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Overtreatment in nonmalignant lesions detected in a colorectal cancer screening program: a retrospective cohort study

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Abstract

Background: Although colorectal cancer (CRC) screening programs reduce CRC incidence and mortality, they are associated with risks in healthy subjects. However, the risk of overtreatment and overdiagnosis has not been determined yet. The aim of this study was to report the surgery rates in patients with nonmalignant lesions detected within the first round of a fecal immunochemical test (FIT) based CRC screening program and the factors associated with it.

Methods: We included in this analysis all patients with nonmalignant lesions detected between May 2013 and June 2019 in the Galician (Spain) CRC screening program. We calculated surgery rate according to demographic variables, the risk classification according to the colonoscopy findings (European guidelines for quality assurance), the endoscopist's adenoma detection rate (ADR) classified into quartiles and the hospital's complexity level. We determined which variables were independently associated with surgery rate and expressed the association as Odds Ratio and its 95% confidence interval (CI).

Results: We included 15,707 patients in the analysis with high (19.9%), intermediate (26.9%) low risk (23.3%) adenomas and normal colonoscopy (29.9%) detected in the analyzed period. Colorectal surgery was performed in 162 patients (1.03, 95% CI 0.87–1.19), due to colonoscopy complications (0.02, 95% CI 0.00–0.05) and resection of colorectal benign lesions (1.00, 95% CI 0.85–1.16). Median hospital stay was 6 days with 17.3% patients developing minor complications, 7.4% major complications and one death. After discharge, complications developed in 18.4% patients. In benign lesions, an endoscopic resection was performed in 25.4% and a residual premalignant lesion was detected in 89.9%. The variables independently associated with surgery in the multivariable analysis were age (≥ 60 years = 1.57, 95% CI 1.11–2.23), sex (female = 2.10, 95% CI 1.52–2.91), the European guidelines classification (high risk = 67.94, 95% CI 24.87–185.59; intermediate risk = 5.63, 95% CI 1.89–16.80; low risk = 1.43; 95% CI 0.36–5.75), the endoscopist's ADR (Q4 = 0.44, 95% CI 0.28–0.68; Q3 = 0.44, 95% CI 0.27–0.71; Q2 = 0.71, 95% CI 0.44–1.14) and the hospital (tertiary = 0.54, 95% CI 0.38–0.79).

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Conclusions: In a CRC screening program, the surgery rate and the associated complications in patients with nonmalignant lesions are low, and related to age, sex, endoscopic findings, endoscopist's ADR and the hospital's complexity.

Keywords: Adenoma detection rate, Colorectal cancer, Overtreatment, Screening, Surgical resection

Background

Colorectal cancer (CRC) is the second most frequent cancer worldwide with almost two million incident cases and one million related deaths in 2020 [1]. In order to reduce the disease burden, population-based CRC screening programs have been established in the Western world. This strategy has demonstrated their efficacy to reduce CRC mortality and incidence in randomized controlled trials [2]. Furthermore, CRC screening programs have demonstrated their efficiency in reducing both CRC mortality and incidence [3, 4].

Screening programs are directed to asymptomatic subjects. A key point is the minimization of risks. The benefit gained by individuals should outweigh any harm [5]. Although complications related to the diagnostic tests are well established in CRC screening [2, 6], there is no such certainty regarding overdiagnosis and overtreatment. Overdiagnosis is defined as the diagnosis of a medical condition or disease that would not cause symptoms or death during a patient's lifetime. In the case of CRC screening, treatment of overdiagnosed CRC and polyps should be called overtreatment [7].

Endoscopic resection of colorectal polyps is the key to reduce CRC incidence and mortality [8]. Although side effects are limited, mainly postpolypectomy syndrome, rectal bleeding and perforation, they account for most colonoscopy-related injury during CRC screening [2]. Endoscopic resection removes up to 90% of advanced complex polyps [9]. However, the introduction of CRC screening programs has increased the number of colectomies due to benign polyps. In the US, up to 25% of colectomies were performed for non-malignant polyps [10]. Related mortality and morbidity attains 0.8 and 25.3%, respectively [11]. However, there is little information regarding the incidence of surgery and associated risks in subjects with benign lesions detected in a CRC screening program [12]. Thus, we decided to perform a retrospective cohort analysis in the first round of the Galician (northwestern Spain) CRC screening program to determine the surgery rate in patients with non-malignant lesions detected on colonoscopy, the surgery-related complications, the motivation for surgery and finally, the factors independently associated with it.

Methods

Study design

We designed a retrospective cohort multicenter study using the Galician (Northwestern Spain) CRC screening program database to identify patients. We included in this analysis all patients that underwent at least one colonoscopy in the first round of the CRC screening program from its implementation (May 2013) until July 2019. We excluded patients with an invasive CRC as the final diagnosis.

Description of the Galician CRC screening program

Galician CRC mass screening and its implementation have been described elsewhere [13]. The CRC screening program includes the central coordination and management of patient follow-up after polyp resection depending on their risk according to EU guidelines for quality assurance on CRC screening recommendations [14]. The Coordination Unit personnel introduces the data obtained from the different sources in the screening program information system regarding CRC stage according to the AJCC classification [15], the final classification of patients with a positive result [14] as well as several quality endoscopist indicators according to Spanish guidelines on quality in screening colonoscopy [16].

Baseline data

From each patient, we collected the information available in the screening program database: sex, age, fecal hemoglobin concentration, performance status, associated medical illnesses graded according to the American Society of Anesthesiologists' Physical Status Classification (ASA grade), number of baseline colonoscopies (colonoscopies performed after the positive FIT result), number of polyps, adenomas and size of the largest adenoma. Patients were classified as high risk (≥ 20 mm or ≥ 5 adenomas), intermediate risk (3 to 4 adenomas, $1 \geq 10$ mm and < 20 mm, with a villous component or high grade dysplasia), low risk (1–2 tubular adenomas < 10 mm in size) and no adenomas according to the European guidelines for quality assurance in CRC screening [17]. Data regarding the center and the endoscopist that performed the first complete colonoscopy were collected. The adenoma detection rate (ADR) and number of colonoscopies performed during the first round were calculated for each endoscopist in the first round. Endoscopists were classified into quartiles according to

their ADR and number of colonoscopies performed. Finally, hospitals were classified according to their complexity level (tertiary versus secondary).

Surgery

We identified all the patients that required surgery after colonoscopy using the Spanish Health System's Hospital Discharge Records Database (CMBD in Spanish) and the CRC screening program database. The CMBD includes information on hospital discharges using a list of clinical codes to establish the diagnosis that justified the admission. The CMBD database receives notifications from approximately 98% of Spanish public hospitals [18]. Mandatory health insurance covers an estimated 99.5% of the Spanish population, although subjects not covered by health insurance can still receive treatment in public hospitals. All subjects included in the Galician CRC screening programme are attended in the Galician Public health System. The International classification of diseases (ICD) codes used to identify colorectal surgeries were: ICD-9-MC 48.6 over the period 2013–2015 and ICD-10-ES ODT(C,E-N,P)(0,4) ZZ; ODB(C,E-N,P)(0,4) ZZ and ODBP7ZZ over the period 2016–2019. We subsequently searched manually the clinical records of identified patients to confirm that colorectal surgery was related to the screening colonoscopy. Moreover, we retrieved the following data: reason for surgery, type of surgery, length of hospital stay and complications either during hospitalization or after discharge (first year). We searched the clinical information in IANUS, the Galician electronic health record system that covers both all the Galician hospitals and the primary healthcare centers. In-hospital complications were classified according to the Clavien-Dindo classification [19]. We classified surgery complications as minor if they were grade I-II and major if they were grade III-V. If surgery was due to resection of colorectal lesions, we collected data regarding size, morphology according to the Paris classification [20], location, endoscopic resection and histologic findings in the endoscopic and surgical specimen. Based on endoscopic reports we calculated the Size, Morphology, Site and Access (SMSA) score and we classified lesions accordingly [21].

Analysis

First, we described the characteristics of the subjects included. We reported continuous and categorical variables as median and interquartile range (IQR), and total number and percentage, respectively. Thereafter, we calculated the surgery rate according to the different variables assessed. We performed a bivariate analysis using the Chi-square test for categorical variables and the Student's *t* test for continuous variables to determine those related to surgery. Finally, we included statistically

significant or clinically relevant variables in a multivariable analysis using logistic regression (forward conditional) to determine which variables were independently related to surgery. We performed a secondary analysis after excluding transanal surgery to determine the colectomy rate, related complications and independently associated factors. Associations were expressed as Odds Ratio (OR) with a 95% confidence interval (CI). Statistical analyses were performed with IBM SPSS Statistics for Windows, Version 22.0. Armonk, NY, USA: IBM Corp.

Ethics issues

The local Institutional Review Board assessed and approved the study (code 2018/593). As long as the study was based on database operation, no informed consent was required. The information was accessed according to prevailing European and Spanish legislation.

Results

Description of the sample

Between May 2013 and June 2019, a total of 16,720 subjects underwent at least one colonoscopy during the first round of the Galician CRC screening program. We excluded 1013 subjects with CRC as the final diagnosis from this analysis. Therefore, we included in the analysis 15,707 patients without a CRC in the first round. After linking this data with the CMBD database, we identified 352 patients with any of the codes related to colorectal surgery. After verifying the clinical records, we confirmed that 162 underwent colorectal surgery related to participation in the screening program, four due to colonoscopy-related complications and 158 due to resection of colorectal lesions (Fig. 1 and Table 1). The surgery rate was as follows: global: 1.03% (95% CI 0.87–

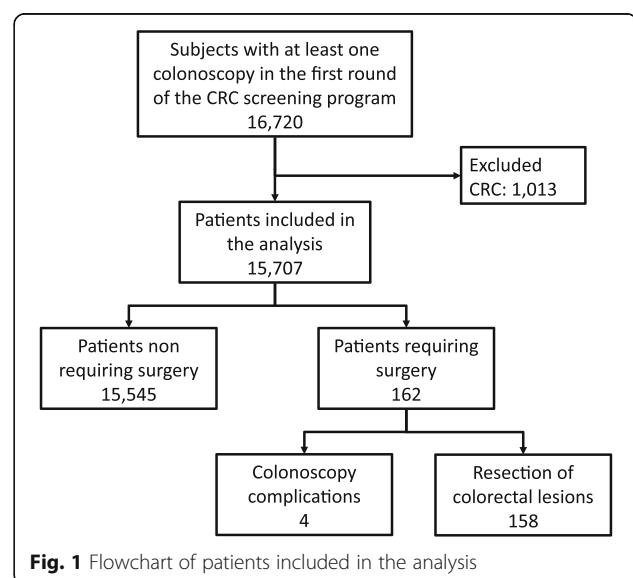


Table 1 Baseline characteristics and surgery rate according to dependent variables

		Patients not requiring surgery (n = 15,545)	Surgery (n = 162)	Surgery rate % (95% CI)	Significance ^a
Sex (n = 15,707)	• Female	6708 (43.2%)	72 (44.4%)	1.06 (0.82–1.31)	0.7
	• Male	8837 (56.8%)	90 (55.6%)	1.01 (0.80–1.22)	
Age (n = 15,707)	• < 60 years	6855 (44.1%)	48 (29.6%)	0.69 (0.50–0.89)	< 0.001
	• ≥60 years	8690 (55.9%)	114 (70.4%)	1.29 (1.06–1.53)	
PS (n = 15, 383)	• 0	12,388 (81.3%)	132 (83.0%)	1.05 (0.87–1.23)	0.8
	• 1	2836 (18.6%)	27 (17.0%)	0.94 (0.59–1.29)	
ASA (n = 15,383)	• I	8876 (58.2%)	96 (60.3%)	1.07 (0.86–1.28)	0.9
	• II	5391 (35.4%)	53 (33.3%)	0.97(0.71–1.23)	
	• III	957 (6.3%)	10 (6.3%)	1.03 (0.40–1.67)	
Fecal Hb (n = 15,707)	• < 100 µg/g	10,388 (66.8%)	79 (48.8%)	0.75 (0.59–0.92)	< 0.001
	• 100–200 µg/g	2935 (18.9%)	41 (25.3%)	1.42 (0.99–1.86)	
	• > 200 µg/g	2222 (14.3%)	42 (25.9%)	1.85 (1.30–2.41)	
N.colonoscopies (n = 15,707)	• One	13,557 (87.2%)	122 (75.3%)	0.89 (0.73–1.05)	< 0.001
	• At least two	1988 (12.8%)	40 (24.7%)	1.97 (1.37–2.58)	
Number of polyps (n = 15,707)		2 (IQR 1–4)	3 (IQR 1–5)		< 0.001
Number of adenomas (n = 15,707)		1 (IQR 0–3)	2 (IQR 1–4)		< 0.001
Adenoma size (mm) (n = 15,707)		5 (IQR 0–12)	19 (IQR 8–31.3)		< 0.001
European guidelines classification (n = 15,707)	• No adenoma	4650 (29.9%)	4 (2.5%)	0.08 (0.00–0.17)	< 0.001
	• Low risk	3626 (23.3%)	4 (2.5%)	0.11 (0.00–0.22)	
	• Intermediate risk	4179 (26.9%)	17 (10.5%)	0.40 (0.21–0.59)	
	• High risk	3090 (19.9%)	137 (84.6%)	4.24 (3.55–4.94)	
Endoscopist's ADR (n = 15,459)	• Q1 (≤60%)	2653 (17.3%)	42 (26.1%)	1.56 (1.09–2.03)	0.02
	• Q2 (60–65.3%)	3989 (26.1%)	40 (24.8%)	0.99 (0.67–1.30)	
	• Q3 (65.3–70.8%)	4181 (27.3%)	34 (21.1%)	0.81 (0.54–1.08)	
	• Q4 (> 70.8%)	4474 (29.2%)	45 (28.0%)	0.99 (0.71–1.28)	
Endoscopist's number of colonoscopies (n = 15,459)	• Q1 (≤57)	198 (1.3%)	2 (1.2%)	1.00 (–0.38–2.38)	0.03
	• Q2 (58–278)	1647 (10.8%)	18 (11.2%)	1.08 (0.58–1.58)	
	• Q3 (279–507)	5340 (34.9%)	39 (24.2%)	0.72 (0.50–0.95)	
	• Q4 (> 507)	8113 (53.0%)	102 (63.4%)	1.24 (1.00–1.48)	
Complexity of hospital (n = 15,707)	• Third level	7150 (46.0%)	52 (32.1%)	0.72 (0.53–0.92)	< 0.001
	• Second level	8395 (54.0%)	110 (67.9%)	1.29 (1.05–1.53)	

ADR Adenoma detection rate, ASA American Society of Anesthesiologists' Physical Status, CI Confidence interval, Hb Hemoglobin, IQR Interquartile range, PS Performance status

^aSignificance in the univariate analysis using the Chi-square test for qualitative variables and the Student's t test for quantitative variables

1.19), due to colonoscopy complications: 0.02% (95% CI 0.00–0.05) due to resection of colorectal lesions: 1.00% (95% CI 0.85–1.16). In the seven hospitals taking part in the CRC screening program, the surgery rate ranged across participating hospitals between 0.27% (95% CI 0.05–0.50) and 1.89% (95% CI 1.36–2.43). After excluding transanal surgeries (31) the colectomy rate was 0.83% (95% CI 0.69–0.98). The colectomy rate again ranged between 0.23% (95% CI 0.03–0.43) and 1.62%

(95% CI 1.06–2.17). In Table 1, we outline the characteristics of the sample as well as the surgery rate according to dependent variables and in Supplementary Table 1 we show the same results referred to colectomies.

Seventy-one endoscopists from seven hospitals took part in the first round of the CRC screening program. The median number of colonoscopies performed was 278 (IQR 56–507) and the median ADR was 65.3% (IQR 60.0–70.08%). We classified endoscopists into quartiles

according to number of colonoscopies performed and ADR. Finally, hospitals were classified into tertiary (three) and secondary (four).

Type of surgery and complications

As we show in Table 2, the main surgical approach was laparoscopy (57.4%). The most common surgeries performed were right-sided interventions (51.3%) and transanal resections (19.1%). The median length of hospitalization was 6 days with minor and major complications in $n = 28$ (17.3%) and $n = 12$ (7.4%) patients, respectively. Only one patient died due to surgery. After discharge, complications were detected in $n = 29$ (18.1%) patients, mainly due to intestinal subocclusion (5), rectal bleeding (3), abdominal wall hernia (11), anastomotic stenosis (2) and change in bowel movements (3). After colectomy, intrahospital complications were detected in $n = 34$ (26%) patients, mostly minor ($n = 23$) and complications after discharge in $n = 28$ patients (21.4%). In contrast, inhospital and out-of-hospital complications were detected in six (19.4%) and one (3.2%) patients after transanal surgery, respectively.

Characteristics of the resected colorectal lesions

As we show in Table 3, most commonly surgically resected lesions were either right-sided (49.6%) or located in the rectum (22.2%). Median endoscopic size was 35 mm and most lesions were either sessile, flat or laterally spreading tumors. The lesions had a SMSA score above 12 in most cases (76.7%). An endoscopic resection was attempted in 23.5% of patients either in the work-up colonoscopy or in scheduled therapeutic colonoscopy. Median surgical size of the lesion was 25 mm and, as in the endoscopic histology, the most common histology was adenomatous (81.8%).

Factors associated with surgery

During bivariate analysis, several factors related to the patient (age), screening program (FIT result and number of baseline colonoscopies performed), characteristics of the lesions detected (number of polyps and adenomas, adenoma size and classification according to the European guidelines for CRC screening), endoscopist quality metrics (ADR and number of colonoscopies performed), and hospital complexity were significantly associated with the surgery rate as shown in Table 2. With respect

Table 2 Surgery indications and complications

		Number (%)	
Indication for surgery ($n = 162$)	• Colonoscopy complications	4 (2.5%)	
	• Resection of colorectal lesions	158 (97.5%)	
Surgical approach ($n = 162$)	• Laparoscopy	84 (51.8%)	
	• Reconverted laparoscopy	9 (5.5%)	
	• Laparotomy	38 (23.1%)	
	• Transanal surgery	31 (19.1%)	
	• Expanded appendectomy	9 (5.6%)	
Type of surgery ($n = 162$)	• Right hemicolectomy	74 (45.7%)	
	• Left hemicolectomy	6 (3.7%)	
	• Sigmoidectomy	15 (9.2%)	
	• Rectum anterior resection	8 (4.9%)	
	• Segmental resection	14 (8.6%)	
	• Subtotal colectomy	5 (3.1%)	
	• Transanal surgery	31 (19.1%)	
	• Transanal surgery	31 (19.1%)	
Length of hospitalization ($n = 162$)		6 (IQR 4–9)	
	In hospital complications ^a ($n = 162$)	• 0	122 (75.3%)
		• I	19 (11.7%)
		• II	9 (5.6%)
		• III	6 (3.7%)
		• IV	5 (3.1%)
• V		1 (0.6%)	
Complications after discharge ($n = 160$)		29 (18.1%)	

^aAccording to the Clavien-Dindo classification [19].

Table 3 Characteristics of colonic lesions resected surgically

		Number (%)	
Location (n = 158)	• Appendix	10 (6.3%)	
	• Cecum	28 (17.7%)	
	• Ascending colon	26 (16.5%)	
	• Hepatic flexure	14 (8.9%)	
	• Transverse colon	13 (8.2%)	
	• Splenic flexure	3 (1.9%)	
	• Descending colon	9 (5.7%)	
	• Sigmoid colon	20 (12.7%)	
	• Rectum	35 (22.2%)	
Endoscopic resection attempt (n = 158)	• Surgery directly	109 (68.9%)	
	• In baseline colonoscopy	29 (18.4%)	
	• In therapeutic colonoscopy	20 (12.7%)	
Type of endoscopic resection (n = 153)	• No resection	118 (74.7%)	
	• Incomplete resection	32 (20.3%)	
	• Piecemeal resection	6 (3.8%)	
	• En bloc resection	2 (1.3%)	
Endoscopic size (mm) (n = 154)		35 (25–50)	
Morphology (n = 155)	• Pedunculated	11 (7.0%)	
	• Sessile	70 (44.3%)	
	• Flat	17 (10.8%)	
	• Flat-depressed	6 (3.8%)	
	• Laterally spreading tumor	51 (32.3%)	
	• Tubular adenoma with LGD	26 (16.4%)	
Endoscopic histology (n = 158)	• Villous adenoma with LGD	51 (32.2%)	
	• Adenoma with HGD	42 (26.5%)	
	• Adenoma with intramucosal carcinoma	6 (3.8%)	
	• Serrated lesion	7 (4.4%)	
	• Serrated lesion with HGD	1 (0.6%)	
	• Other histology	1 (0.6%)	
	• No biopsy	24 (15.2%)	
	SMSA classification (n = 150)	• 6–8	4 (2.7%)
		• 9–12	31 (20.7%)
• > 12		115 (76.7%)	
Surgical size (mm) (n = 136)		25 (20–40)	
Surgical histology (n = 158)	• No residual lesion	10 (6.3%)	
	• Tubular adenoma with LGD	19 (12.0%)	
	• Villous adenoma with LGD	45 (28.5%)	
	• Adenoma with HGD	53 (33.5%)	
	• Adenoma with intramucosal carcinoma	12 (7.8%)	
	• Serrated lesion	9 (5.7%)	
	• Serrated lesion with HGD	4 (2.5%)	
	• Other	6 (3.8%)	

HGD High grade dysplasia, LGD Low grade dysplasia, SMSA Size, Morphology, Site and Access

to colectomy, we also identified several associated variables as shown in supplementary Table 1.

Finally, in the multivariable logistic regression analysis we identified several variables independently associated with the risk of surgery: age ≥ 60 years (OR = 1.57, 95% CI 1.11–2.23), female sex (OR = 2.10, 95% CI 1.52–2.91), the European guidelines classification (high risk OR = 67.94, 95% CI 24.87–185.59; intermediate risk OR = 5.63, 95% CI 1.89–16.80; low risk OR = 1.43; 95% CI 0.36–5.75), the endoscopist's ADR (Q4 OR = 0.44, 95% CI 0.28–0.68; Q3 OR = 0.44, 95% CI 0.27–0.71; Q2 OR = 0.71, 95% CI 0.44–1.14) and a tertiary hospital (OR = 0.54; 95% CI 0.38–0.79) (Table 4). After excluding transanal surgeries, the same variables were independently related to risk of colectomy: age ≥ 60 years (OR = 1.93, 95% CI 1.30–2.89), female sex (OR = 2.21, 95% CI 1.54–3.16), the European guidelines classification (high risk OR = 53.21, 95% CI 19.36–146.18; intermediate risk OR = 5.33, 95% CI 1.77–16.03; low risk OR = 1.07; 95% CI 0.24–4.78), the endoscopist's ADR (Q4 OR = 0.37, 95% CI 0.23–0.61; Q3 OR = 0.48, 95% CI 0.29–0.79; Q2 OR = 0.58, 95% CI 0.34–1.00) and a tertiary hospital (OR = 0.57; 95% CI 0.38–0.85).

Discussion

Our study reports the surgery rate in patients with non-malignant lesions detected within a mass CRC screening program and the factors related to it. Most surgeries are related to resection of colorectal lesions and, exceptionally, to endoscopic complications. This information is extremely relevant to measure overtreatment risks in this setting. Fortunately, the surgery rate is low and the

associated risk of mortality is as expected: one related death in 15,000 subjects. However, we have determined that not only factors associated with the patient and endoscopic findings but also the endoscopist's performance measured with the ADR and hospital level of complexity are independently associated with surgery rate.

Our study has several strengths. The first is related to its population-based perspective. We have collected data from the first round of the Galician CRC screening program. During this initial round, FIT was offered to 721,349 subjects aged 50–69 years, colonoscopies were performed in seven hospitals and quality indicators of seventy-one endoscopists were collected in a centralized database. This database enabled us to calculate surgery rate according to the different variables available. Thus, we could accurately determine the risk of overtreatment in a mass screening program and the side effects related to surgery. There is not much information available to compare our data. As an example, in a retrospective study performed within the scope of the national English Bowel Cancer Screening Program, surgery rate in large polyps (≥ 20 mm flat or sessile) attained 21.7% [22]. Our data are not comparable because the European guidelines high risk group includes adenomas of any morphology ≥ 20 mm in size and/or ≥ 5 adenomas. In fact, most surgically resected lesions in our study were either sessile, flat or laterally spreading tumors (93%) with a SMSA > 12 in most cases. A French study evaluated the frequency and risk factors for the surgical resection of non-malignant polyps detected in a FIT based mass CRC screening program [12]. In this study, the surgery rate in patients with any polyp detected was 4.1% and

Table 4 Factors independently associated with colorectal surgery and colectomy in the logistic regression analysis

		Colorectal surgery (<i>n</i> = 162) Odds Ratio (95% CI) ^a	Colectomy (<i>n</i> = 131) Odds Ratio (95% CI) ^a
Sex (<i>n</i> = 15,707)	• Male	1	1
	• Female	2.10 (1.52–2.91)	2.21 (1.54–3.16)
Age (<i>n</i> = 15,707)	• < 60 years	1	1
	• ≥ 60 years	1.57 (1.11–2.23)	1.93 (1.30–2.89)
European guidelines classification (<i>n</i> = 15,707)	• No adenoma	1	1
	• Low risk	1.43 (0.36–5.75)	1.07 (0.24–4.78)
	• Intermediate risk	5.63 (1.89–16.80)	5.33 (1.77–16.03)
	• High risk	67.94 (24.87–185.59)	53.21 (19.36–146.18)
Endoscopist's ADR (<i>n</i> = 15,459)	• Q1 ($\leq 60\%$)	1	1
	• Q2 (60–65.3%)	0.71 (0.44–1.14)	0.58 (0.34–1.00)
	• Q3 (65.3–70.8%)	0.44 (0.27–0.71)	0.48 (0.29–0.79)
	• Q4 ($> 70.8\%$)	0.44 (0.28–0.68)	0.37 (0.23–0.61)
Complexity of hospital (<i>n</i> = 15,707)	• Second level	1	1
	• Third level	0.54 (0.38–0.79)	0.57 (0.38–0.85)

ADR Adenoma detection rate, CI Confidence interval

^aOdds Ratio and 95% CI calculated in the multivariable logistic regression analysis (forward conditional)

was related with factors related to the size, location, histology, endoscopy center and the endoscopist. In our study, the surgery rate in the patients with at least one adenoma was clearly lower.

We have detected an association between the ADR and the surgery rate independent from the endoscopic findings. ADR is the endoscopist's main quality indicator and has been associated with the risk of interval CRC [23], CRC death [24], detection of serrated polyps [25] and the adenoma detection during surveillance [26]. Although ADR is considered a surrogate for meticulous inspection of the colorectal mucosa, correlation with other important outcomes has never been found. In our case, we hypothesize that our findings reflect an association between the assessment of the mucosa and the endoscopists' resection skills. Our results confirm that endoscopists are a risk factor for surgery in patients with polyps detected in a screening program [12]. Nevertheless, we must draw attention to the high ADR of the endoscopists taking part in the Galician screening program. Although an ADR above 45% is recommended in a FIT-based screening programs [27], in our case 75% of endoscopists attained a 60% ADR.

Our study has several limitations related to quality of the data collected in the CRC screening database. First, we used the CMBD to identify all the colorectal surgeries. Although we do not have information regarding the accuracy of the data obtained from the Spanish CMBD, an evaluation of the ICD-9-CM for CRC in an Italian administrative database showed a sensitivity ranging between 98 and 99% [28]. Unfortunately, information regarding location, morphology of the most advanced lesion, SMSA classification or the visual predicted histology of the lesions detected was not stored. We cannot provide information regarding on the visual suspicion of malignancy of the polyp that could explain some of the referrals to surgery. Additionally this information could explain one of the most striking findings of our study. Although males have an increased risk of advanced neoplasia detection in CRC screening [29] and account for 75% of the high risk lesions detected [30], in our study, females have an increased risk of surgery. The reason is unclear and we suggest it may be related to differences in the natural history of CRC. There is evidence that the serrated carcinogenic pathway, through hypermethylation and BRAF V600E mutation, with flat or sessile serrated lesions located proximally [31, 32], is more common among females and this could explain our findings. In fact, as the study by Le Roy et al. [12] shows, location is a risk factor for surgery in polyps detected in a screening program. Unfortunately, this information was unavailable for patients not requiring surgery.

Colorectal complications and mortality in our study are within the ranges expected. Data analyzed from a

National Surgical Quality Improvement Program from 2011 to 2014, including 12,732 patients who underwent elective surgery for nonmalignant colorectal lesions, revealed a 0.7% 30-day mortality rate and 14% risk of major postoperative adverse events [10]. We also analyzed the long term complications that mainly impair the subject's quality of life [33]. In contrast, endoscopic resection is more cost-effective, has few side effects, complications no greater than 1 to 2% and mortality below 1/10,000 [2]. In large colorectal lesions, endoscopic resection-related mortality ranges between 0 and 0.08% [34, 35]. Despite professional society guidelines and recommendations [9, 36], colectomies for benign colon lesions have increased in the last few years. In the US, surgery incidence for nonmalignant lesions has increased from 5.9/100,000 to 9.4/100,000 adults in 2000 and 2014, respectively [10].

Our study highlights the need for improved endoscopic resection techniques. First, endoscopists need to be trained specifically in visual assessment of colorectal lesions and in resection techniques and their results should be continuously monitored. In this sense, we require contrasted quality indicators adapted to each screening scenario (FIT, colonoscopy). Quality indicators such as visual diagnostic yield, complete resection, complications, relapse and colectomy rates in large colorectal polyps should be monitored both per endoscopist and per endoscopy unit. However, complex endoscopic resection techniques such as submucosal dissection and endoscopic full thickness resection should be available and patients should be referred to centralized units where these techniques are performed on a regular basis [36].

Conclusions

To conclude, the surgery rate in patients with nonmalignant lesions detected in a mass screening program is low and mainly associated with treatment of unresectable polyps. Although complications related to surgery are acceptable, this is an area both endoscopists and endoscopy units can improve upon. In order to reduce the number of subjects referred to surgery, we need to improve the endoscopist resection skills and centralized units for complex techniques should be available. Finally, we require endoscopic resection quality indicators that enable us to continuously monitor endoscopic resection results.

Abbreviations

ADR: Adenoma detection rate; AJCC: American Joint Committee on Cancer; ASA: American Society of Anesthesiologists' Physical Status; CI: Confidence interval; CRC: Colorectal cancer; FIT: Fecal immunochemical test; Hb: Hemoglobin; HGD: High grade dysplasia; IQR: Interquartile range; LGD: Low grade dysplasia; OR: Odds ratio; PS: Performance status; SMSA: Size, Morphology, Site and Access

Supplementary Information

The online version contains supplementary material available at <https://doi.org/10.1186/s12885-021-08606-w>.

Additional file 1: Supplementary Table 1. Baseline characteristics and colectomy rate according to dependent variables.

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Authors' contributions

The authors' contributions were as follows: JC, AG, RA, ERC, IPRL and RZ participated in the study design and search for financial support; AG, RA, ERC, took part in operation of the CRC screening database; JC and AG participated in design of the study database; JC, took part in the clinical records search; JC performed the statistical analysis and wrote the first draft. Finally, all the authors made comments on the article and approved the submitted version of the manuscript. All authors had full access to all the data (including statistical reports and tables) in the study and can take responsibility for the integrity of the data and accuracy of the data analysis. JC had full access to all of the data in the study and takes responsibility for the integrity of the data and accuracy of the data analysis. JC acts as guarantor of the article. The author(s) read and approved the final manuscript.

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Availability of data and materials

The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request.

Declarations

Ethics approval and consent to participate

The local Institutional Review Board of Pontevedra-Vigo-Ourense, Spain assessed and approved the study (code 2018/593). As long as the study was based on database operation, no informed consent was required. The information was accessed according to prevailing European and Spanish legislation.

Consent for publication

Not required.

Competing interests

The authors have no conflict of interest to declare. Joaquín Cubiella has financial support from Instituto de Salud Carlos III but has no financial relationships with any organizations that might have an interest in work submitted in the previous five years, and no other relationships or activities that could appear to have influenced the submitted work.

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