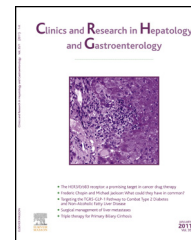




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ORIGINAL ARTICLE

# Management of antithrombotic agents for colonoscopic polypectomies in Israeli gastroenterologists relative to published guidelines

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## Summary

**Background:** Endoscopic procedures are commonly performed in patients taking antithrombotic agents.

**Objective:** To examine the correlation between the management of antithrombotic drugs for colonoscopic polypectomies and the published guidelines.

**Design and settings:** A structured survey delivered to gastroenterologists in 15 major Israeli hospitals and three central HMO clinics.

**Results:** We collected 100 filled out surveys. Polypectomies on aspirin were performed by 78%. Most physicians did not perform polypectomies on clopidogrel. None of the physicians performed polypectomies on warfarin. Cessation of aspirin for  $\geq 3$  days post-polypectomy was recommended by 60%. Renewal of LMWH or warfarin was recommended  $\geq 2$  days post-polypectomy in 91% and 71%, respectively. The greatest variation in recommendations was found for clopidogrel, where the majority of gastroenterologists advised renewal after 1–2 days (38%). Years in practice and increasing colonoscopy volume work had no significant association with management of antithrombotic agents. Working in a HMO clinic was associated with lower rates of polypectomies on aspirin ( $P=0.036$ ).

**Discussion:** When the guidelines are clear, most gastroenterologists practice according to the existing recommendation. However, lack of prospective studies limits the ability to publish evidence-based recommendation and guidelines. We found that the practice of our cohort study varies in these situations.

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**Abbreviations:** LMWH, Low molecular weight heparin; HMO, Health maintenance organization; ASGE, American Society for Gastrointestinal Endoscopy; ESGE, European Society for Gastrointestinal Endoscopy; NSAID, Non-steroidal anti-inflammatory drugs; GI, Gastrointestinal.

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## Introduction

Endoscopic procedures are commonly performed in patients taking antithrombotic agents. The management of antithrombotic therapy in these patients is challenging, since the physician has to weigh the increased risk of gastrointestinal bleeding against the risk of thromboembolism caused by withholding the antithrombotic agent. A survey conducted prior to publication of the American Society for Gastrointestinal Endoscopy (ASGE) guidelines in 1997 found a wide variation regarding the management of aspirin, non-steroidal anti-inflammatory drugs (NSAIDs), and anticoagulants in the periendoscopic period [1]. However, no significant difference in management of anticoagulant agents among gastroenterologists was found after publication of these guidelines [2]. In 2009, the ASGE issued the latest official guidelines on the management of antithrombotic agents for endoscopic process [3]. It is of interest to note that for the main recommendations for the management of antithrombotic agents in elective endoscopies, seven were rated as having low quality evidence and only one as having moderate quality evidence, mainly due to the paucity of randomized controlled trials in

which there was evidence for the superiority of a particular strategy. Table 1 summarizes the current guidelines for the management of antithrombotic drugs during colonoscopic polypectomies.

It is unknown whether Israeli endoscopists manage antithrombotic agents for colonoscopic polypectomies according to the published guidelines. Therefore, we conducted a survey of the management strategies of antithrombotic therapy in elective interventional colonoscopies in Israeli gastroenterologists.

## Methods

Two hundred and twenty fully trained gastroenterologists practice in Israel. Most practice in hospitals and in health maintenance organizations (HMO). A structured survey (Table 2) was sent by mail to gastroenterology departments in all major academic hospitals in Israel ( $n=15$ ) and to three central HMO GI clinics. A representative in each department or clinic was contacted prior to dispatching the survey and was asked to hand the questioners to their colleagues and to send back the filled surveys. The survey was conducted between January 2011 to November 2011. The

**Table 1** Current guidelines for antithrombotic drug management during colonic polypectomies.

Colonic polypectomies	ESGE [4]	ASGE [3]
Aspirin	Aspirin should not be discontinued irrespective of the size of the polyp	Aspirin may be continued for all endoscopic procedures. When high-risk procedures are planned, clinicians may elect to discontinue aspirin for 5 to 7 days before the procedure, depending on the underlying indication for antiplatelet therapy
Thienopyridines	Should be withheld if polyps > 1 cm have to be resected, provided that the patient is not at high risk for thrombotic events When polyps must be resected in patients who cannot discontinue thienopyridines, preventive measures should be readily available In patients with large polyps, biopsy sampling with deferral of polypectomy should be considered	May be continued for low-risk procedures, but should be discontinued for approximately 7 to 10 days before higher-risk procedures. For those patients not taking aspirin, the addition of aspirin during the periendoscopic period may reduce the risk of thromboembolic events
Anticoagulants (warfarin and LMWH)	No guidelines exist	Anticoagulation should be discontinued in patients with a low risk of thromboembolic events in whom it is safe to do so in the periendoscopic period. Anticoagulants should be continued in patients at higher risk of thromboembolic complications
Post-polypectomy reinitiation of antiplatelet therapy	No guidelines exist	Thienopyridines may be reinitiated as soon as deemed safe with consideration of the patient's condition and any therapy performed at the time of endoscopy
Post-polypectomy reinitiation of anticoagulants	No guidelines exist	There is no consensus as to the optimal timing of reinitiation of anticoagulant therapy after endoscopic interventions, and decisions are likely to depend on procedure-specific circumstances as well as the indications for anticoagulation

**Table 2** The survey questionnaire.

1. Do you perform polypectomy if the patient is on aspirin?  
If not- How many days off aspirin do you recommend?  
If you do- Does the size of the polyp matter?  
If it does- What size of polyp is eligible for excision?  
< 10 mm, 10–20 mm, 21–30 mm, > 30 mm  
If you do- Does the morphology of the polyp matter?  
If it does- What morphology is eligible for excision?  
Sessile, pedunculated, all
2. Do you perform polypectomy if the patient is on clopidogrel?  
If not- How many days off clopidogrel do you recommend?  
If you do- Does the size of the polyp matter?  
If it does- What size of polyp is eligible for excision?  
< 10 mm, 10–20 mm, 21–30 mm, > 30 mm  
If you do- Does the morphology of the polyp matter?  
If it does- What morphology is eligible for excision?  
Sessile, pedunculated, all
3. Do you perform polypectomy if the patient is on warfarin?  
If not- How many days off warfarin do you recommend?  
If you do- Does the size of the polyp matter?  
If it does- What size of polyp is eligible for excision?  
< 10 mm, 10–20 mm, 21–30 mm, > 30 mm  
If you do- Does the morphology of the polyp matter?  
If it does- What morphology is eligible for excision?  
Sessile, pedunculated, all
4. How many days off aspirin do you recommend after polypectomy?
5. How many days off clopidogrel do you recommend after polypectomy?
6. How many days off low molecular weight heparin do you recommend after polypectomy?
7. How many days off warfarin do you recommend after polypectomy?

study was approved by the local ethics committee. Analysis was conducted using the SPSS for windows program (16.0; SSS Inc., Chicago, IL) with use of the Chi square test or Fisher's exact probability test for dichotomous variables.  $P$  value < 0.05 was reported as significant. Logistic regression models with type of practice, years in practice, and colonoscopy volume per year as independent variables were used to investigate any association between management strategies for antithrombotic therapy and gastroenterologist experience.

## Results

One hundred physicians filled out the survey (45% of the practicing gastroenterologists) in 13 of the 15 academic centers (87%) and in all three HMO GI clinics (100%). Unfortunately, we did not get any completed surveys from two small size centers. All physicians indicated that they were practicing gastroenterologists who perform colonoscopy. All responders had completed fellowship training and were in active practice. Twenty-six percent had been in gastroenterology practice at the time of the survey for 1 to 5 years, 21% for 6 to 10 years, 13% for 10 to 15 years, 18% for 16 to

**Table 3** Polypectomy practices on antithrombotic agents.

Polypectomy on aspirin	
No	22 (22%)
Yes	78 (78%)
Polyp morphology	
All morphology	70 (70%)
Sessile	3 (3%)
Pedunculated	27 (27%)
Polyp size	
< 10 mm	50 (50%)
10–20 mm	36 (36%)
20–30 mm	10 (10%)
> 30 mm	4 (4%)
Polypectomy on clopidogrel	
No	68 (68%)
Yes	32 (32%)
Polyp morphology	
All morphology	8 (50%)
Sessile	0
Pedunculated	8 (50%)
Polyp size	
< 10 mm	14 (63%)
10–20 mm	5 (23%)
20–30 mm	3 (14%)
> 30 mm	0
Polypectomy on warfarin	
No	100 (100%)
Yes	0

20 years and 22% for more than 20 years. Eighty-seven percent of the physicians worked in academic hospitals and 13% in HMO GI clinics. Eighty-six percent of the physicians were performing more than 300 colonoscopies/year and 50% more than 600 colonoscopies/year.

Polypectomies on aspirin were performed by 78% of gastroenterologists, regardless of the morphology of the polyp, but 86% limited their practice to polyps less than 2 cm ( $P < 0.001$ ). Thirty-two percent of the physicians performed polypectomies on clopidogrel. However, most endoscopists excised only polyps smaller than 1 cm. Cessation of clopidogrel for  $\geq 5$  days prior to colonoscopy was advised by 96% ( $P < 0.0001$ ). None of the physicians performed polypectomies on warfarin (Table 3). Cessation of aspirin for  $\geq 3$  days post-polypectomy was recommended by 60% of the physicians ( $P = 0.015$ ). Reinitiating low molecular weight heparin (LMWH) or warfarin was recommended at or even before 2 days post-polypectomy in 90% and 72%, respectively ( $P < 0.0001$  for both). The greatest variation in recommendations was found for clopidogrel, where 38% of the physicians advised renewal of treatment 1–2 days post-polypectomy, 28% after 3–5 days, 21% after more than 5 days and 13% immediately after the procedure (Table 4).

Working in a hospital was associated with higher rates of polypectomies on aspirin ( $P = 0.02$ ). Years in practice and increasing colonoscopy volume work had no significant association with management of antithrombotic agents during and post-polypectomy (Table 5).

**Table 4** Post-polypectomy reinitiation of antithrombotic agents.

	No (Percent)
Aspirin renewal after polypectomy	
Immediate	12
1–2 d	28
3–5 d	33
> 5 d	27
Clopidogrel renewal after polypectomy	
Immediate	13
1–2 d	38
3–5 d	28
> 5 d	21
LMWH renewal after polypectomy	
Immediate	37
1–2 d	53
3–5 d	7
> 5 d	3
Warfarin renewal after polypectomy	
Immediate	44
1–2 d	28
3–5 d	25
> 5 d	3

LMWH: low molecular weight heparin.

**Table 5** Association of practice type, years in practice, and annual colonoscopy volume with antithrombotic therapy strategy.

Predictor	OR	95% CI	P value
Polypectomy on aspirin			
Hospital vs. HMO	5	1.3–19.8	0.02
Years in practice	1.4	0.5–3.8	0.64
Colonoscopy volume	3	0.85–10	0.13
Polypectomy on clopidogrel			
Hospital vs. HMO	1.7	0.3–8.7	0.7
Years in practice	0.84	0.36–2	0.86
Colonoscopy volume	2.7	0.6–1.9	0.3
Polypectomy on warfarin			
Hospital vs. HMO	—	—	1
Years in practice	—	—	1
Colonoscopy volume	—	—	1

OR: Odds ratio; CI: confidence interval.

## Discussion

We found that most gastroenterologists perform polypectomies on aspirin, but not on clopidogrel or anticoagulant therapy. Post-polypectomy cessation of antithrombotic therapy is advised by most gastroenterologists with the greatest variation regarding clopidogrel.

Bleeding is the most common complication of colonoscopic polypectomy, ranging from 0.6% to 6.1% per polyp [5]. The impact of aspirin use on post-polypectomy bleeding was analyzed in case control studies that consisted of a total of 30,000 patients [6–10]. Although the results varied

in many aspects, all studies found that the risk for post-polypectomy bleeding was not increased significantly by concomitant use of aspirin. However, large prospective studies on post-polypectomy bleeding have not been conducted. Therefore, the ASGE guidelines recommend continuation of aspirin for all endoscopic procedures, but also comment that clinicians may elect to discontinue aspirin for 5 to 7 days before high-risk procedures [3], while the European Society of Gastrointestinal Endoscopy (ESGE) guidelines recommend continuation of aspirin irrespective of the size of the polyp [4]. Correspondingly, we found that most of clinicians in Israel remove polyps without discontinuation of aspirin.

The use of clopidogrel has grown considerably in the last decade with concomitant prolongation of the period of therapy [11]. The influence of clopidogrel on post-polypectomy bleeding was reported in three retrospective studies [12–14], with the findings of significantly increased rates of delayed post-polypectomy bleeding up to 14 days post-polypectomy in two studies, and low (<1%) post-polypectomy bleeding in one study which was limited mainly to small polyps (<1 cm). Therefore, the ASGE guidelines recommend discontinuation of clopidogrel for 7–10 days prior to high-risk procedure [3], and the ESGE guidelines advocate discontinuation of clopidogrel before excision of polyps of more than 1 cm [4]. Correspondingly, we found that physicians usually do not perform polypectomies in patients who continue clopidogrel. Furthermore, most clinicians who excised polyps without discontinuation of clopidogrel limited their practice to polyps of less than 1 cm.

Current guidelines recommend that clotting parameters should be normalized at the time of polypectomy [3,15]. These recommendations are based mainly on expert opinion, as prospective studies had not been conducted. Moreover, retrospective studies demonstrate conflicting results. While increased rates of post-polypectomy bleeding were found even if warfarin was stopped 4 days before procedure [10,16], other studies demonstrated low rates of post-polypectomy bleeding after discontinuation of warfarin for 4 days [17] and even after excision of polyps of more than 1 cm during active treatment with warfarin [18]. None of the practicing gastroenterologists in our study perform polypectomies during anticoagulation treatment, regardless of polyp size or morphology.

There is no consensus as to the timing for reinitiation of antithrombotic therapy after polypectomy. Although it remains to be proven, withholding aspirin for 3 to 5 days may reduce the likelihood of early rebleeding after initial hemostasis, whereas the residual antiplatelet effects might continue to provide cardiovascular protection. However, although discontinuation of aspirin after achieving homeostasis reduced recurrent bleeding, it was associated with higher mortality rates due to thromboembolic events [19]. A recently published study found higher mortality rates among patients with cardiovascular disease who stopped aspirin due to upper gastrointestinal bleeding [20]. We found that most gastroenterologists recommend aspirin discontinuation for more than 3 days post-polypectomy, most probably in order to avoid post-polypectomy bleeding. The greatest diversity in practice was found in the recommendations for resumption of clopidogrel after polypectomy. There is no data regarding the appropriate time to resume clopidogrel,

but it may be appropriate to restart the drug the day after the procedure because of the slow onset of its action [3,15].

There is no consensus as to the optimal timing of reinitiation of anticoagulant agents after polypectomies. The risk of thromboembolism was found to be low when warfarin was stopped up to 15 days [21,22], while post-polypectomy bleeding rates were found to be higher even if INR levels were found to be in sub-therapeutic levels, regardless of the time of the reinitiation of warfarin [15,16]. We found that our study cohort tended to restart warfarin early, usually up to 2 days post-polypectomy.

Our study has few limitations. The main limitation of the study is the possibility of a recall bias, which is typical for survey type studies.

Another limitation is the lack of information regarding the prevalence of post-polypectomy bleeding. However, previous large case control studies did not find a significant increase of post-polypectomy bleeding with concomitant use of aspirin [6–10]. Although clopidogrel was not stopped prior to polypectomy in 32% of the endoscopists, the vast majority limited their practice to excision of small polyps of less than 10 mm. As previously mentioned, the reported prevalence of post-polypectomy bleeding after the excision of polyps of less than 10 mm during clopidogrel treatment was very low [14].

In conclusion, our findings demonstrate that when the published guidelines are clear, most gastroenterologists practice according to the existing recommendation. However, lack of prospective studies limits the ability to publish evidence-based recommendation and guidelines. We found that the practice of our cohort study varies in these situations. Our findings call for performance of large population prospective studies in order to clear these issues and choose the best available practice for our patients in relation to their condition which has a risk for thromboembolic events.

## Disclosure of interest

The authors declare that they have no conflicts of interest concerning this article.

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