



Appendix orifice polyps: a study of 691 lesions at a single institution

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Abstract

Purpose Data on the management of appendix orifice lesions are limited. We present our experience on the management of appendix orifice lesions focusing on the range of size, histology, treatment, and outcomes for polyps at the appendix orifice.

Methods Retrospective descriptive study at a tertiary referral center. *Patients:* Those having appendix orifice lesion removed and sent for histology between 2000 and 2017. *Interventions(s):* Polypectomy, surgery. *Main outcome measures:* Polyp size, shape, histology, treatment.

Results In total, 691 patients matched our inclusion criteria. Screening was the most common indication for colonoscopy (49.1%). Mean size was 10.1 mm. The most common excision method was cold biopsy forceps (36.3%), followed by hot snare (9.3%), cold snare (8.5%), jumbo cold forceps (6.7%), hot biopsy (6.8%), and endoscopic mucosal resection (EMR)/endoscopic submucosal dissection (ESD) (4%). Recurrence was seen in 19/184 (10.3%) patients. Index polyps ≥ 10 mm had a significantly higher risk of recurrence compared to those ≤ 5 mm (odds ratio 3.2 95% CI 1.1–9.2, $p = 0.027$). None of the patients had complications. Surgery was performed in 45/691 (6.5%). Polyps > 5 mm (41/45) were more likely to require surgery than polyps ≤ 5 mm (4/45 6.67%), $p < 0.001$.

Limitations Retrospective study.

Conclusion Appendix orifice polyps can usually be managed by conventional endoscopic polypectomy methods without the need for ESD.

Keywords Appendix orifice polyps

Background

Colorectal cancer (CRC) occurs due to an accumulation of genetic abnormalities in clones of colonocytes, leading to increasing dysregulation of cell growth, death, and division. Precancerous benign neoplasms are the first clinically obvious manifestation of the genetic events and one or more of these may ultimately acquire the ability to invade and spread outside the colorectum. This carcinogenic sequence can be stopped before cancer develops by discovery and removal of the cancer precursor, usually by colonoscopic screening [1].

However, not all premalignant colorectal lesions can be resected. Some may be too large for endoscopic removal, and some may be too flat, while others may be awkwardly placed. One of the locations notorious for making polypectomy difficult is the region of the appendix orifice.

Traditionally, polyps are excised using biopsy forceps or snares (either hot or cold). Certain flat polyps or polyps on mucosal folds may need a saline lift injection to ensure complete and safe polypectomy [2]. Other lesions might require more technically demanding methods such as endoscopic submucosal dissection (ESD). The final option is surgical resection [3]. Exact indications for endoscopic mucosal resection (EMR)/ESD are not clear, but generally large polyps (> 20 mm), flat lesions, and laterally spreading tumors are chosen [4]. However, both EMR/ESD are associated with an increased risk of bleeding and perforation compared to conventional biopsy forceps and snares [5].

The most difficult polyps of all to manage are either those that extend into the lumen of the appendix itself, or those that arise completely from within the lumen. It seems as if EMR/ESD would be of limited use for appendix orifice polyps due

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to the presence of the appendix itself and the unusual shape of the base of the cecum. We would anticipate that most appendix orifice polyps are treated with biopsy forceps and simple snares.

There are few studies in the literature that explore the topic of appendix orifice polyps. In this study, we aim to describe the range of histology to be found in this location, the ways that such polyps are managed, and the outcomes of their management.

Methods

This is a retrospective analysis of all patients with lesions at the appendix orifice that were submitted to the Department of Pathology at the Cleveland Clinic for histologic evaluation in the years 2000–2017. After IRB approval, patients were accessed by review of the institutional histology database searching for reports with the term “appendix orifice lesion/polyp.” The definition of “appendix orifice polyp” was based on the pathology request form, the histology report, and a review of the patient record. We excluded all patients with inflammatory bowel disease, Lynch syndrome, and polyposis syndromes. Multiple pathologists and endoscopists from the Departments of Anatomic Pathology, Colorectal Surgery, and Gastroenterology are represented in this report. All endoscopists performing the procedures are experts with a volume of at least 300 procedures per year.

The following variables were abstracted from the patient record: age and sex of the patients; their history of appendectomy; the size, number, and shape of the appendix orifice lesions; indication of colonoscopy; the quality of bowel preparation; excision method; pathology; follow-up; use of additional interventions (such as clips or epinephrine injection); recurrence of the excised polyp; and need for excisional surgery for the appendix orifice lesion.

Statistical analysis

Categorical variables were summarized as proportions and percentages. Continuous variables were summarized as mean \pm standard deviation (SD) for normal distribution or median (interquartile range [IQR]) for non-parametric distribution. Tests of the significance of differences between groups and categorical variables were performed using the chi-square method and Fisher’s exact test. For quantitative variables, groups were compared by Student’s *t* tests or Wilcoxon rank sum tests. $p < 0.05$ was accepted as statistically significant. All analyses were done using SAS (version 9.4; The SAS Institute, Cary, NC), and p values < 0.05 were considered statistically significant.

Results

During this 17-year period, 691 patients matched our inclusion criteria. The mean age at polypectomy was 59.8 ± 11 years; male to female ratio is 1:1. Details about indication for colonoscopy, size, shape, and excision method of appendix orifice lesions are shown in Table 1. Size distribution favors diminutive polyps with relatively few lesions larger than 1 cm.

Table 1 Endoscopic characteristics of appendix orifice lesions

| Variable | Total number (691 lesions) |
|---------------------------------------|----------------------------|
| Indication | |
| Screening | 341 (49.3%) |
| Personal history of polyps | 231 (33.4%) |
| Personal history of colorectal cancer | 11 (1.6%) |
| Change in bowel habits | 33 (4.8%) |
| Anemia | 15 (2.2%) |
| Bleeding per rectum/melena | 36 (5.2%) |
| Abdominal pain | 21 (30.4%) |
| Weight loss | 2 (0.3%) |
| Pelvic mass | 1 (0.1%) |
| Size (mean = 6.2 mm) | |
| Not reported | 121 (17.5%) |
| ≤ 5 mm | 380 (55.0%) |
| 6–9 mm | 100 (14.5%) |
| ≥ 10 mm | 90 (13.0%) |
| Excision method | |
| Cold biopsy forceps | 461 (66.7%) |
| Jumbo cold forceps | 46 (6.7%) |
| Hot snare | 64 (9.3%) |
| Cold snare | 48 (7.0%) |
| Snare (unspecified) | 11 (1.6%) |
| Hot biopsy | 33 (4.8%) |
| EMR | 26 (3.7%) |
| ESD | 2 (0.3%) |
| Shape of the lesion | |
| Sessile | 439 (63.5%) |
| Flat | 40 (5.8%) |
| Carpet-like | 11 (1.6%) |
| Semi-sessile | 11 (1.6%) |
| Pedunculated | 12 (1.7%) |
| Semi-pedunculated | 4 (0.6%) |
| Lipoma | 2 (0.3%) |
| Prominent mucosal fold | 42 (6.1%) |
| Granular mucosa | 45 (6.5%) |
| Nodule | 22 (3.2%) |
| Mass | 4 (0.58%) |
| Submucosal mass/nodule | 15 (2.17%) |
| Polyp unspecified | 44 (6.4%) |
| Complete resection | 469 (67.9%) |

Most polyps were removed by biopsy forceps, while 17.9% were snared. EMR/ESD was performed in approximately 4% of lesions. Most lesions were sessile or flat, with only a few that were pedunculated. There were 265 non-neoplastic lesions including 153 lymphoid follicles, 86 normal mucosa, and 26 inflammatory polyps. There were 426 neoplasms including 227 adenomas (209 tubular, 17 tubulo-villous, and 1 villous), 123 sessile serrated adenomas/polyps, 61 hyperplastic polyps, and 8 traditional serrated adenomas. Three adenomas contained high-grade dysplasia. There was one leiomyoma and six cancers including three adenocarcinoma and three carcinoid tumors. Elective surgical resection was performed in 45 patients: details are shown in Table 2.

The quality of bowel preparation was fair in 80/691 patients (11.6%) and poor in 20/691 patients (2.9%). A total of 90 patients (13%) had a history of appendectomy, and details about the size and pathology of lesions in patients with history of appendectomy are shown in Table 3. None of the patients in our study suffered from perforation or postprocedural bleeding, or needed readmission.

Complications

In order to avoid or treat postprocedural bleeding, 27 patients needed active hemostasis. This was done using endoscopic

Table 2 Surgical management

| Variable | Total (N = 45) |
|-----------------------------------|----------------|
| Operation | |
| Appendectomy only | 4 (8.9%) |
| Appendectomy + partial cecectomy | 22 (48.9%) |
| Right hemi-colectomy | 19 (42.2%) |
| Margins | |
| Positive | 1* |
| Free | 44 |
| Pre-operative pathology | |
| Neoplastic (n = 36) | |
| Tubular adenoma | 10 (22.2%) |
| Tubulo-villous adenoma | 5 (11.1%) |
| SSA/P | 12 (26.7%) |
| Villous adenoma | 1 (2.22%) |
| Adenoma with high-grade dysplasia | 1 (2.22%) |
| Traditional serrated adenoma | 1 (2.22%) |
| Adenocarcinoma | 3 (6.7%) |
| Carcinoid tumor | 3 (6.7%) |
| Non-neoplastic (n = 9) | |
| Normal mucosa | 6 (13.3%) |
| Lymphoid follicles | 2 (4.4%) |
| Inflammatory | 1 (2.2%) |

*Tubulo-villous adenoma following appendectomy and partial cecectomy, scheduled for follow-up colonoscopy 1 year after surgery

Table 3 Polyps in patients with previous appendectomy

| | Total (n = 90) | Percentage of all lesions | Percentage of neoplastic lesions |
|---------------------------------|----------------|---------------------------|----------------------------------|
| Pathology | | | |
| Neoplastic lesions (n = 35) | | | |
| Tubular adenoma | 14 | 15.6 | 40 |
| Adenoma (NOS) | 2 | 2.2 | 5.7 |
| SSA/P | 11 | 12.2 | 31.4 |
| High-grade dysplasia | 1 | 1.1 | 2.9 |
| Hyperplastic polyp | 7 | 7.8 | 20 |
| Non-neoplastic lesions (n = 55) | | | |
| Inflammatory | 3 | 3.3 | – |
| Lymphoid aggregates | 39 | 43.3 | – |
| Normal mucosa | 13 | 14.4 | – |
| Size | | | |
| Not reported | 26 | 28.9 | – |
| ≤ 5 mm | 35 | 38.9 | – |
| 6–9 mm | 14 | 15.6 | – |
| ≥ 10 mm | 15 | 16.7 | – |

clips in 19 patients (14 had a single clip and 5 had two clips), while 2 patients had argon plasma coagulation (APC) and 6 had injection of 1:10,000 epinephrine solution. The size of lesions in the patients who had hemostatic treatment was > 10 mm in 14/27 patients (51.9%). The most common method of excision complicated by bleeding was snaring in 15/27 patients (55.6%). There were no cases of perforation or postpolypectomy syndrome. No patient developed acute appendicitis after polypectomy.

Surgical management

Following endoscopy, 45 patients (6.5%) underwent surgery. Preoperative pathology is shown in Table 2, along with the type of surgeries performed. In 9 patients, the biopsy was non-neoplastic, but these cases had been associated with a mass on colonoscopy/imaging, and surgery was performed because of

Table 4 Multivariable logistic regression for association of different variables with surgical management

| Effect | Odds ratio (95% CI) | p value |
|------------------------|---------------------|----------|
| Age | 1.00 (0.98, 1.03) | 0.81 |
| AA vs Caucasian | 0.69 (0.20, 2.4) | 0.55 |
| ≥ 10 mm vs ≤ 5 mm | 19.3 (6.3, 59.7) | < 0.001* |
| Non-sessile vs sessile | 2.8 (1.3, 6.1) | 0.008 |

*Polyps ≥ 10 mm are more likely to require surgery compared to polyps ≤ 5 mm

Table 5 Recurrent polyps

| Variable | Total <i>N</i> = 19 (%) |
|-----------------------|-------------------------|
| Size (mean = 10.1 mm) | |
| ≤5 mm | 9(47.4%) |
| 6–9 mm | 2(10.5%) |
| ≥ 10 mm | 8(42.1%) |
| Shape | |
| Sessile | 13 (68.4%) |
| Flat | 1(5.3%) |
| Carpet-like | 3 (15.8%) |
| Semi-pedunculated | 1(5.3%) |
| Polyp (unspecified) | 1(5.3%) |
| Excision method | |
| Cold biopsy forceps | 2 (10.5%) |
| Jumbo cold forceps | 3 (15.8%) |
| EMR | 5 (26.3%) |
| Hot biopsy | 2 (10.53%) |
| Hot snare | 5 (26.32%) |
| Cold snare | 2 (10.53%) |

the mass. All operated cases but 1 had a free resection margin in the specimen. The case with the positive margin was a tubulovillous adenoma that had undergone an appendectomy with partial colectomy; final pathology was the same with no high-grade dysplasia. The patient is scheduled for follow-up 1 year following surgery. On multivariate analysis (Table 4), we found that patients with lesions ≥ 10 mm are more likely to require surgery compared to patients with smaller lesions. Also, flat lesions are more likely to require surgery than sessile lesions (odds ratio 2.8, 95% CI 1.3–6.1,

$p = 0.008$). In all cases, postoperative diagnosis was the same as preoperative.

Follow-up and recurrence after complete colonoscopic excision

Colonoscopic follow-up was done in 183/646 (28.3%) patients, excluding the 45 patients who underwent surgery. This relatively low rate of follow-up is due to the large number of patients (70%) whose index lesion had been removed within the last 4 years and who had not yet returned for their scheduled or recommended surveillance. Median follow-up duration was 34 months with 66/183 (36.1%) patients having their first follow-up within 1 year of index procedure. Recurrence after complete excision of the index lesion was seen in 19/183 patients (10.4%) (Table 5). On univariate analysis, size was the only significant factor associated with recurrence (Table 6). In a multivariable analysis, shape was removed from the model, as it was the least significant of the other three, in order to maintain appropriate number of events per variable. A large size was a significant risk factor for recurrence (Table 7). All recurrences were managed endoscopically.

Analysis of lesions ≥ 10 mm in size (*n* = 90)

Complete excision was done in 53/90 patients (58.8%). Of these 53, snare polypectomy was used in 36/53 (67.9%). Surgical resection was the definitive management in 19/90 (21.1%). Recurrence rate was high in this group; 8/29 (27.6%) patients. Details are presented in Table 8 and Fig. 4.

Table 6 Univariate analysis for recurrence

| Factor | Total (<i>N</i> = 183) | No (<i>N</i> = 164) | | Yes (<i>N</i> = 19) | | <i>p</i> value |
|--------------|-------------------------|----------------------|-------------|----------------------|-------------|--------------------|
| | | <i>n</i> | | <i>n</i> | | |
| Age (years) | 60.8 ± 10.5 | 164 | 60.5 ± 10.4 | 19 | 63.4 ± 11.3 | 0.25 ^a |
| Race | | 164 | | 19 | | 0.17 ^b |
| White | 168 (91.8) | | 149 (90.9) | | 19 (100.0) | |
| Black | 15 (8.2) | | 15 (9.1) | | 0 (0.0) | |
| Shape | | 164 | | 19 | | 0.50 ^b |
| Other shape | 71 (38.8) | | 65 (39.6) | | 6 (31.6) | |
| Sessile | 112 (61.2) | | 99 (60.4) | | 13 (68.4) | |
| Size | | 164 | | 19 | | 0.027 ^b |
| Not reported | 34 (18.6) | | 34 (20.7) | | 0 (0.0) | |
| ≤ 5 mm | 86 (47.0) | | 77 (47.0) | | 9 (47.4) | |
| 6–9 mm | 26 (14.2) | | 24 (14.6) | | 2 (10.5) | |
| 10+ mm | 37 (20.2) | | 29 (17.7) | | 8 (42.1) | |

Statistics presented as mean ± SD, median [P25, P75], median (min, max), or *N* (column %). *p* values: ^a ANOVA, ^b Pearson's chi-square test

Table 7 Multivariable logistic regression for recurrence

| Effect | Odds ratio (95% CI) | <i>p</i> value |
|-------------------|---------------------|----------------|
| Age | 1.02 (0.98, 1.07) | 0.36 |
| ≥ 10 mm vs ≤ 5 mm | 3.2 (1.1, 9.2) | 0.027* |
| 6–9 mm vs ≤ 5 mm | 1.02 (0.21, 5.0) | 0.98 |

*Polyps ≥ 10 mm are more likely to recur with an odds ratio of 3.2 (*p* = 0.027) compared to polyps ≤ 5 mm

Discussion

Most of the issues with lesions located near or in the appendix orifice concern their removal, as the contour of the region

Table 8 Lesions ≥ 10 mm

| | Lesions ≥ 10 mm (<i>n</i> = 90) | | |
|----------------------------------|----------------------------------|---------------------------|----------------------------------|
| | Total (<i>N</i> = 90) | Percentage of all lesions | Percentage of neoplastic lesions |
| Mean age (years) | 61.1 ± 11.4 | | |
| Male:female ratio | 1:1.5 | | |
| Excision | | | |
| Complete | 53 | 58.8 | – |
| Incomplete | 37 | 41.1 | – |
| Excision method (<i>n</i> = 53) | | | |
| CBF | 1 | 1.9 | – |
| Hot/cold snare | 36 | 67.9 | – |
| Hot biopsy | 2 | 3.8 | – |
| EMR | 13 | 24.5 | – |
| ESD | 1 | 1.9 | – |
| Pathology | | | |
| Neoplastic | | | |
| Tubular adenoma | 23 | 25.5 | 33.3 |
| Tubulo-villous adenoma | 12 | 13.3 | 17.4 |
| Villous adenoma | 1 | 1.1 | 1.4 |
| HGD | 3 | 3.3 | 4.4 |
| SSA/P | 23 | 25.6 | 33.3 |
| Hyperplastic polyp | 4 | 4.4 | 5.8 |
| Adenocarcinoma | 1 | 1.1 | 1.4 |
| Carcinoid | 2 | 2.2 | 2.9 |
| Non-neoplastic | | | |
| Lymphoid follicle | 14 | 15.6 | – |
| Normal mucosa | 4 | 4.4 | – |
| Inflammatory polyp | 3 | 3.3 | – |
| Surgery (<i>N</i> = 19) | | | |
| Appendectomy | 1 | 5.2 | – |
| Appendectomy + partial cecectomy | 9 | 47.4 | – |
| Right hemicolectomy | 9 | 47.4 | – |



Fig. 1 A 3-mm sessile serrated adenoma/polyp (SSA/P) adjacent to the appendix orifice, removed with cold biopsy forceps excision

around the appendix orifice and the fact that some polyps grow into or out of the appendix make complete excision potentially challenging. There is also a concern that causing postpolypectomy edema of the appendix orifice may precipitate acute appendicitis. Our study showed that it is possible to safely remove most appendix orifice polyps endoscopically and that postprocedure appendicitis did not occur. Larger polyps were sometimes more of a challenge. Figure 1 shows a small serrated adenoma/polyp (SSA/P) near the appendix orifice, simply removed with cold biopsy forceps. Figure 2 shows a large SSA/P completely surrounding the appendix orifice. It was possible to remove this completely with a diathermy snare (Fig. 3) without sublesional injection of fluid.

Data on the optimal management of appendix orifice (AO) polyps are quite limited. Two recent studies from Asia report



Fig. 2 A 12-mm SSA/P surrounding the appendix orifice. Removed by simple diathermy snare excision



Fig. 3 Postpolypectomy view of the appendix orifice after snare of the lesion seen in this image. The site healed without any adverse effects

on the use of EMR and ESD. In a multicenter study from Korea, Song et al. report on 131 lesions with a median size of 10 mm (3–60 mm) [6]. Endoscopic treatment was possible in 93% but was mainly EMR/ESD with only 15% of lesions

excised using biopsy forceps and simple snare excision. This was a completely different pattern of treatment to ours. In their series, Song et al. reported a recurrence rate of 15.6%. Involvement of $\geq 75\%$ of AO circumference was the only significant risk factor for recurrence on multivariate analysis. There were 3 cases (2.3%) of postprocedural bleeding, 2 of perforation (1.5%), and no postprocedural appendicitis [6].

A Japanese study reported by Jacob et al. describes 76 lesions near the appendix orifice; 29 were at the orifice or extending into the appendix with a median size of 35.5 mm (10–110 mm). All were managed using ESD with a complication rate of 13.8% (1 bleeding, 1 perforation, and 2 postprocedural appendicitis) [7].

Our study adds to these two studies by providing a broad and comprehensive review of all polyps submitted to histology. This allows us to report the spectrum of size, shape, and histology of polyps seen in and near the appendix orifice. The most clinically important polyps are those that measure ≥ 10 mm. We have broken these out to provide a more valid group for comparison with the other studies (Table 8). Our large polyps (≥ 10 mm) had a higher recurrence rate (8/29, 27.6%) and a higher chance of surgery (Table 4). However, only 1 had an ESD and 13 had EMR (Table 8). Overall,

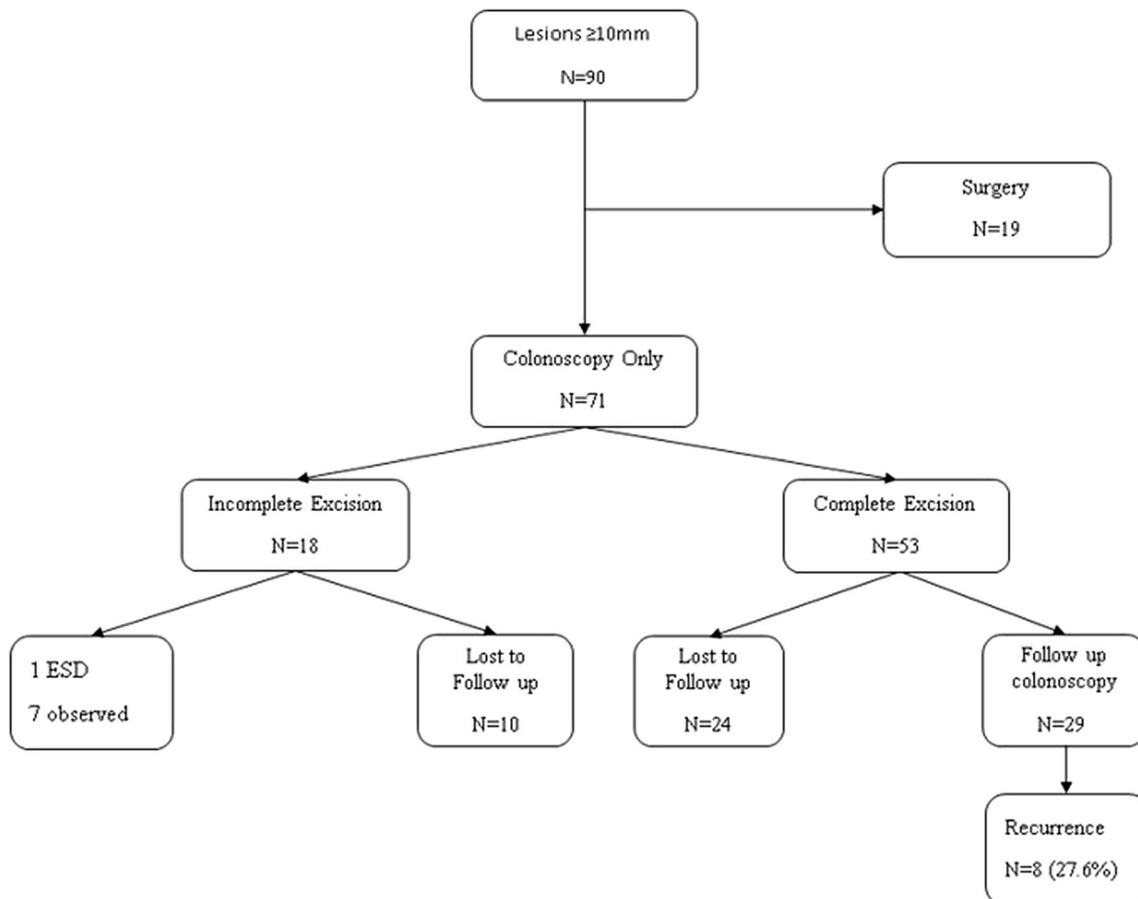


Fig. 4 Lesions ≥ 10 mm

complete polyp resection was achieved in 469/691 patients (67.9%) but the Asian data reflect the advantages of the ESD technique for larger and especially circumferential polyps at this location. Our overall recurrence rate in patients with documented follow-up was 10.3%. Several factors have been implicated in polyp recurrence such as proximity of polyp to the orifice, polyp number, and size [8, 9]. Our data show that patients with lesions larger than 10 mm have an increased risk of recurrence (odds ratio 3.2, 95% CI 1.1–9.2, $p = 0.027$).

Management of large polyps in difficult locations like the appendix orifice can be challenging. Our study showed that although they are amenable to resection by conventional techniques, these polyps have a significantly higher risk of recurrence and surgery compared to small lesions. Trial of complete excision using conventional polypectomy techniques (mainly snaring for large-sized polyps) is the first option. However, should this trial fail, surgery must be considered. Some authors recommend surgery after a second attempt at colonoscopy [10]. Others believe that patients should be referred to expert surgical endoscopists. Should colonoscopy absolutely fail to control the lesion, combined laparoscopy and polypectomy may be worthwhile [11, 12]. Surgery was done in only 6.5% of our patients, including 9 with normal mucosa, colitis, or lymphoid follicles on colonoscopic biopsies since they were associated with a mass on colonoscopy/imaging. Interestingly, all appendectomy cases ($n = 4$) had free margins. This was achieved by frozen section (2/4), examination of appendix on side table following excision (1/4), and gross examination of cecal mucosa before closure of cecotomy (1/4). As expected, patients with flat lesions ≥ 10 mm were more likely to undergo surgery.

One of the weaknesses of our study is that it is based on a database of histology. Numerous endoscopists are involved, with different levels of endoscopic experience and skill. The outcome data are therefore an integral of multiple endoscopists. The retrospective nature of this study makes knowing the intent of the endoscopist unattainable (intentional incomplete excision with biopsies only versus unsuccessful attempt at endoscopic resection). The primary author (JC) has treated polyps of the appendix orifice with simple snare excision as well as hot and cold biopsies (Figs. 2 and 3). Polyps going into the appendix can be pulled out with a cautery snare or hot biopsy. The instrument is quickly reapplied and coagulation used to excise part of the polyp. The fraction that is left often stays prolapsed out into the cecum due to the edema caused by the coagulation. The instrument can then be reapplied and the process repeated until the entire polyp has been removed. Large polyps arising from inside the appendix often cause dilation of the orifice, facilitating snare or forceps insertion. The use of coagulation is possibly less risky than elsewhere in the colon due to the presence of a complete longitudinal muscle coat in the appendix and at its base.

Another weakness of our study is that only 183 (28.6%) patients had a follow-up colonoscopy. Still, these are reasonable numbers of patients as a base to draw conclusions.

Conclusions

Appendix orifice polyps can be safely managed endoscopically using cold/hot biopsy forceps, cold/hot snares, and saline lift injection techniques without the need for special expertise in the form of ESD. Further studies regarding the efficacy of ESD in the management of large appendix orifice polyps are needed.

Author's contribution Both authors contributed by:

- Substantial contributions to the conception or design of the work; or the acquisition, analysis, or interpretation of data for the work;
- Drafting the work or revising it critically for important intellectual content;
- Final approval of the version to be published;
- Agreement to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

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