

## Colonoscopic polypectomy in anticoagulated patients

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### Abstract

**AIM:** To review our experience performing polypectomy in anticoagulated patients without interruption of anticoagulation.

**METHODS:** Retrospective chart review at the Veterans Affairs Palo Alto Health Care System. Two hundred and twenty five polypectomies were performed in 123 patients. Patients followed a standardized protocol that included stopping warfarin for 36 h to avoid suprathreshold anticoagulation from the bowel preparation. Patients with lesions larger than 1 cm were generally rescheduled for polypectomy off warfarin. Endoscopic clips were routinely applied prophylactically.

**RESULTS:** One patient (0.8%, 95% CI: 0.1%-4.5%) developed major post-polypectomy bleeding that required transfusion. Two others (1.6%, 95% CI: 0.5%-5.7%) had self-limited hematochezia at home and did not seek medical attention. The average polyp size was  $5.1 \pm 2.2$  mm.

**CONCLUSION:** Polypectomy can be performed in therapeutically anticoagulated patients with lesions up to 1 cm in size with an acceptable bleeding rate.

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**Key words:** Colon cancer; Colonic polyps; Colonoscopy; Early detection of cancer; Endoscopy; Hemorrhage; Thrombosis; Warfarin

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### INTRODUCTION

Current guidelines for the management of anticoagulants during colonoscopic polypectomy recommend that clotting parameters should be normalized at the time of the procedure<sup>[1,2]</sup>. These guidelines are based largely on expert opinion: polypectomy is considered to be a high risk procedure, and the risk of temporary discontinuation of anticoagulants was previously considered low<sup>[3-5]</sup>. However, recent data suggest that the risk of thromboembolic events is significant when anticoagulants are discontinued for endoscopic and other procedures: the risk of stroke was 1% in a study of 987 patients with atrial fibrillation undergoing 1137 endoscopic procedures, and the risk of thromboembolic events was 0.7% in a study of 1293 warfarin interruptions in 1024 patients<sup>[6,7]</sup>.

One strategy that may decrease this risk by shortening the period of subtherapeutic anticoagulation, is to use intravenous heparin or subcutaneous low-molecular-weight heparin in the perioperative period, rather than simply holding warfarin for several days before and resuming warfarin after the procedure<sup>[8,9]</sup>. An alternative strategy to decrease the thromboembolic risk is to perform polypectomy on lesions up to 1 cm in size while patients remain anticoagulated. In 2007, we reported a series of 41 polypectomies performed in 21 patients with an average international normalized ratio (INR) of 2.3 (range 1.4-4.9)<sup>[10]</sup>. The patients were maintained on warfarin until 36 h before the procedure; the medication was held for 36 h in order to avoid suprathreshold anticoagulation as a result of dietary restriction during colonoscopy preparation. Endoscopic clipping was performed prophylactically immediately after polypectomy. There were no episodes of post-polypectomy bleeding in that small case series. In this study we report our experience of performing polypectomy in a significantly larger number of patients who were anticoagulated.

## MATERIALS AND METHODS

We reviewed available data from all anticoagulated patients from July 2004 to May 2008 who underwent colonoscopy at the Veterans Affairs Palo Alto Health Care System. Informed consent for the procedure was obtained from all patients, including discussion of the potentially high risk of bleeding due to anticoagulation. Institutional review board approval was obtained for retrospective data analysis. Our clinical protocol, which was followed by all patients, was to continue warfarin until 36 h before the procedure, when a clear liquid diet was initiated in preparation for the procedure. Warfarin was not taken while patients were on a clear liquid diet in order to avoid supratherapeutic anticoagulation during this period of potentially low vitamin K intake. In the first 21 patients, as reported in our original case series, INR was measured on the day of the procedure<sup>[10]</sup>. Subsequently, INR was no longer routinely measured. Colonoscopic polypectomy was generally only performed on polyps up to 1 cm in size (the size was estimated by comparison to a fully opened 1 cm snare), and patients with larger lesions were rescheduled at a later date with cessation of anticoagulation. On five occasions, lesions larger than 10 mm were removed and these patients were also included in the series. Immediately after polypectomy, one or more endoclips were placed prophylactically to close the polypectomy defect. Following the procedure, warfarin anticoagulation was continued on the patient's standard schedule. Follow-up was available on all patients *via* telephone and/or clinic visits.

## RESULTS

Two hundred and twenty five polypectomies were performed in 123 patients (Table 1). The most common indications for colonoscopy were screening, history of polyps, iron-deficiency anemia, hematochezia and occult bleeding. The most common indications for warfarin therapy were atrial fibrillation, history of thromboembolism and mechanical heart valves. Characteristics of resected polyps are described in Table 2. The average diameter of resected polyps was  $5.1 \pm 2.2$  mm, with a range of 2-15 mm. Most of the polyps were removed by cold snare (snare removal without cautery or submucosal saline injection) or by snare with cautery following submucosal saline injection. Seventy percent of the resected polyps were neoplastic, consisting mainly of tubular adenomas. Twenty percent of the resected polyps were non-neoplastic. Ten percent of the specimens were lost.

One patient (0.8%, 95% CI: 0.1%-4.5%) developed major post-polypectomy bleeding. He was a 79-year-old man with atrial fibrillation, dilated cardiomyopathy, emphysema and a history of alcohol abuse who had 6 mm, 8 mm and 12 mm tubular adenomas removed. The smallest polyp was removed by cold snare and the larger two were removed by snare with cautery after saline injection. A subsequent upper endoscopy on the same day as the colonoscopy demonstrated

Table 1 Patient characteristics

| Patient characteristics  | Number or percentage  |
|--------------------------|---|
| Number of patients       | 123   |
| Average age (range)      | 68.4 ± 9 (49-90) yr   |
| Male, female             | 122, 1  |
| Indication for procedure | Screening (48%)<br>History of polyps (24%)<br>Iron def anemia (9%)<br>Hematochezia (7%)<br>Occult-blood positive stool (7%)<br>Other (5%) |
| Indication for warfarin  | Atrial fibrillation (65%)<br>Thromboembolism (16%)<br>Mechanical valve (9%)<br>Other indications (13%)                                    |

Table 2 Polypectomy characteristics

| Polyp characteristics    | Number or percentage   |
|--------------------------|--|
| Number of polyps         | 225  |
| Polyps per patient       | 1.8  |
| Average polyp size (mm)  | 5.1 ± 2.2  |
| Range of polyp size (mm) | 2-15   |
| Polypectomy method       | Cold snare (48%)<br>Snare/cautery after saline injection (30%)<br>Snare/cautery, no saline injection (16%)<br>Cold biopsy (4%)<br>Cold snare after saline injection (1%) |
| Polyp histology          | Neoplastic (70%)<br>Non-neoplastic (20%)<br>Lost specimen (10%)  |

portal hypertensive gastropathy. On post-procedure day 4, he developed hematochezia. He was admitted to a local hospital and received 2 units of packed red blood cells. Repeat colonoscopy was not performed, and the bleeding resolved without further treatment. Two patients (1.6%, 95% CI: 0.5%-5.7%) had self-limited hematochezia at home and did not seek medical attention; these were classified as minor bleeding complications. No thromboembolic events were observed.

## DISCUSSION

Current practice guidelines for the management of anticoagulation during colonoscopy are largely based on expert opinion. According to current guidelines, colonoscopy with or without biopsy can be performed in anticoagulated patients, but polypectomy is considered a high risk procedure for which anticoagulation must be temporarily discontinued in order to achieve normalization of coagulation function at the time of the polypectomy. The risk of withholding warfarin for several days has generally been estimated based on extrapolation from the annual incidence of thromboembolic events in patients with various clinical conditions who do not receive anticoagulants. However, more recent data suggest that actual observed thromboembolic complication rates in patients who have interruption of anticoagulation for endoscopic

procedures are higher than the theoretical predictions; this may be due to a rebound increase in clotting factors in this setting<sup>[6-7,11]</sup>.

Post-polypectomy bleeding is a relatively common complication of colonoscopic polypectomy, with a reported incidence of approximately 0.3%-2% that depends on multiple factors including lesion size<sup>[12,13]</sup>. A multivariate regression analysis suggested that anticoagulation increases this risk<sup>[14]</sup>. Post-polypectomy bleeding is generally divided into two types: immediate bleeding following the polypectomy, and delayed bleeding that can occur up to 2-3 wk following the procedure. Immediate bleeding is familiar to therapeutic endoscopists, as it is particularly common following endoscopic mucosal resection of large lesions<sup>[15]</sup>. In this situation, it is generally treated very effectively by methods such as clip application<sup>[15-17]</sup>. In contrast, delayed bleeding typically occurs when the patient is already at home and is therefore a significant concern when polypectomy is undertaken in patients who require anticoagulation. Even when current guidelines are followed and warfarin is held in anticipation of polypectomy, it is quite possible that the patient will be therapeutically anticoagulated at the time that delayed bleeding occurs several days after the procedure. The major issues with performing polypectomy while patients are anticoagulated are therefore as follows: will there be difficulty in controlling any immediate bleeding, will there be a significantly increased risk of delayed bleeding, and are the bleeding risks outweighed by the risk of thromboembolic events that could occur if anticoagulation was interrupted? This study systematically evaluated the risks associated with performing polypectomy while patients were anticoagulated.

Our study demonstrated that polypectomy of lesions up to approximately 1 cm in size can be performed with relative safety in anticoagulated patients. Because we anticipated some degree of immediate bleeding, our uniform practice was to immediately apply endoscopic clips to the polypectomy sites rather than observing the site and waiting to see if bleeding developed. With this strategy, we did not observe any extraordinary episodes of immediate bleeding that could not be controlled with clip application. There was only 1 episode of major delayed bleeding out of 123 patients and 225 polypectomies, a major bleeding rate of 0.8% (CI: 0.1%-4.5%). There were no thromboembolic events, although follow-up was often performed by telephone and typically did not include a neurological exam. The complication profile observed in this study suggests that the strategy of removing small lesions up to 1 cm in size may compare favorably with the standard practice of discontinuation of warfarin for elective procedures, where two major recent studies found thromboembolic rates of 0.7% and 1%<sup>[6,7]</sup>.

It must be emphasized that in our patients warfarin was withheld for approximately 36 h in order to avoid supratherapeutic anticoagulation due to dietary restriction and possibly other factors relating to bowel

preparation. We previously published our experience with the first 21 patients in our series, in whom INR was routinely measured before the procedure<sup>[10]</sup>. In those patients the average INR at the time of colonoscopy was 2.3. Following this experience, we stopped routine measurement of INR before colonoscopy as this involved significant logistical difficulty. The polypectomy techniques utilized in our series varied, with cold snare, standard snare with cautery and inject & cut mucosectomy comprising the majority of polypectomies. Although our data suggest that all three techniques may be safe, our current preference is to perform cold snare in lesions smaller than 5 mm and to perform submucosal injection for larger lesions in which cautery is used in order to minimize potential injury to the bowel wall. In addition, prophylactic clipping was performed immediately at all polypectomy sites. While there is no data to demonstrate the efficacy of clipping in this circumstance, and a randomized study of clipping in average-risk patients demonstrated no benefit, we felt compelled to perform clipping because of the absence of data in anticoagulated patients<sup>[18]</sup>. The drawbacks of clipping include additional endoscopy time, clip cost, and in our case also the practice of immediate clipping before specimen retrieval may have contributed to a relatively large fraction, 10%, of lost specimens.

Limitations of our study include the retrospective, single center design. It is possible that the bleeding rate could be higher in different patient populations, with alternative polypectomy techniques, and/or with less experience in clip placement. Anecdotally, we have observed that endoscopists in our unit apply significantly less cautery during polypectomy than many of our colleagues and it is possible that this will influence delayed bleeding rates due to cautery ulcers. An additional limitation is the absence of INR measurements on patients after the first 21 in the series. However, there were no changes in our colonoscopy preparation during the study period so we expect that the INR levels in subsequent patients would have been similar.

Our study suggests that a reasonable strategy for screening and surveillance colonoscopy in anticoagulated patients may be to perform the procedure while patients are anticoagulated. Small polyps can be removed with a relatively low risk of bleeding. The proportion of patients with lesions larger than 1 cm is relatively low in most clinical settings, so only a relatively small number of patients would undergo a repeat colonoscopy with normalization of coagulation parameters to resect these larger lesions<sup>[19,20]</sup>. A more refined strategy, which would be ideal, would be to develop a highly predictive algorithm to determine which patients are likely to harbor a lesion larger than 1 cm and proceed directly to colonoscopy with interruption of anticoagulation only in these select patients. This strategy could potentially resolve a dilemma facing endoscopists and patients who follow current American Society for Gastrointestinal Endoscopy guidelines: whether to perform screening/surveillance colonoscopy while patients are anticoagulated and repeat

the procedure off anticoagulation in the large number of patients who have small polyps, or to risk thromboembolic complications by normalizing coagulation parameters even in screening/surveillance colonoscopies where potentially no polyps may be found.

A recent survey of endoscopists in the United Kingdom demonstrated a wide variation in the management of anticoagulants for colonoscopy, with 49% of responding physicians routinely stopping anticoagulants and 37% routinely continuing anticoagulants<sup>[21]</sup>. This wide variation in practice suggests that the management of anticoagulants is a significant clinical dilemma. A prospective randomized trial would be the ideal method to resolve this dilemma, and by demonstrating that polypectomy of small lesions can be performed with relative safety, our series demonstrated that it would be reasonable to prospectively compare a strategy of anticoagulant interruption to one of colonoscopy in anticoagulated patients where small polyps can be removed at the discretion of the endoscopist.

## COMMENTS

### Background

Current guidelines recommend discontinuation of anticoagulation prior to colonoscopic polypectomy. However, small colon polyps are exceedingly common and the risk of significant complications from anticoagulant interruption may outweigh the benefit in these patients.

### Research frontiers

In this study, the authors report their experience with resection of small colon polyps up to 1 cm in diameter without interruption of anticoagulation.

### Innovations and breakthroughs

The authors report that the bleeding risk is very low (0.8%) when small polyps are removed in this setting. This suggests that it is reasonable to perform polypectomy without interruption of anticoagulation.

### Applications

Patients who are on chronic anticoagulation and are undergoing screening colonoscopy can be considered for colonoscopy without interruption of anticoagulation, and if small polyps are found then polypectomy can be considered.

### Terminology

Polyps are growths in the colon that are often precancerous. During colonoscopy, the colon is examined for polyps using an endoscope. Polyps are usually removed using a variety of instruments during colonoscopy. Bleeding is a relatively common complication of polyp removal, so there is widespread concern about performing polyp removal in patients who are taking anticoagulants.

### Peer review

The authors performed a retrospective review that demonstrated that the risk of post-polypectomy bleeding is low in patients with small polyps who are anticoagulated. A comparison to published risk estimates for anticoagulant interruption suggests that it may be favorable to perform polypectomy in this setting rather than interrupting anticoagulation.

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