplatelet and anticoagulant therapy days before the examination, depending on the treatment and dosage (Rodrigo, 2011).

2.2. Study design: cases and controls

Cases consisted of all SC related to diagnostic colonoscopy identified in the participating population that underwent diagnostic colonoscopy in the cohort analyzed in the CRIBEA project. Following the criteria established by the European guidelines for quality of colorectal cancer screening, we defined SC as any complication requiring hospital admission or causing death due to perforation, bleeding requiring transfusion, vagal syndrome or peritonitis, and occurring between 0 and 30 days after colonoscopy (Segnan et al., 2010). We distinguished among SC according to time of onset, as follows: immediate-SC were those occurring on the same day as colonoscopy and late-SC were those occurring between 1 and 30 days after colonoscopy.

SC were identified through the endoscopic report of the CRCSP or through linking of the information on the colonoscopies performed in the CRCSP and the information on hospital admissions in the period between the performance of the colonoscopy and up to 30 days later. All SC in the study population were identified. Specifically, perforations and bleeding events requiring transfusion were detected, while there were no cases of vagal syndrome or peritonitis. There was one death that resulted from a perforation.

Controls were selected from diagnostic colonoscopies without SC, and were matched by age (in 5-year strata), sex, CRCSP, and the period when the colonoscopy was performed (before 2010/ from 2010 to 2013).

Two controls were selected for each case, we excluded cases and controls with colonoscopies performed in private centers and with non-severe complications and finally, cases were matched with 1 or 2 controls (Table 1). The total number of cases and controls varied according to whether they were immediate or late and according to whether the SC consisted of a perforation or bleeding event.

Table 1
Number of cases and matched controls.

	Cases	Matched controls
Total SC	161	314
Immediate SC	83	161
Late SC	78	153
Perforation SC	98	189
Hemorrhagic SC	63	125

SC, Severe complication.

2.3. Exposure variables

An active search was made in the clinical histories of cases and controls and information was gathered on personal history, the characteristics of the procedure and the findings of the test, specifically:

- History of symptoms (6 months prior to the colonoscopy): change in bowel habits; rectorrhagia, melena and/or anemia.
- History of investigations performed (last 5 years): colonoscopy and/or sigmoidoscopy.
- History of prior disease: colon disease (chronic inflammatory disease, colorectal polyps, presence of diverticula); coagulation disorders; lung disease; heart disease; diabetes mellitus; alcoholism and other addictions.
- History of regular treatment prior to colonoscopy: antiplatelet agents (eg, clopidogrel, ASPIRIN at antiplatelet doses); anticoagulants (SINTROM, heparins or others); oral iron therapy; sedatives or hypnotics.
- History of Abdominal-pelvic-surgery and/or abdominal-radiotherapy.
- Characteristics of the procedure: information on bowel cleansing (better/worse); type of cleansing (magnesium-citrate/disodium phosphate/polyethylene-glycol); type of sedation and analgesia (none/deep/superficial); health professional administering the sedation (anestesiologist/endoscopist/nurse/others); quality of cleaning (excellent/good/acceptable/poor or inadequate); type of colonoscopy (diagnostic without polypectomy/diagnostic with polypectomy).
- Colonoscopy findings: number of extirpated polyps; final diagnosis (normal for screening or low-risk adenoma/medium-high-risk adenoma or CCR).

2.4. Statistical analysis

The study population and the number of SC are described by age, sex, and period when the colonoscopy was performed, and the rate of SC was calculated as the proportion of participants developing a SC among diagnostic colonoscopies performed among participants with a positive FOBT between 2000 and 2012. Rates are expressed per 1000 diagnostic colonoscopies.

To analyze the association between an exposure factor and SC, data were described through contingency tables. The statistical technique used to analyze the relationship between two variables was based on Bayes' theorem, calculating the probability of association (PA) as posteriori probability of the null hypothesis (H_0: relationship between the two variables) being valid, given the difference observed giving rise to the data (d_0), that is, calculating: $P(H_0/d_0)$ (Albert, 2007), In this study, high probability was defined when values above 0.8. Conditional logistic regression models were adjusted for SC. The models included those exposure factors showing a high a posteriori PA. We excluded those variables with an expected frequency of less than 5 in at least one of its categories.

Table 2
Proportion of SC in diagnostic colonoscopies with respect to the total number of diagnostic colonoscopies in CRCSP with a positive FOBT test.

	Diagnostic colonoscopies	SC		Immediate SC		Late SC	
	N	N	Rate(‰)	N	Rate(‰)	N	Rate(‰)
Total	48730	161	3.30	83	1.70	78	1.60
Sex							
Male	28402	101	3.56	50	1.76	51	1.80
Female	20328	60	2.95	33	1.62	27	1.33
Age (years)							
50–59	22707	55	2.42	31	1.37	24	1.06
60–70	26023	106	4.07	52	2.00	54	2.08
Year of colonoscopy							
2000–2009	6143	19	3.09	7	1.14	12	1.95
2010–2013	42586	142	3.33	76	1.78	66	1.55

SC, Severe complication.

Table 3
Distribution and PA of cases and controls according to personal history.

	All SC			Immediate SC			Late SC			Perforation-related SC			Hemorrhagic SC		
Antecedentes, n(%)	Controls (n = 314)	Cases (n = 161)	PA	Controls (n = 161)	Cases (n = 83)	PA	Controls (n = 153)	Cases (n = 78)	PA	Controls (n = 189)	Cases (n = 98)	PA	Controls (n = 125)	Cases (n = 63)	PA
Prior symptoms															
Change in bowel habits															
No	310 (98.7)	158 (98.1)		158 (98.1)	81 (97.6)		152 (99.3)	77 (98.7)		186 (98.4)	96 (98.0)		124 (99.2)	62 (98.4)	
Yes	4 (1.3)	3 (1.9)	0.05	3 (1.9)	2 (2.4)	0.07	1 (0.7)	1 (1.3)	0.05	3 (1.6)	2 (2.0)	0.06	1 (0.8)	1 (1.6)	0.07
Rectorrhagia, Melena or Anemia															
No	297 (94.6)	145 (90.1)		152 (94.4)	76 (91.6)		145 (94.8)	69 (88.5)		179 (94.7)	88 (89.8)		118 (94.4)	57 (90.5)	
Yes	17 (5.4)	16 (9.9)	0.30	9 (5.6)	7 (8.4)	0.14	8 (5.2)	9 (11.5)	0.35	10 (5.3)	10 (10.2)	0.30	7 (5.6)	6 (9.5)	0.18
Prior tests															
Colonoscopy or sigmoidoscopy															
No	307 (97.8)	156 (96.9)		157 (97.5)	82 (98.8)		150 (98.0)	74 (94.9)		185 (97.9)	97 (99.0)		122 (97.6)	59 (93.7)	
Yes	7 (2.2)	5 (3.1)	0.06	4 (2.5)	1 (1.2)	0.07	3 (2.0)	4 (5.1)	0.16	4 (2.1)	1 (1.0)	0.06	3 (2.4)	4 (6.3)	0.20
Prior diseases															
Colon disease															
No	240 (97.6)	142 (89.9)		117 (97.5)	76 (93.8)		123 (97.6)	66 (85.7)		137 (97.2)	88 (91.7)		103 (98.1)	54 (87.1)	
Yes	6 (2.4)	16 (10.1)	0.94	3 (2.5)	5 (6.2)	0.19	3 (2.4)	11 (14.3)	0.95	4 (2.8)	8 (8.3)	0.37	2 (1.9)	8 (12.9)	0.87
Coagulation disorders															
No	314 (100.0)	154 (95.7)		161 (100.0)	83 (100.0)		153 (100.0)	71 (91.0)		189 (100.0)	97 (99.0)		125 (100.0)	57 (90.5)	
Yes	0 (0.0)	7 (4.3)	0.96	0	0	0.02	0	7 (9.0)	0.98	0	1 (1.0)	0.06	0	6 (9.5)	0.96
Lung disease															
No	279 (88.9)	137 (85.1)		142 (88.2)	76 (91.6)		137 (89.2)	61 (78.8)		169 (89.4)	87 (88.8)		110 (88.0)	50 (79.4)	
Yes	35 (11.1)	24 (14.9)	0.18	19 (11.8)	7 (8.4)	0.16	16 (10.5)	17 (21.8)	0.69	20 (10.6)	11 (11.2)	0.12	15 (12.0)	13 (20.6)	0.38
Heart disease															
No	236 (75.2)	101 (62.7)		125 (77.6)	60 (72.3)		111 (72.5)	41 (52.6)		160 (84.7)	77 (78.6)		76 (60.8)	24 (38.1)	
Yes	78 (24.8)	60 (37.3)	0.88	36 (22.4)	23 (27.7)	0.23	42 (27.5)	37 (47.4)	0.95	29 (15.3)	21 (21.4)	0.27	49 (39.2)	39 (61.9)	0.95
Diabetes mellitus															
No	292 (93.0)	145 (90.1)		151 (93.8)	80 (96.4)		141 (92.2)	65 (83.3)		180 (95.2)	96 (98.0)		112 (89.6)	49 (77.8)	
Yes	22 (7.0)	16 (9.9)	0.14	10 (6.2)	3 (3.6)	0.12	12 (7.8)	13 (16.7)	0.52	9 (4.8)	2 (2.0)	0.12	13 (10.4)	14 (22.2)	0.64
Alcoholism or drug addiction															
No	259 (82.5)	134 (83.2)		131 (81.4)	70 (84.3)		128 (83.7)	64 (82.1)		154 (81.5)	85 (86.7)		105 (84.0)	49 (77.8)	
Yes	55 (17.5)	27 (16.8)	0.11	30 (18.6)	13 (15.7)	0.17	25 (16.3)	14 (17.9)	0.16	35 (18.5)	13 (13.3)	0.22	20 (16.0)	14 (22.2)	0.26
Regular treatment															
Antiplatelets[a]															
No	295 (93.9)	129 (80.1)		153 (95.0)	74 (89.2)		142 (92.8)	55 (70.5)		181 (95.8)	84 (85.7)		114 (91.2)	45 (71.4)	
Yes	19 (6.1)	33 (19.9)	1.00	8 (5.0)	9 (10.8)	0.32	11 (7.2)	23 (29.5)	1.00	8 (4.2)	14 (14.3)	0.89	11 (8.8)	18 (28.6)	0.99
Anticoagulants[a]															
No	301 (95.9)	143 (88.8)		154 (95.7)	79 (95.2)		147 (96.1)	64 (82.1)		179 (94.7)	95 (96.9)		122 (97.6)	48 (76.2)	
Yes	13 (4.1)	18 (11.2)	0.83	7 (4.3)	4 (4.8)	0.09	6 (3.9)	14 (17.9)	0.98	10 (5.3)	3 (3.1)	0.11	4 (2.4)	15 (23.8)	1.00
Oral iron therapy															
No	309 (98.4)	158 (98.1)		157 (97.5)	83 (100.0)		152 (99.3)	75 (96.2)		184 (97.4)	96 (98.0)		125 (100.0)	62 (98.4)	
Yes	5 (1.6)	3 (1.9)	0.04	4 (2.5)	0 (0.0)	0.11	1 (0.7)	3 (3.8)	0.20	5 (2.6)	2 (2.0)	0.06	0	1 (1.6)	0.09
Sedatives or hypnotics															
No	243 (77.4)	131 (81.4)		125 (77.6)	72 (86.7)		118 (77.1)	59 (75.6)		146 (77.2)	88 (89.8)		97 (77.6)	43 (68.3)	
Yes	71 (22.6)	30 (18.6)	0.18	36 (22.4)	11 (13.3)	0.43	35 (22.9)	19 (24.4)	0.17	43 (22.8)	10 (10.2)	0.84	28 (22.4)	20 (31.7)	0.37
Prior treatment															
Pelvic-surgery or abdominal-radiotherapy															
No	273 (86.9)	101 (62.7)		143 (88.8)	50 (60.2)		130 (85.0)	51 (65.4)		175 (92.6)	57 (58.2)		98 (78.4)	44 (69.8)	
Yes	41 (13.1)	60 (37.3)	1.00	18 (11.2)	33 (39.8)	1.00	23 (15.0)	27 (34.6)	0.98	14 (7.4)	41 (41.8)	1.00	27 (21.6)	19 (30.2)	0.34

SC, severe complications; PA, probability of association.

[a] All patients had an indication to suspend treatment in the days before the colonoscopy.

A multivariate model was adjusted for each of the case-control groups. The conditional model allowed control of the correlation between matched data. The results are shown as odds ratios (OR) and 95% confidence intervals. The data analysis was performed using the R program.

3. Results

SC occurred in 3.3‰ of diagnostic colonoscopies; 3.56‰ in men and 2.95‰ in women, 2.42‰ in participants aged 50–59 years and 4.07‰ in those aged 60–70 years. SC occurred in 3.09‰ of colonoscopies performed between 2000 and 2009 and in 3.33‰ of those carried out between 2010 and 2013 (Table 2).

A total of 83 SC were immediate. Of these, 75.9% were perforations and 24.1% were bleeding events requiring transfusion. There were 78 late-SC, of which 44.9% were perforations occurring at a mean of 3.3 ± 4.6 days after the colonoscopy, and 55.1% were bleeding events with 6.0 ± 5.6 days after the procedure.

The characteristics of personal antecedents are shown in Table 3. There was a very low probability of an association between SC and symptoms 6 months before colonoscopy and investigations performed in the last 5 years. Overall SC, and late and hemorrhagic *SC* were more common in persons with prior colonic disease, coagulation disorders, and heart disease (PA above 0.87), these complications were more frequent when the patient was taking regular anticoagulant therapy (PA above 0.83). Overall SC, late, perforation-related and hemorrhagic SC were more frequent in patients taking regular antiplatelet therapy (PA above 0.89). Perforation-related SC showed a PA = 0.84 with regular treatment with sedation and hypnotics. Overall SC, immediate, late and perforation-related SC were more common in patients with prior pelvic-surgery or abdominal-radiotherapy (PA above 0.98).

Procedural characteristics in cases and controls are shown in Table 4. The percentage of persons who were poorly informed was higher in cases with hemorrhagic-SC (PA = 0.91). For overall SC, immediate, late, perforation-related and hemorrhagic SC, there was a high PA with the professional performing the sedation, the quality of bowel cleansing, and the type of colonoscopy (PA higher than 0.93). The percentage of SC was lower when the professional performing the sedation was an endoscopist, when the quality of bowel cleansing was excellent and when the colonoscopy was purely diagnostic (PA higher than 0.84). The number of polyps found showed a PA above 0.99 with overall SC, late, perforation and hemorrhagic SC, the final diagnosis showed PA = 1 with overall SC, and immediate, late and perforation-related SC and PA = 0.82 with hemorrhagic-SC.

The results of multivariate models are shown in Table 5. Variables of previous diseases that had a high PA with patients' regular treatment were not included. The models included the most relevant predictors and provided the most precise estimates. The OR for the occurrence of a SC was 5.35(CI 1.40–20.46) in patients with colon disease, 3.83(CI 1.62–9.05) in patients taking regular antiplatelet therapy versus those not receiving this treatment, OR = 3.56(CI 1.21–10.43) for anticoagulant therapy, OR = 5.45(CI 2.78–10.70) for a history of pelvic-surgery or abdominal-radiotherapy, and OR = 9.36(CI 4.44–19.69) for a diagnosis of adenoma or CRC, colonoscopy type was not statistically significant. The risk of an immediate-SC was higher if there was a history of pelvic-surgery or abdominal-radiotherapy, OR = 8.49(CI 3.52–20.52), and if the diagnosis was adenoma or CRC, OR = 12.67(CI 4.32–38.65), colonoscopy type was not statistically significant. The risk of a late-SC was higher in patients taking regular antiplatelet therapy versus those not receiving this treatment, OR = 9.26(CI 3.10–27.65), in those taking anticoagulants, OR = 7.36(CI 1.60–33.87), in those with a history of pelvic-surgery or abdominal-radiotherapy OR = 4.65(CI 1.70–12.70), in those

Table 4
Distribution and PA of cases and controls according to procedural characteristics and colonoscopy results.

	All SC			Immediate SC			Late SC			Perforation-related SC			Hemorrhagic SC		
Procedure, n(%)	Controls (n = 314)	Cases (n = 161)	PA	Controls (n = 161)	Cases (n = 83)	PA	Controls (n = 153)	Cases (n = 78)	PA	Control (n = 189)	Cases (n = 98)	PA	Controls (n = 125)	Cases (n = 63)	PA
Characteristics															
Information on preparation															
Worse	32 (10.2)	22 (14.0)		16 (9.9)	11 (13.6)		16 (10.5)	11 (14.5)		24 (12.7)	9 (9.5)		8 (6.4)	13 (21.0)	
Better	282 (89.8)	135 (86.0)	0.18	145 (90.1)	70 (86.4)	0.17	137 (89.5)	65 (85.5)	0.19	165 (87.3)	86 (90.5)	0.15	117 (93.6)	49 (79.0)	0.91
Type of preparation															
Magnesium citrate	84 (39.8)	43 (40.2)		48 (43.6)	25 (44.6)		36 (35.6)	18 (35.3)		55 (39.0)	30 (39.5)		29 (42.4)	13 (41.9)	
Disodium phosphate	37 (17.5)	17 (15.9)		15 (13.6)	7 (12.5)		22 (21.8)	10 (19.6)		18 (12.8)	8 (10.5)		19 (27.1)	9 (29.0)	
Polyethylene glycol	90 (42.7)	47 (43.9)	0.04	47 (42.7)	24 (42.9)	0.07	43 (42.6)	23 (45.1)	0.09	68 (48.2)	38 (50.0)	0.06	22 (31.4)	9 (29.0)	0.12
Type of sedation-analgesia															
None	11 (4.2)	6 (4.1)		9 (6.3)	5 (6.4)		2 (1.7)	1 (1.5)		2 (1.2)	3 (3.2)		9 (8.7)	3 (5.8)	
Deep sedation	180 (68.2)	105 (71.9)		102 (71.3)	61 (78.2)		78 (64.5)	44 (64.7)		121 (75.2)	74 (78.7)		59 (57.3)	31 (59.6)	
Superficial sedation	73 (27.7)	35 (24.0)	0.02	32 (22.4)	12 (15.4)	0.07	41 (33.9)	23 (33.8)	0.03	38 (23.6)	17 (18.1)	0.05	35 (34.0)	18 (34.6)	0.07
Professional sedation															
Anesthesiologist	215 (72.9)	116 (73.4)		117 (79.1)	63 (78.8)		98 (66.7)	53 (67.9)		143 (79.4)	75 (78.1)		72 (62.6)	41 (66.1)	
Endoscopist	30 (10.2)	3 (1.9)		13 (8.8)	1 (1.3)		17 (11.6)	2 (2.6)		13 (7.2)	1 (1.0)		17 (14.8)	2 (3.2)	
Nurse	46 (15.6)	20 (12.7)		17 (11.5)	7 (8.8)		29 (19.7)	13 (16.7)		23 (12.8)	10 (10.4)		23 (20.0)	10 (16.1)	
Other (not specified)	4 (1.4)	19 (12.0)	1.00	1 (0.7)	9 (11.3)	1.00	3 (2.0)	10 (12.8)	0.94	1 (0.6)	10 (10.4)	0.99	3 (2.6)	9 (14.5)	0.93
Quality of preparation															
Excellent	144 (68.2)	4 (3.1)		79 (68.1)	2 (2.8)		65 (68.4)	2 (3.6)		98 (73.1)	1 (1.2)		46 (59.7)	3 (7.1)	
Good	40 (19.0)	104 (81.3)		24 (20.7)	62 (86.1)		16 (16.8)	42 (75.0)		22 (16.4)	72 (83.7)		18 (23.4)	32 (76.2)	
Satisfactory	16 (7.6)	10 (7.8)		8 (6.9)	5 (6.9)		8 (8.4)	5 (8.9)		10 (7.5)	7 (8.1)		6 (7.8)	3 (7.1)	
Poor or inadequate	11 (5.2)	10 (7.8)	1.00	5 (4.3)	3 (4.2)	1.00	6 (6.3)	7 (12.5)	1.00	4 (3.0)	6 (7.0)	1.00	7 (9.1)	4 (9.5)	1.00
Type of associated colonoscopy															
Diagnostic	102 (32.5)	18 (11.4)		53 (32.9)	14 (17.5)		49 (32.0)	4 (5.1)		64 (33.9)	12 (12.6)		38 (30.4)	6 (9.5)	
Diagnostic/therapeutic =	212 (67.5)	140 (88.6)	1.00	108 (67.1)	66 (82.5)	0.84	104 (68.0)	74 (94.9)	1.00	125 66.1)	83 (87.4)	1.00	87 (69.6)	57 (90.5)	0.98
Findings															
Number of polyps found															
0	163 (51.9)	50 (31.1)		84 (52.2)	32 (38.6)		79 (51.6)	18 (23.1)		105 (55.6)	40 (40.8)		58 (46.4)	10 (15.9)	
1	42 (13.4)	23 (14.3)		22 (13.7)	8 (9.6)		20 (13.1)	15 (19.2)		27 (14.3)	12 (12.2)		15 (12.0)	11 (17.5)	
2–3	61 (19.4)	44 (27.3)		31 (19.3)	20 (24.1)		30 (19.6)	24 (30.8)		36 (11.1)	24 (24.5)		25 (20.0)	20 (31.7)	
4+	48 (15.3)	44 (27.3)	1.00	24 (14.9)	23 (27.7)	0.47	24 (15.7)	21 (26.9)	0.99	21 (11.1)	22 (22.4)	1.00	27 (21.6)	22 (34.9)	1.00
Diagnosis															
Normal/LRA/IRA	225 (71.7)	54 (34.4)		114 (70.8)	20 (25.3)		111 (72.5)	34 (43.6)		137 (72.5)	32 (34.0)		88 (70.4)	22 (34.9)	
HRA/CRC	89 (28.3)	103 (65.6)	1.00	47 (29.2)	59 (74.7)	1.00	42 (48.8)	44 (56.4)	1.00	52 (27.5)	62 (66.0)	1.00	378 (29.6)	41 (65.1)	0.82
Diagnosis															
Normal	158 (50.3)	17 (10.8)		79 (49.1)	8 (10.1)		79 (51.6)	9 (11.5)		97 (51.3)	14 (14.9)		61 (48.8)	3 (9.1)	
Adenoma or CRC	156 (49.7)	140 (89.2)	1.00	82 (50.9)	71 (89.9)	1.00	74 (48.4)	69 (88.5)	1.00	92 (48.7)	80 (85.1)	1.00	64 (51.2)	30 (90.9)	1.00

SC, severe complications; PA, probability of association; LRA, low-risk adenoma; IRA, intermediate-risk adenoma; HRA, high-risk adenoma; CRC, colorectal cancer.

with a diagnosis was adenoma or CRC, OR = 4.08(CI 1.69–9.84) and if the colonoscopy was diagnostic-therapeutic OR = 2.59(CI 1.29–5.20). The risk of perforation was higher in patients with a history of pelvic-surgery or abdominal-radiotherapy, OR = 21.59(CI 7.99–58.32), if the diagnosis was adenoma or CRC, OR = 4.69(CI 2.07–10.61) and if the type of colonoscopy was diagnostic-therapeutic OR = 2.77(CI 1.02–7.51), while the risk of perforation was lower in patients receiving regular treatment with sedatives or hypnotics, OR = 0.34(CI 0.12–0.93). A high risk of hemorrhage was conferred by regular antiplatelet therapy, OR = 3.74(CI 1.27–11.01), anticoagulants, OR = 10.34(CI 1.82–58.80) and a diagnosis of adenoma or CRC, OR = 17.02(CI 4.13–70.23), while the risk of hemorrhage was lower in patients who were better informed about bowel cleansing, OR = 0.18(CI 0.04–0.79). Like the model for overall SC and immediate SC, in the model for bleeding, colonoscopy type was not statistically significant when other factors were considered OR = 1.09(CI 0.25–4.80).

4. Discussion

This study shows that risk factors for SC in screening colonoscopy are a prior pelvic-surgery or abdominal-radiotherapy, colonoscopy with polypectomy, detection of adenoma or CRC and regular antiplatelet and anticoagulant therapies. The study also shows that the factors influencing the appearance of late-SC differ from those influencing immediate-SC, with a history of regular antiplatelet and anticoagulant use before colonoscopy and diagnostic-therapeutic colonoscopy increasing the risk of late-SC. The factors influencing the development of perforations and bleeding events also differ, regular antiplatelet and anticoagulant treatment before colonoscopy increased bleeding risk the type of information on bowel preparation was a protective factor for bleeding, while diagnostic-therapeutic colonoscopy and pelvic-abdominal surgery increased perforation risk.

The overall rate of SC in our study was 3.3‰ (in the context of a population-based screening program using guaiac or immunological FOBT and colonoscopy for diagnostic confirmation), which is lower than the rates reported in European guideline ranging between 5‰ and 16‰ in subjects undergoing colonoscopy in screening programs using guaiac FOBT (Segnan et al., 2010). There is no information on SC rates in screening programs using immunological FOBT. One study found an SC rate of 4.7% of colonoscopies in the population screened with different methods (Rutter et al., 2012). The fact that patients who undergo colonoscopy after a positive FOBT have a higher risk of having adenomas or CRC could explain why the rate in our study was higher than that in other studies analyzing the SC rate in healthcare colonoscopies rather than screening colonoscopies (Singh et al., 2009; Ko et al., 2010).

As expected, a higher number of extirpated lesions were associated with a higher complications risk, consistent with a study showing that patients with 2 or more polyps had a higher risk of complications than patients with 1 polyp (Heldwein et al., 2005). In this study, more advanced adenomas conferred a higher risk of complications. Several studies have shown that age, the number of polyps, and polyp size are risk factors for a finding of more advanced lesions (Portillo et al., 2017).

Few studies have evaluated the association between colonoscopy type (diagnostic/diagnostic-therapeutic) and the appearance of complications. As expected, diagnostic colonoscopy with polypectomy conferred a higher risk of complications, in agreement with Chan, AO (Chan et al., 2015; Rutter et al., 2012). Although most studies have analyzed complications in colonoscopies with polypectomy only (Heldwein et al., 2005; Hui et al., 2004). Like other studies, we found that patients under regular anticoagulant therapy had a higher risk of late bleeding (Tong et al., 2015; Yousfi et al., 2004). Although Hui et al. studied the effect of ASPIRIN use and found no relationship with bleeding events after polypectomy, in the present study we found an association between prior antiplatelet treatment and the appearance of late-SC. A possible reason for this discrepancy is that this study included ASPIRIN as an antiplatelet agent only when the dose was sufficiently high to have an antiplatelet effect. Another study also analyzed the association of post-polypectomy bleeding and the use of prior ASPIRIN administration and concluded that there was no significant association (Yousfi et al., 2004).

Prior regular use of sedatives-hypnotics was a protective factor against perforation. According to the clinical practice guidelines for quality of colonoscopy in CRCSP, sedation is recommended during the procedure as it improves patients' experience and can make endoscopic examination easier (Rodrigo, 2011). Sedatives-hypnotics make patients feel calm or sedated and, possibly because of this effect, patients receiving regular prior sedative-hypnotic therapy have a lower risk of perforation.

Patients receiving poorer information on bowel cleansing before colonoscopy had a higher bleeding risk, which could be because information on screening, the informed consent form and instructions for bowel cleansing are components of colonoscopy quality (Rodrigo, 2011).

We found no relationship between SC and the type of sedation-analgesia (None/Deep sedation/Superficial sedation). Unlike our study, Wernli et al. compared patients with anesthesia administered by the anesthesia service (which is similar to what we consider to be deep sedation) and patients with standard sedation (superficial sedation) and found a higher risk of SC in patients with sedation administered by the anesthesia

Table 5
Multivariate conditional logistic regression model.

		OR (95% CI)
All SC	Colon disease (yes)	5.35 (1.40–20.46)
	Regular antiplatelet therapy (yes)	3.83 (1.62–9.05)
	Regular anticoagulant therapy (yes)	3.56 (1.21–10.43)
	Prior pelvic-surgery or abdominal-radiotherapy (yes)	5.45 (2.78–10.70)
	Diagnosis (adenoma or CRC)	9.36 (4.44–19.69)
	Type of colonoscopy (diagnostic-therapeutic)	1.82 (0.79–4.22)
Immediate SC	Prior pelvic-surgery or abdominal-radiotherapy (yes)	8.49 (3.52 to 20.52)
	Diagnosis (adenoma or CRC)	12.67 (4.32 to 38.65)
	Type of colonoscopy (diagnostic-therapeutic)	0.96 (0.32 to 2.81)
Late SC	Regular antiplatelet therapy (yes)	9.26 (3.10 to 27.65)
	Regular anticoagulant therapy (yes)	7.36 (1.60 to 33.87)
	Prior pelvic-surgery or abdominal-radiotherapy (yes)	4.65 (1.70 to 12.70)
	Diagnosis (adenoma or CRC)	4.08 (1.69 to 9.84)
	Type of colonoscopy (diagnostic-therapeutic)	4.45 (1.20 to 15.55)
Perforation SC	Regular treatment with sedatives or hypnotics (yes)	0.34 (0.12 to 0.93)
	Prior pelvic-surgery or abdominal-radiotherapy (yes)	21.59 (7.99 to 58.32)
	Diagnosis (adenoma or CRC)	4.69 (2.07 to 10.61)
	Type of colonoscopy (diagnostic-therapeutic)	2.77 (1.02 to 7.51)
Hemorrhagic SC	Regular antiplatelet therapy (yes)	3.74 (1.27 to 11.01)
	Regular anticoagulant therapy (yes)	10.34 (1.82 to 58.80)
	Information on bowel preparation (better)	0.18 (0.04 to 0.79)
	Diagnosis (adenoma or CRC)	17.02 (4.13 to 70.23)
	Type of colonoscopy (diagnostic-therapeutic)	1.09 (0.25 to 4.80)

SC, severe complications; OR, odds ratio; CI, confidence intervals.

service (Wernli et al., 2016). We did find a relationship with the health professional administering the sedation and with the quality of bowel cleansing, with the percentage of SC being lower when sedation was administered by an endoscopist rather than by an anesthesiologist or nurse and when the quality of bowel cleansing was excellent. Another study concluded that administration by an anesthesia professional did not appear to confer a safety benefit to patients undergoing colonoscopy (Vargo et al., 2017).

Unlike other studies, we found no relationship between the type of preparation and SC. One study analyzed the type of preparation in bowel cleansing and reported a higher percentage of adverse effects such as nausea, vomiting and abdominal pain after colonoscopy in the group using “Fleet Phospho-Soda” than in groups using “Klean-Prep” and “Endofalk” (Ell et al., 2003).

Our study is limited by the low frequencies in the categories of some exposure variables that could not be analyzed in greater depth, specifically variables such as the health professional administering sedation and the quality of bowel preparation. In the descriptive analysis, we found a relationship between SC and the quality of the procedure, with the number of complications being lower when the quality was excellent according to the Aronchick scale. One study found an association between colonoscopy quality and complications (Rajasekhar et al., 2016).

Another limitation was the impossibility of including body mass index as a risk factor as well as certain variables related to the characteristics of extirpated polyps, since this information was not always recorded in the clinical histories.

Our study shows that lesions diagnosed at colonoscopy as adenoma or CRC confer a higher risk of complications than if no lesions are found. One of the aims of CRCSP is to detect early-stage tumors or precursor lesions. The cohort analyzed in this study included data from the start of CRCSP to 2012 and it could be expected that more advanced lesions would be detected in the first screening round than in successive rounds. A study showed that the complication rate decreases with time and that some of this decrease was due to a reduction in the complexity of the procedure (Blanks et al., 2015), probably because successive rounds identified earlier-stage disease.

SC are an infrequent but important adverse effect of CRCSP that should be minimized. Our study provides information on the factors influencing the occurrence of these complications and has analyzed differences between risk factors associated with immediate-SC and late-SC independently, as well as risk factors for different types of complications. The results could help to target prevention measures, bearing in mind certain patient-related and procedural factors that could help to minimize the risk of SC by adopting organizational and information measures that take account of the patient's risk of having an SC during colonoscopy and the next 30 days. Immediate-SC are more frequently consisted of perforations and to occur in patients with a history of surgery or radiotherapy and in patients with adenoma or CRC. Late-SC are also influenced by prior medication, specifically regular antiplatelet and anticoagulant therapy and type of colonoscopy. Knowledge of the medical history of persons undergoing colonoscopy is needed for post-procedural follow-up.

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Ethics considerations

This study was performed in accordance with the principles of the declaration of Helsinki and the Spanish legal requirements of confidentiality.

Conflict of interest statement

The authors disclose no conflicts interests.

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