# Risk of cancer in small and diminutive colorectal polyps

Prasanna L. Ponugoti, M.D.[1]

Oscar W. Cummings, M.D.[2]

Douglas K. Rex, M.D.[1]

Indiana University School of Medicine,
[1]Division of Gastroenterology and Hepatology, Indianapolis, IN
[2]Division of Surgical Pathology, Indianapolis, IN

Address correspondence and reprint requests to:
Douglas K. Rex
550 N. University Blvd, Suite 4100
Indianapolis, IN 46202
Phone: 317-948-8741
Fax: 917-944-5449
Email: drex@iupui.edu

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Abstract

The prevalence of cancer in small and diminutive polyps is relevant to “resect and discard” and CT colonography reporting recommendations.

We evaluated a prospectively collected colonoscopy polyp database to identify polyps < 10 mm and those with cancer or advanced histology (high-grade dysplasia or villous elements)

Of 32,790 colonoscopies, 15,558 colonoscopies detected 42,630 polyps < 10 mm in size. A total of 4,790 lesions were excluded as they were not conventional adenomas or serrated class lesions. There were 23,524 conventional adenomas < 10 mm of which 22,952 were tubular adenomas. There were 14,316 serrated class lesions of which 13,589 were hyperplastic polyps and the remainder were sessile serrated polyps. Of all conventional adenomas, 96 had high-grade dysplasia including 0.3% of adenomas ≤ 5 mm in size and 0.8% of adenomas 6-9 mm in size. Of all conventional adenomas, 2.1% of those ≤ 5 mm in size and 5.6% of those 6-9 mm in size were advanced. Among 36,107 polyps ≤ 5 mm in size and 6,523 polyps 6-9 mm in size, there were no cancers.

These results support the safety of resect and discard as well as current CT colonography reporting recommendations for small and diminutive polyps.

Key words: Diminutive polyps, small polyps, colorectal cancer, adenomas, serrated lesions, resect and discard, CT colonography.

## INTRODUCTION

The risk of cancer in small and diminutive colorectal polyps remains an important factor in several polyp management paradigms. For example, the risk of cancer in the resect and discard paradigm is important, since resect and discard [1] could potentially result in a small polyp with cancer being discarded after resection, and the cancer thus going unrecognized. Such an event could result in an adverse outcome for a patient if a cancer recurrence developed. Similarly, the prevalence of cancer in diminutive and small polyps is important in computed tomography (CT) colonography management paradigms, where diminutive polyps are not reported [2], and small polyps may not be recommended for immediate resection [2].

Early studies of cancer prevalence in small and diminutive polyps found a substantial cancer risk, which exceeded 0.4% in polyps 6 to 9 mm in size in some studies [3-7]. However, more recent colonoscopic studies found a much lower prevalence [8-15]. These differences may reflect in part the improved potential for polyp identification resulting from progressive improvements in colonoscope imaging. Thus, increasing emphasis on maximizing adenoma detection could result in a broader range of lesions removed, including many with a more subtle and flat morphology than was detectable in early studies. Contrary to some suggestions, flat morphology without depression is not associated with an increased risk of advanced pathology and may be associated with a lower risk of advanced pathology [16-18].

The prevalence of cancer in diminutive polyps is of great interest to some patients who are considering whether to participate in the resect and discard paradigm of small polyp management [19]. Determining this risk of cancer within narrow confidence limits is an important goal. We now report the largest single experience on the prevalence of cancer in small and diminutive polyps. This study exceeds the size of all prior studies on this topic combined.

## MATERIALS AND METHODS

We prospectively maintained a database of colonoscopies and polyp findings continuously since the year 2000 in our endoscopy units. The current report describes colonoscopies performed beginning in February 2004 and extending to September 2015. Permission to review the database was granted by the Institutional Review Board at Indiana University School of Medicine on September 29, 2015.

The database includes the endoscopist performing the examination, polyp size (as measured by endoscopist estimate), polyp location in the colon (by endoscopist estimate), and pathology as reported by our university pathologists.

Conventional adenomas were those interpreted by the pathologists as tubular, tubulovillous, or villous. Serrated class lesions were those interpreted as hyperplastic polyp, sessile serrated polyp, sessile serrated adenoma, or serrated adenoma, or traditional serrated adenoma.

Statistical analysis was descriptive.

## RESULTS

A total of 32,790 colonoscopies were performed during the study period by 53 different endoscopists. There were 15,558 procedures that identified 42,630 polyps < 10 mm in size for which the polyp was resected and a pathology report was created. The mean age was 60.1 years (59.7 years in females, 60.2 years in males). There were 1,890 procedures in persons < 50 years of age, and 649 in persons 80 years and older.

Polyps (n=4,790) that were not considered conventional adenomas or serrated class lesions were excluded from further analysis. These included normal tissue/mucosa (n = 3,833),

inflammatory polyps (n = 574), lymphoid follicles (n = 293), granulation tissue (n = 60), hamartoma (n = 14), carcinoid tumor (n=13), metastatic malignant melanoma (n = 2), and granular cell tumor (n = 1).

There were 23,524 conventional adenomas < 10 mm in size, of which 22,952 (97.6%) were tubular adenomas. There were 14,316 serrated class lesions < 10 mm in size, of which 13,589 (95%) were interpreted as hyperplastic polyps, and the remainder were sessile serrated polyps or "serrated adenoma" (Table 1). Polyps < 10 mm in size comprised 88.4% of all resected polyps.

Among all conventional adenomas, 96 had high-grade dysplasia, including 0.3% of adenomas ≤ 5 mm in size and 0.8% of conventional adenomas 6 to 9 mm in size. The fraction of conventional adenomas ≤ 5 mm in size that were advanced (had either villous elements or high-grade dysplasia) was 2.1%. The fraction of 6-9 mm conventional adenomas that were advanced was 5.6%.

There were no cancers among 36,107 polyps ≤ 5 mm in size and 6,523 polyps 6 to 9 mm in size.

## DISCUSSION

In this report, we describe the largest reported experience with identification of cancer in colorectal polyps < 10 mm in size. This study exceeds the size of all previous studies on this topic combined (Table 2). We found no cancers in nearly 36,000 polyps ≤ 5 mm in size, and none in 6,523 polyps 6 to 9 mm in size. Our results indicate that the risk of cancer in diminutive and small polyps is very low. These results substantially improve the projected safety of resect and discard paradigm [1] and of current reporting recommendations for CT colonography [2].

Our results are consistent with much of the previously published literature [3-15,20-27], particularly reports from the last 10 years (Table 2). As noted earlier, the trends toward decreasing prevalence rates of cancer in small and diminutive polyps may reflect the improved imaging capabilities of colonoscopes, and increasing emphasis on identification of flat lesions which do not increase the risk of cancer compared to polypoid lesions [16-18].

The overall distribution of polyp sizes in this study suggests that the tendency of endoscopists in our unit is to underestimate polyp size, particularly since the percentage of all polyps < 1 cm in size was comparable to other studies [3-15,21-27], despite our center receiving many referrals for large and complex polypectomies [28]. Further the fraction of polyps ≤ 5 mm and 6-9 mm in size was comparable to or higher than prior studies [3-17,22-29]. Any underestimation of polyp size would tend to cause the apparent prevalence of cancer in polyps of different size ranges to increase. Despite this apparent tendency to underestimate polyp size, no cancers were identified in small and diminutive polyps.

The prevalence of villous elements and high-grade dysplasia in small and diminutive polyps in the study was very low, and lower than noted in a number of other reports (Table 2). However, we have demonstrated that interpretation of villous elements and dysplasia grade in small polyps is subject to extreme interobserver variation and poor agreement even among experts [29]. These features have caused the British Society of Gastroenterology to ignore villous elements and dysplasia grade in their post polypectomy surveillance guideline [30]. We previously reported that experts in gastrointestinal pathology do not use the same definitions of high-grade dysplasia [29]. Specifically, pathologists who utilize cytologic criteria for high-grade dysplasia report much higher prevalence rates of high-grade dysplasia compared to those who use only morphologic criteria [29]. At the direction of the gastrointestinal pathologists in our unit, our

pathologists utilize only morphologic criteria for high-grade dysplasia, which undoubtedly contributes to the low prevalence of high-grade dysplasia in our study. Similarly, there is marked interobserver variation in the interpretation of sessile serrated polyp vs. hyperplastic polyp [31,32]. We had previously demonstrated that experts identify a higher percentage of sessile serrated polyps than are identified by our own pathologists [32]. However, experts also exhibit significant interobserver variation [31]. Therefore, our data on the prevalence of sessile serrated polyp reflect a conservative approach to interpretation of this lesion, as well as evolving awareness of sessile serrated polyp by pathologists during the study period. Our focus in this paper is on the prevalence of cancer in small and diminutive polyps. Interpretation of cancer by community pathologists in colorectal polyps appears to be consistent and reliable [33], as does the assignment of colorectal polyps to the conventional adenoma vs. serrated class [1,33]. Thus, the pathology reports with regards to the prevalence of cancer in diminutive and small polyps should be reliable.

Strengths of our study include its large size, which far exceeds the size of any previous study on this topic, and is slightly larger than the size of all previous studies on this topic combined (Table 2). There are few databases available that include pathology results on individual polyps < 10 mm in size.

Limitations include the retrospective nature of the study, though the database was accumulated prospectively. Additionally, polyp size was estimated endoscopically, though as we noted above the distribution of polyp sizes does not suggest any tendency to overestimate lesion size.

In summary, we did not identify any cancers in a large sample of diminutive and small colorectal polyps. This result favors the feasibility of strategies such as resect and discard [1], and

favors the appropriateness of current CT colonography reporting recommendations for diminutive and small polyps [2].

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Table 1. Prevalence of cancer in diminutive and small colorectal polyps

| Polyp Pathology | Size | Total number of polyps | Tubular adenoma n (%) | Tubulovillous adenoma n (%) | Villous adenoma n (%) | High-grade Dysplasia n (%) | Cancer n (%) | Hyperplastic polyp n (%) | Sessile serrated polyp n (%) |
|---|---|---|---|---|---|---|---|---|---|
| | ≤ 5 mm | 19,559 | 19,191 (98.1%) | 357 (1.8%) | 11 (0.1%) | 66 (0.3%) | 0 | - | - |
| | 6-9 mm | 3,965 | 3,761 (94.9%) | 202 (5.1%) | 2 (0.1%) | 30 (0.8%) | 0 | - | - |
| | ≤ 5 mm | 12,214 | - | - | - | - | 0 | 11,772 (96.4%) | 442 (3.6%) |
| | 6-9 mm | 2,102 | - | - | - | - | 0 | 1,817 (86.4%) | 285 (13.6%) |

Table 2: Previously published data on the prevalence of advanced adenomas and caner in small and diminutive polyps

| Study | Number of Diminutive Adenomas (Size Range) | Number of Diminutive Adenomas with Advanced Histology (%) | Number of Diminutive Carcinomas (%) | Number of Small Adenomas (Size Range) | Number of Small Adenomas with Advanced Histology (%) | Number of Small Carcinomas (%) |
|---|---|---|---|---|---|---|
| Shinya et al. 1979 [3] | | | | 1661 (5-9 mm) | 249 (15%)** | 8 (0.5%) |
| National Polyp Study, 1990 [20] | 1270 (<6 mm) | 25 (2%)** | | 1230 (6-10 mm) | 155 (12.6%)** | - |
| Weston et al. 1995 [21] | 1964 (<= 5 mm) | 5 (0.3%) | 0 | | | |
| Aldridge et al. 2001 [22] | 194 (<= 5 mm) | 71 (36.5%)** | 0 | 163 (6-10 mm) | 99 (60.7%)** | 2 (0.01%) |
| Gshwantler et al. 2002 [4] | 3016 (<5 mm) | 561 (18.6%)** | 0 | 2789 (5-10 mm) | 1080 (38.7%)** | 26 (0.9%) |
| Kapsoritakis et al. 2002 [23] | 293 (<= 5 mm) | 6 (2%)* | 0 | | | |
| Pickhardt et al. 2003 [24] | 966 (<=5 mm) | 1 (0.1%) | 0 | 262 (6-9 mm) | | 0 |
| Church et al. 2004 [25] | 4381 (<6 mm) | 91 (2.1%) | 2 (0.05%) | 666 (6-10 mm) | 65 (9.8%) | 1 (0.15%) |
| Odom et al. 2005 [5] | 2851 (<= 5 mm) | | 1 (0.03%) | 152 (6-10 mm) | | 1 (0.65%) |
| Butterly et al. 2006 [7] | 1305 (<6 mm) | 34 (2.6%)** | 1 (0.08%) | 487 (6-9 mm) | 38 (7.8%)** | 2 (0.4%) |
| Sprung et al. 2006 [26] | | | | 6694 (5-10 mm) | | 2 (0.03%) |
| Yoo et al. 2007 [6] | 3303 (<= 5 mm) | 5 (0.15%) | 1 (<0.01%) | 1432 (6-9 mm) | 31 (2.2%) | 7 (0.49%) |
| Kim et al. 2007 [8] | 2006 (<=5 mm) | 4 (0.2%) | 0 | | | |
| Lieberman et al. 2008 [9] | 3744 (<=5 mm) | 62 (1.7%)*** | 1 (0.02%) | 1198 (6-9 mm) | 77 (6.4%)*** | 2 (0.2%) |
| Graser, 2009 [10] | 418 (<= 5 mm) | 7 (1.7%)** | 0 | 56 (6-9 mm) | 6 (10.7%)** | 0 |
| Bretagne et al. 2010 [11] | 535 (<=5 mm) | 15 (2.8%)* | 0 | 219 (6-9 mm) | 34 (15.5%)* | 0 |
| Chaput et al. 2011 [12] | 342 (<=5 mm) | 16 (4.7%) | 0 | 72 (6-9 mm) | 25 (35.2%) | 0 |
| Tsai et al. 2011 [13] | 1025 (<= 5 mm) | 105 (10%) | 0 | 247 (6-9 mm) | 67 (27%) | 0 |
| Denis et al. 2011 [14] | 180 (<= 5 mm) | 22 (12.2%) | | 29 (6-9 mm) | 13 (44%) | 0 |
| Gupta et al. 2012 [15] | 1620 (<= 5 mm) | 9 (0.6%)** | 0 | 455 (6-9 mm) | 7 (1.5%)** | 0 |
| Kaltenbach et al. 2014 [27] | 975 (<= 5 mm) | 1 (0.10%) | 0 | | | |
| ***Pooled data*** | ***30,388*** | ***1,040 (3.42%)*** | ***6 (0.02%)*** | ***17,812*** | ***1,946 (10.9%)*** | ***51 (0.28%)*** |

*: High grade dysplasia only

**: High grade dysplasia, villous and tubulovillous category

***: High grade dysplasia, villous and tubulovillous, serrated category