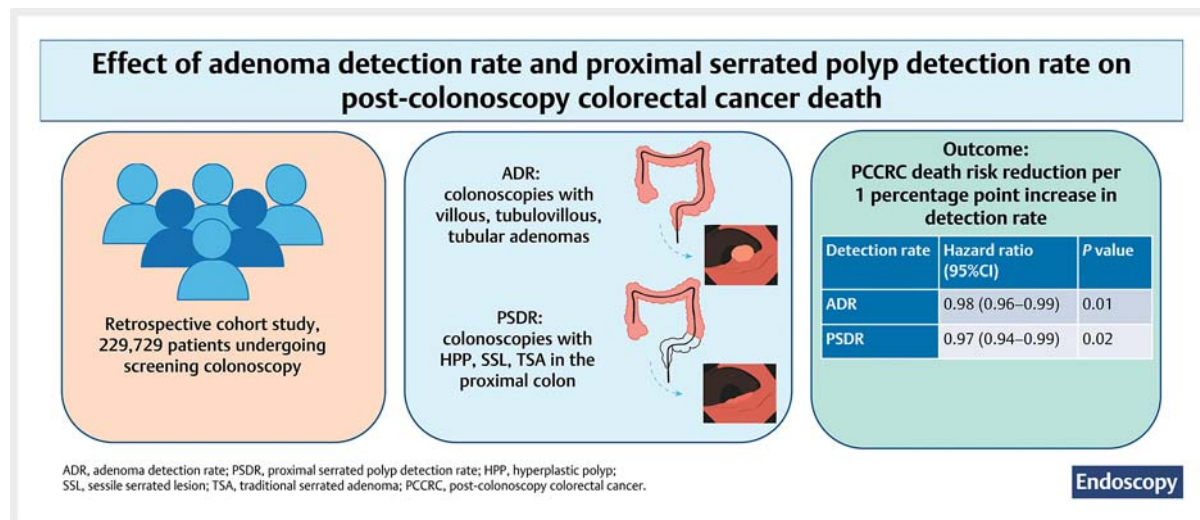


Comparison of adenoma detection rate and proximal serrated polyp detection rate and their effect on post-colonoscopy colorectal cancer mortality in screening patients

GRAPHICAL ABSTRACT



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submitted 22.2.2022

accepted after revision 12.10.2022

published online 8.12.2022

Bibliography

Endoscopy 2023; 55: 434–441

DOI 10.1055/a-1974-9979

ISSN 0013-726X

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Georg Thieme Verlag KG, Rüdigerstraße 14, 70469 Stuttgart, Germany

Supplementary material

Supplementary material is available under <https://doi.org/10.1055/a-1974-9979>

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ABSTRACT

Background Patients with serrated polyps are at increased risk for post-colonoscopy colorectal cancer (PCCRC); however, evidence for a dedicated serrated polyp detection rate is lacking. The aim of this study was to investigate the association of the proximal serrated polyp detection rate (PSDR) and adenoma detection rate (ADR) with PCCRC death.

Methods This was a retrospective analysis within the Austrian quality assurance program for screening colonoscopy. Spearman's rank coefficient was calculated for the assessment of association between ADR and PSDR. Whether ADR or PSDR were associated with colorectal cancer mortality was assessed by Cox proportional hazards model.

Results 229/729 screening colonoscopies performed by 308 endoscopists were analyzed. The ADR (hazard ratio [HR] per 1 percentage point increase 0.98, 95%CI 0.96–0.99) as well as the PSDR (HR per 1 percentage point increase 0.97, 95%CI 0.94–0.99) were significantly associated with PCCRC death. The correlation coefficient of the ADR and PSDR calculated at every colonoscopy was 0.70 (95%CI 0.70–0.71), and the corresponding PSDR value for an ADR performance standard of 25% was 11.1%. At the end of the study period, 86 endoscopists (27.9%) reached an ADR of >25% and a PSDR of >11.1%.

Conclusions The ADR as well as the PSDR were associated with PCCRC death. Striving for a high PSDR in addition to a high ADR might reduce the risk for PCCRC mortality in patients undergoing screening colonoscopy.

Introduction

Screening colonoscopy with subsequent polypectomy is considered the gold standard for the prevention of colorectal cancer (CRC), especially when performed under high quality standards [1]. Serrated polyps are CRC precursor lesions and recently obtained new diagnostic criteria from the World Health Organization (WHO); thus, the current classification of serrated polyps comprises hyperplastic polyps (HPPs), traditional serrated adenomas (TSAs), and sessile serrated lesions (SSLs) [1,2]. Compared with conventional adenomas, serrated polyps arise from the serrated pathway, which is associated with the activation of mitogenic pathways by means of mutations in the *BRAF* gene in SSLs, and more rarely, *KRAS* in TSAs. Tumors evolving through the serrated pathway account for 10%–33% of all new CRCs [3–5]. Mutations in *BRAF* are associated with the CpG island mutator phenotype, leading to microsatellite instability in SSLs, progressing to SSL with dysplasia [6]. These hallmarks might enable rapid growth of serrated polyps, and make them prone to the development of interval-type post-colonoscopy colorectal cancer (PCCRC) [7–9]. However, the risk for progression of serrated polyps to PCCRC is not attributed exclusively to molecular features, but can also be attributed to high miss rates and incomplete resection, highlighting the importance of adequate performance metrics for serrated polyp management. The detection and removal of serrated polyps is often more challenging than that of adenomas, owing to smooth edges, a similar color to that of healthy colonic mucosa, and a flat appearance; furthermore, SSLs are located in the right colon more often than adenomas [10]. Due to the dissimilarities with colorectal adenomas, and the need for quality standards for serrated polyp detection, parameters such as the serrated polyp detection rate, the proximal serrated polyp detection rate (PSDR), and the clinically significant serrated polyp detection rate have been proposed [11–14]. None of these measures has been implemented in performance recommendations, and there was only a weak recommendation for a minimum PSDR of 5% from the British Society of Gastroenterology (BSG) [15]. Ideally, a

quality standard for the detection of serrated polyps would be associated with reduced risk of long-term PCCRC mortality, and would be easy to calculate and report. So far, the PSDR has been well characterized; however, the PSDR suffers from high endoscopist and center variability in the literature [11, 13]. Most previous studies have included small sample sizes, and no study has yet established a connection between ADR/PSDR and an outcome measure such as PCCRC death. The aim of the current study was to investigate the correlation between ADR and PSDR (quantifying the amount of proximally detected serrated polyps). Furthermore, we assessed the association of ADR and PSDR at screening colonoscopy with PCCRC mortality.

Methods

Study population

This was a retrospective cohort study of a prospectively built database within the Austrian quality assurance program for screening colonoscopy. In Austria, screening colonoscopy is recommended from the age of 50 years for both men and women. For the purpose of standardization and quality control, a monitoring program to which colonoscopy details are submitted was founded in 2007 by the Austrian Society of Gastroenterology and Hepatology, the Austrian Cancer Aid, and the Austrian Federation of Statutory Insurance Institutions. Since then, 401 941 colonoscopies from 353 endoscopists (surgeons, internists, and gastroenterologists) have been collected in the database.

Colonoscopy records of patients aged ≥ 50 years who undergo screening are uploaded to the database. Endoscopists take part in the program on a voluntary basis, and approximately half of all Austrian inpatient and outpatient endoscopy services currently participate. Participating endoscopists are required to meet standards of performance such as ≥ 200 supervised colonoscopies and ≥ 50 supervised polypectomies, and at least 100 colonoscopies and 10 polypectomies annually must be performed and submitted to the database in order to maintain participant status. Each record comprises information on age and

sex of patients, location, size, and number of lesions detected, quality of bowel preparation, cecal intubation rate, and histologic characteristics of the most severe finding. The most severe finding is determined by the presence of dysplasia. When multiple polyps with dysplasia occur, they are ranked as: sessile serrated adenoma > villous adenoma > tubulovillous adenoma > TSA > tubular adenoma. All histologic types are recorded as one category except for HPPs; therefore, patients can have synchronous adenomas and HPPs. Records are submitted via a standardized form.

If quality standards of the program are not met, endoscopists are informed about insufficient compliance and reminded of current guidelines and/or program requirements. Details of the quality program can be read in detail elsewhere [16, 17]. Written informed consent from patients for data processing is obtained prior to colonoscopy. This study was approved by the Institutional Review Board of the Medical University of Vienna (EK 1794/2019).

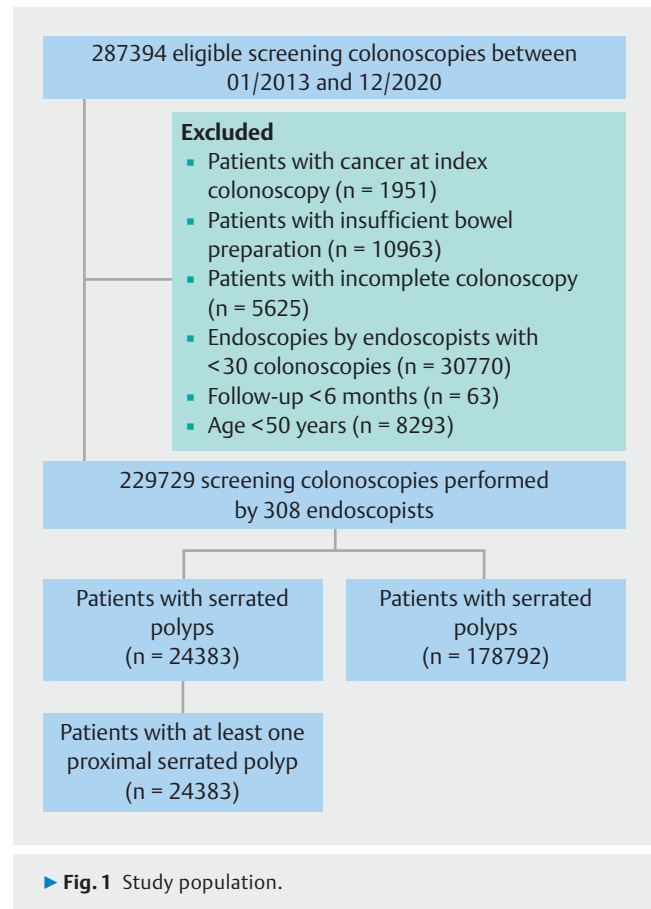
Study design and definitions

Patients aged 50 years or older, who underwent screening colonoscopy between 01/2013–12/2020 as participants of the Austrian national CRC screening and quality assurance program were enrolled in the current study. We chose the study period to start in 2013 as examinations prior to this did not explicitly record sessile serrated adenomas and TSAs in the histologic diagnosis. Patients were included if they had complete records of age, sex, presence or absence of polyps or adenomas, location, size, and number of polyps, as well as histologic reports. Patients were excluded if they had insufficient bowel preparation, had cancer present at screening colonoscopy, or if colonoscopy was incomplete (defined as not reaching the cecum). Polyp location was categorized into: 1) proximal – in these colonoscopies, polyps were found proximal to the border of the descending colon and sigmoid, 2) distal – in these colonoscopies, polyps were found distal to the border of the descending colon and sigmoid, 3) in these colonoscopies, patients had polyps in the distal and the proximal colon (distal and proximal). The proximal colon was hence the sum of the descending colon, transverse colon, ascending colon, and cecum. Patients with histologic reports of HPP(s), TSA(s), or sessile serrated adenoma(s) were classified as having serrated polyps. Follow-up started at the first colonoscopy record of a patient in our database (i. e. index colonoscopy) and ended at death of the patient from CRC or other causes, or at the end of the study period (31/12/2020). Only patients with a minimum follow-up period of 6 months were included. Details of the study cohort are shown in ► Fig. 1.

► Fig. 1.

ADR

The ADR was calculated for each endoscopist by determining the number of colonoscopies with at least one adenoma detected (tubular, villous, tubulovillous) divided by the total number of colonoscopies performed by the endoscopist. The ADR was calculated dynamically, meaning the ADR was recalculated at every colonoscopy performed, to account for variability in performance over time. Furthermore, to reduce variability in the



detection rate at the beginning of participation, the detection rate for the first 30 colonoscopies for each endoscopist was approximated to the detection rate at the 31st procedure. Endoscopists with fewer than 30 colonoscopies overall were not eligible for the database. The dynamic ADR calculation has been described in detail previously [18].

PSDR

The PSDR was calculated for each endoscopist by determining the number of colonoscopies with at least one serrated polyp detected in the proximal colon, either exclusively or in both the proximal and distal segments, divided by the total number of colonoscopies performed by the endoscopist. Colonoscopies detecting serrated polyps only in the distal colon were not included in the calculation. We computed the PSDR in a dynamic manner, using the same approach as for the ADR.

SSL detection rate

SSLs as precursors are overrepresented in patients who develop PCCRC [7–9]. Therefore, we aimed to assess whether the SSL detection rate has a similar effect on PCCRC mortality as the PSDR. The SSL detection rate was calculated for each endoscopist as the number of colonoscopies with at least one SSL detected, irrespective of location, divided by the total number of colonoscopies performed by the endoscopist.

Outcome measures

CRC mortality

We linked our database to a central registry from Statistics Austria, where cause of death of every individual is recorded according to the coding system of the tenth version of the International Classification of diseases (ICD-10). We assigned a cause of death from CRC when an ICD-10 code was recorded as either C18, C19, or C20. A death from any other ICD code was considered a death from other causes. Data on CRC mortality in our cohort was available until 12/2020.

Statistical analysis

Mean and SD as well as median and interquartile range (IQR) were reported for continuous variables, and proportions for categorical variables, as appropriate. We investigated the association between ADR and PSDR, and quantified the extent of correlation by Spearman's rank coefficient of all dynamically calculated values. Currently, the European Society of Gastrointestinal Endoscopy (ESGE) suggests a performance target for ADR of >25% [19]. Linear regression was performed to identify the PSDR that corresponds to an ADR of 25%. To describe the association of ADR, PSDR, or SSL detection rate with PCCRC death, we fitted a cause-specific Cox proportional hazards model, including ADR, PSDR, and SSL detection rate, respectively. Additionally, we estimated the association of meeting an ADR of 25% and the corresponding PSDR value (11.1%), as well as meeting either the ADR of 25% or the corresponding PSDR of 11.1% with PCCRC death. In this analysis, we considered meeting neither an ADR nor PSDR target as the reference. Hazard ratios (HRs) with 95% CIs were obtained from the model with time to PCCRC death as the outcome. Survival time was defined as the elapsed time from screening colonoscopy to death from PCCRC or death from other causes, where death from other causes was considered a competing event. The model estimates were adjusted for patient sex and patient age. Patient age was included as a continuous variable. The sandwich estimator was employed to obtain robust standard errors of the resulting estimators to account for single endoscopists contributing multiple observations to the dataset. The proportional hazards assumption was assessed by tests based on scaled Schoenfeld residuals. $P < 0.05$ was considered statistically significant for all tests. The statistical analyses were performed using R version 4.1.0 with the survival package version 3.2–11 (R Foundation for Statistical Computing, Vienna, Austria).

Results

Characteristics of patients with serrated polyps

Of 229 729 screening colonoscopies by 308 endoscopists between 01/2013 and 12/2020, the median age of patients was 59.9 years (IQR 54.1–67.7) and 51.1% of patients were female (► **Table 1**). A total of 50,937 patients had a serrated polyp detected at screening colonoscopy. The median age of these patients was 59.8 years (IQR 54.3–67.0) and 51.9% were men. By histologic type, 5315 patients had an SSL, 929 had a TSA, and 34 147 patients had at least one HPP. Of all patients with at

► **Table 1** Baseline cohort characteristics.

| | Colonoscopies with serrated polyps (n = 50,937) | Overall (n = 229 / 729) |
|--------------------------------|---|-------------------------|
| Age | | |
| Age, median (IQR), years | 59.8 (54.3–67.0) | 59.9 (54.1–67.7) |
| Sex, n (%) | | |
| ▪ Female | 24/486 (48.1) | 117/310 (51.1) |
| ▪ Male | 26/451 (51.9) | 112/419 (48.9) |
| Histology | | |
| ▪ Negative colonoscopy | – | 130/737 (56.9) |
| ▪ Synchronous HPP and adenoma, | | |
| ▪ Tubulous | 9218 (18.1) | – |
| ▪ Tubulovillous | 1221 (2.4) | – |
| ▪ Villous | 107 (0.2) | – |
| ▪ HPP | 34/147 (67.0) | – |
| ▪ SSL | 5315 (10.4) | – |
| ▪ TSA | 929 (1.8) | – |
| Location of polyps | | |
| ▪ Distal and proximal | 15/824 (31.1) | 32/364 (32.6) |
| ▪ Distal | 26/492 (52.0) | 43/906 (44.3) |
| ▪ Proximal | 8559 (16.8) | 22/722 (23) |
| Polyp count | | |
| ▪ 1–2 | 35/305 (69.3) | 72/834 (73.5) |
| ▪ 3–4 | 9426 (18.5) | 15/832 (16) |
| ▪ ≥5 | 6144 (12.1) | 10/326 (10.4) |
| Polyp size | | |
| ▪ <5 mm | 35/505 (69.7) | 62/064 (62.7) |
| ▪ 5–9 mm | 12/251 (24.1) | 26/979 (27.2) |
| ▪ 10–20 mm | 2308 (4.5) | 6933 (7.0) |
| ▪ >20 mm | 810 (1.6) | 3015 (3.0) |

IQR, interquartile range; HPP, hyperplastic polyp; SSL, sessile serrated lesion; TSA, traditional serrated adenoma.

least one serrated polyp, 8559 had polyps located proximally, 15 824 had polyps in both colonic segments, and 26 492 had polyps located distally (sigmoid colon and rectum). The largest proportion of serrated polyps was small (69.7% <5 mm; n = 35 / 505), and in 12/251 (24.1%) colonoscopies a polyp of 5–9 mm was detected. In 3118 colonoscopies, serrated polyps larger

► **Table 2** Screening adenoma detection rate and proximal serrated polyp detection rate. Both parameters were assessed for each endoscopist over the whole study period.

| | Female screening patients n = 117/310 | Male screening patients (n = 112/419) | Overall |
|----------------|--|--|------------------|
| ADR, % | | | |
| ▪ Mean (SD) | 17.5 (7.09) | 28.7 (10.5) | 23.0 (10.5) |
| ▪ Median (IQR) | 17.1 (13.3–22.6) | 28.8 (22.3–36.2) | 22.3 (15.6–30.1) |
| PSDR, % | | | |
| ▪ Mean (SD) | 9.78 (7.40) | 11.5 (8.41) | 10.6 (7.95) |
| ▪ Median (IQR) | 8.31 (4.36–13.6) | 9.41 (5.60–15.8) | 8.51 (4.99–14.4) |

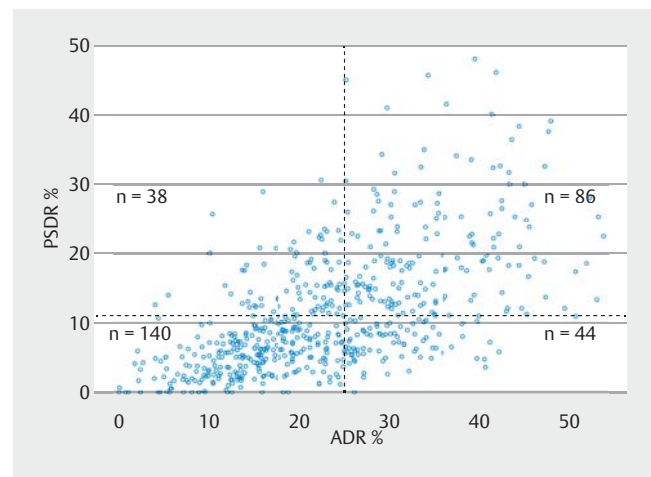
ADR, adenoma detection rate; IQR, interquartile range; PSDR, proximal serrated polyp detection rate.

than 10 mm were diagnosed, with 2308 polyps (4.5%) being 10–20 mm, and 810 polyps (1.6%) being >20 mm. Patients with any serrated polyp had ≥ polyps detected in 6144 colonoscopies (12.1%).

The median ADR of screening colonoscopies was 22.3% (IQR 15.6–30.1), and the median PSDR was 8.51% (IQR 4.99–14.4). The median ADR was higher in men (28.8%, IQR 22.3–36.2) than in women (17.1%, IQR 13.3–22.6) (► **Table 2**). A similar pattern was observed for the PSDR, with a median PSDR of 9.41% (IQR 5.60–15.8) in men and 8.31% (IQR 4.36–13.6) in women.

PSDR by setting and specialty

Screening colonoscopies were mainly performed in private practices (79.1%). The median PSDR of endoscopists was 9.37% (IQR 5.75–13.5) in hospitals, 7.30% (IQR 4.19–11.3) in outpatient clinics, and 8.45% (IQR 4.99–15.0) in private practices. When assessed by specialty, the median PSDR was 8.84% (IQR 5.01–14.9) for endoscopists practicing internal medicine or



► **Fig. 2** Overall adenoma detection rate (ADR) and proximal serrated polyp detection rate (PSDR) for each endoscopist. Dashed lines represent an ADR target of 25% (x axis) and the corresponding PSDR value of 11.1% (y axis). Every dot represents one endoscopist.

► **Table 3** Mean and median adenoma detection rate and proximal serrated polyp detection rate by setting and by specialty. Both parameters were assessed for each endoscopist over the whole study period.

| | Setting | | | Specialty | |
|----------------|------------------------------|---------------------|---------------------------|----------------------------|------------------|
| | Outpatient clinics (4.7%) | Hospital (16.2%) | Private practice (79%) | Internal medicine (57%) | Surgery (43%) |
| ADR, % | | | | | |
| ▪ Mean (SD) | 23.9 (9.34) | 22.8 (9.28) | 22.8 (10.8) | 23.2 (10.5) | 22.3 (11.1) |
| ▪ Median (IQR) | 22.7 (15.8–29.7) | 22.9 (15.8–30.2) | 22.1 (15.5–30.1) | 22.1 (15.6–30.8) | 22.4 (15.5–29.0) |
| PSDR, % | | | | | |
| ▪ Mean (SD) | 7.91 (4.99) | 10.4 (6.52) | 10.8 (8.31) | 10.1 (8.43) | 10.4 (8.14) |
| ▪ Median (IQR) | 7.30 (4.19–11.3) | 9.37 (5.75–13.5) | 8.45 (4.99–15.0) | 8.84 (5.01–14.9) | 8.25 (4.87–15.2) |

ADR, adenoma detection rate; IQR, interquartile range; PSDR, proximal serrated polyp detection rate.

gastroenterology and 8.25% (IQR 4.87–15.2) for surgeons (► **Table 3**).

Correlation between ADR and PSDR in screening colonoscopy

The PSDR showed a correlation with the ADR at every screening colonoscopy (correlation coefficient 0.70, 95%CI 0.70–0.71). In screening colonoscopy, the PSDR corresponding to a minimum performance cutoff for ADR of $\geq 25\%$ was 11.1%. At the end of the study period, the PSDR and ADR target was met or exceeded by 86 of 308 endoscopists (27.9%) (► **Fig. 2**).

Association of PSDR and ADR with PCCRC mortality

During a maximum follow-up period of 7.9 years and a median follow-up of 3.89 years (95%CI 3.78–3.90), 134 CRC deaths were observed, of which 46 were in female patients and 88 were in male patients. When assessed separately, a one percentage point increase in ADR was associated with a 2 percentage point decrease in hazard of PCCRC death (HR 0.98, 95%CI 0.96–0.99; $P=0.01$). A similar association was observed for a one percentage point increase in PSDR, leading to 3 percentage point lower hazard of PCCRC death (HR 0.97, 95%CI 0.94–0.99; $P=0.02$) (► **Table 4**). The SSL detection rate (irrespective of proximal or distal location) had a similar estimate to the PSDR; however, the association with PCCRC death was not significant (HR 0.97, 95%CI 0.89–1.06; $P=0.53$) (see Table 1s in the online-only Supplementary material). When endoscopists were categorized according to an ADR of 25% and corresponding PSDR cutoff of 11.1%, meeting the ADR of 25% as well as PSDR target of 11.1% had a strong association with PCCRC death (HR 0.58, 95%CI 0.35–0.99; $P=0.04$) (Table 2s).

Discussion

In this study, we found that both the ADR and the PSDR were significantly associated with PCCRC death. We assessed the correlation of these parameters and determined the proportion of endoscopists meeting a target ADR and PSDR.

The importance of serrated polyps as significant contributors to PCCRC incidence has been highlighted by many recent cohort studies on screening patients, showing a clearly elevated risk for PCCRC and PCCRC mortality for patients with serrated polyps [20]. Owing to the distinct biology and appearance of serrated polyps on colonoscopy compared with conventional

adenomas, concerns have been raised that the ADR might not accurately reflect the ability of endoscopists to detect serrated polyps, especially as SSLs are not included in the ADR definition [21]. Furthermore, the ADR does not encompass the detection of HPPs, which are considered high risk if they are larger than 10 mm [22]. Efforts have been made to introduce quality standards specifically for the detection of serrated polyps, such as the sessile serrated adenoma detection rate, serrated polyp detection rate, clinically significant serrated polyp detection rate, and the PSDR [12]. The PSDR has been established because the miss rate for proximal serrated polyps is very high, and proximal serrated polyp detection requires distinct endoscopic skills [23]. However, uncertainties about the reliability of the PSDR exist, as variability and dependence on endoscopy specialty have been demonstrated by some authors [13, 24–26] but not others [27]. Furthermore, comparing previous studies of serrated polyp detection should be done with caution, as the numerators vary, with some only considering SSLs and TSAs but not HPPs for their calculations. As a result of these inconsistencies, the mean overall PSDR ranges from 2.8% to 10.4% in the literature [12, 13, 25]. In our study, we used the border of the descending and sigmoid colon as our cutoff for the definition of proximal polyps, and we summarized HPP, SSL, and TSA as one category, as supported by current ESGE guidelines, and because the correct classification of HPP and SSL histology is often challenging. There has been a rise in the awareness of SSL as a CRC precursor, and the distinction from HPP has changed over time in WHO definitions [5, 22, 28, 29]. Payne et al. showed that the detection of SSL significantly varied by center, with some pathologists classifying serrated polyps more frequently as SSL than others [13]. Our definition of serrated polyps avoided the possibility of histologic misclassification of SSLs as HPPs, and ensured that all serrated polyps were included in our PSDR calculation.

Two recent studies found that the PSDR is well correlated with the ADR, and with the detection of clinically significant serrated polyps (as determined by the number of SSL/TSA and HPP > 5 mm located proximally to the sigmoid colon) [12, 25]. This makes the PSDR an attractive proxy for high risk serrated polyp detection, as it is easy to calculate and report. Although assessment of proximal serrated polyps might yield some advantages, it excludes SSLs and TSAs that are located in the distal colon. This might lead to imprecision when tying the PSDR to long-term patient outcome, as distal lesions might also lead to PCCRC. Furthermore, proximal serrated polyps rarely occur, which might add to the complexity of estimating the effect on PCCRC death.

In our study, we found that a 1 percentage point increase in the PSDR alone led to a reduction in hazard of PCCRC death; a similar reduction was found for an increase in the ADR. However, the effect was higher for the PSDR (3 percentage points) compared with the ADR (2 percentage points). These values should be interpreted with caution, as the PSDR has a much smaller range than the ADR, hence it is much harder to achieve a 1 percentage point higher PSDR compared with a 1 percentage point increase in ADR. Our data suggest that low ADRs or PSDRs are indicators associated with unfavorable patient out-

► **Table 4** Association of adenoma detection rate and proximal serrated polyp detection rate at screening colonoscopy with post-colonoscopy colorectal cancer death. Model estimates are adjusted for age and sex.

| Detection rate | HR (95%CI) | P value |
|----------------|------------------|---------|
| ADR | 0.98 (0.96–0.99) | 0.01 |
| PSDR | 0.97 (0.94–0.99) | 0.02 |

HR, hazard ratio; ADR, adenoma detection rate; PSDR, proximal serrated polyp detection rate.

come. For endoscopists meeting an ADR $\geq 25\%$ and PSDR $\geq 11.1\%$ concomitantly, significantly lower hazards for PCCRC death were found (HR 0.58, 95%CI 0.35–0.99; $P = 0.04$). However, we found that only 27.9% of the endoscopists in the cohort achieved an ADR of 25% and the corresponding PSDR target of 11.1%.

It has long been held that the association of serrated polyps with PCCRC can be attributed to features of their pathway, given the high prevalence of microsatellite instability in tumors classified as PCCRC [30]. However, recent evidence has shown that the mutational landscape of interval cancers might not differ from noninterval CRCs [31]. This would imply that physician performance plays a bigger role in PCCRC occurrence than molecular characteristics alone. Furthermore, incomplete resection has been found to be more prevalent in serrated polyps, with one study showing that almost half (46.7%) of all serrated polyps were incompletely removed [32]. Given the risk for PCCRC arising from serrated polyps, there is a need for an accurate detection metric that captures the identification of these lesions. However, whether the PSDR will be the most accurate tool to reflect physician performance in serrated polyp detection needs further validation.

Two recent studies found a PSDR as high as 10.4%–10.8% with an ADR cutoff of 25% [12, 33]; however, only the study from Anderson et al. was derived from a screening cohort. We confirm that in our study the PSDR corresponding to an ADR of $\geq 25\%$ was similar to that reported by Anderson et al. (our study 11.1% and Anderson et al. 10.8%) [12]. The BSG published a position statement including a weak recommendation for a PSDR cutoff of 5%, with the known caveats of detection rate variability depending on correct pathological diagnosis, endoscopist, patient population, and ethnicity [15]. In our study, a performance PSDR cutoff of $\geq 11.1\%$ and ADR of $\geq 25\%$ was reached by 27.9% of endoscopists; however, the BSG-recommended cutoff would have been met by 40% of our endoscopists.

A strength of our study is the large number of quality-assured screening and surveillance colonoscopies included, with many endoscopists from different specialties contributing to our database. Furthermore, we used a dynamic calculation of ADR and PSDR. We assessed these performance measures at every timepoint where a colonoscopy was performed, which ensures that no false-low ADR and PSDR values are reported. This is the first study to assess the association of a proposed quality parameter with long-term CRC mortality, underscoring that the current performance measure, the ADR, could be supplemented by an additional indicator dedicated to proximal serrated polyp detection.

A main limitation of the study is the relatively short time of follow-up for the assessment of CRC mortality. Serrated polyps were not accurately defined in our screening database at its initiation in 2007, reflecting the increase in awareness of distinct colorectal polyp histology later in time. The serrated pathway, with its discrimination between sessile serrated adenomas and HPPs has evolved over the past decade, with the classification term “sessile serrated adenoma/polyp” being first introduced by the WHO in 2010 [34]. However, our outcome data con-

firmed the risk reduction of PCCRC mortality by the ADR, reflecting that a follow-up period of 7.9 years was sufficient to determine effects of screening colonoscopy parameters on patient outcome. Another limitation of our study is the lack of adjustment for confounders that are associated not only with the occurrence of serrated polyps, but also with higher rates of PCCRC mortality. For example, smoking is one of the strongest risk factors for the development of serrated polyps, and simultaneously increases the risk for the development of microsatellite instability CRC [35]. A limitation of the reporting of SSLs and TSAs with conventional adenomas in one category is that it does not allow for assessment of synchronous adenomas and SSLs. Synchronous adenomas are frequently observed in patients with SSLs [36]. However, we were able to capture HPPs separately. Given the possibility that SSLs may be misclassified as HPPs, the distinction between these histologic types is relevant for estimating the effect of PCCRC risk reduction by the PSDR.

In conclusion, we found that some endoscopists performed well, with ADRs of $\geq 25\%$ and PSDRs of $\geq 11.1\%$. A rise in PSDR was associated with a decrease in risk of PCCRC death. A high ADR together with a sufficiently high PSDR might be an appropriate quality measure for endoscopist performance and the assurance of long-term PCCRC risk reduction.

Acknowledgments

The authors would like to thank Statistics Austria for providing data on mortality in the study cohort. The authors further express gratitude to Aleksandra Syzmanska and Arno Asaturi for their efforts in project coordination and management of participating endoscopists for the quality certificate for screening colonoscopy.

Competing interests

The authors declare that they have no conflict of interest.

Funding

Austrian Main Association of Statutory Insurance Institutions
Austrian Cancer Aid
Österreichische Gesellschaft für Gastroenterologie und Hepatologie
<http://dx.doi.org/10.13039/501100020617>

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