



NATIONAL HEMOPHILIA FOUNDATION
for all bleeding disorders

MASAC Document #261

MASAC RECOMMENDATIONS FOR BLEEDING PROPHYLAXIS IN BLEEDING DISORDER PATIENTS UNDERGOING GI ENDOSCOPY

The document was approved by the Medical and Scientific Advisory Council (MASAC) of the National Hemophilia Foundation (NHF) on February 28, 2020, and adopted by the NHF Board of Directors on March 16, 2020.

A. Background:

The need for prophylaxis is expanding in persons with hemophilia (PWH) due to the relatively frequent use of endoscopy in general medical care of patients with gastrointestinal signs and symptoms and the implementation of population-based colorectal cancer screening with surveillance colonoscopies. Furthermore, endoscopic variceal ligation is commonly performed given the increased prevalence of hepatitis C infection acquired from plasma-derived factor concentrates administered in the 1980s. Formal guidance regarding prophylaxis for GI endoscopy is not extensive, and they are not covered in the World Federation of Hemophilia (WFH) guidelines likely due to the paucity of prospective studies. There is previously a MASAC recommendation for liver biopsy (#223), but it does not address endoscopy.

In developing MASAC recommendations, it is first informative to review the baseline risk of bleeding after GI endoscopy in terms of the specific procedure per the American Society of Gastrointestinal endoscopy classification¹:

Low risk procedures

- Diagnostic endoscopy (EGD, colonoscopy, flexible sigmoidoscopy) including mucosal biopsy
- Push enteroscopy and diagnostic balloon-assisted enteroscopy
- Capsule endoscopy
- Endoscopic ultrasound without fine needle aspirate
- Enteral stent deployment
- Argon plasma coagulation
- Barrett's ablation

Higher risk procedures

- Polypectomy
- Biliary or pancreatic sphincterotomy
- Treatment of Varices
- PEG placement
- EUS with fine needle aspirate
- Therapeutic balloon-assisted enteroscopy
- Endoscopic hemostasis
- Tumor ablation
- Cystgastrostomy

- Ampullary resection
- Endoscopic mucosal resection
- Endoscopic submucosal dissection
- Pneumatic or bougie dilation
- Percutaneous endoscopic jejunostomy.

Low risk procedures like gastroscopy or colonoscopy without polypectomy have a bleeding risk between 0 and 0.02%. In general, a number of variables increases the risk of bleeding, independent of an underlying bleeding disorder, including older age, male gender, polypectomy > 7 mm, and colonoscopy performed by a low- volume endoscopist.¹ The continued development of endoscopes and equipment is likely to reduce the bleeding risk further.

Historically, specific prophylactic regimens in bleeding disorder patients have not been validated in controlled clinical trials and management must be individualized with respect to the underlying disorder, the underlying severity, the bleeding phenotype and other relevant clinical factors like concurrent HCV-related chronic liver disease.²

Three studies published in the past 7 years may now inform prophylaxis further.³⁻⁵ Two studies reported a total of 75 patients (majority with moderate to severe hemophilia) undergoing a total of 137 procedures with factor given pre-procedure at the minimum with subsequent doses if biopsy or polypectomy done and tranexamic acid (TxA) given pre-procedure for the most part and continued for 3-5 days if biopsy or polypectomy done. In the Tintillier et al study³ (no antifibrinolytic therapy given), the biopsy bleed rate was 0% but the polypectomy bleed rate was 31% (6/19 with 2/6 inhibitors) all with polyps > 7 mm. In the more recent Tomaszewski et al study⁴, the post-polypectomy bleed rate for hemophilia patients was 10% (CI 95% 0.2-40.0%) (1/10).

A third study⁵ involving 16 EGD procedures (14/16 low risk) did not infuse factor pre-procedure but rather used tranexamic acid 1 g oral 8 hourly started the night prior to the procedure with subsequent management based on type of procedure; if no biopsy TxA was continued for 24 hrs. Only two patients (both in the low risk procedure group) experienced bleeding- grade 1 bleeding in one patient and grade 2 in the other. In just using tranexamic acid alone, there is considerable cost saving, but it carries risk of intraluminal hemorrhage particularly in children.^{6,7}

In summary, infusing to a higher target of 80-100%⁴ and using concurrent tranexamic acid pre-procedure^{4,5} should be incorporated in any recommendations as well as infusing for 7-10 days if a high-risk procedure.

B. Recommendations:

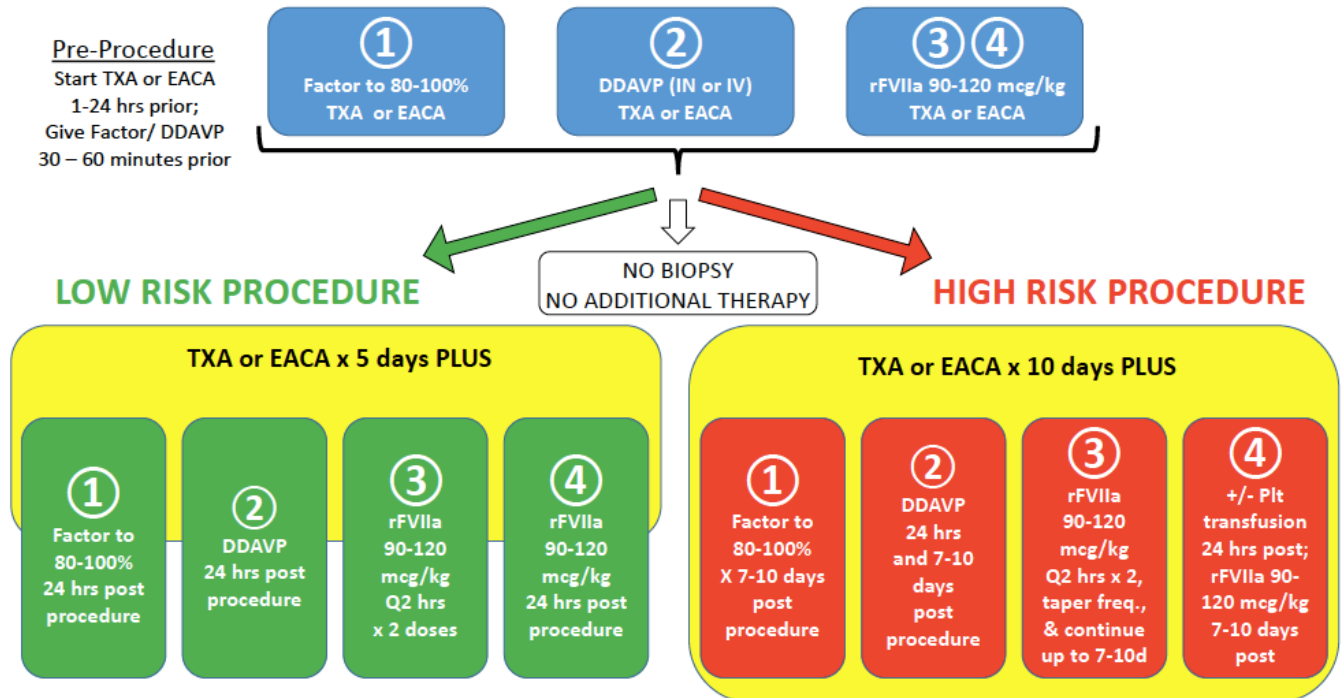
1. For all bleeding disorder patients: Advise pre-treatment with antifibrinolytic therapy*, continue for 5 days if forceps biopsy or polypectomy for polyp < 8 mm, up to 10 days if

larger polyp or endoscopic mucosal resection or endoscopic variceal ligation or ERCP with sphincterotomy or hemorrhoidectomy.

2. For moderate or severe hemophilia or severe VWD on prophylaxis: Advise moving the prophylactic factor dose to the day of the procedure adjusting to goal of 80-100% 1 hr pre-procedure and repeat same dose 24 hrs later if forceps biopsy or polypectomy done; if polyp > 7 mm or endoscopic mucosal resection or ERCP with sphincterotomy continue for up to 7 days and up to 10 days if bleeding,
 - If patient with moderate or severe hemophilia or severe VWD not on factor prophylaxis, infuse dose as above or if feasible, have available in endoscopy suite and infuse during procedure if biopsy/polypectomy done.
3. For the non-inhibitor hemophilia A patient on emicizumab: Advise infusing with FVIII to goal 80-100% pre-procedure and repeat same dose 24 hrs later as above and possibly longer pending type and size of lesion as above.
4. For the inhibitor hemophilia A patient on emicizumab: infuse rVIIa pre-procedure 90 - 120 mcg/kg and repeat the same dose q 2 hrs x 2 doses on the day of procedure and consider weaning dose to every 8-12 hours for several more days pending the type and size of lesion as above.
5. For the known DDAVP responsive Type 1 VWD, low VWF or mild hemophilia patient: administer IN or IV DDAVP 60-90 min pre-procedure and consider repeat dose based on bleeding phenotype and likelihood of adequate fluid restriction 24 hrs later if forceps biopsy or polypectomy; if polyp >7 mm or endoscopic mucosal resection consider repeat dose post-procedure day # 7-9
6. For endoscopic variceal ligation or hemorrhoidectomy: infuse 100% pre-dose and continue to infuse daily x 7 days
7. For mild platelet function disorders: pre-administer IN/IV DDAVP 60-90 min pre- and repeat dose 24 hrs later if forceps biopsy or polypectomy; if polyp >7 mm or endoscopic mucosal resection and consider repeat dose DDAVP post-procedure day # 7-9
8. For severe platelet function disorders (Glanzmann thrombasthenia, Bernard Soulier Syndrome): pre-administer rVIIa 90-120 mcg/kg then q 2 hours x 2 more doses (minimum) and repeat dose 24 hrs later if forceps biopsy or polypectomy; if polyp >7 mm or endoscopic mucosal resection consider platelet transfusion (HLA matched, leuco-reduced) pre-procedure based on bleeding phenotype and consider repeat dose of rVIIa post-procedure day # 7-9

*antifibrinolytic therapy- tranexamic acid 1.3 g po tid or epsilon aminocaproic acid 50-100mg/kg PO q6 hours beginning 1-24 hrs pre-procedure

C. Flowchart summary



Group definitions:

- ① Hemophilia A, Hemophilia B, VWD / low VWF (non-DDAVP responsive)
- ② DDAVP responsive disorders: mild hemophilia A, VWD / low VWF, or mild platelet function disorders (known to be DDAVP responsive)
- ③ Hemophilia A with inhibitor, Hemophilia B with inhibitor
- ④ Severe platelet function disorder (Glanzmann, Bernard-Soulier, etc)

D. References

1. Committee of the American Society of Gastrointestinal Endoscopy-Acosta RD, Abraham NS, et al. The management of antithrombotic agents for patients undergoing GI endoscopy. *Gastrointest Endosc.* (2016);83:3-16.
2. Fogarty PF, Kouides P. How we treat: patients with haemophilia undergoing screening colonoscopy. *Haemophilia* (2010); 16: 363-5.
3. Tintillier V, Branche J, Maunoury V, et al. Colonoscopy in patients with haemophilia: the duration of clotting factor coverage must be adjusted to suit the procedure. *Haemophilia.* (2013);19:e296.e298.
4. Tomaszewski M, Bienz M, Kherad O, et al. Low endoscopy bleeding risk in patients with congenital bleeding disorders. *Haemophilia.* (2019);25:289-295.
5. Davis A, Walsh M, McCarthy P et al. Tranexamic acid without prophylactic factor replacement for prevention of bleeding in hereditary bleeding disorder patients undergoing endoscopy: a pilot study *Haemophilia* (2013), 19, 583-589
6. Shema Hameed S, McHugh K et al. Duodenal haematoma following endoscopy as a marker of coagulopathy. *Pediatr Radiol* (2014), 44:392-397
7. Osman M, Mantor C and O'Connor J. Duodenal and retroperitoneal hematoma after upper gastrointestinal endoscopy: First presentation of a child with Hemophilia B. *J Ped Surg Case Reports* (2014), 2, 421-423