Oncology

The mean number of adenomas per procedure should become the gold standard to measure the neoplasia yield of colonoscopy: A population-based cohort study

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ABSTRACT

Background: Measuring adenoma detection is a priority in the quality improvement process for colonoscopy. Our aim was (1) to determine the most appropriate quality indicators to assess the neoplasia yield of colonoscopy and (2) to establish benchmark rates for the French colorectal cancer screening programme.

Methods: Retrospective study of all colonoscopies performed in average-risk asymptomatic people aged 50–74 years after a positive guaiac faecal occult blood test in eight administrative areas of the French population-based programme.

Results: We analysed 42,817 colonoscopies performed by 316 gastroenterologists. Endoscopists who had an adenoma detection rate around the benchmark of 35% had a mean number of adenomas per colonoscopy varying between 0.36 and 0.98. 13.9% of endoscopists had a mean number of adenomas above the benchmark of 0.6 and an adenoma detection rate below the benchmark of 35%, or inversely. Correlation was excellent between mean numbers of adenomas and polyps per colonoscopy (Pearson coefficient $r = 0.90$, $p < 0.0001$), better than correlation between mean number of adenomas and adenoma detection rate ($r = 0.84$, $p = 0.01$).

Conclusion: The mean number of adenomas per procedure should become the gold standard to measure the neoplasia yield of colonoscopy. Benchmark could be established at 0.6 in the French programme.

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1. Introduction

A growing number of countries undertake colorectal cancer (CRC) screening programmes with faecal occult blood test (FOBT), flexible sigmoidoscopy or colonoscopy. These screening methods lead to colonoscopy for detection of early-stage cancers and removal of adenomatous polyps. However, colonoscopy is an operator-dependent examination, and adenoma and polyp detection vary dramatically between endoscopists [1–10]; high adenoma detection rate (ADR) and polypectomy rate (PR) are associated with a lower risk of interval CRC [11,12]. Measuring the neoplasia yield is a priority in the quality improvement process for colonoscopy but there is no agreement concerning which quality indicator should be used, nor the standard threshold that should be attained [13]. There is no ideal and universal neoplasia yield indicator; the same is true for benchmarks set for minimum detection rates which depend on the details of CRC screening programmes. Adenoma detection rate (ADR) is the most commonly recommended neoplasia-related quality indicator [14–16]. However, the mean number of adenomas (MNA) per colonoscopy is a better reflect of full length of

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colon examination and "could prove to be the ideal measure of adenoma detection" [14,16]. Moreover, both MNA and ADR are seldom measured in routine practice because their calculation is rather complex as they share the same drawback of waiting for the pathology report before determination. Other indicators such as polyp detection rate (PDR), PR and mean number of polyps (MNP) per colonoscopy have been proposed [17–20]. In a previous exploratory study, we advocated the use of MNP, which is well correlated with ADR and MNA and much easier to measure [19]. In our prior work, we examined a relatively small number of endoscopists practicing in a few geographic areas.

The aim of this study was (1) to determine on a larger scale the most appropriate quality indicators to assess the neoplasia yield of colonoscopy and (2) to establish benchmark rates for the French organized CRC screening programme with guaiac-based FOBT (gFOBT).

2. Patients and methods

2.1. Screening programme

A pilot gFOBT CRC screening programme was implemented in several French administrative areas from 2002 on. Its design has been previously described [21]. Briefly, residents aged 50–74 years were invited by mail every other year to participate. People with serious illness, recent CRC screening or high CRC risk were excluded. The gFOBT (Hemoccult II) was used without dietary restriction and was processed without rehydration. Faecal material was assessed from two samples from each of three consecutive stools. The test was defined as positive if at least one window was positive. People with a positive gFOBT were referred for colonoscopy.

2.2. Colonoscopies

All the colonoscopies performed within the gFOBT screening programme in eight administrative areas (Supplementary Fig. S1) (2.0 million residents aged 50–74 years) from December 2002 to December 2010 were assessed to compare different yield indicators, specify their determinants and determine a threshold between higher and lower detectors. Endoscopists who had performed 30 procedures or more were evaluated. As usual in France, all colonoscopies were performed by gastroenterologists and most of them (95%) under sedation/anaesthesia provided by an anaesthetist.

2.3. Pathological classification

The pathological examination of detected polyps and CRCs was performed as usual, mostly by community general pathologists. The result of each colonoscopy was classified according to the lesion with the worst prognosis. Cancer was defined as carcinoma invading at least the submucosa across the muscularis mucosa [22]. In situ and intramucosal carcinomas were classified as high-grade neoplasia. Advanced adenoma was defined as an adenoma measuring ≥10 mm or with a villous component >20% or with high-grade dysplasia.

2.4. Yield indicators

ADR and PDR were defined respectively as the percentages of colonoscopies where at least one adenoma and one polyp were found. MNA and MNP were defined respectively as the overall number of adenomas and polyps detected divided by the number of colonoscopies performed. Colonoscopies displaying invasive cancer were excluded for the calculation of these yield indicators. ADR,

PDR and MNP were measured in all eight administrative areas, whereas MNA was measured in five areas only.

2.5. Statistical methods

Qualitative variables (ordered or nominal) were described by their frequency and quantitative variables by their median, range, mean and standard deviation (SD). Pearson coefficients were determined to search for correlations between variables and compared using a normal Fisher transformation. The chi-square test was used for comparison of caecal intubation rates and frequencies of higher detectors between the eight administrative areas.

The goal of multivariate analysis was to find among age and sex of patients, number of positive windows, number of previous tests performed before the positive gFOBT, year of colonoscopy, administrative area and number of colonoscopies performed by the endoscopist, those variables having an effect on the number of polyps and adenomas detected. There were however two levels of data since several colonoscopies (first level) were performed by endoscopists (second level) practicing in a given administrative area. Therefore, we built Bayesian multilevel mixed models [23]. In Bayesian analyses, a prior knowledge on parameters is updated by gathered data and yields posterior knowledge. The prior knowledge is summarized under prior distribution on each parameter (here rather vague distributions). Using simulation techniques (Markov chains and Monte Carlo integration), the posterior distributions are summarized with their empirical means (posterior mean in the sequel of the article) and some of their percentiles: 2.5th and 97.5th percentiles give rise to a 95% credible interval (CI) (analogous to confidence interval in frequentist statistics). The Bayesian framework allows fitting complex multilevel models. In a linear regression model including covariates, we added nested effects for endoscopists and for administrative areas. Comparison between models used a deviance information criterion (DIC), the Bayesian version of the Akaïke score (AIC) [24]. Using the cut-off established at 0.8 for MNP for the definition of higher detectors in our previous study [19], we estimated the cut-off for MNA, ADR and PDR by maximizing each of the corresponding kappa agreement statistics. Comparing the percentages of endoscopists classified similarly as higher or lower detectors with each indicator and with the gold standard, MNA, gave an assessment of their relative performances. These analyses used Bayesian inference for agreement models [25]. The benchmark rates were then calculated for all indicators by rounding the corresponding cut-off while maintaining an acceptable rate of higher detectors situated around 60–65%.

3. Results

A total of 42,817 colonoscopies were performed by 316 endoscopists. Table 1 shows their distribution by administrative area. A measure of MNA was available in 202 endoscopists. The mean age of the patients was 62.5 years (SD 7.0); 22,554 (52.7%) colonoscopies were performed in men. The mean number of procedures by endoscopist was 135 (SD 105; range 30–543). The caecal intubation rate was 96.7%. It varied from 95.2% to 97.8% depending on the administrative area ($p = 0.99$) (Table 1). Overall, 17,090 colonoscopies (39.9%) displayed a neoplasia, 2438 (5.7%) a cancer, 9184 (21.4%) an advanced adenoma, and 5468 (12.8%) a non-advanced adenoma. The overall ADR was 36.3% (26.6% in women, 45.0% in men).

Table 1 shows the median, mean, and SD of the main yield indicators observed in both sexes in the whole study. ADR ranged from 12.8% to 73.1% (mean 36.8%; SD 9.9), PDR from 12.8% to 88.5% (mean 49.2%; SD 13.5), MNA from 0.2 to 1.7 (mean 0.71; SD 0.28) and MNP from 0.2 to 3.6 (mean 1.03; SD 0.47). Using the overall cut-off of 0.8

Table 1
Results observed in the eight administrative areas.

Administrative area	Number of endoscopists	Number of colonoscopies	Caecal intubation rate (%)	ADR median–mean (SD) (%)	PDR median–mean (SD) (%)	MNA median–mean (SD)	MNP median–mean (SD)	Higher detectors (%)
Alpes Maritimes	46	3216	97.0	31.9–34.4 (12.4)	40.9–43.9 (16.1)	–	0.82–0.89 (0.48)	52.2
Côte d'Or	25	5136	95.2	33.9–32.2 (8.3)	46.3–49.4 (15.8)	–	0.91–1.16 (0.75)	68.0
Finistère	40	5068	97.3	37.0–38.3 (7.6)	50.5–50.9 (10.1)	0.60–0.64 (0.23)	1.00–1.02 (0.33)	67.5
Ille-et-Villaine	40	6956	97.1	38.0–38.3 (10.6)	49.7–52.1 (13.3)	0.64–0.74 (0.35)	0.97–1.18 (0.55)	72.5
Isère	48	7058	97.0	35.9–35.2 (9.7)	47.8–47.1 (13.4)	0.74–0.73 (0.26)	1.02–1.03 (0.45)	68.8
Bas-Rhin	40	3149	97.8	39.4–40.6 (9.3)	50.8–50.6 (12.9)	0.76–0.76 (0.26)	1.03–1.08 (0.45)	75.0
Haut-Rhin	34	7220	95.9	35.6–36.8 (9.1)	47.4–46.9 (11.9)	0.63–0.66 (0.25)	0.96–0.95 (0.36)	61.7
Essonne	43	5014	97.1	38.7–37.9 (8.7)	52.8–53.5 (12.3)	–	0.92 –1.00 (0.41)	60.5
Whole study	316	42817	96.7	36.5–36.8 (9.9)	48.7–49.2 (13.5)	0.67–0.71 (0.28)	0.96–1.03 (0.47)	65.5

ADR, adenoma detection rate; MNA, mean number of adenomas per colonoscopy; MNP, mean number of polyps per colonoscopy; PDR, polyp detection rate; SD, standard deviation.

for MNP, established for the distinction between higher and lower detectors in our previous study, 65.5% of the gastroenterologists were classified as higher detectors. This rate varied from 52.2% to 75.0% depending on the administrative area ($p = 0.3$) (Table 1).

Multivariate analysis showed that both the number of adenomas and the number of polyps per colonoscopy varied significantly according to patient age and sex, number of positive windows, number of previous tests performed before the positive gFOBT, and year of colonoscopy (Table 2 for adenomas, data not shown for polyps). Table 2 shows for example that the number of adenomas increased significantly by 0.016 a year (95% CI 0.009–0.024). For the number of adenomas per colonoscopy, the posterior mean of the administrative area variance was 0.013 (95% CI 0.0005–0.0370) and that of endoscopist variance 0.043 (95% CI 0.033–0.056). The posterior mean of the ratio of these variances was about 9. Taking into account those two variances increased the model's goodness of fit (better DIC). In summary, it was better to include two additional levels of variability in the number of adenomas per colonoscopy: administrative area and endoscopist. These results indicate that both variables influenced independently and significantly the number of adenomas per colonoscopy, the endoscopist much more than the administrative area. Similar results were observed for the number of polyps per colonoscopy.

There was a good linear relation between MNA and MNP (coefficient of determination $R^2 = 0.80$) and an excellent correlation (Pearson coefficient $r = 0.90$, $p < 0.0001$) (Supplementary Fig. S2). The correlation between MNA and MNP was significantly better than that between MNA and ADR (Pearson coefficient $r = 0.84$, $p < 0.0001$) ($p = 0.01$) (Supplementary Fig. S3). There was a good linear relation between ADR and PDR ($R^2 = 0.72$) and a good correlation (Pearson coefficient $r = 0.85$, $p < 0.0001$).

Table 3 shows the cut-off values for each indicator for the distinction between lower and higher detectors, the corresponding benchmark rates and percentages of higher detectors. The kappa concordance between classifications of endoscopists as higher or lower detectors was 0.74 (95% CI 0.64–0.84) between MNA and MNP (with 89.6% of endoscopists well classified) and 0.66 (95% CI 0.56–0.76) between MNA and ADR (with 85.2% of endoscopists well

classified). With respect to MNA, the percentage of well classified endoscopists was higher with MNP than with ADR ($p = 0.07$). Endoscopists who had an ADR around the benchmark of 35% exhibited a broad range of MNA, varying between 0.36 and 0.98 (Supplementary Fig. S3). Of 202 endoscopists, 16 (7.9%) had a MNA above the benchmark of 0.6 and an ADR below the benchmark of 35%, and 12 (5.9%) stood in the inverse situation (Supplementary Fig. S3).

The positive predictive value of colonoscopy for invasive cancer was the same between higher and lower detectors (5.7% in both groups), whereas it was significantly higher for advanced neoplasia (28.7% vs. 24.2%, respectively) and for all neoplasia (43.5% vs. 33.2%) ($p < 0.001$).

4. Discussion

4.1. Main findings

Our main findings were dramatic inter-endoscopist differences observed in adenoma and polyp detection in the French organized CRC screening programme. There were also significant temporal and geographical differences of much lesser magnitude. We further found that there was an excellent correlation between MNP and MNA, better than that between ADR and MNA. Moreover, MNA and MNP offered better discrimination between higher and lower detectors than ADR and PDR, respectively.

4.2. Comparison with other studies

Large inter-endoscopist differences in adenoma and polyp detection have been observed in different settings, including the French and English organized gFOBT CRC screening programmes [7,10,19,26]. Whereas ADR is the most commonly recommended neoplasia-related quality indicator, MNA is a better indicator of full length of colon examination and "could prove to be the ideal measure of adenoma detection" as mentioned in the recommendations made by the ASGE/ACG Taskforce on Quality in Endoscopy [14]. We have demonstrated that MNA offers better discrimination between higher and lower detectors than ADR [19]. Likewise,

Table 2
Results of Bayesian multilevel models for the number of adenomas per colonoscopy.

Covariate	Mean	95% credible interval	*p*-Value
Sex (female is the reference category)	0.450	0.422–0.476	<0.0001
Age	0.018	0.016–0.020	<0.0001
Year	0.016	0.009–0.024	<0.0001
Number of positive windows	0.023	0.012–0.034	<0.0001
Number of previous FOBTs	−0.073	−0.088 to −0.058	<0.0001
Number of colonoscopies/endoscopist	−0.0004	−0.0008 to −0.0001	0.005

FOBT, faecal occult blood test.

Table 3
Cut-off values for the distinction between lower and higher detectors and benchmark rates (in bold) proposed for the French guaiac faecal occult blood test colorectal cancer screening programme. The numbers in brackets represent the percentages of endoscopists exceeding the corresponding threshold in our study.

Yield indicator	Cut-off values			Benchmark rates (% higher detectors)		
	Overall	Men	Women	Overall	Men	Women
MNA	0.57	0.85	0.32	**0.6**(61.4)	**0.8**(66.3)	**0.4**(54.5)
MNP	0.80	1.00	0.50	**0.8**(65.5)	**1.0**(68.7)	**0.5**(67.7)
ADR	35.0%	41.1%	23.2%	**35%**(56.6)	**42%**(59.8)	**25%**(61.4)
PDR	44.4%	53.8%	33.8%	**45%**(62.7)	**55%**(59.8)	**35%**(60.4)

ADR, adenoma detection rate; MNA, mean number of adenomas per colonoscopy; MNP, mean number of polyps per colonoscopy; PDR, polyp detection rate.

Lee et al. showed that the relative increase of adenoma detection associated with longer mean withdrawal times was larger when measured with MNA (25%) than with ADR (11%) [26]. MNA provides additional information over ADR about the performance of endoscopists [10,27]. Several studies found, as we did (Supplementary Fig. S3), that some endoscopists who have an ADR around the benchmark exhibit a broad range of MNA, giving evidence that some endoscopists are able to find more adenomas per patient than others [10,27]. In our study, 13.9% of endoscopists had a MNA above the benchmark of 0.6 and an ADR below the benchmark of 35%, or inversely. ADR has several limitations and drawbacks. It is binary and thus provides a rather rough assessment compared with the finer MNA, potentially without maximal value. When counting adenomas with ADR the detection of a single adenoma is enough to get the maximal score of one, whereas counting with MNA will encourage the endoscopists to detect as many adenomas as possible. Last, MNA is not more difficult to measure than ADR and is the only yield indicator that cannot be "gamed". All other indicators, ADR included, are susceptible to "gaming" in prospective studies. The correlations between ADR and PR and the risk of interval cancer have been observed in retrospective studies only [11,12]. Unfair endoscopists could easily boost both indicators in prospective studies. MNA should therefore be considered the "gold standard" for measuring adenoma detection.

In routine practice MNA and ADR are however seldom measured because they share the same drawback of waiting for the pathology report before determination. Until now, their calculation has been a time-consuming process, which cannot be automated. Several recent studies have demonstrated that the measure of adenoma detection can be simplified by measuring polyp detection [17–20]. They found strong correlations between ADR and PDR [18,19], PR and ADR [17,20], and MNA and MNP [19]. Moreover, measures of PR based on administrative data are significantly associated with risk of proximal postcolonoscopy CRC [12]. PR, which is equivalent to PDR, is the simplest indicator that could be used in routine practice to replace ADR as it could be automatically derived from administrative data [12,20]. However, administrative data for measuring PR lack precision and would have to be checked before evaluating individual endoscopists [28,29]. Besides, PDR and ADR correlate well in the proximal colon only, not in the distal colon [30]. We found that MNP could be an interesting alternative: it is as easy to measure as PR or PDR and offers a more precise assessment of the quality of colon examination.

There is no ideal indicator. In our opinion, the best indicator is the one, which is actually measured in routine practice. MNA would be rather difficult to measure in the French CRC screening programme; it is not measured by most screening centres in charge of the organization of the programme. By contrast, MNP and ADR could be measured by all the screening centres so that endoscopists could be easily informed of their own performance results without the expense of additional resources or time.

The best concordance for classification of endoscopists as higher detectors with a benchmark MNP at 0.8 was obtained with a benchmark ADR at 35%, exactly the same as the benchmark ADR recommended by the quality assurance guidelines for colonoscopy in the National Health Service (NHS) Bowel Cancer Screening Programme with gFOBT [15]. This convergence reinforces the validity of the benchmarks proposed in both programmes.

4.3. Strengths and limitations of the study

This was a population-based study, which together with the fact that all gastroenterologists practicing in the administrative areas studied participated, is its main strength. Other strengths include the large number of endoscopists and colonoscopies evaluated and the number of different geographical areas studied. Our study is not without weaknesses however. First, some factors influencing the neoplasia yield were not included in our analysis. For instance, certain patient-related factors such as body mass index, smoking habits or quality of bowel preparation, endoscopist-related factors such as withdrawal time and technique, and endoscope-related factors such as instrument generation (e.g. standard vs. high-definition) were not examined. This should however not modify our findings because the principal demographic features predictive of neoplasia at colonoscopy are age and gender, which were analysed, and to a lesser extent family history of colorectal neoplasia, which was excluded from our screening programme. Besides, the size of the adenomas and polyps removed was not included in our analysis. One could argue that the difference in neoplasia yield observed between higher and lower detectors could be related to diminutive polyps, without impact on the risk of interval CRC. This is however unlikely since the positive predictive value of colonoscopy for advanced neoplasia was significantly higher in higher detectors than in lower detectors. Moreover, this would not modify our findings since the objection is identical regardless the neoplasia yield indicator used and the correlation between neoplasia yield and risk of interval CRC was demonstrated without taking into account the adenoma or polyp size [11,12]. Another weakness is that we could not analyse the proximal serrated polyp detection rate which has been proposed as a new neoplasia yield indicator given the importance of these polyps in colorectal carcinogenesis and their contribution to interval CRCs [31]. However, this indicator is difficult to measure in routine practice and its use will probably be restricted for research and academic studies. Another weakness is the way we calculated the yield indicators: on the one hand colonoscopies displaying invasive cancer were excluded from both numerator and denominator and, on the other hand, incomplete colonoscopies were not excluded. However, as these procedures represent a minor proportion of the overall procedures, a different calculation method would not modify our findings, except for the threshold values which would be slightly modified. Besides, one could consider that our findings are specific of the subset of population studied, i.e. people with a positive gFOBT. In fact, there is a priori no reason why the correlations between indicators should be different in other populations. In contrast, the proposed thresholds are specific of our population. Despite small but significant geographical disparities, we have chosen to propose a unique and rather low national threshold, so that most gastroenterologists,

52.2–75.0% depending on the geographic area, would be classified as higher detectors. Indeed, the main goal of measuring the neoplasia yield of colonoscopy is to encourage lower detectors to enhance their performances. Benchmark rates remain to be established in other countries, adapted to their CRC prevalences and screening programmes. Likewise, the French CRC screening programme will move from gFOBT to immunochemical FOBT, so that new benchmark rates will have to be determined.

4.4. Future research

Future research should be directed at determining the cost-effectiveness and benefit–risk balance of prospectively measuring adenoma detection in routine practice, i.e. the correlation between MNA, or in its absence of MNP or ADR, and the risk of post-colonoscopy CRC.

The low adenoma yield observed in a non-negligible percentage of endoscopists is a problem in organized CRC screening programmes, since they are supposed to offer the screened population a better quality assurance than opportunistic screening. The reduction of the percentage of lower detectors should be a priority for quality improvement programmes. The first step is the assessment of individual endoscopists' performances, but what next? Previous studies have been quite pessimistic about the efficacy of most interventions for improving adenoma and polyp detection rates, with the exception of one small study that paired enhanced inspection techniques with an 8-min targeted colonoscopy withdrawal time using an audible timer [32,33]. Another small pilot study suggested that video recording colonoscopy withdrawal might improve adenoma detection among lower detectors [34]. Even the English Screening Programme involving a few accredited endoscopists reported considerable variation in adenoma detection between colonoscopists [10,26].

CRC screening is the only homogeneous setting that allows comparison between endoscopists and the establishment of benchmarks for adenoma detection. To date, the French CRC screening programme lacks neoplasia yield quality standards for colonoscopy such as those of the NHS Bowel Cancer Screening Programme, the ASGE or the ESGE [14–16]. Gastroenterologists should take the lead in setting quality indicators and benchmarks for CRC screening, otherwise others such as payers or consumers will impose them. The ESGE recently recommended that "national screening boards should monitor quality indicators and use them to license individual colonoscopists and endoscopy units" [16]. Our results will contribute to establish adenoma detection benchmarks for the French programme.

Another point deserving further investigation is the minimum number of colonoscopies required for the evaluation of an individual endoscopist's yield. Do et al. have demonstrated that large numbers are required for a reliable assessment [27]. They proposed that the 95% confidence intervals should be reported when calculating yield indicators to account for uncertainty and better reflect endoscopist performance.

4.5. Conclusions and policy implications

All agree that measuring the neoplasia yield is a priority in the quality improvement process for colonoscopy, but only a minority of endoscopists are actually aware of their own yield. CRC screening programmes are the only setting that allows the assessment of neoplasia yield indicators and the establishment of benchmarks. MNA, which best reflects the full-length quality of colon examination and is the only indicator that cannot be "gamed", should become the gold standard to measure the neoplasia yield of colonoscopy. However, where MNA is difficult to measure, MNP may be a suitable alternative, as well as ADR and even better than

ADR. The periodic measurement of MNA, or failing that, of MNP or ADR should be included in the quality improvement process for colonoscopy conducted by all endoscopists in the setting of CRC screening programmes. Benchmarks could be established at 0.6 for MNA, 0.8 for MNP and 35% for ADR in the French colorectal cancer screening programme with gFOBT.

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Competing interests

None declared.

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Appendix A. Supplementary data

Supplementary material related to this article can be found, in the online version, at http://dx.doi.org/10.1016/j.dld.2013.08.129.

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