The Size of Colon Polyps Revisited: Intra- and Inter-observer Variations

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Abstract. *Background: It has been postulated that the occurrence of invasive carcinoma in a colon adenoma can be predicted by estimating the size of the resected polyp. Recently, significant intra- and inter-observer differences in size were found when 22 pathologists estimated the size of 12 polyp phantoms. In this work, the size of a large cohort of endoscopically-resected colon polyps was assessed with a novel method. Patients and Methods: Three pathologists measured photocopies of 148 resected polyps (adenomas at histology) in two independent trials. Results: The size recorded by the three participants was congruent in only 50% of the measurements in trial 1, and in 62% in trial 2. A significant difference in size asessment was found between the three investigators ($p \leq 0.05$). When 6 possible combinations (the 3 size limits proposed for predicting cancer risk in adenomas, and 2 different trials) were tested for the 13 adenomas showing invasive carcinoma, merely one of the three participants recorded the same size, but only in 11% of the 6 possible combinations. Conclusion: Present and previous investigations indicate that the lack of reproducibility makes the use of size limits in predicting cancer risk in polyps removed at colonoscopy unreliable.*

Colorectal adenomas are foci of atypical cells with aberrant proliferation and the main source of colorectal invasive carcinoma, the third most commonly diagnosed type of cancer in Europe and the US (1-3).

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In a seminal work published more than 30 years ago (4), it was postulated that the risk of villous adenomas harbouring an invasive growth at histology was approximately 1% for lesions measuring ≤9 mm in diameter, nearly 10% for adenomas measuring between 10 mm and 19 mm in diameter and 46% for those measuring ≥20 mm. The limits proposed in that work were considered valuable in the management of polyps and consequently readily implemented by radiologists (5-13), endoscopists (14-28) and pathologists (29-32).

To explore the reliability in assessing polyp size, 22 participants (18 pathologists and 4 surgeons) recently measured the largest diameter of 12 artificial polyp phantoms with the aid of a conventional millimetre ruler on two different trials (33). The results, compared to the gold standard-size assessed at the Department of Production Engineering, The Royal Institute of Technology in Stockholm, showed substantial variations in size assessment of single polyp phantoms from ±1 mm to ±7 mm, not only by different participants but even by the same participant, in two different trials.

Due to the clinical implications of the adenoma size regarding the expected risk of tumor invasion being found at histology (4) and in view of the poor performance in size assessment of polyp phantoms with a conventional ruler (33), it was considered desirable to search for a more robust and simpler method that could permit, in daily praxis, the size of removed clinical polyps to be assessed with an acceptable degree of reproducible accuracy.

Recently, we reported preliminary (encouraging) results using a novel method of size assessment of endoscopically removed colorectal polyps (34). In the present work, this method was further tested by three pathologists working in different countries, in a large cohort of consecutive colonic polyps removed at colonoscopy.

Patients and Methods

Between 2004 and 2006, 148 colonic polyps (adenomas as proven at histology) were removed at colonoscopy in 143 patients. After measuring each removed polyp with a conventional millimetre ruler for reporting purposes, the formalin-fixed polyp was placed on a piece of translucent paper together with the laboratory registration number and a millimetre ruler and then covered with white paper to avoid any contact of the polyp with the photocopier. The preparation was then photocopied on a Ricoh, Afficio, 2020D (Ricoh Europe, London, UK). The lid of the apparatus was brought down without exerting any pressure on the polyp. The lightest exposure (longest time exposure) was chosen to photocopy the preparation. To explore whether diffraction of a photocopied object influenced the registered size, a millimetre ruler was placed on the photocopied ruler. The size of the millimetre ruler corresponded exactly to the size of the ruler on the photocopy, indicating that the procedure caused no diffraction error.

Two short lines were then traced on each photocopy by one of us (CAR) to denote the apparent largest diameter of the polyp (Figure 1). To measure the polyp, one of the demarcating lines was placed on the 0 mark of a ruler. When the other traced line lay between two mm lines on the ruler, the more distal line on the ruler was chosen to record the largest diameter of the polyp. The three participants carried out a second measurement between these two lines independently, one week apart. Each participant registered the results and was blinded to the results of the other two. Measurements were transferred onto charts carrying the registration number of the Department of Pathology, Stockholm, Sweden. The three sets of charts with the measurements remained sealed until the compilation of results.

When all three participants (identified as participants A, B and C in the text and in the Tables) registered the same size, the values were considered to be congruent. When only two out of the three participants registered the same size, the values were registered as partially congruent and when all three participants registered a different size, the values were regarded as incongruent.

The Karolinska Institute Ethical Committee approved this investigation.

Statistical analysis. Two unbiased statisticians working in different countries (JM, EO) tested the results with a two-factor within subjects ANOVA (repeated tests) for measurements. The software used was Stata 10.0 for Windows (Stata Corporation, College Station, TX, USA) and SPSS version 14.0 (IBM Acquires SPSS Inc., Armonk, NY, USA).

ANOVA was used to test if the measurements differed for the three investigators in trials 1 and 2. The hypothesis was accepted at p=0.0001 and rejected at p=0.0511.

Results

Table I shows that in trial 1, only 50.0% of the values obtained for the 148 adenomas by the 3 participants were congruent. The percentage of congruency in trial 2 was 62%.

When the size of the polyps was catalogued according to Muto *et al*. (4), differences in the number of polyps measuring ≤9 mm and ≥20 mm in size were recorded among participants in trial 1 (Table II) and for those measuring ≤9 mm, 10-19 mm and ≥20 mm in size in trial 2 (Table III). When ANOVA was applied for all the measurements, significant differences in measurement at the millimetre level were found in the values provided by the three investigators (p=<0.05).

Comparing trials 1 and 2: When the results of trials 1 and 2 were compared (Tables II and III), it is seen that for polyps measuring ≤9 mm and 10-19 mm in diameter, all three participants recorded different numbers of polyps in both trials. For polyps measuring ≥20 mm in diameter, two participants reported different numbers of polyps in both trials while only one participant (participant A, in Tables II and III) found the same number of polyps with that size (n=44) in both trials. When ANOVA was applied for all the measurements in both trials, significant differences at the millimetre level were found in the values provided by the three investigators (p=<0.05).

Adenomas with invasive carcinoma: Invasive carcinoma was detected at histological evaluation in 13 out of the 148 adenomas (8.8%). Tables II and IIII show that the polyp size given by the three participants in these 13 cases, differed in trials 1 and 2. Difference in polyp size given by each participant was also different in the two trials (except for polyps measuring ≥20 mm, participant A in Tables II and III). Significant differences were found at the millimetre level in measurements made by the three investigators, as well as for each investigator, in individual trials (p=<0.05).

Discussion

More than 30 years ago three pathologists (4), one of them also an endoscopist, postulated that the risk of colorectal adenomas harbouring an invasive growth was relatively low for lesions measuring ≤9 mm in diameter but high for those measuring ≥20 mm in diameter. More recently, while re-reading that canonical document (4), we noticed that the size of all polyps was assessed either from examinations of clinical records and/or surgical notes or from the reports of the department of pathology. The material also included "some cases" in which the size was assessed from histological sections (4). Whether the size appearing in the clinical records (including surgical notes) was obtained using different methods, or if a discrepancy occurred between the sizes appearing in the clinical records, in the surgical operation notes, in the pathology reports or/and in histological sections, was not specified. Possible intra-observer or inter-observer variations in size were not explored. Recently, Lieberman *et al*. (25, 26) investigated the size of 6360 colorectal polyps, 5977 of them with histological evaluation. Patients from 17 different practice sites were assigned groups based on the size of the largest polyp found at colonoscopy. They concluded that patients whose largest polyp is 6 to 9 mm will have and would undergo surveillance at 3 years, based on current guidelines (25, 26).

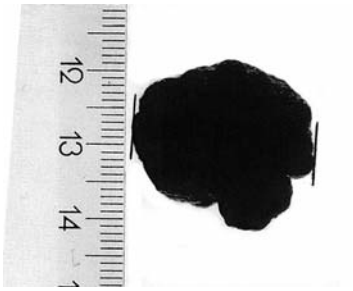

Figure 1. *Photocopy of endoscopically-resected polyp (adenoma at histological examination). Two lines were tracaed to demarcate the largest dimension of the polyp. The largest size between the two lines was recorded.*

Table I. *Congruity recorded for the measurements of polyp size by three different pathologists. Congruent, all three participants recorded the same polyp size in mm; partially congruent, one observer diverged by ≥1 mm from the size given by the other two observers; incongruent, all three participants recorded different sizes. The number of polyp measurements of the two individual trials obtained for 148 polyps (adenoma at histological examination) are given, with percent age in brackets.*

	Congruent	Partially congruent	Incongruent	Total
Trial 1	74 (50.0%)	73 (49.3%)	1 (0.7%)	148 (100%)
Trial 2	92 (62.2%)	56 (37.8%)	0 (0%)	148 (100%)

Table II. *The size distribution of polyps as assessed in trial 1 by the three participants. The percentage of total polyps is given in brackets. The number of adenomas found to have invasive carcinoma at histological evaluation are also given.*

Size (mm)	Participant A	Participant B	Participant C	No. of invasive carcinoma/ no. of adenomas
≤9	22 (14.9%)	21 (14.2%)	21 (14.2%)	1/21
10-19	82 (55.4%)	82 (55.4%)	82 (55.4%)	8/82
≥20	44 (29.7%)	45 (30.4%)	45 (30.4%)	4/45
All	148 (100%)	148 (100%)	148 (100%)	13/148

Table III. *The size distribution of polyps as assessed in trial 2 by the three participants. The percentage of total polyps is given in brackets. The number of adenomas found to have invasive carcinoma at histological evaluation, are also given.*

Size (mm)	Participant A	Participant B	Participant C	No. of invasive carcinoma/ no. of adenomas
≤9	23 (15.5%)	22 (14.9%)	23 (15.5%)	1/23
10-19	81 (54.7%)	80 (54.1%)	81 (54.7%)	8/81
≥20	44 (29.7%)	46 (31.0%)	44 (29.7%)	4/44
All	148 (100%)	148 (100%)	148 (100%)	13/148

In a recent critical evaluation (33) of the validity of these limits, it was inferred that if a pathologist measured a polyp at routine examination (an adenoma at histology) as being 9 mm in its largest diameter, the expected cancer risk is less than 1%, but if another pathologist measured the same adenoma as being 10 mm, the expected risk of detecting an invasive carcinoma at histology would then be nearly 10% (4). Similarly if a pathologist measured a polyp (an adenoma at histology) as being 19 mm, the expected risk is only 10%, but if another pathologist measured the same poly as being 20 mm, the expected risk for detecting an invasive carcinoma at histology would be then 46% (4).

In this study, although the three participants were urged to focus exclusively on measuring the distance between the two lines demarcating the largest diameter of the polyp on the photocopy, differences of 1 mm between participants were often recorded. Hence, a 1 mm difference between individual values seems to be an unavoidable human error. If congruent values are regarded as *bona fide* values, the results in trial 1 showed that the 9 mm limit was overscored by one of the three participants and that the not less important limit 20 mm was underscored by one of the three participants. In the second trial, the 9 mm limit was underscored by one of the three participants and the limit 20 mm was overscored by one of the three participants. Consequently, despite optimal, standardized conditions in size assessment, the values recorded differed by ≥1 mm for the same participant in the two different trials (intra-observer variation) and between the three participants (inter-observer variation) in individual trials as well as in both trials. These results question the validity of the limits given in the literature (4-27) to predict cancer in colonic adenomas.

It should be understood that in clinical praxis, pathologists calculate the size of polyps with a conventional millimetre ruler. This procedure, however, might be influenced by several confounding factors such as: i) the skill of the pathologist on duty, ii) the time given to measure the polyp (much influenced by differences in the daily workload) and iii) the technique used to measure a polyp (some pathologists place the polyp on the working bench facing the ruler, others place the polyp

on the ruler and a third group hold the soft, formalin-fixed polyp between two fingers to make the measurement). The latter procedure may exert lateral pressures that might reduce the actual maximal diameter of the polyp. Similarly, when callipers are used, the arms of the instrument may compress the sides of the soft polyp and induce its deformation, the result being an unwanted error in size estimation. Pathologists, moreover, do not re-check or double-check the size recorded with another pathologist before the polyp is cut and processed for histological evaluation and yet their measurements are added to the histological report and subsequently used in scientific publications (5-28, 33).

In conclusion, despite choosing the most optimal conditions for size assessment, the congruence between the values provided by the three participants was low in trial 1. A better congruence was, however, recorded between the values given in trial 2 suggesting that experience might have improved the readings. However, in trial 1, only two of the values provided by one of the participants differed ≥2 mm from the values found by the two other participants but in trial 2, as many as seven of the values provided by one of the participants differed ≥7 mm from the values found by the two other participants.

When 6 possible combinations (the 3 size limits proposed for cancer risk in adenomas, and 2 different trials) were tested for the 13 adenomas showing invasive carcinoma, merely one of the three participants recorded the same size, but only in 11% of the 6 possible combinations.

As a corollary, the encouraging preliminary results obtained by one of us (CAR) with this method (34) could not be confirmed when a large cohort of adenomas were measured by three independent observers in two separate trials.

Present and previous investigations (28, 33) indicate that the lack of intra- and inter-observer reproducibility makes the use of size limits unreliable in predicting cancer risk in polyps removed at colonoscopy.

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