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Relationship between the polyp detection rate and the post-colonoscopy colorectal cancer rate

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ABSTRACT

Aim: the adenoma detection rate is the quality indicator of colonoscopy that is most closely related to the development of interval colorectal cancer or post-colonoscopy colorectal cancer. However, the recording of this indicator in different units of gastrointestinal endoscopy is obstructed due to the large consumption of resources required for its calculation. Several alternatives have been proposed, such as the polyp detection rate. The objective of this study was to evaluate the relationship between the polyp detection rate and its influence on post-colonoscopy colorectal cancer rate.

Patients and methods: in this study, 12,482 colonoscopies conducted by 14 endoscopists were analyzed. The polyp detection rate was calculated for each endoscopist. Endoscopists were grouped into quartiles (Q1, Q2, Q3, and Q4), from lowest to highest polyp detection rate, in order to evaluate whether there were any differences in the development of post-colonoscopy colorectal cancer.

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Results: the lowest polyp detection rate was 20.66% and the highest was 52.16%, with a median of 32.78 and a standard deviation of ± 8.54. A strong and positive association between polyp endoscopy diagnosis and adenoma histopathology result was observed and a linear regression was performed. A significantly higher post-colonoscopy colorectal cancer rate was observed in the group of endoscopists with a lower polyp detection rate ($p < 0.02$).

Conclusion: polyp detection rate is a valuable quality indicator of colonoscopy and its calculation is much simpler than that of the adenoma detection rate. In our study, the prevalence of post-colonoscopy colorectal cancer was inversely and significantly related to the endoscopists' polyp detection rate.

Key words: Colorectal neoplasms. Polyp detection rate. Post-colonoscopy colorectal cancer.

INTRODUCTION

Currently, colorectal cancer (CRC) is the third most common cancer worldwide for both sexes and is the fourth leading cause of death by cancer (1). At present, colonoscopy is the diagnostic technique of choice for CRC. Although it may produce false-negative results (2,3), leading to late detection. Post-colonoscopy colorectal cancer (PCCRC) is diagnosed within a relatively short period after a negative colonoscopy, or identified when lesions are completely removed. Diagnosis periods are not well defined in the literature but are between 36 and 60 months post-colonoscopy (4). The causes of PCCRC are not completely defined and accurately identifying the etiology has been a great challenge.

There are three pathways through which PCCRC occur (4-7) and the algorithm published by Pabby et al. is as follows (8,9):

1. Existing lesions in the index colonoscopy, not visualized by the endoscopist (missed lesions, 50-60%):
   - CRCs diagnosed 6-36 months post-colonoscopy independent of size.
   - CRCs greater than 2 cm or advanced stage that were diagnosed 36-60 months after a negative colonoscopy.

2. Lesions identified but not completely excised, with local recurrence of the lesion (~20%): lesions located where a polypectomy was previously performed.

3. *De novo* lesions that occur over a short period with molecular characteristics that allow for rapid tumor growth (~25%): lesions less than 2 cm and with a non-advanced TNM stage that were diagnosed 36-60 months post-colonoscopy.

Although the current rate of unidentified lesions in colonoscopy in the clinical practice is unknown, it is paramount to establish an adequate follow-up of patients with adenomas (3). The scientific community and the European Society of Gastrointestinal Endoscopy (ESGE) have detailed the quality indicators of colonoscopy that determine a reduction in the development of PCCRC. They recommend all endoscopy units to develop recording procedures of these indicators in order to facilitate the internal audit of the scientific and technical conditions under which endoscopic explorations are performed. This measure will allow for the correction of existing deficits and could prevent most "interval lesions" (10).

According to the literature, the adenoma detection rate (ADR) is the most important indicator to measure colonoscopy quality (11). This is defined as the proportion of patients undergoing a colonoscopy in which at least one adenoma is detected. However, its calculation requires intense manual work, reviewing colonoscopies in which a polyp is detected and later histologically confirming that the detected polyp is an adenoma. Due to this limitation, alternatives to the ADR have been proposed and the polyp detection rate (PDR) deserves a special mention (12).

The objective of this study was to demonstrate that it is possible to obtain an approximation of the ADR by calculating the endoscopists' PDR in a gastrointestinal endoscopy unit at a third-level hospital. The relationship between the PDR and the development of PCCRC was also evaluated.

METHODS AND MATERIALS

Study design and data collection

This was an observational retrospective study. The patient cohort was identified in a third-level hospital in an area with approximately 300,000 inhabitants (Hospital Santa

Lucía, Murcia, Spain). Data collection was performed via access to the following digital files:

- Endoscopic reports of the colonoscopies performed in our Digestive Endoscopy Unit from January 1st 2011 to December 31st 2014, recorded in the Medical Explorer form.
- Medical records and Pathology reports obtained from the Selene computer program used by the hospital.

Study variables

Initially, 12,482 computer-assisted colonoscopies were analyzed that were performed for any indication and conducted by 14 endoscopists. PDR, defined as the number of patients in which at least one polyp was found and removed, was calculated for each endoscopist and expressed as a percentage. Every hyperplasic polyp smaller than 5 mm located in the rectum or sigma were not included following the endoscopist's diagnosis.

Calculating the PDR does not require as much effort for endoscopy units with capture and recording systems for the endoscopic report. In Spain, this tool is available in many endoscopy units and several studies report an adequate correlation with the ADR using the Pearson's correlation coefficient (12,19). A Pearson's correlation test was performed to analyze whether the endoscopists' diagnoses of polyps were associated with the histopathologic result of adenoma. A random sample of 60 colonoscopies were selected and the detected polyps were counted. The necessary sample size was previously calculated by statistical analysis in order to reach a suitable power higher than 95%. Those polyps that histologically matched an adenoma were identified. A linear regression analysis was performed after finding a strong and positive association.

The PDR was calculated and its relationship with the development of PCCRC was also evaluated. In this study, PCCRC was defined as colorectal cancers diagnosed within 6 to 60 months following a negative colonoscopy that was performed due to any indication. This is consistent with other studies in the literature in which colonoscopy quality and molecular features are considered. The prevalence of PCCRC diagnosed between

January 1st 2012 and December 31st 2014 was calculated. Patients with a known high risk of CRC were excluded, including personal or family history of CRC, inflammatory bowel disease and polyposis syndrome, among others. People younger than 18-years-old were also excluded.

The endoscopists were grouped into quartiles according to their PDR (Q1, Q2, Q3 and Q4) in order to evaluate whether there was a relationship between the PDR and the development of PCCRC. The relationship between the endoscopists' PDR and the sporadic detection of CRC was also analyzed. This was performed in order to avoid a bias resulting from an endoscopist with a high PDR and a greater number of colonoscopies and therefore, a greater possibility of PCCRC. The "PCCRC rate" of each group of endoscopists was obtained as follows: *number of PCCRC/PCCRC + sporadic CRC* expressed in percentage.

In order to complete the evaluation of the relationship between PDR and PCCRC development, those cases that were not determined by endoscopy quality following Pabby's algorithm were excluded, i.e., any PCCRC less than 2 cm in size and early stage, diagnosed 36-60 months post-colonoscopy.

Statistical analysis

Categorical variables were summarized by the median, frequencies and absolute values. The mean and standard deviation were calculated for continuous variables. For statistical analysis, univariate tests of association were assessed using the Student's t-test for continuous variables and the Chi-square test for categorical variables. The relationship between the diagnosis of a polyp and an adenoma histopathological result was analyzed by using a Pearson's correlation test as explained previously. Values were considered as statistically significant when the p value was < 0.05. The statistical analysis was performed using the SPSS software 20v (IBM, USA).

This study was approved by the Ethics Committee clinical research of the reference institution.

RESULTS

In this study, 12,482 computer-assisted colonoscopies were analyzed. The endoscopists' PDR was obtained after identifying the colonoscopies performed by each endoscopist. The lowest rate was 20.66% and the highest was 52.16%; the median and standard deviation were 32.78 and ± 8.54, respectively (Table 1). Subsequently, a linear regression analysis was performed from a sample of 60 random colonoscopies that included 4-5 colonoscopies by each endoscopist. Of these, 35 had at least one polyp removed and a total of 59 polyps were analyzed. In the case of colonoscopies in which polyps had been removed, the number of polyps corresponding to an adenoma in the anatomopathological report was determined. A linear correlation equation between polyp and adenoma was obtained and Pearson's correlation coefficient was 0.927, $p < 0.01$ (Fig. 1).

In order to calculate PCCRC prevalence, 325 CRCs diagnosed between January 1st 2012 and December 31st 2014 were analyzed. Thirty-four cases were excluded, as they did not fulfill the inclusion criteria; 291 CRCs were considered for the study and 17 PCCRCs of 291 CRCs were identified (5.84%). Endoscopists were divided into four groups, by quartiles, according to their PDR in order to facilitate the analysis (Table 2). The "PCCRC rate" for each endoscopist group is shown in table 3 and there was a higher PCCRC prevalence for endoscopists with lower PDRs. The differences were not statistically significant, but the p value was 0.06, which indicates that significant differences may be obtained if the size of the study population was increased. PCCRCs were classified according to the etiology, as described by the algorithm by Pabby et al.:

1. Missed lesions: 12 cases (70.59%).
2. Previous incomplete resection: one case (5.88%).
3. *De novo* lesions: four cases (23.53%).

Endoscopists were grouped in two groups (G1 = Q1+Q2 y G2 = Q3+Q4) and PCCRC classified as new lesions (i.e., those that do not depend on endoscopy performance quality) according to the Pabby et al. algorithm (8) were excluded from the analysis (four cases of 17 PCCRC). A significantly higher PCCRC prevalence was observed in G1 (nine PCCRC, 69.2%) *versus* G2 (four PCCRC, 30.8%), $p < 0.02$. It is important to note that three of four PCCRC which do not depend on endoscopy performance quality (*de*

novo lesions) were in the Q4 endoscopist group.

DISCUSSION

Current evidence suggests that PCCRC are more frequent due to lesions unidentified during colonoscopy and to a lesser extent, a rapid carcinogenesis pathways (14,15). "Interval CRC" represents between 3.5% and 9% of all cancers diagnosed. The overall prevalence was 3.7% (95% CI, 2.8-4.9%) according to a recent meta-analysis of population studies (4,16,17). A retrospective study performed in Spain by Ferrández et al. found that up to 13% of advanced adenomas were not detected during colonoscopies performed two years prior to the diagnosis of these lesions (3).

The factors related to the endoscopic technique that result in undetected lesions include size, location, cathartic preparation, withdrawal time and endoscopist experience (18). Endoscopists who spend more time inspecting the colon mucosa have a higher ADR (19-21). Many studies relate ADR with PCCRC and Kaminski et al. demonstrated that an ADR lower than 20% was associated with a higher risk of developing interval cancer (22). The recommended ADR to meet quality standards is 25%. When stratified by sex, this increases to 30% in males and is 20% in females (4,23). Computer tools facilitate the calculation using capture and recording systems of the endoscopic and histological reports (24). However, these programs are not available in most endoscopy units. The quality indicator most closely related to the incidence of PCCRC according to the literature is the least recorded and well known by endoscopists. Based on the results of this study, the PDR is thought to be a valuable quality indicator of colonoscopy for digestive endoscopy units in which endoscopists' ADRs are unknown. Prospective studies are needed to verify the relationship between the PDR and quality improvement in colonoscopies in order to consider it as a quality indicator (25). Nevertheless, the ADR can be estimated with reliable statistical tools such as linear regression equations when the endoscopist's PDR is known. This measure is characteristic for each endoscopy unit, although the correlation coefficient between ADR and PDR is generally very high (23). Therefore, the two metrics are comparable. One of the most criticized characteristics of PDR is the inclusion of hyperplastic polyps smaller than 5 mm located in the rectum-sigma as a "polyp".

Despite this controversy, the studies show that the histological correlation of the lesions identified (polyp-adenoma) is high.

At least one of the two indicators should be known in endoscopy units. This would allow for interventions that aim to improve the training of professionals in units that do not reach the minimum PDR required. ADR had not been calculated in this study. However, the correlation between the polyp endoscopy diagnosis and adenoma histopathologic result was high (Pearson's correlation coefficient was 0.927). Further multicenter studies are needed in order to establish a translatable polyp-adenoma correlation. Thus, each Endoscopy Unit could omit this calculation in the future.

PCCRC prevalence was similar to that previously reported in the literature (16). The PCCRC rate has been reported in a few studies (26), although leading quality indicators of colonoscopy are shown. There was a higher PCCRC rate in this study among endoscopists with a lower PDR but there were no significant differences. Nevertheless, significant differences were found when only PCCRCs related with colonoscopy performance were considered. The main hypothesis for this observation is that there were more technical deficits for endoscopists that had performed fewer explorations.

The main limitation of this study was the low number of PCCRC cases and the single center retrospective study design. Thus, further studies are needed and the conclusions from this cannot be extrapolated. Methodology design is complex as there is not a single model of a PCCRC study (4). Thus, scientific societies must establish a common design to perform homogeneous multicenter studies. Currently, PCCRC is not only important in screening programs. Colonoscopies performed due to any indication are analyzed in several studies (27,28). All colonoscopies performed by endoscopists were included in this study. Therefore, those endoscopists who performed screening colonoscopy were highlighted.

A rapid access to each endoscopist' ADR or PDR may be a valuable parameter to monitor the technical improvements implemented for colonoscopy equipment, modify preparation guidelines and detect technical difficulties in the daily clinical practice that increase the number of unidentified lesions (29). As shown in the literature, PCCRC incidence is significant. Most cases are due to lesions that were not identified in a previous colonoscopy, which may have a significant medical-legal impact. This

incidence also reflects the scientific and technical quality of the endoscopy unit that performs the exploration. The common goal should be to provide as much information as possible in the endoscopic report, implementing a common structure and routine reporting of intra-procedure quality indicators.

CONCLUSION

The most closely related indicator for the development of PCCRC is the ADR (23). However, the available indicators should be used to monitor scientific and technical quality in the daily clinical practice. This study demonstrates that the calculation is not complex when computer tools are available that aid the calculation. PDR is an alternative to ADR and is significantly related to PCCRC incidence.

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ETHICAL STANDARDS

The study was evaluated by the Clinical Research Ethics Committee (CREC) of the hospital and approval was obtained to perform the consultation, obtain clinical data from patients and subsequently publish the findings.

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Table 1. Colonoscopies performed by each endoscopist in the digestive endoscopy unit and endoscopist PDR; those who perform colonoscopy screening for CRC are identified

Endoscopist	Total colonoscopies in the period (n)	Colonoscopies with at least one polyp (n)	PDR (%)	Screening (Yes/No)
1	2,558	1,129	44.13	Yes
2	1,447	414	28.61	No
3	577	301	52.16	Yes
4	989	316	31.95	Yes
5	1,112	338	30.39	No
6	565	198	35.04	No
7	594	206	34.68	No
8	331	98	29.6	No
9	292	69	23.63	No
10	1,286	410	31.78	Yes
11	695	177	25.46	No
12	784	162	20.66	No
13	304	82	26.97	No
14	948	209	22.39	No

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Table 2. Endoscopists stratified by their PDR and the quartile to which they were classified

Endoscopist	PDR (%)	Quartiles
12	20.66	Q1
14	22.39	Q1
9	23.63	Q1
11	25.46	Q1
13	26.97	Q2
2	28.61	Q2
8	29.60	Q2
5	30.39	Q3
10*	31.78	Q3
4*	31.95	Q3
7	34.68	Q4
6	35.04	Q4
1*	44.13	Q4
3*	52.16	Q4

*Endoscopists who performed colonoscopies for CRC screening.

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Table 3. PCCRC rate of each group of endoscopists (quartiles)

Endoscopists (quartiles)	PCCRC (n)	S-CRC (n)	PCCRC + S-CRC	PCCRC rate (%) (PCCRC/PCCRC + S-CRC)
Q1	6	68	74	6/74 (8.1%)
Q2	4	33	37	4/37 (10.81%)
Q3	2	64	66	2/66 (3.03%)
Q4	5	107	112	5/112 (4.46%)
TOTAL	17	272*	289	17/289 (5.88%)

*Two cases of S-CRC (sporadic CRC) in which the endoscopist was not reported.

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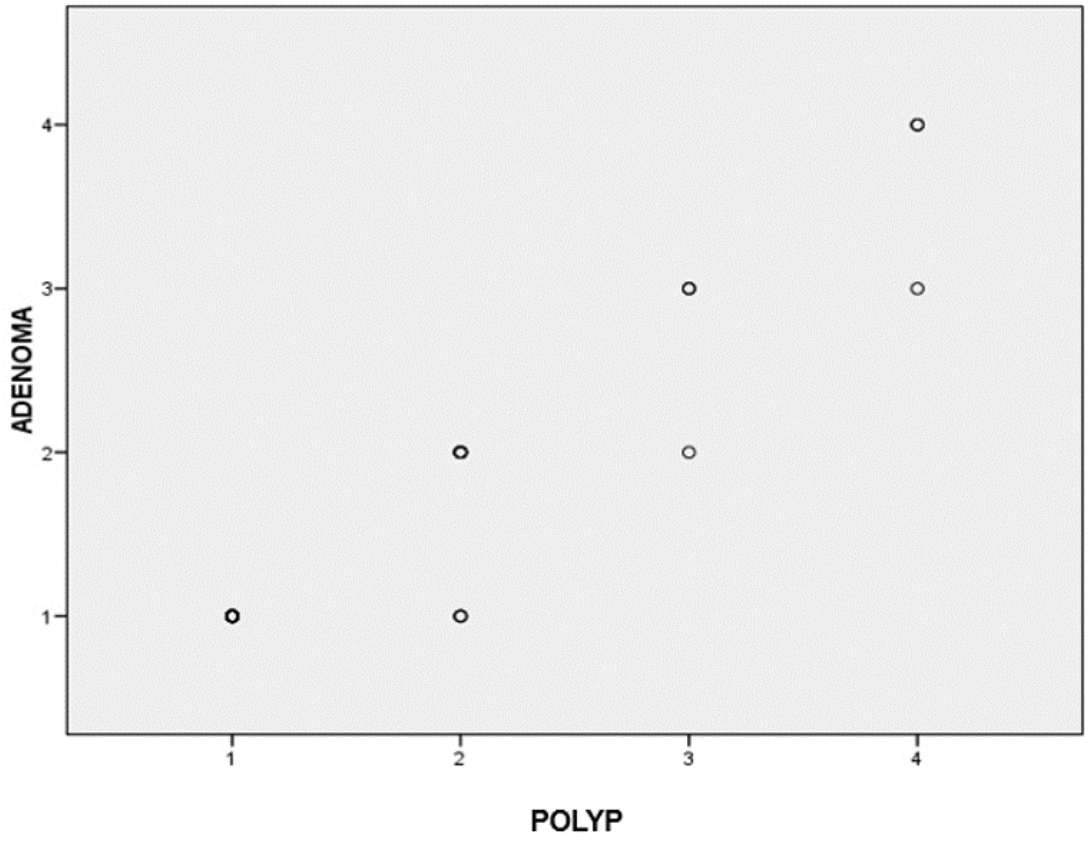

Fig. 1. Linear regression graph that resulted from the polyp-adenoma correlation equation.