

Number of polyps detected is a useful indicator of quality of clinical colonoscopy



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ABSTRACT

Background and study aims Adenoma detection rate (ADR) is a well-known quality indicator (QI) for colonoscopy. It is, however, difficult to evaluate ADR during practice.

The aim of this study was to investigate the number of endoscopically detected polyps as a QI for colonoscopy.

Patients and methods This was a retrospective single-center cohort study of 5,190 consecutive patients who underwent colonoscopy from January 2015 to May 2016. Among these patients, we ultimately enrolled 1,937 patients for initial colonoscopy. We evaluated QIs including bowel preparation, cecum intubation time, withdrawal time, number of endoscopically detected polyps, ADR and advanced neoplasia detection rate (ANDR)

Results The mean number of endoscopically detected polyps, ADR and ANDR were 1.5 ± 2.3 (95% confidence interval (CI) 1.4–1.6), 38.6% (95% CI 36.5–40.8), and 18.3% (95% CI 16.6–20.1), respectively. ADR and ANDR increased with the number of endoscopically detected polyps, but the correlation reached a plateau at five or more polyps. We divided the patients into three groups based on the number of polyps (1 to 2, 3 to 4, and 5 or more). Logistic regression analysis adjusted by age and sex revealed that presence of a large number of polyps was a strong predictor of advanced neoplasia (odds ratio: 3.1 [95% CI 2.2–4.3] for 3 to 4 polyps and 7.9 [95% CI 5.4–11.8] for 5 or more polyps when using the presence of 1 or 2 polyps as a reference).

Conclusion The number of endoscopically detected polyps can predict risk of advanced neoplasia and may thus be a new QI for colonoscopy.

Introduction

Colorectal cancer (CRC) is one of the leading causes of death due to cancer worldwide [1]. Removal of adenomatous colorectal polyps, which are precursor lesions for CRC, is known to be important for reducing both incidence and mortality of CRC, particularly advanced neoplasia [2]. Colonoscopy is an important screening modality for detecting and removing adenomatous polyps [3] and for reducing interval CRC [4, 5]. Therefore, an endoscopist is required to perform high-quality colonoscopy and evaluate the quality of his or her performance based on clinical parameters, such as adenoma detection rate (ADR). ADR and withdrawal time (WT) are well known as important

quality indicators (QIs) of colonoscopy [6–9]. Specifically, a 25% or higher ADR is required (higher than 30% for men and 20% for women) for initial colonoscopies, and a WT of at least 6 minutes with intact colons is desired [10–13]. There is excellent correlation between ADR and WT and prevention outcomes, which is reflective of careful examination via colonoscopy [14]. Kaminski et al. reported that an ADR of 20% or higher is significantly associated with a reduced risk of interval CRC compared with an ADR below 20% [7]. However, a considerable number of colonoscopic examinations and pathological evaluations and a large amount of time are required for each endoscopist to evaluate the quality of his or her performance. In addition, endoscopic reports and histological reports are not

linked in most clinical practices. Therefore, an endoscopist must review and combine two separate reports. Consequently, it is difficult for endoscopists to know the daily ADR in clinical practice. Furthermore, it is possible that once endoscopists detect an adenoma, they become less motivated to find subsequent adenomas [15, 16]. However, it is possible to evaluate the number of endoscopically detected polyps without histologic evaluation, and it is easy to count the number of polyps per colonoscopy during routine colonoscopy. The aim of this study was to investigate the number of endoscopically detected polyps as a new QI of colonoscopy and as a surrogate marker to ADR and advanced neoplasia detection rate (ANDR).

Patients and methods

Patients

This was a retrospective single-center cohort study. We conducted this study based on routine clinical practice in an educational hospital certified by the Japan Gastroenterological Endoscopy Society (JGES). From January 2015 to May 2016, 5,190 patients underwent colonoscopy at Toyonaka Municipal Hospital. Among these patients, we consecutively enrolled patients who underwent initial colonoscopy. The study was approved by the institutional review board of Toyonaka Municipal Hospital. Exclusion criteria were as follows: advanced CRC, presence of inflammatory bowel disease, history of colorectal resection, urgent colonoscopy without bowel preparation or inadequate preparation to evaluate QI for total colonoscopy, prior knowledge of lesions or prior colonoscopy.

Outcomes

We evaluated quality of bowel preparation with the Boston Bowel Preparation Scale (BBPS), cecum intubation time, WT, the number of endoscopically detected polyps, polyp detection rate (PDR), ADR, non-neoplastic polypectomy rate (NNPR) and ANDR. We measured PDR, ADR, and ANDR and then studied the correlation between these indicators and the number of endoscopically detected polyps to evaluate the benefit of polyp number as a QI.

Definitions

Cecum intubation is defined as the passage of the colonoscope tip from the rectum to the ileocecal valve. WT is the period from when the cecum was reached to when the scope was withdrawn from the rectum. This period included time required for maneuvers such as endoscopic resection performed during the withdrawal phase of the examination [12]. An attending endoscopist evaluated the quality of bowel preparation using the BBPS [16]. The number of endoscopically detected polyps is defined as the total number of polyps confirmed at the time of each colonoscopy irrespective of removal. However, hyperplastic polyps smaller than 5 mm, which were endoscopically diagnosed with white-light imaging (WLI) or narrow-band imaging (NBI) in the sigmoid colon or rectum, were not counted because considerable evidence suggests that patients with only sigmoid colon or rectum hyperplastic polyps appear to represent a low-risk cohort [17]. PDR is defined as the proportion of

colonoscopies that led to detection of at least one polyp without histological confirmation. ADR is defined as the proportion of colonoscopies that led to removal of at least one histologically confirmed colorectal adenoma per colonoscopy. Advanced neoplasia is defined as cancer or adenoma measuring at least 10 mm in diameter with high-grade dysplasia, villous or tubulovillous histologic characteristics, or any combination of these features [18]. A polyp is defined as villous when 25% or more of its mass is composed of villi. ANDR was defined as the proportion of colonoscopies that led to detection of at least one histologically confirmed advanced neoplasm per colonoscopy. Sessile serrated polyps (SSPs) were not counted toward the ADR, as recommended by the American Society for Gastrointestinal Endoscopy/American College of Gastroenterology Task Force on Quality in Endoscopy [6, 10]. NNPR is defined as the proportion of colonoscopies that led to detection of at least one histologically confirmed colorectal non-neoplastic polyp. Non-neoplastic polyps comprise mucosal tissue and inflammatory polyps but not hyperplastic polyps or SSPs [19].

Procedures

Before the scheduled colonoscopy appointment, a hospital pharmacist instructed all patients on use of drugs to prepare for the procedure. The standard bowel cleansing regimen included polyethylene glycol (PEG) plus ascorbic acid (1.5 L of Moviprep [EA Pharmaceutical Co., Ltd., Tokyo, Japan] liquid state) or PEG (2 L of Muben [Nihon Pharmaceutical Co., Ltd., Tokyo, Japan] liquid state) taken within 2 hours after 6 a.m. for colonoscopy in the morning or after 9 a.m. for colonoscopy in the afternoon. Colonoscopy was performed by nine full-time expert endoscopists who were board-certified at the Japan Gastroenterological Endoscopy Society and 10 full-time non-expert endoscopists (trainees) at Toyonaka Municipal Hospital during the study period. All trainees were supervised by expert endoscopists over a 1-year training interval (during at least 300 colonoscopies) before participation in this study. We routinely used Olympus CF-Q260AI or CF-H290I series (Olympus Optical Co., Tokyo, Japan) colonoscopic instruments for colonoscopy and evaluated by conventional WLI and NBI. If a patient preferred sedation, we used intravenous midazolam under electrocardiographic monitoring and oxygen saturation detection under conscious sedation. Anticonvulsants, such as scopolamine butyl bromide or glucagon, were used unless contraindicated. Carbon dioxide insufflation was employed for all colonoscopies. Polyp size was endoscopically measured using standard clinical practices, such as by visual estimation, the open biopsy forceps method or use of a polypectomy snare. When we detected colorectal polyps during colonoscopy, the indication for endoscopic resection (ER) was >5 mm for polyp size, and diminutive polyps were allowed to be followed up without resection based on the judgement of each endoscopist at our institution, adhering to the JGES guideline [20]. However, flat and depressed lesions that were difficult to distinguish from adenoma or carcinoma were resected. The final decision to perform ER was made by each physician based on the patient's condition and bowel preparation. However, we did not adopt a resect-and-discard

strategy [21] in this study. All removed specimens were evaluated and diagnosed by full-time pathologists at our hospital.

Statistical analyses

All continuous variables are presented as means \pm standard deviation (SD). Categorical variables are presented as the number in each category or the frequency. A receiver operating characteristic (ROC) curve analysis was used to determine the cut-off value for polyp number for detecting advanced neoplasia. Multiple logistic regression analysis was performed to determine the odds ratios adjusted by age and sex for advanced neoplasms comparing fewer than three polyps with a higher number of polyps. Spearman's rank-order correlation was used to evaluate the relationship between ADR and mean number of endoscopically detected polyps or ANDR. Statistical analyses were performed using JMP software (ver. 13.1.0, SAS Institute, Inc., Cary, North Carolina, United States).

Results

A total of 5,190 consecutive patients underwent colonoscopy in our hospital during the study period. We excluded 754 patients who had inadequate or insufficient QIs for total colonoscopy because of incomplete performance or previous knowledge of lesions, including 166 patients with advanced CRC, 222 patients with inflammatory bowel disease, 62 patients with post-operation status, 166 patients with urgent colonoscopy without bowel preparation and 138 patients with inadequate preparation for colonoscopy. Furthermore, we excluded 745 patients who underwent endoscopic mucosal resection, 68 patients who underwent endoscopic submucosal dissection and 1,686 patients with colonoscopy for evaluation of known lesions ($n=76$) and scheduled surveillance ($n=1,610$). Ultimately, we enrolled 1,937 patients (53.3% male; mean age, 64 ± 13 years) undergoing initial colonoscopies for positive fecal immunochemical test (FIT) ($n=1,000$, 51.6%), primary screening ($n=260$, 13.4%) and symptoms ($n=677$, 35.0%). Among the enrolled patients, Muben was used in 1,216 (62.8%) and Moviprep was used in 721 (37.2%). The sedative midazolam was used in 50.6% of patients. ► **Table 1** shows the patient characteristics and the QIs of colonoscopies. The cecum intubation rate was 98.6%, and average total time was 24 ± 11 minutes. The average cecum intubation time was 10 ± 7.8 minutes, and average WT was 13 ± 8.1 minutes.

Bowel preparation and number of endoscopically detected polyps

The average BBPS was 7.2 ± 1.5 , and adequate bowel preparation (a score of ≥ 2 in each segment of the colon) was achieved in 88.2% of patients (1709/1937). The mean number of endoscopically detected polyps per procedure was 1.5 ± 2.3 (95% confidence interval [CI] 1.4–1.6). The cecum intubation rate was significantly better in the adequate bowel preparation group than that in the poor bowel preparation group (BBPS < 6) (99.8% vs. 88.4%, $P < 0.0001$), as were the intubation times (10.2 ± 7.5 minutes vs. 13.9 ± 10.0 minutes, $P < 0.0001$). There was no significant difference between experts and trainees in

► **Table 1** Characteristics of 1,937 patients undergoing initial colonoscopy and quality indicators.

Variable	Total (n=1,937)
Age (years), mean \pm SD	64 ± 13
Sex, male (%)	1,032 (53.2)
Sedative drug use ¹ , n (%)	982 (50.6)
Cecum intubation rate, n (%)	1911 (98.6)
Intubation time, min	10 ± 7.8
BBPS	7.2 ± 1.5
Total procedure time, min	24 ± 11
▪ With polyp, min	26 ± 11
▪ Without polyp, min	22 ± 10
Total withdrawal time, min	13 ± 8.1
▪ With polyp, min	16 ± 8.6
▪ Without polyp, min	11 ± 6.2
Total number of detected polyps	2,907
Total number of resected polyps	657
PDR, % (95% CI)	57.5 (55.2–59.6)
ADR, % (95% CI)	38.6 (36–40)
ADR/PDR ratio	0.67
ANDR, % (95% CI)	18.3 (16.6–20.1)
NNPR, % (95% CI)	1.3 (0.9–2.0)

PDR, polyp detection rate; ADR, adenoma detection rate; NNPR, non-neoplastic polypectomy rate; ANDR, advanced neoplasia detection rate; CI, confidence interval

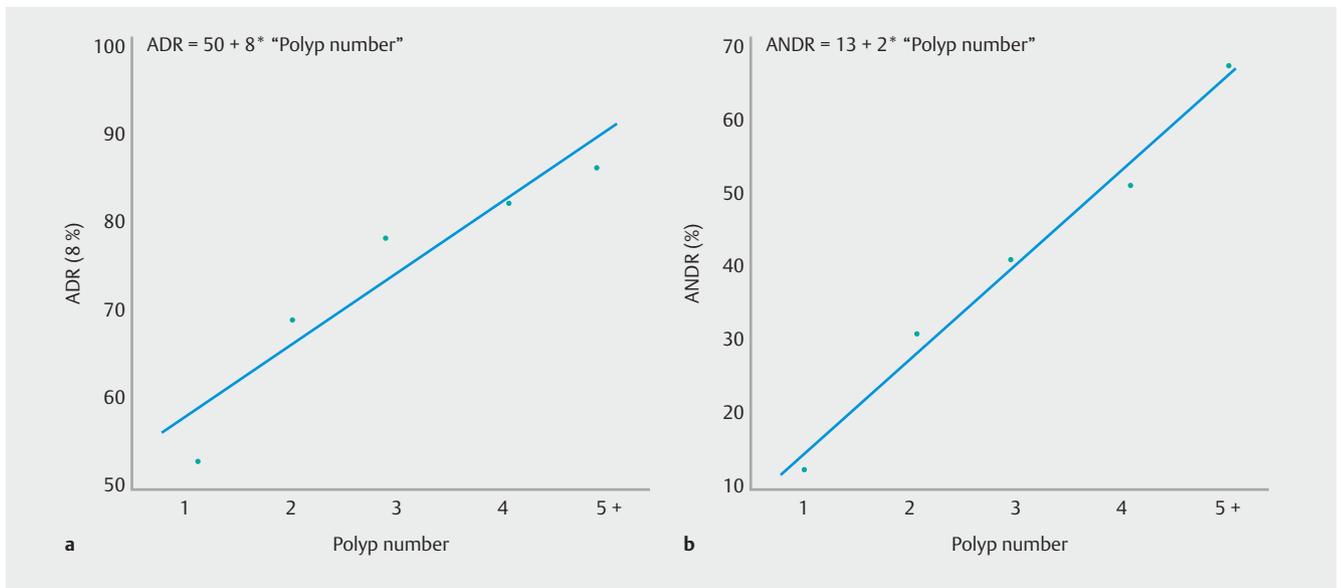
When we detected colorectal polyps during colonoscopy, the indication for endoscopic resection was > 5 mm for polyp size, and diminutive polyps were allowed to be followed up without resection, adhering to the JGES guideline [20]. This procedure may have resulted in a lower ADR than that observed in reality.

¹ Midazolam

number of endoscopically detected polyps (1.5 ± 2.3 vs. 1.3 ± 2.1 , $P=0.2838$).

QIs

The overall PDR, ADR, NNPR and ANDR were 57.5% (95% CI 55.2–59.6), 38.6% (95% CI 36.5–40.8), 1.3% (95% CI 0.9–2.0) and 18.3% (95% CI 16.6–20.1), respectively. All endoscopists except for two trainees had an ADR of 25% or higher (data not shown). There was no significant difference in ADR and ANDR between experts and trainees ($P=0.3725$ and $P=0.4848$, respectively). Therefore, we evaluated QIs to address experts and trainees together. We found that number of polyps was positively correlated with ADR and ANDR, but the association plateaued at five or more polyps (approximately 86% and 67%, respectively). ► **Fig. 1** shows the relationship between number of polyps and ADR (**a**) and that between number of polyps and ANDR (**b**). When one or more polyps were detected, the linear approximation equations describing those relationships were



► **Fig. 1** **a** Relationship between the number of polyps and ADR and **b** between the number of polyps and ANDR.

► **Table 2** Association of number of detected polyps with older age, male sex, and higher ADR and ANDR¹.

Polyp number	Total	0	1	2	3	4	5+
n (%)	1937	823 (42)	481 (25)	248 (13)	144 (7.4)	82 (4.2)	159 (8.2)
Age (years), mean ± SD	64 ± 13	61 ± 15	64 ± 12	67 ± 11	69 ± 9	71 ± 9	70 ± 9
Sex, male (%)	53	46	51	60	63	62	73
ADR, % (95% CI)	38 (36–40)	0	53 (48–57)	69 (63–74)	78 (71–84)	82 (73–89)	86 (80–91)
ANDR, % (95% CI)	18 (16–20)	0	13 (11–17)	31 (25–37)	41 (33–49)	51 (40–61)	67 (60–74)

ADR, adenoma detection rate; ANDR, advanced neoplasia detection rate; CI, confidence interval
¹ The association plateaued at 5 polyps.

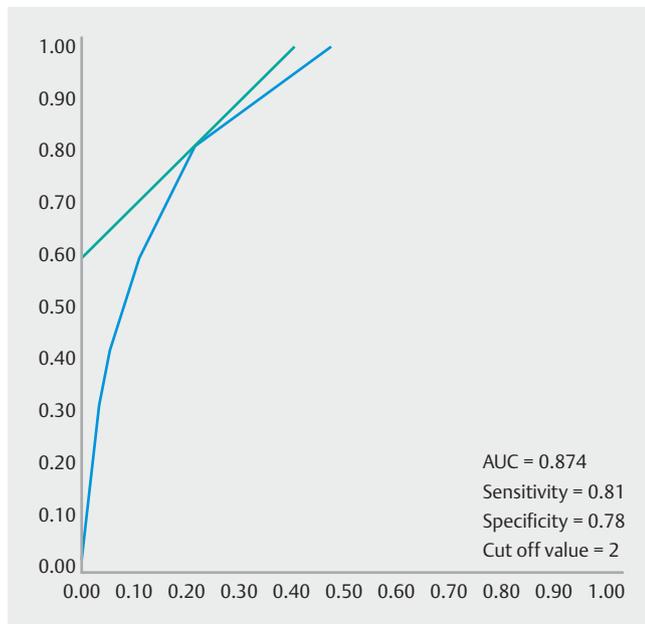
$ADR(\%) = 50 + 8 \times \text{the number of polyps}$ and $ANDR(\%) = 13 + 2 \times \text{the number of polyps}$, respectively.

Age and male sex were positively correlated with number of detected polyps (► **Table 2**). Next, using ROC analysis, we evaluated the performance of the number of detected polyps per procedure, stratified into groups according to cut-off values, in predicting presence of at least one advanced neoplasm. The ideal cut-off value for polyp number was two (area under the ROC curve (AUC) 0.874, sensitivity 81% and specificity 78%) (► **Fig. 2**). Accordingly, we divided the patients into three groups based on the number of polyps detected (1 to 2, 3 to 4, and 5 or more) (► **Table 3**). Logistic regression analysis adjusted by age and sex revealed that presence of three or more polyps was a stronger predictor of adenoma and advanced neoplasia than presence of fewer than three polyps, and the risk increased with the number of detected polyps (odds ratio for ADR: 2.9, 95% CI 2.0–4.2 for 3 to 4 polyps and 4.8, 95% CI 3.0–8.1 for 5 or more polyps and odds ratio for AADR: 3.1, 95% CI 2.2–4.3 for 3 to 4 polyps and 7.9, 95% CI 5.4–11.8 for 5 or more polyps) (► **Table 3**).

We studied the relationship between number of endoscopically detected polyps per procedure and ADR or ANDR across the 19 endoscopists (► **Fig. 3a**, ► **Fig. 3b**), and the R^2 value was 0.36 or 0.60, respectively, based on the linear approximation curve. An ADR of 25%, the recommended screening threshold, corresponded to an average of 1.1 endoscopically detected polyps per procedure.

Discussion

All endoscopists are required to self-evaluate their quality of colonoscopy and make efforts to reduce CRC incidence and mortality. The ADR is well known as one of the most important QIs of colonoscopy. Each 1% increase in ADR has been shown to be associated with a 3% reduction in CRC incidence and a 5% reduction in fatal interval CRC [8]. Consequently, an ADR of 25% or higher is necessary for reducing risk of fatal interval cancer [8]. The American Society for Gastrointestinal Endoscopy recommends an ADR of 30% for men and 20% for women [10]. Therefore, an endoscopist should evaluate the quality of his or her performance regarding colonoscopy in clinical prac-



► **Fig. 2** ROC curve of the number of endoscopically detected polyps representing advanced neoplasms (AUC 0.87, sensitivity 81 %, specificity 78 %).

tice. Recent studies have shown that patients with advanced neoplasia are often recommended for more frequent colonoscopic evaluation than are patients without advanced neoplasia [11, 22–24] because most CRCs arise from advanced neoplasms. Therefore, we may have to evaluate advanced ADRs in addition to ADRs in daily practice. In the current study, increasing age, male sex and number of detected polyps were strongly correlated with advanced neoplasia, although ADR was also strongly correlated with ANDR. In everyday clinical practice, it is difficult to evaluate the quality of a colonoscopic procedure using ADR, ANDR or adenomas per colonoscopy (APC) in a timely manner because many of these procedures and the associated histological assessment are time-consuming. However, it is easy to quickly evaluate quality using the total number of endoscopically detected polyps every day without requiring

histology. In the current study, the number of endoscopically detected polyps was correlated with both ADR and ANDR. In addition, we can evaluate QIs in a cost- and time-efficient manner. Therefore, the number of endoscopically detected polyps may be a useful QI of each colonoscopic procedure.

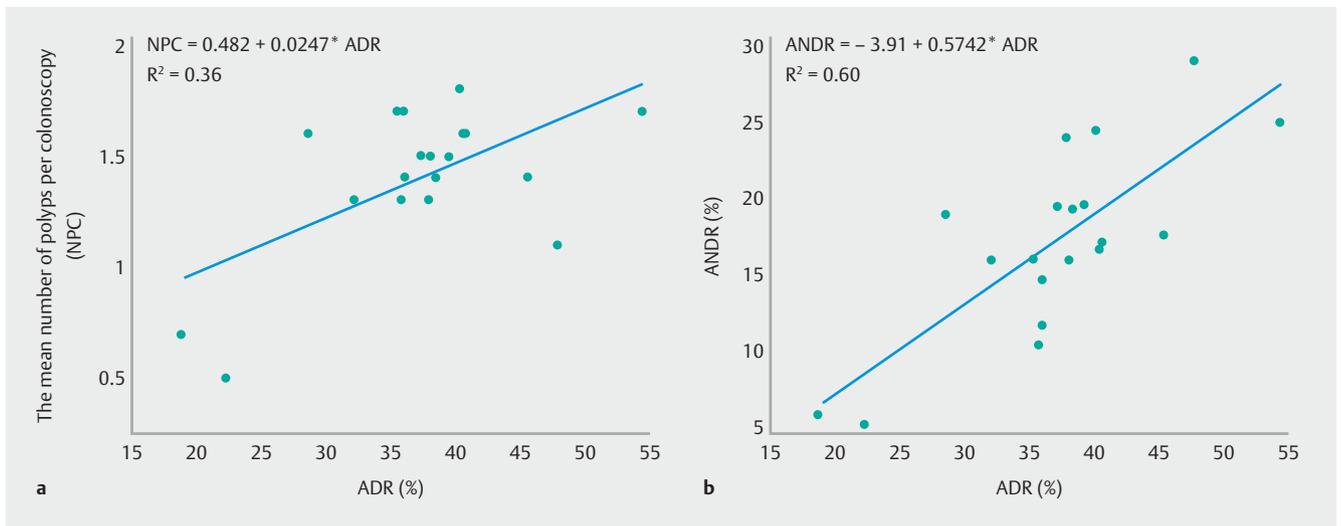
ADR and ANDR have several limitations as QIs. Regarding ADR, it is possible that when an endoscopist detects one adenoma, he or she loses the motivation to find subsequent adenomas (“one and done”) [15, 16]. The same reasoning can be applied to PDR. When we discarded some diminutive polyps, it was difficult to calculate the correct ADR because of lack of histology. Histological evaluation of all diminutive polyps may become time-consuming and expensive. Regarding ANDR, an endoscopist may overestimate the size of polyps as larger than 10 mm; such polyps are indicative of advanced neoplasms.

Similarly, number of APC has been proposed as a QI because of its comprehensive nature and because it is significantly associated with ADR and ANDR [25, 26]. However, APC calculation also requires histologic evaluation. Recently, Denis et al. reported a strong correlation between the number of polyps and adenomas and showed that mean number of polyps per colonoscopy offers a better delineation than does the PDR between higher and lower detectors. The authors concluded that mean number of polyps per colonoscopy could be an attractive alternative to the ADR for assessment of adenoma detection in routine practice [27]. A strong correlation between ADR and PDR has been observed in recent studies [27, 28] that have reported a mean ADR/PDR ratio of 0.64 and 0.66, which is consistent with the value obtained in our study (0.67). Moreover, detection of more than one polyp may motivate endoscopists in daily practice. Therefore, the number of polyps could be an alternative to the ADR as a QI. In the current study, we showed that an ADR of 25% (30% for men and 20% for women) corresponds to an average of 1.1 (1.2 for men and 1.0 for women) endoscopically detected polyps per procedure (► **Fig. 3**). Assuming that an endoscopist performs five colonoscopies on a daily basis, to reach an ADR of 25%, more than five to six polyps must be detected for every five colonoscopies. Alternatively, because the PDR was approximately 60% in the current study, polyps need to be detected in at least three of those five colonoscopies.

► **Table 3** Three groups based on number of polyps (1 to 2, 3 to 4, and 5 or more) and results of logistic regression analysis adjusted by age and sex.

Polyp number	1–2	3–4	5+
n (%)	471 (65)	112 (20)	289 (14)
Age (yr)	65 ± 12	69 ± 9	70 ± 9
Male sex (%)	53	62	73
ADR (%)	58	80	86
Adjusted OR for ADR ¹ (95% CI)	1	2.9 (2.0–4.2)	4.8 (3.0–8.1)
ANDR (%)	19	45	67
Adjusted OR for ANDR ¹ (95% CI)	1	3.1 (2.2–4.3)	7.9 (5.4–11.8)

ADR, adenoma detection rate; ANDR, advanced neoplasia detection rate; CI, confidence interval
¹ Adjusted by age and sex



► **Fig. 3** Relationship between **a** mean number of endoscopically detected polyps and ADR and **b** between ANDR and ADR all 19 endoscopists.

This figure corresponds to detection of more than two polyps for each polyp-positive colonoscopy, although the number of polyps is a QI for number of colonoscopies but not for an isolated colonoscopy.

There are several limitations to the current study. First, diminutive polyps could be followed up without resection based on the judgment of each endoscopist in this study, adhering to the JGES guideline [20]. This procedure may have resulted in a lower ADR than that observed in reality, which may affect the absolute number of polyps observed in this study. However, we found the number of polyps was positively correlated with ADR and ANDR. Second, this study was based on a single referral center with a moderate cohort size. Therefore, it may be difficult to apply the results to a different cohort. Third, the most common indication for colonoscopy was a positive FIT test (51.6%), followed by diagnostic colonoscopy performed as a result of symptoms (35%), and only 13.4% of all initial colonoscopies were primary screening colonoscopies. Therefore, the ADR and ANDR for this study may have seemed high because half the patients had positive FIT. However, the ADR for primary screening colonoscopies was also 33.9% (88/260, 39.4% for men and 25.9% for women), above the recommended screening threshold. Thus, further study may be needed to evaluate whether the number of detected polyps can be used in different settings, including in surveillance colonoscopy, and among different patient groups and to assess the generalizability of the results. Recently, Rex DK et al. described that the need to confine ADR to screening procedures is not yet established and that an overall ADR encompassing screening, surveillance, and diagnostic examinations would be as effective as the ADR alone [29].

Conclusion

In conclusion, the number of endoscopically detected polyps can be used to predict risk of advanced neoplasia and may be a new QI for daily colonoscopy practice in the clinic. Detection of

a large number of polyps and not simply one adenoma during daily colonoscopy may motivate endoscopists and thus increase detection of advanced neoplasia. An endoscopist should thus be encouraged to detect two or more polyps in patients with colorectal polyps during colonoscopy to maintain an adequate ADR.

Competing interests

None

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