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COMMENTARY

Should Procedures or Patients Be Safe? Bias in Recommendations for Periprocedural Discontinuation of Anticoagulation

Andrew J. Doorey, MD; William S. Weintraub, MD; and J. Sanford Schwartz, MD

From Christiana Care Health Systems, Newark, DE (A.J.D.); MedStar Health System, Washington, DC (W.S.W.); and Perelman School of Medicine at the University of Pennsylvania and Wharton School of Business, Philadelphia, PA (J.S.S.).

Medical decisions require balancing expected benefits and harms of alternative management strategies, weighted according to effect on patient outcomes. In practice, however, clinical decisions frequently appear also to be driven by other factors. This issue is illustrated by clinical guidelines and practice patterns for interruption of chronic oral anticoagulation when patients undergo procedures or operations. Each year, more than 250,000 patients in North America undergo procedures or operations for which prescribed anticoagulation is interrupted.[1] Deciding whether to interrupt anticoagulation requires weighing the risk and resultant consequences of experiencing a thromboembolic event during therapy interruption against those of bleeding from the procedure without anticoagulation interruption.

Clinical practice guidelines exist to assist with these decisions.[2] However, for many procedures, assumptions about the dangers of periprocedural bleeding often lead to a recommendation for anticoagulation interruption, despite limited evidence of the incremental risks of bleeding while continuing anticoagulation therapy.

Colonoscopy is one of the most common reasons for anticoagulation interruption. The American Society for Gastrointestinal Endoscopy (ASGE) 2016 guidelines for anticoagulation interruption are based on the estimated relative risk of experiencing a bleeding or embolic complication.[2] These guidelines classify diagnostic colonoscopy without biopsy as low risk for bleeding and, thus, do not recommend anticoagulation interruption. In contrast, colonoscopy with polypectomy is classified as high risk, and anticoagulation interruption is recommended (5 days for warfarin and a varying interval for the novel oral anticoagulant drugs—dabigatran, rivaroxaban, apixaban, and edoxaban—adjusted for renal function).

Many guidelines seek to balance number needed to treat (NNT) with number needed to harm (NNH). Based on published studies, the ASGE guidelines estimate a 1% absolute risk of an embolic event (primarily stroke) in patients with warfarin interruption for 4 to 7 days.[3,4] This surprisingly high number has been consistently confirmed in other studies.[5,6] Although data are limited, there seems to be an equal thromboembolic risk with temporary interruption of novel oral anticoagulant drugs for procedures.[7] In comparison, the references provided in the ASGE guideline report only an average 0.6% (range, 0%-1.4%; references 61, 101, 103, and 105) rate of significant bleeding (generally defined as requiring transfusion or hospitalization) with polypectomy and uninterrupted anticoagulation (Table).[8-11] Thus, the NNT and NNH seem to favor uninterrupted anticoagulation.

However, such a simple numerical comparison of possible complications with and without anticoagulation interruption is not sufficient to guide clinical decision making. The outcomes of these potential adverse sequelae often are of markedly different magnitude. This is especially important because strokes associated with atrial fibrillation (the most common indication for anticoagulation use) frequently are large, devastating events.[12] Although there is variability, patients also generally express a clear preference to avoid stroke even at the cost of significant bleeding—assessing the outcomes of stroke to be much more severe than those of a significant gastrointestinal bleed.[13] However, the ASGE guidelines implicitly weight procedural bleeding as the greater harm. Thus, despite emphasis on a patient-centric approach to

TABLE. Risks of Periprocedural Bleeding or Major Emboli/Stroke From References in ASGE Guidelines.[a]

Reference, year[b]	Patients (No.)	Anticoagulation indication	Duration of follow-up (d)	INR at procedure	Bleeding risk with uninterrupted anticoagulation (%)	Major embolic/stroke risk with interruption of anticoagulation (%)
Bleeding risk						
Friedland et al,[8] 2006	21	NR	21-56	2.3	0.0	
Howell et al,[9] 2006	71	NR	30	1.5	1.4	
Friedland et al,[10] 2009	123	Afib 65% TE 16% Valve 9% Other 13%	21-56	NA	0.8	
Horiuchi et al,[11] 2014	35	Afib 74% TE 20% Other 6%	14	2.4	0	
Average					0.6	
Stroke risk						
Garcia et al,[3] 2008	1024	Afib 54% TE 14% MV 13%	30	NR		0.7
Blacker et al,[4] 2003	1137	Afib	30	1.3		1.1
Average						0.9

[a]Afib = atrial fibrillation; INR = international normalized ratio; MV = mechanical valve; NA = not applicable; NR = not reported; TE = thromboembolism.
[b]From Acosta et al.[2]

medicine, with patient preferences helping guide decisions when no clearly superior medical approach exists, current guidelines for anticoagulation discontinuation for colonoscopy not only do not consider but actually conflict with patient preferences.

In clinical practice, anticoagulation discontinuation deviates ever further from optimal care. In an effort to avoid the potential of having to reschedule a repeated procedure, many practitioners in our communities discontinue anticoagulation for all colonoscopies because of the possibility of having to perform a polypectomy. Because only approximately one-third of all screening and diagnostic colonoscopy patients undergo a polypectomy, only approximately 0.2% (0.6% ÷ 3) of such colonoscopy patients interrupting anticoagulation therapy potentially benefit via a reduced bleeding risk compared with a 1% chance of experiencing a stroke or other serious thromboembolic event with anticoagulation interruption. We acknowledge that bleeding risks of polypectomy higher than those mentioned previously herein have been reported and likely are related to the anatomical complexity of the polyps. Yet the low bleeding risks noted previously herein, cited in the endoscopy guidelines, show that many polyps, especially most that are smaller than 10 mm, can be safely removed without anticoagulation interruption.[11] This fact is rarely discussed when the risks and benefits of anticoagulation interruption for colonoscopy are considered. Delayed bleeding occurs more often in patients receiving oral anticoagulation after polypectomy even when anticoagulation was interrupted for the procedure.[14] But this bleeding is generally not associated with significant morbidity or mortality, and it typically occurs at a time when anticoagulation would have been resumed regardless of an interruption strategy.

The current ASGE guidelines generally are evidence based and clinically nuanced (eg, including recommendations for heparinoid "bridging" in patients at high thromboembolic risk). However, evidence for bridging is weak, with most studies showing no benefit and often increased periprocedural bleeding risk. And bridging, if it does not decrease periprocedural thromboembolic risk, will likewise offer no benefit regarding the delayed bleeding risk after polypectomy at 7 to 10 days because almost uniformly full oral anticoagulation would have been resumed by

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