

# Colorectal endoscopic mucosal resection outcomes in octogenarians versus younger patients referred for removal of large ( $\geq 20$ mm) nonpedunculated polyps

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## Abstract

### Background and Aims

There are limited data on safety and outcomes of colorectal endoscopic mucosal resection (EMR) in octogenarians ( $\geq 80$  years old). We sought to review outcome data for patients aged 80 and over in a prospectively collected database of patients referred for large polyp removal.

### Methods

We retrospectively evaluated a database of patients referred for large ( $\geq 20$  mm) nonpedunculated polyp removal. For years 2000 to 2019, we compared the rates of follow-up, recurrence, adverse events, and synchronous neoplasia detection between younger patients and patients aged 80 and over.

### Results

There were 167 patients  $\geq 80$  years old and 1686  $< 80$  years. Patients in the elderly group returned for surveillance less often (67.1% vs 75.1%,  $p=0.024$ ), had greater first follow-up recurrence rates (27.5% vs 13.8%,  $p<0.001$ ) but had similar adverse event rates (1.8% vs 2.8%,  $p=0.619$ ) compared with younger patients. Rates of synchronous neoplasia were similar and high in both groups.

### Conclusion

EMR is safe and well tolerated for large polyp removal in patients over 80 years old. Patients  $\geq 80$  years of age are less likely to present for follow-up after EMR. They had a higher recurrence rate and a similarly high prevalence of synchronous precancerous lesions. Follow-up after EMR should be encouraged in the elderly, and an attempt to clear the colon of synchronous disease at the time of the initial EMR may be warranted.

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## **Introduction**

Endoscopic mucosal resection (EMR) is the first-line treatment for large sessile and flat colorectal lesions<sup>1-6</sup>. The prevalence of colorectal adenomas increases with age<sup>7</sup>, and colorectal cancer incidence increases sharply with age<sup>8</sup>. Advanced colorectal adenomas transform into cancer faster in the elderly than in younger persons<sup>9, 10</sup>, probably because they have accumulated more mutations. Patients  $\geq 80$  years of age are often found to harbor large nonpedunculated colorectal lesions, which are candidates for EMR. In our anecdotal experience, endoscopists may be fearful of adverse events in elderly patients, which might be poorly tolerated in the elderly. Our anecdotal experience is that some referring physicians only refer patients to our center for EMR who are elderly or who have serious comorbidities. This may reflect either unwillingness to perform colonoscopy and EMR in elderly patients, or perhaps referral of younger patients with large sessile and flat lesions for surgical resection<sup>11</sup>. Currently, EMR is the first-line treatment for large sessile or flat lesions in the colorectum in patients of any age<sup>12</sup>.

There are limited data on the safety and outcomes of colorectal EMR in elderly patients<sup>13-17</sup>.

Gomez et al<sup>13</sup> reported the success and safety of colon EMR on 131 lesions  $\geq 2$  cm in size in 99

elderly patients but there was no control group under the age of 80. They noted many patients did not follow up for various reasons (eg, not being medically fit, death, or unknown reasons). Xie et al<sup>14</sup> investigated the short-term outcomes of EMR in 63 lesions  $\geq 2$  cm in 46 patients  $\geq 80$  years old compared with patients  $< 80$  years old. Adverse event rates were similar in the 2 groups, but follow-up rates were not reported.

We sought to evaluate the outcomes of EMR in older patients, with regard to efficacy (recurrence rates), adverse event rates, and follow-up surveillance rates. We also report synchronous neoplasia burden in older patients compared with patients  $< 80$  years old matched for gender and year of large polyp resection.

## **Methods**

We retrospectively evaluated a database of patients referred for removal of large flat or sessile polyps. The database has been described elsewhere<sup>18</sup>. The database was collected prospectively and contains patient demographic information, polyp specific information, removal methods, adverse events and pathology. For the current study we included all patients in the database who had a nonpedunculated polyp  $\geq 20$  mm in size which was completely removed by snare resection (with ablation of residual flat or fibrotic lesion that resisted snaring in 2014 and prior and avulsion of flat lesion in 2015 and after) at index examination and did not have a submucosal invasion as indicated by pathology report. Ablation of flat or fibrotic residual polyp that resisted snaring was treated by argon plasma coagulation (APC) before 2015 and by avulsion using electrocautery (“hot avulsion”) from January 2015. The database also records information on up

to 4 follow-up examinations after polyp removal. During the follow-up examination, the endoscopist records any visible recurrence at the site of polypectomy, removes any residual lesion, and performs biopsies on those portions of the scar that are normal or have clip artifact. Any visible polyp tissue on the scar was deemed residual polyp, regardless of whether it was verified by pathology (electrocautery used to remove the recurrence sometimes destroys the recurrence). If the endoscopist did not see a recurrence but a biopsy from the scar revealed neoplastic tissue (adenoma or sessile serrated lesion), we counted that as recurrence as well. Adverse events included delayed bleeding (defined as hospitalization or requiring transfusion or repeat colonoscopy for managing bleeding symptoms after departing the endoscopy unit), and perforation. A return examination was defined as a colonoscopy examination at our center for examining the polypectomy site and clearing the remaining colon.

#### Synchronous neoplasia

For the purpose of calculating synchronous neoplasia burden, we included all neoplasia removed at the index colonoscopy (when EMR was performed) or at any follow-up examination within 1 year of the index colonoscopy at our center. Among the 112 elderly patients with a follow-up examination, we identified 97 with a follow-up colonoscopy within a year of the index examination. We matched by gender, index polyp histology, and year of examination, 97 patients from the group of people less than 80 years old who also had a follow-up colonoscopy within a year of the index colonoscopy to compare synchronous neoplasia. The number of synchronous lesions, therefore, reflects these selected 194 patients. We report number of patients with additional adenomas (ADR, adenoma detection rate; number of patients with  $\geq 1$  synchronous conventional adenoma divided by total number of patients), with additional advanced adenomas

(AADR, advanced adenoma detection rate; number of patients with  $\geq 1$  synchronous conventional advanced adenoma divided by total number of patients), and with additional sessile serrated lesions (SSLDR, sessile serrated lesion detection rate; number of patients with  $\geq 1$  synchronous sessile serrated lesion divided by total number of patients). We defined advanced adenomas as adenomas measuring 10 mm or larger or having high-grade dysplasia or villous elements.

### Statistical analysis

The chi-squared test was used to compare return rate for follow-up, the recurrence rate at follow-up, rate of adverse events and rate of synchronous lesions for patients  $\geq 80$  years compared with patients  $< 80$  years of age. For comparing time to first follow-up and size of polyps among both groups we used the nonparametric Mann-Whitney test. We used the chi-squared test and Student t-test, respectively, to compare polyp detection rates and polyps per colonoscopy among the groups for synchronous neoplasia. We report 95% confidence intervals (CIs) for polyp detection rates. All analyses were performed using SPSS, Version 26 (IBM, NY, USA).

### Results

During the study interval, 1852 patients underwent EMR of 2191 colorectal polyps. A total of 1989 colonoscopies were performed for initial removal of large ( $\geq 20$  mm) lesions (some patients had more than 1 lesion removed in a single colonoscopy and others had more than 1 lesion removed over multiple colonoscopies, with 184 colonoscopies in patients aged 80 years and over (Group A) and 1805 colonoscopies in patients under 80 years (Group B) . The average age of

Group A patients was 83.3 years (SD = 2.7) and Group B was 63.8 years (SD = 9.1) ( $p < 0.001$ ). Women comprised 55% of Group A and 48% of Group B ( $p = 0.115$ ) (Table 1). Adverse events were similar in the 2 groups (1.8% in Group A vs 2.8% in Group B,  $p = 0.480$ ) (Table 1). There were 6 perforations in the younger group and none in the elderly. The majority of polyps removed in both groups were in the right colon segment (58% in Group A vs 61% in Group B,  $p = 0.170$ ) (Table 1). The percentage of patients who had a follow-up colonoscopy at our center was 67.1% in Group A and 75.1% in Group B ( $p = 0.024$ ).

Among polyps with at least 1 follow-up examination, there was no difference between the groups for polyp size (mean size 29.7 mm and 29.9 mm in Group A and Group B,  $p = 0.816$ ). The prevalence of high-grade dysplasia (HGD) in the baseline lesions was 12.4% in the elderly and 11.7% in the younger patients. The median time to first follow-up was similar between the groups (6.05 vs 6.07 months,  $p = 0.159$ ). Residual polyp was present at first follow-up (in those presenting to our center) in 27.5% of resected polyps in Group A versus 13.8% in Group B ( $p < 0.001$ ) (Table 2).

Before 2015, lesions with flat or fibrotic polyp that resisted snaring were treated by ablation with APC. Early in the experience, APC was used to treat all or part of the normal edge of the EMR defect in some lesions. Among 906 lesions treated through December 2014, there were no significant differences between the elderly and younger patients in use of APC, but APC use to treat flat residual polyp was numerically less likely in elderly patients (29% vs 33%) and APC use to treat all or part of the normal appearing rim of the EMR defect was numerically more likely in elderly patients (39% vs 28%).

Synchronous additional neoplasia burden in the elderly and the matched controls is shown in Table 3. Both groups had a high prevalence of synchronous or additional adenomas and sessile serrated lesions, and the rates were similar between the groups (Table 3).

### **Discussion:**

In this report, we demonstrate that EMR in patients  $\geq 80$  years is associated with a higher recurrence rate but a similar rate of adverse events compared with EMR in patients  $< 80$  years, and elderly patients were less likely to return to our center for follow-up. The exact reasons for being less likely to return for follow-up are unclear, but could include factors such as more comorbidities, poor tolerance of prep, more difficulty arranging transportation from substantial distances, or a difference in patient attitude toward follow-up. Some patients, particularly those traveling significant distances to our center, could have undergone follow-up by their referring colonoscopist. However, given the size of the study, we expect the differences in follow-up rates are real. Xie et al<sup>14</sup> also noted that substantial numbers of elderly patients did not undergo follow-up after EMR. Hence, our data suggest that special measures should be considered to help ensure that elderly patients undergo follow-up after EMR. Recent breakthroughs in EMR technique,<sup>19-22</sup> such as application of snare tip soft coagulation thermal injury to the margin of the EMR defect, should result in lower recurrence rates and reduce the implications of lower follow-up rates after EMR in elderly patients. Rates of synchronous disease were similar to younger patients with large sessile or flat colorectal lesions and high in both groups (18). Because of lower rates of follow-up attendance and the high rate of synchronous disease, there is a rationale for clearing the colon of synchronous disease at the index examination in the elderly

whenever feasible, although this rationale is arguably in play for all patients with large nonpedunculated lesions.

The higher recurrence rate at first follow-up in the elderly was not expected, although we did identify a prior study that reported age >70 years was an independent predictor of recurrence<sup>23</sup>. When we adjusted for histologic type (looking at adenomas only) and eliminating a small group of elderly patients whose lesions were removed without electrocautery (data not shown), the difference in recurrence and magnitude of difference persisted. The reasons for this result are currently not clear. Previous reports found that HGD in the baseline lesion was a predictor of recurrence<sup>3,24</sup>. However, HGD prevalence was similar at baseline in the 2 groups in this study. Certain factors such as intraprocedural bleeding<sup>25</sup> and attempts at resection (with resultant fibrosis)<sup>3</sup> that might affect the risk of recurrence were not recorded in the database for much of the study interval. Thus, we are uncertain whether there were differences in these factors in the elderly. It is possible that we applied resection techniques less aggressively in the elderly, with the goal of reducing the adverse events, and because of fear of adverse events in the elderly. For example, until 2015, our usual practice was to ablate flat residual polyp with the argon plasma coagulator (APC). Since then, we have used hot avulsion rather than ablation<sup>26</sup> because avulsion was shown in uncontrolled studies to be more effective than ablation of residual tissue<sup>27,28</sup>. Anecdotally, the senior author's impression is that APC ablation is generally associated with less risk of delayed hemorrhage compared with resection. Thus, any subconscious tendency to switch from snaring to ablation earlier during EMR (to reduce the risk of adverse events) in the elderly could increase the recurrence rate. However, we did not identify increased use of APC to treat residual polyp in the elderly before 2015. Thus, although we have no actual evidence to support



the suggestion that any technique we used for EMR differed in the elderly, a subconscious bias with regard to technique could potentially have contributed to the differences in residual polyp rates. Because our study is a retrospective assessment of a database, it is possible that other unseen factors account for the recurrence difference. It also seems possible, given that evidence indicates that advanced adenomas become cancer faster in the elderly<sup>9, 10</sup>, that some biologic differences in polyps in the elderly drive a higher recurrence rate, just as HGD is associated with a higher recurrence rate<sup>3, 24</sup>. Finally, as noted above, a previous study found that age >70 years was an independent predictor of recurrence<sup>23</sup>. Thus, our finding of a higher recurrence rate in the elderly is not novel. Additional study and prospective evaluation of recurrence rates after EMR in the elderly are warranted.

Limitations of our study include its retrospective nature. However, the database was accumulated prospectively. All of the EMRs were performed by a single endoscopic expert, which could limit the generalizability of the results. However, the large size of the study and the inclusion of control group for the prevalence of synchronous lesions are strengths of the study, and we expect that the results with regard to follow-up rates and synchronous disease are likely to be generalizable.

Currently, EMR is the treatment of choice for large benign flat and sessile colorectal lesions. These results suggest that in patients age  $\geq 80$  years, where mortality from surgical resection is about 3% in the United States<sup>29</sup>, EMR is safe and well tolerated. Because of higher recurrence rates, lower follow-up rates, and higher rates of synchronous neoplasia, special measures are appropriate to encourage follow-up in patients age  $\geq 80$  years undergoing EMR. When feasible,

patients undergoing EMR at referral centers should have their colons cleared of synchronous disease at the index examination, particularly if they are elderly.

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Table 1. Patient and polyp characteristics among patients undergoing EMR

	≥80 years, n=167*	<80 years, N=1686	<i>P</i> value
Women, n (%)	91 (54.5)	811 (48.1)	.115
Mean age, years (SD)	83.3 (2.7)	63.8 (9.1)	<.001
No. of examinations, no. of polyps	184, 210	1805, 1981	
Location of the polyps, n (%)			.170
Left colon segment	32 (15.2)	343 (17.3)	
Transverse colon (includes hepatic and splenic flexures)	57 (27.1)	427 (21.6)	
Right colon segment	121 (57.6)	1211 (61.1)	
Pathology of polyps, n (%)			.015
Adenomatous	171 (81.4)	1471 (74.3)	
Sessile serrated polyp	27 (12.9)	420 (21.2)	
Hyperplastic	12 (5.7)	90 (4.5)	
Adverse events, n (%)	3 (1.8)	48 (2.8)	.619 <sup>†</sup>
Bleeding	3	42	
Perforation	0	6	
Patients with at least one follow-up examination, n (%)	112 (67.1)	1266 (75.1)	.024

EMR, Endoscopic mucosal resection; SD, standard deviation.

\* One patient is included in both groups as they had a large polyp removed when they were under and over 80 years old.

<sup>†</sup>Fisher exact test.

Table 2. Characteristics of polyps with a follow-up examination

	Polyps among persons $\geq$ 80 years old	Polyps among persons <80 years old	<i>P</i> value
N	142	1486	
Median time to first follow-up examination, months (minimum-maximum)	6.05 (2-59)	6.07 (0.8-178)	.159*
Mean size, mm (SD)	29.7 (10.1)	29.9 (11.3)	.716*
Residual polyp present at first follow-up examination, n (%)	39 (27.5)	205 (13.8)	< 0.001

SD, Standard deviation.

\*Mann-Whitney U-test

Table 3. Synchronous lesions in patients  $\geq$  and under 80 years

	Patients $\geq$ 80 years, n=97	Patients less than 80 years, n=97*	P value
ADR, n (% , 95% CI)	83 (85.6, 77.6-91.5)	78 (80.4, 71.7-87.4)	.339
APC, $\mu$ (SD)	5.02 (5.88)	4.58 (6.71)	.625
AADR, n (% , 95% CI)	46 (47.4, 37.7-57.3)	35 (36.1, 27.0-45.9)	.109
AAPC, $\mu$ (SD)	1.12 (2.04)	0.88 (1.87)	.380
SSLDR, n (% , 95% CI)	11 (11.3, 6.2- 18.8)	11 (11.3, 6.2-18.8)	1.000
SSLPC, $\mu$ (SD)	0.22 (0.74)	0.37 (1.19)	.279

AADR, Advanced adenoma detection rate; AAPC, advanced adenomas per colonoscopy; ADR, Adenoma detection rate; APC, adenomas per colonoscopy; CI, confidence interval; SD, standard deviation; SSLDR, sessile serrated lesions detection rate; SSLPC, sessile serrated lesions per colonoscopy.

\*Matched with patients  $\geq$ 80 years group for gender, index polyp histology, and year of examination.

Colorectal endoscopic mucosal resection outcomes in octogenarians versus younger patients referred for removal of large ( $\geq 20$  mm) nonpedunculated polyps

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