DOACs and Obesity in 2021: Updates from the ISTH SSC Subcommittee on Control of Anticoagulation

Wednesday | September 15, 2021 | 12:00 – 1:00pm ET

Authors & Presenters:

Karlyn Martin, MD | Stephan Moll, MD

Moderators:

Arthur Allen, PharmD, CACP | Deborah Siegal, MD, MSc
Andrea Van Beek, RN, DNP, AGPCNP-BC

Presenters

Karlyn Martin, MD

- Assistant Professor of Medicine, Division of Hematology-Oncology, Northwestern University.

Stephan Moll, MD

- Professor of Medicine, Division of Hematology-Oncology, University of North Carolina

Arthur Allen, PharmD, CACP

- Anticoagulation Program Manager, VA Salt Lake City Health Care System

Deborah Siegal, MD, MSc

- Associate Professor, University of Ottawa
- Associate Scientist, The Ottawa Hospital

Andrea Van Beek, RN, DNP, AGPCNP-BC

- Anticoagulation Clinic Nurse Practitioner, Visalia Medical Clinic/Kaweah Health Medical Group

Astronaut with Blood Clot on Space Station treated by Dr. Stephan Moll

Stephan Moll, MD, visiting NASA facilities in Houston after the agency asked for his help in treating an astronaut with a blood clot.

Disclosures & Notification of Support

The speakers have the following relevant financial relationships with commercial interests:

Karlyn Martin, MD
Janssen | Penumbra

Stephan Moll, MD
Bristol-Myers Squibb

Arthur Allen, PharmD, CACP
Alexion Pharmaceuticals | BMS/Pfizer Alliance | Boehringer-Ingelheim Pharmaceuticals | Janssen Pharmaceuticals
Roche Diagnostics

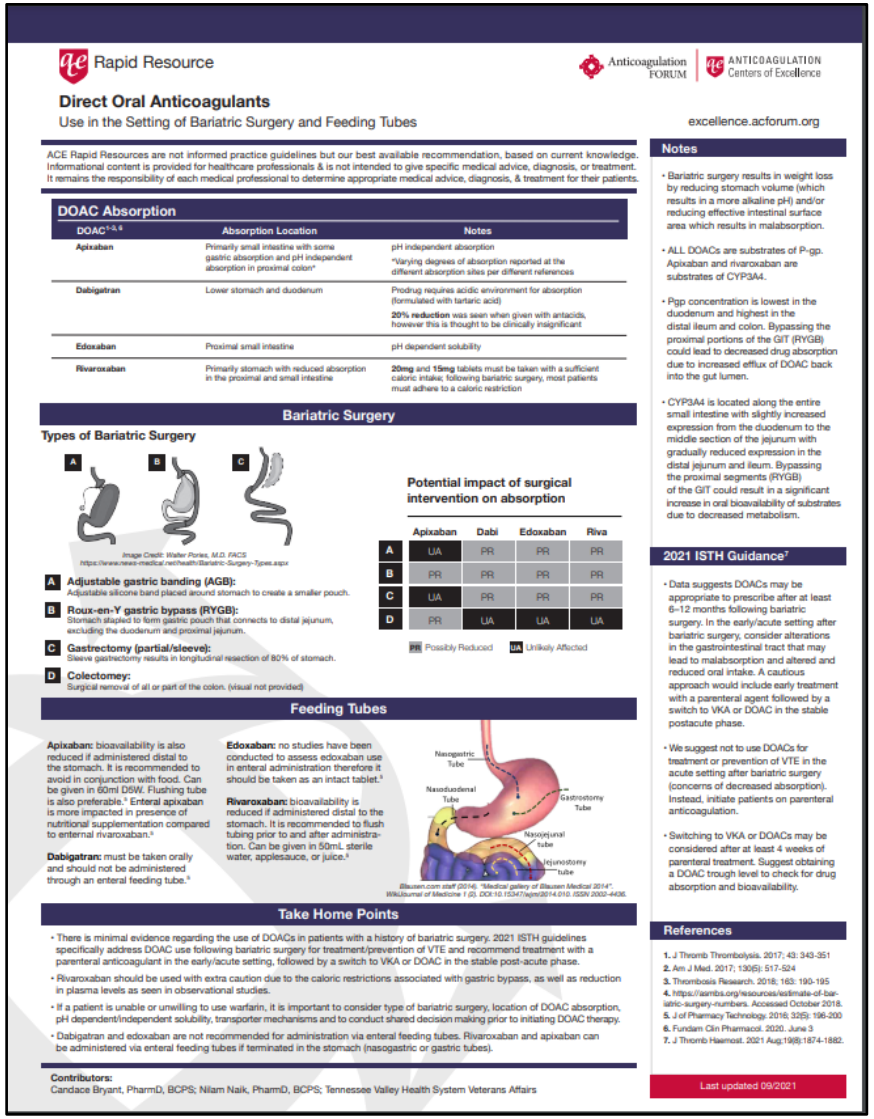
Deborah Siegal, MD, MSc
Aspen Pharma | Bayer | BMS/Pfizer Alliance | LEO Pharma | Novartis | Portola | Servier

Andrea Van Beek, RN, DNP, AGPCNP-BC
None

DOAC Use in the Setting of Bariatric Surgery and Feeding Tubes

AC Forum Rapid Resource

https://acforum-excellence.org/Resource-Center/



Rapid Resource

Anticoagulation FORUM | ANTICOAGULATION Centers of Excellence

Direct Oral Anticoagulants

Use in the Setting of Bariatric Surgery and Feeding Tubes

excellence.acforum.org

ACE Rapid Resources are not informed practice guidelines but our best available recommendation, based on current knowledge. Informational content is provided for healthcare professionals & is not intended to give specific medical advice, diagnosis, or treatment. It remains the responsibility of each medical professional to determine appropriate medical advice, diagnosis, & treatment for their patients.

DOAC Absorption

DOAC[1-3,8]	Absorption Location	Notes
Apixaban	Primarily small intestine with some gastric absorption and pH independent absorption in proximal colon*	pH independent absorption *Varying degrees of absorption reported at the different absorption sites per different references
Dabigatran	Lower stomach and duodenum	Prodrug requires acidic environment for absorption (formulated with tartaric acid) **20% reduction** was seen when given with antacids, however this is thought to be clinically insignificant
Edoxaban	Proximal small intestine	pH dependent solubility
Rivaroxaban	Primarily stomach with reduced absorption in the proximal and small intestine	**20mg** and **15mg** tablets must be taken with a sufficient caloric intake; following bariatric surgery, most patients must adhere to a caloric restriction

Bariatric Surgery

Types of Bariatric Surgery

Image Credit: Walter Portes, M.D. FACS
https://www.news-medical.net/health/Bariatric-Surgery-Types.aspx

A **Adjustable gastric banding (AGB):** Adjustable silicone band placed around stomach to create a smaller pouch.

B **Roux-en-Y gastric bypass (RYGB):** Stomach stapled to form gastric pouch that connects to distal jejunum, excluding the duodenum and proximal jejunum.

C **Gastrectomy (partial/sleeve):** Sleeve gastrectomy results in longitudinal resection of 80% of stomach.

D **Colectomey:** Surgical removal of all or part of the colon. (visual not provided)

Potential impact of surgical intervention on absorption

	Apixaban	Dabi	Edoxaban	Riva
A	UA	PR	PR	PR
B	PR	PR	PR	PR
C	UA	PR	PR	PR
D	PR	UA	UA	UA

PR Possibly Reduced UA Unlikely Affected

Feeding Tubes

Apixaban: bioavailability is also reduced if administered distal to the stomach. It is recommended to avoid in conjunction with food. Can be given in 60ml D5W. Flushing tube is also preferable.[4] Enteral apixaban is more impacted in presence of nutritional supplementation compared to enternal rivaroxaban.[5]

Dabigatran: must be taken orally and should not be administered through an enteral feeding tube.[6]

Edoxaban: no studies have been conducted to assess edoxaban use in enteral administration therefore it should be taken as an intact tablet.[7]

Rivaroxaban: bioavailability is reduced if administered distal to the stomach. It is recommended to flush tubing prior to and after administration. Can be given in 50mL sterile water, applesauce, or juice.[8]

Blausen.com staff (2014). "Medical gallery of Blausen Medical 2014". WikiJournal of Medicine 1 (2). DOI:10.15347/wjm/2014.010. ISSN 2002-4436.

Take Home Points

- There is minimal evidence regarding the use of DOACs in patients with a history of bariatric surgery. 2021 ISTH guidelines specifically address DOAC use following bariatric surgery for treatment/prevention of VTE and recommend treatment with a parenteral anticoagulant in the early/acute setting, followed by a switch to VKA or DOAC in the stable post-acute phase.
- Rivaroxaban should be used with extra caution due to the caloric restrictions associated with gastric bypass, as well as reduction in plasma levels as seen in observational studies.
- If a patient is unable or unwilling to use warfarin, it is important to consider type of bariatric surgery, location of DOAC absorption, pH dependent/independent solubility, transporter mechanisms and to conduct shared decision making prior to initiating DOAC therapy.
- Dabigatran and edoxaban are not recommended for administration via enteral feeding tubes. Rivaroxaban and apixaban can be administered via enteral feeding tubes if terminated in the stomach (nasogastric or gastric tubes).

Contributors:
Candace Bryant, PharmD, BCPS; Nilam Naik, PharmD, BCPS; Tennessee Valley Health System Veterans Affairs

Notes

- Bariatric surgery results in weight loss by reducing stomach volume (which results in a more alkaline pH) and/or reducing effective intestinal surface area which results in malabsorption.
- ALL DOACs are substrates of P-gp. Apixaban and rivaroxaban are substrates of CYP3A4.
- Pgp concentration is lowest in the duodenum and highest in the distal ileum and colon. Bypassing the proximal portions of the GIT (RYGB) could lead to decreased drug absorption due to increased efflux of DOAC back into the gut lumen.
- CYP3A4 is located along the entire small intestine with slightly increased expression from the duodenum to the middle section of the jejunum with gradually reduced expression in the distal jejunum and ileum. Bypassing the proximal segments (RYGB) of the GIT could result in a significant increase in oral bioavailability of substrates due to decreased metabolism.

2021 ISTH Guidance[7]

- Data suggests DOACs may be appropriate to prescribe after at least 6–12 months following bariatric surgery. In the early/acute setting after bariatric surgery, consider alterations in the gastrointestinal tract that may lead to malabsorption and altered and reduced oral intake. A cautious approach would include early treatment with a parenteral agent followed by a switch to VKA or DOAC in the stable postacute phase.
- We suggest not to use DOACs for treatment or prevention of VTE in the acute setting after bariatric surgery (concerns of decreased absorption). Instead, initiate patients on parenteral anticoagulation.
- Switching to VKA or DOACs may be considered after at least 4 weeks of parenteral treatment. Suggest obtaining a DOAC trough level to check for drug absorption and bioavailability.

References

1. J Thromb Thrombolysis. 2017; 43: 343-351
2. Am J Med. 2017; 130(5): 517-524
3. Thrombosis Research. 2018; 163: 190-195
4. https://asmbs.org/resources/estimate-of-bariatric-surgery-numbers. Accessed October 2018.
5. J of Pharmacy Technology. 2016; 32(5): 196-200
6. Fundam Clin Pharmacol. 2020. June 3
7. J Thromb Haemost. 2021 Aug;19(8):1874-1882.

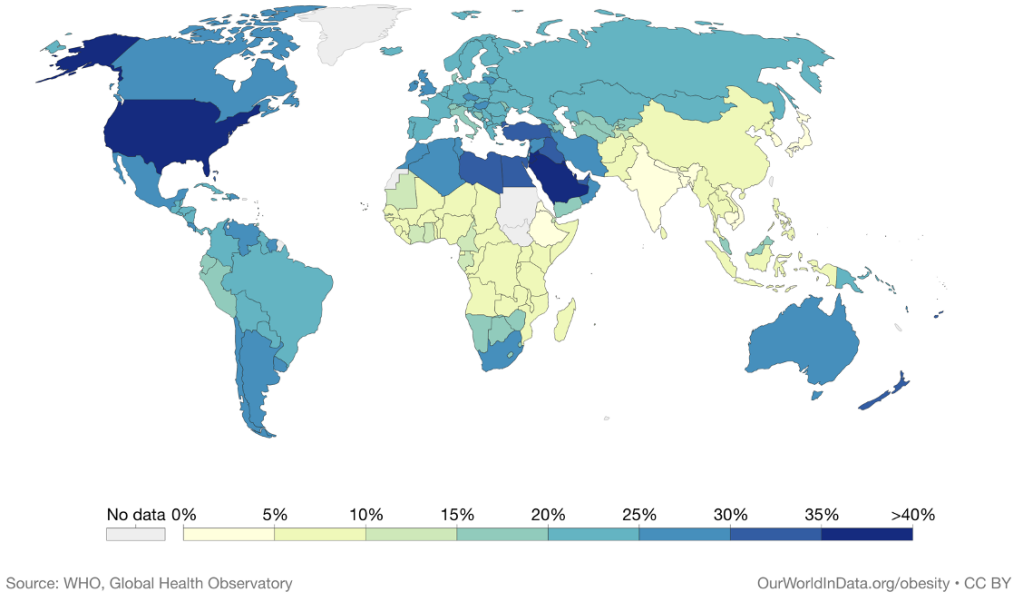
Last updated 09/2021

Anticoagulation FORUM | Webinar

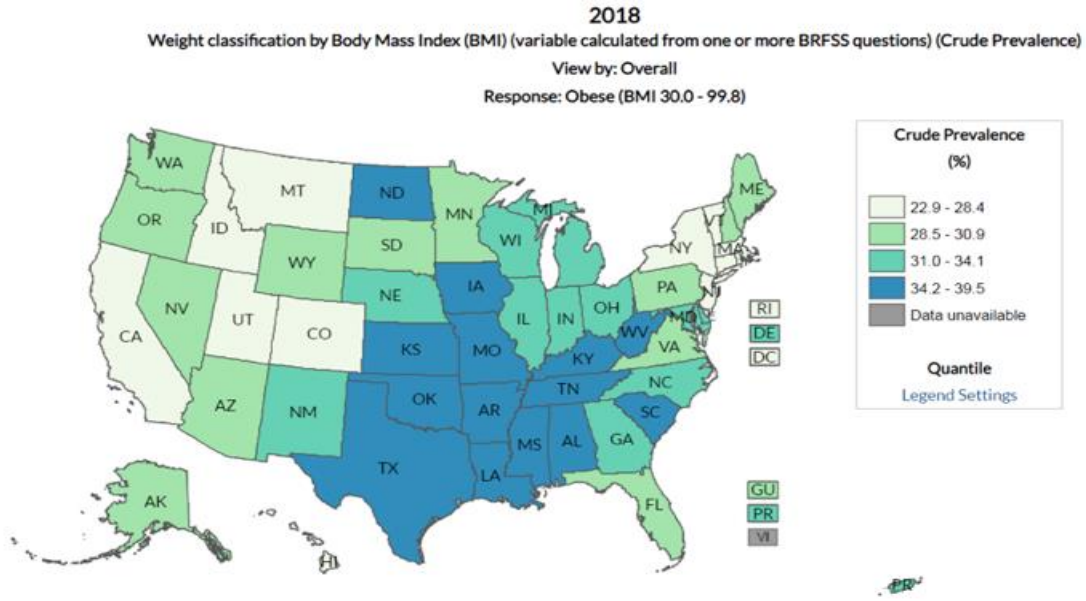
acforum.org

Impact of obesity

- In 2016 worldwide-
  - >1.9 billion overweight adults, of whom 650 million are obese (BMI ≥ 30 kg/m^{2})



- In 2018, US-



WHO Facts Obesity and Overweight
Our World Our Data
CDC BRFSS Prevalence & Trends Data 2018

Journal of Thrombosis and Haemostasis, **14**: 1308–1313 DOI: 10.1111/jth.13323

2016

RECOMMENDATIONS AND GUIDELINES

Use of the direct oral anticoagulants in obese patients: guidance from the SSC of the ISTH

- Recommend appropriate standard dosing of direct oral anticoagulants (DOACs) in patients with BMI ≤ 40 kg/m^2 and weight ≤ 120 kg.
- Suggest not using DOACs in patients with BMI >40 kg/m^2 or weight >120 kg.
- If DOACs are used in BMI >40 kg/m^2 or weight >120 kg, suggest checking drug-specific peak and trough level.

➢ *DOACs= apixaban, dabigatran, edoxaban, rivaroxaban*

➢ *Based on limited clinical data and available PK data at the time*

Summary of Clinical Data

	Phase 3 Studies Comparing DOACs with VKA in VTE		Phase 4 Studies Comparing DOAC with VKA in VTE (Including Retrospective and Prospective Studies and Meta-analyses)	
	BMI >35 or BW >120 kg	BMI >40	BMI >35 or BW >120 kg	BMI >40
Apixaban	X	X	Similar outcomes[6]	Similar outcomes[5,6]
Dabigatran	X	X	X	X
Edoxaban	X	X	X	X
Rivaroxaban	Similar outcomes[7]	X	Similar outcomes[5,8-10]	Similar outcomes[5,9]
Pooled DOAC	Similar outcomes[11]	X	Similar outcomes [12-16]	Similar outcomes[12]

Note: Similar outcome = DOAC compared with LMWH/VKA; X = no available data.

Abbreviations: BMI, body mass index, expressed in kg/m^2; BW, body weight; DOAC, direct oral anticoagulant; LMWH, low molecular weight heparin; VKA, vitamin K antagonist; VTE, venous thromboembolism.

X= no available data

Martin et al *J Thromb Haemst* 2021

Rivaroxaban- post-hoc analysis of EINSTEIN DVT and PE

- Similar outcomes of recurrent VTE and major bleeding in those treated with rivaroxaban compared with VKA, across BMI and body weight
  - Outcomes by BMI:

Recurrent VTE	
Whole study period	Rivaroxaban Enoxaparin/VKA
First 21 days	Rivaroxaban Enoxaparin/VKA
Major bleeding	
Whole study period	Rivaroxaban Enoxaparin/VKA
First 21 days	Rivaroxaban Enoxaparin/VKA

BMI ≥35		P-value for interaction
Incidence n/N (%)	HR (95 %CI)	
13/427 (3.0) 9/434 (2.1)	1.45 (0.62–3.39)	0.60
9/427 (2.1) 4/434 (0.9)	2.22 (0.68–7.26)	0.19
5/426 (1.2) 7/432 (1.6)	0.71 (0.22–2.24)	0.74
3/426 (0.7) 3/432 (0.7)	0.96 (0.19–4.78)	0.45

  - By Weight: ≥120–140 kg- no difference in VTE recurrence (2/119 vs 3/103)

DiNisio *Thromb Haemost.* 2016

Apxiaban- post-hoc analysis of AMPLIFY*

*Not included in ISTH guidance

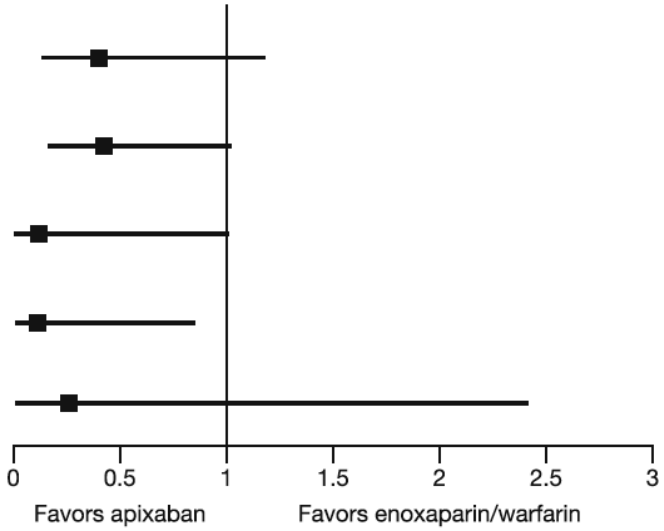
- Similar rates of recurrent VTE/ VTE-related death and lower rates of bleeding for apixaban compared with VKA across body weight and BMI categories

VTE or VTE-related death

BMI category	Apixaban, n/N	Enoxaparin/ warfarin, n/N
⩽ 25 kg/m²	16/693	16/694
> 25 to 30 kg/m²	27/985	26/1014
> 30 to 35 kg/m²	9/568	16/575
> 35 to 40 kg/m²	4/227	6/201
> 40 kg/m²	3/122	6/134

Major bleeding

BMI category	Apixaban, n/N	Enoxaparin/ warfarin, n/N	RR (95% CI)	$P_{interaction}$
⩽ 25 kg/m²	5/725	12/711	0.41 (0.15, 1.18)	0.66
> 25 to 30 kg/m²	7/999	17/1029	0.43 (0.18, 1.02)	
> 30 to 35 kg/m²	1/575	8/587	0.13 (0.02, 1.01)	
> 35 to 40 kg/m²	1/236	8/206	0.12 (0.02, 0.85)	
> 40 kg/m²	1/126	4/137	0.27 (0.03, 2.40)	



Cohen et al *Adv in Therapy* 2021

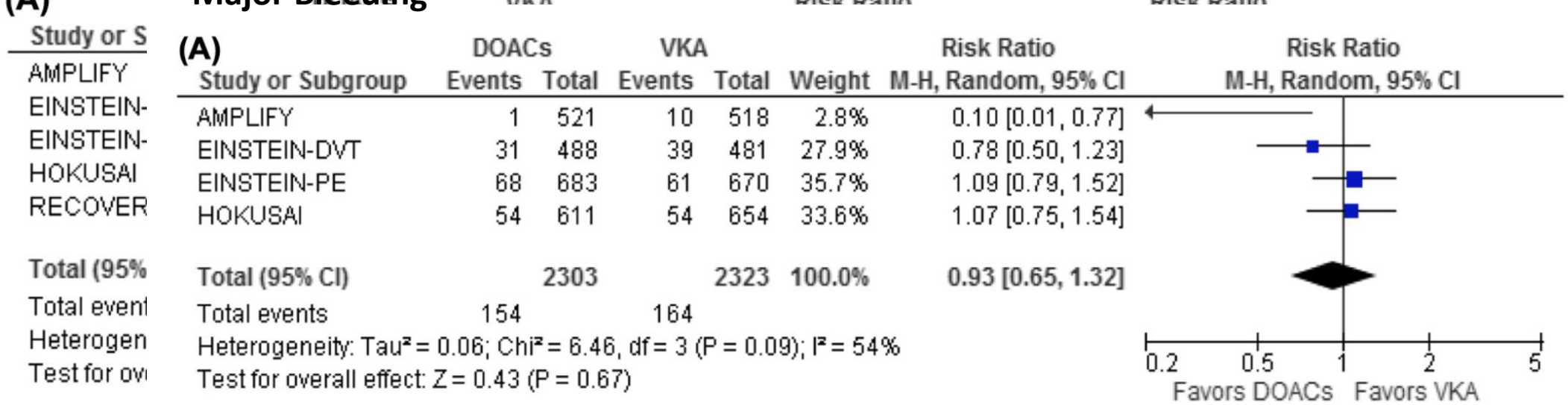
Meta-analysis of VTE RCT shows similar outcomes

Citation	Sample	Context	Conclusions
Di Minno Ann Med 2015	>5,400 patients in high-body weight (HBW)	Meta-analysis of RCT DOAC vs VKA	In HBW (>90-100 kg) subgroup: • VTE and VTE-related death: RR 0.98 (0.72-1.35) • MB + clinically relevant, non-major bleeding: RR 0.9 (0.65-1.32)

VTE: venous thromboembolism; MB: major bleeding

VTE and VTE-related death

Major Bleeding



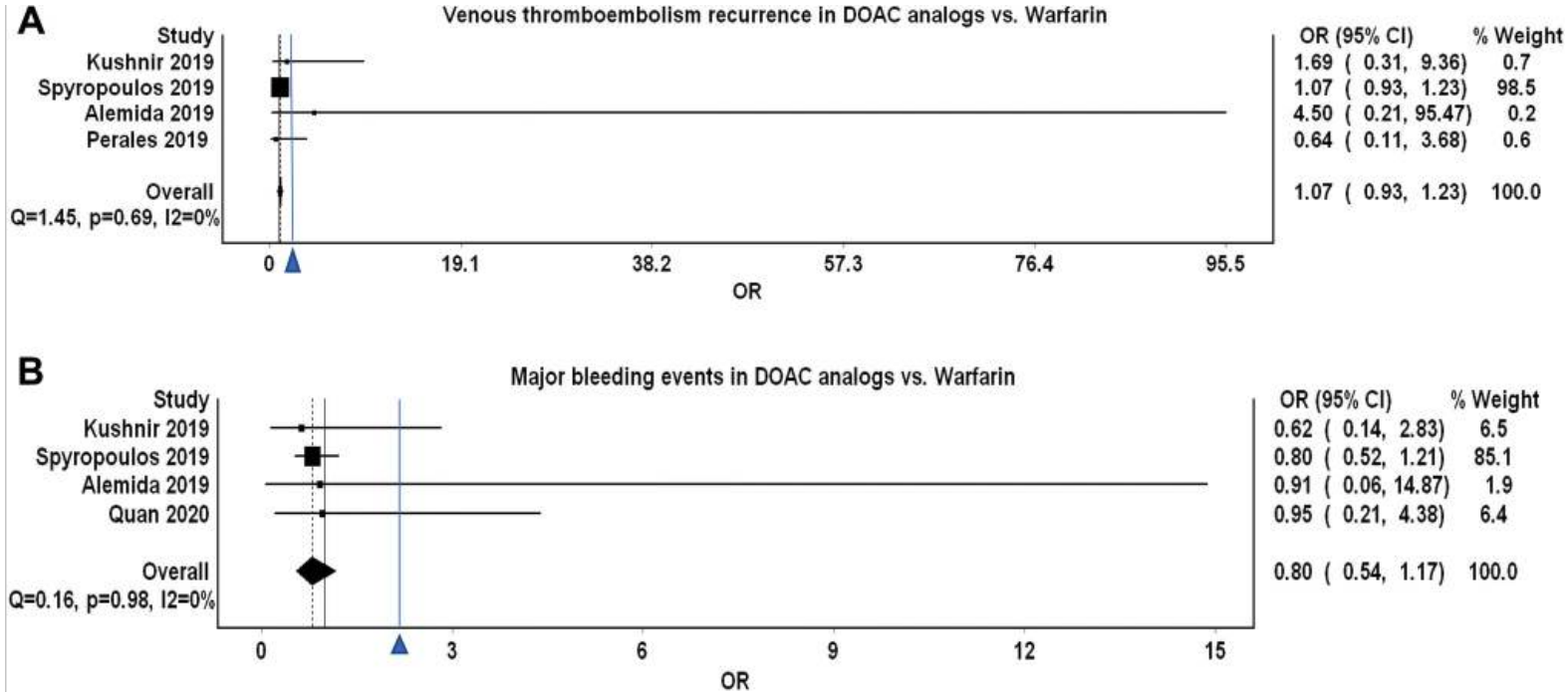
Similar outcomes in observational studies pooling DOAC vs VKA

Citation	Sample	Context	Conclusions
Tittl Int J Cardiol 2018	>1000 patients BMI ≥30 kg/m^2 vs BMI <30	prospective registry	similar rates of stroke/TIA/recurrent VTE (6/285 [2.1%] vs 24/770 [3.1%]) MB: (9/285 [3.2%] vs 24/770 [3.1%]
Wysokinski Eur J Haematol 2020	N= 230 vs 2123 >120 (HBW) vs 60-120 kg	prospective observational; DOACs = rivaroxaban and apixaban	similar rates of VTE in HBW group (4.91 per 100 patient-years [0.1-9.7]) compared with RBW (3.19 per 100 patient-years [1.94-4.44] similar rates of MB
Coons Pharmacotherapy 2020	>1,840 patients weighing 100-300 kg	retrospective matched cohort study conducted at >40 institutions, DOAC vs VKA	similar VTE recurrence at 1 year (6.5% vs 6.4%, p=0.93) and bleeding (1.7% vs 1.2%; p=0.31)
Aloi J Pharm Practice 2019	N= 133 vs ≥ 1,000 ≥120 kg vs <120 kg	retrospective study; DOAC= apixaban, dabigatran, or rivaroxaban	similar VTE recurrence (0.8% vs 1.1%, OR 0.66; 0.09- 5.14)

VTE: venous thromboembolism;
MB: major bleeding

Meta-analysis of observational studies

Citation	Sample	Context	Conclusions
Elshafei J Thromb Thrombolysis 2020	6,500 patients; BMI ≥ 40 kg/m^2 or weight >120 kg	Meta-analysis of 5 observational studies; DOAC (rivaroxaban, apixaban, dabigatran) vs VKA	recurrent VTE: OR 1.07; 0.93–1.23 MB: trend toward reduced risk (OR 0.80; 0.54–1.17)



Summary of Clinical Data

	Phase 3 Studies Comparing DOACs with VKA in VTE		Phase 4 Studies Comparing DOAC with VKA in VTE (Including Retrospective and Prospective Studies and Meta-analyses)	
	BMI >35 or BW >120 kg	BMI >40	BMI >35 or BW >120 kg	BMI >40
Apixaban	X	X	Similar outcomes[6]	Similar outcomes[5,6]
Dabigatran	X	X	X	X
Edoxaban	X	X	X	X
Rivaroxaban	Similar outcomes[7]	X	Similar outcomes[5,8-10]	Similar outcomes[5,9]
Pooled DOAC	Similar outcomes[11]	X	Similar outcomes [12-16]	Similar outcomes[12]

Note: Similar outcome = DOAC compared with LMWH/VKA; X = no available data.

Abbreviations: BMI, body mass index, expressed in kg/m^2; BW, body weight; DOAC, direct oral anticoagulant; LMWH, low molecular weight heparin; VKA, vitamin K antagonist; VTE, venous thromboembolism.

X= no available data

Martin et al *J Thromb Haemst* 2021

Conclusions from clinical data

- When compared individually to VKA, rivaroxaban and apixaban have at least similar efficacy and safety in patients with obesity.
- Studies pooling DOACs show similar rates of efficacy and safety outcomes either compared with VKA or across weight categories.
- No studies limiting analysis to betrixaban, dabigatran or edoxaban individually for treatment of VTE.

Bariatric surgery and DOACs

DOAC	Site of absorption in gastrointestinal tract	Surgical intervention and anticipated effect on absorption		
		Gastric banding	Partial /Sleeve gastrectomy	RYGB
Apixaban	Primarily upper GI tract, with possible limited absorption in the colon; absorption decreased by when delivered to the distal small bowel compared with oral administration[39]	unlikely affected	unlikely affected	possibly reduced
Dabigatran	Lower stomach and proximal small intestine[41,42,49]	possibly reduced	possibly reduced	possibly reduced
Edoxaban	Proximal small intestine, dependent on acidic environment [43,44]	possibly reduced	possibly reduced	possibly reduced
Rivaroxaban	Largely stomach, some small intestine, but absorption reduced when released distal to stomach[43-45]	possibly reduced	possibly reduced	possibly reduced

Martin et al *J Thromb Haemst* 2021

Updated Summary Guidance Statements for use of DOACs for VTE in patients with obesity

1) Consistent with the 2016 ISTH SSC recommendations, we conclude that the use of any DOAC is appropriate for patients with BMI up to 40 kg/m^2 or weight 120 kg. For patients with BMI > 40 kg/m^2 or weight >120 kg, we recommend that the individual DOACs should be used as follows:
2) For treatment of VTE, we suggest that standard doses of rivaroxaban or apixaban are among appropriate anticoagulant options regardless of high BMI and weight. Less supportive data exist for apixaban than rivaroxaban. VKA, weight-based LMWH (per manufacturers' recommendations), and fondaparinux are also options.
3) For primary prevention of VTE, we suggest that standard doses of rivaroxaban or apixaban are among appropriate anticoagulant options regardless of high BMI and weight. Drug approval is restricted to elective hip and knee arthroplasty and (in some countries) extended VTE prevention following acute medical illness.
4) We suggest not to use dabigatran, edoxaban or betrixaban for VTE treatment and prevention in patients with BMI >40 kg/m^2 or weight >120 kg, given unconvincing data for dabigatran, and lack of clinical or PK/PD data for edoxaban and betrixaban.
5) We suggest not to regularly follow peak or trough drug-specific DOAC levels because there are insufficient data to influence management decisions.
6) We suggest not to use DOAC for treatment or prevention of VTE in the acute setting after bariatric surgery (because of concerns of decreased absorption), and instead, to initiate such patients on parenteral anticoagulation in the early postsurgical phase. We suggest that switching to VKA or DOAC may be considered after at least 4 weeks of parenteral treatment, and if so, suggest obtaining a DOAC trough level to check for drug absorption and bioavailability.

Martin et al *J Thromb Haemst* 2021

Questions?

How to Claim Credit

1) Go to: http://acf.cmecertificateonline.com/
2) Select "**DOACs and Obesity in 2021**"
3) Evaluate the program
4) Print certificate for your records

This program is accredited for Physicians, Pharmacists, and Nurses for enduring accreditation for 1.0 hours

Claim Credit:
http://acf.cmecertificateonline.com/

2021 National Conference

October 28-30, 2021

Join Us for a Virtual Experience!

Benefits of meeting:

- **Live Q&A panel after each session – same format as this webinar**
- **All attendees will receive 30-Day extended access to view recordings**
- **30+ Speakers**
- **13.75 hours credit – ACCME, ACPE, ANCC**

REGISTER NOW

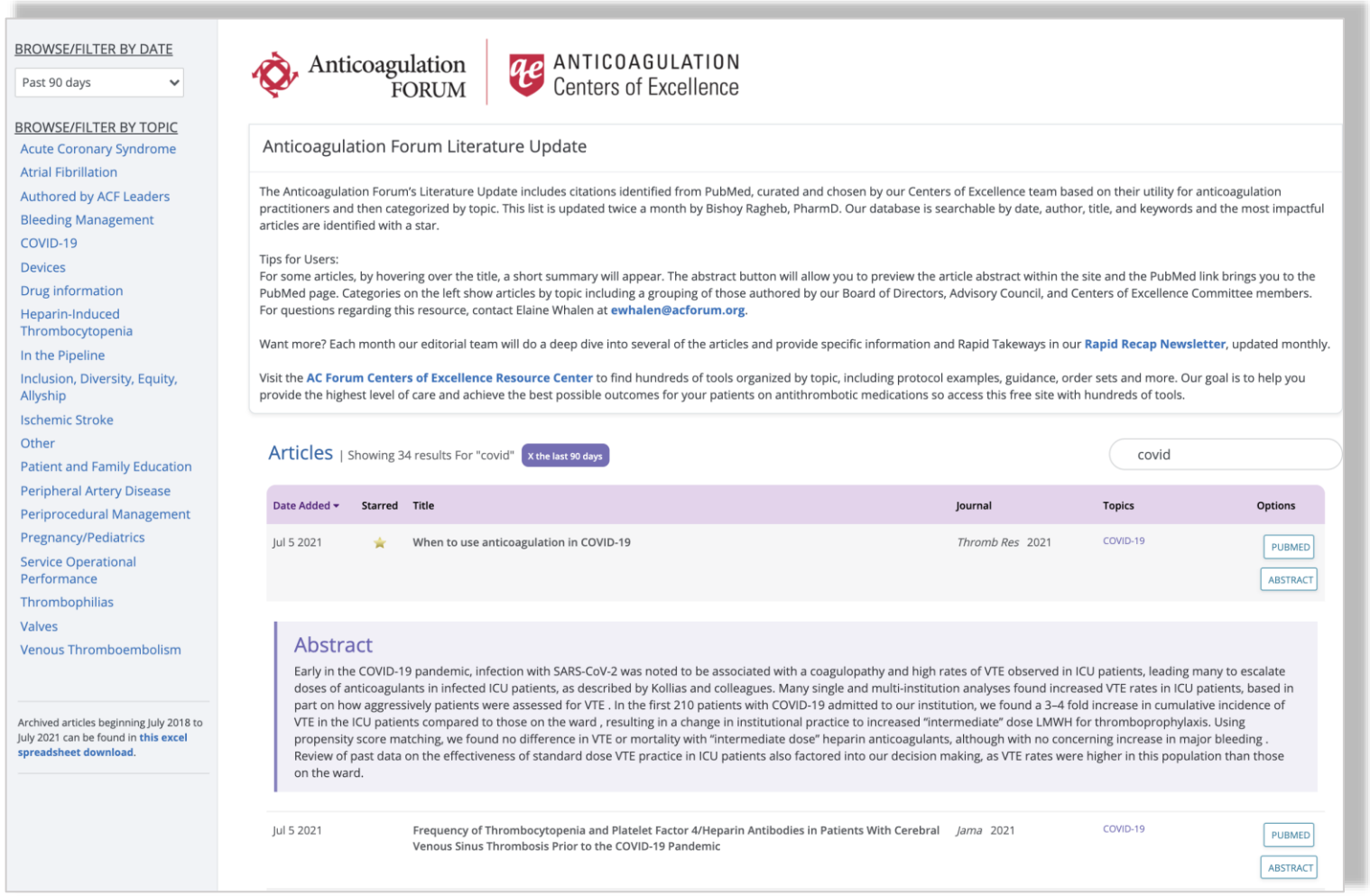
Register today!

Visit our Conference Website to learn more: acforum.org/2021

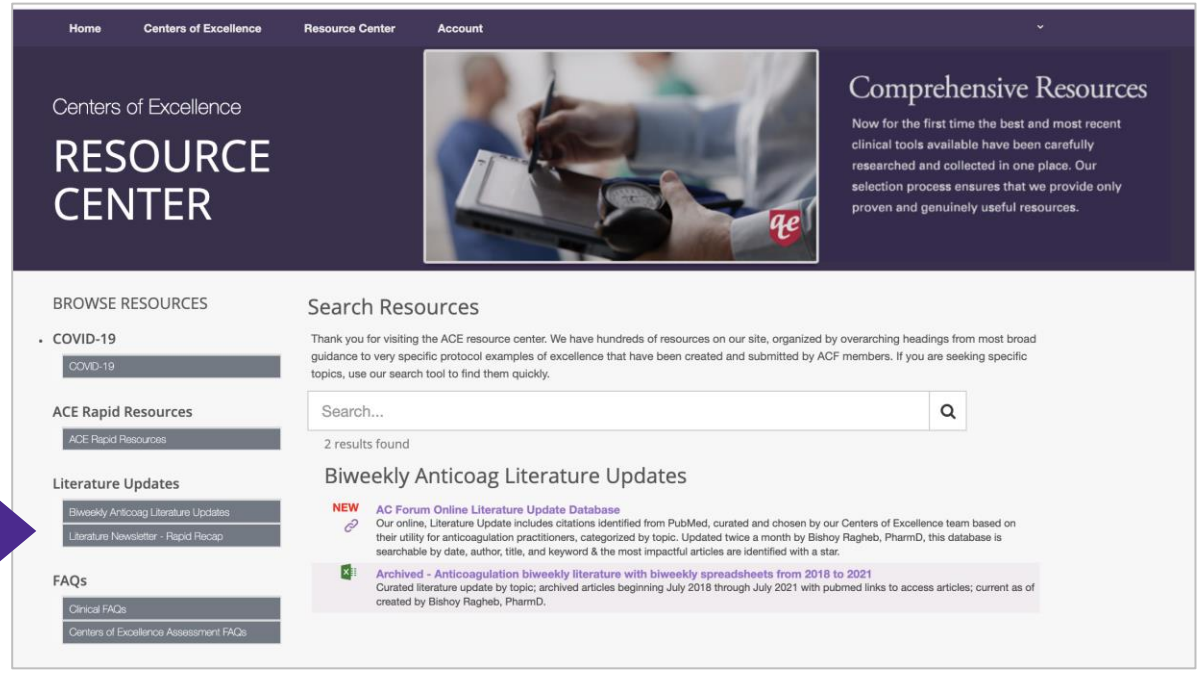
If you have questions, contact info@acforum.org

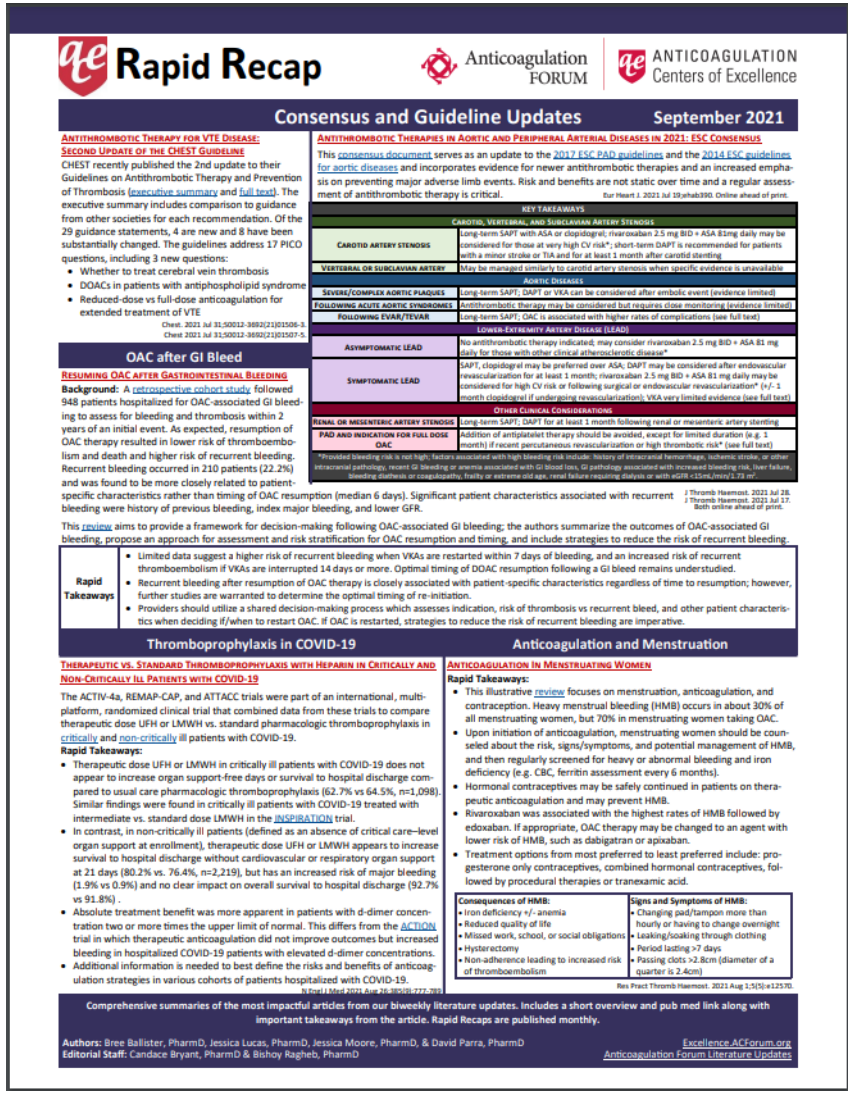
Online Literature Update

- Launched July 1st
- Evolved from our twice-monthly lit search
- Lots of features
  - Most important articles starred
  - Searchable
  - Abstract can be read on site
  - View by date range
  - Includes ACF authored papers
- Links to our new Rapid Recap Newsletter
- This curated literature overview is game changing!
- Thank you Dr. Bishoy Ragheb and Elaine Whalen for this vision



Where are these resources?




Rapid Recap
Anticoagulation FORUM
ANTICOAGULATION Centers of Excellence
Consensus and Guideline Updates September 2021
ANTITHROMBOTIC THERAPY FOR VTE DISEASE: SECOND UPDATE OF THE CHEST GUIDELINE
CHEST recently published the 2nd update to their Guidelines on Antithrombotic Therapy and Prevention of Thrombosis (executive summary and full text). The executive summary includes comparison to guidance from other societies for each recommendation. Of the 29 guidance statements, 4 are new and 8 have been substantially changed. The guidelines address 17 PICO questions, including 3 new questions:
Whether to treat cerebral vein thrombosis
DOACs in patients with antiphospholipid syndrome
Reduced-dose vs full-dose anticoagulation for extended treatment of VTE
Chest. 2021 Jul 31;S0012-3692(21)01506-3.
Chest 2021 Jul 31;S0012-3692(21)01507-5.
ANTITHROMBOTIC THERAPIES IN AORTIC AND PERIPHERAL ARTERIAL DISEASES IN 2021: ESC CONSENSUS
This consensus document serves as an update to the 2017 ESC PAD guidelines and the 2014 ESC guidelines for aortic diseases and incorporates evidence for newer antithrombotic therapies and an increased emphasis on preventing major adverse limb events. Risk and benefits are not static over time and a regular assessment of antithrombotic therapy is critical.
Eur Heart J. 2021 Jul 19;ehab390. Online ahead of print.
KEY TAKEAWAYS
CAROTID, VERTEBRAL, AND SUBCLAVIAN ARTERY STENOSIS
CAROTID ARTERY STENOSIS: Long-term SAPT with ASA or clopidogrel; rivaroxaban 2.5 mg BID + ASA 81mg daily may be considered for those at very high CV risk*; short-term DAPT is recommended for patients with a minor stroke or TIA and for at least 1 month after carotid stenting
VERTEBRAL OR SUBCLAVIAN ARTERY: May be managed similarly to carotid artery stenosis when specific evidence is unavailable
AORTIC DISEASES
SEVERE/COMPLEX AORTIC PLAQUES: Long-term SAPT; DAPT or VKA can be considered after embolic event (evidence limited)
FOLLOWING ACUTE AORTIC SYNDROMES: Antithrombotic therapy may be considered but requires close monitoring (evidence limited)
FOLLOWING EVAR/TEVAR: Long-term SAPT; OAC is associated with higher rates of complications (see full text)
LOWER-EXTREMITY ARTERY DISEASE (LEAD)
ASYMPTOMATIC LEAD: No antithrombotic therapy indicated; may consider rivaroxaban 2.5 mg BID + ASA 81 mg daily for those with other clinical atherosclerotic disease*
SYMPTOMATIC LEAD: SAPT, clopidogrel may be preferred over ASA; DAPT may be considered after endovascular revascularization for at least 1 month; rivaroxaban 2.5 mg BID + ASA 81 mg daily may be considered for high CV risk or following surgical or endovascular revascularization* (+/- 1 month clopidogrel if undergoing revascularization); VKA very limited evidence (see full text)
OTHER CLINICAL CONSIDERATIONS
RENAL OR MESENTERIC ARTERY STENOSIS: Long-term SAPT; DAPT for at least 1 month following renal or mesenteric artery stenting
PAD AND INDICATION FOR FULL DOSE OAC: Addition of antiplatelet therapy should be avoided, except for limited duration (e.g. 1 month) if recent percutaneous revascularization or high thrombotic risk* (see full text)
*Provided bleeding risk is not high; factors associated with high bleeding risk include: history of intracranial hemorrhage, ischemic stroke, or other intracranial pathology, recent GI bleeding or anemia associated with GI blood loss, GI pathology associated with increased bleeding risk, liver failure, bleeding diathesis or coagulopathy, frailty or extreme old age, renal failure requiring dialysis or with eGFR <15mL/min/1.73 m².
J Thromb Haemost. 2021 Jul 28.
J Thromb Haemost. 2021 Jul 17.
Both online ahead of print.
OAC after GI Bleed
RESUMING OAC AFTER GASTROINTESTINAL BLEEDING
Background: A retrospective cohort study followed 948 patients hospitalized for OAC-associated GI bleeding to assess for bleeding and thrombosis within 2 years of an initial event. As expected, resumption of OAC therapy resulted in lower risk of thromboembolism and death and higher risk of recurrent bleeding. Recurrent bleeding occurred in 210 patients (22.2%) and was found to be more closely related to patient-specific characteristics rather than timing of OAC resumption (median 6 days). Significant patient characteristics associated with recurrent bleeding were history of previous bleeding, index major bleeding, and lower GFR.
This review aims to provide a framework for decision-making following OAC-associated GI bleeding; the authors summarize the outcomes of OAC-associated GI bleeding, propose an approach for assessment and risk stratification for OAC resumption and timing, and include strategies to reduce the risk of recurrent bleeding.
Rapid Takeaways
Limited data suggest a higher risk of recurrent bleeding when VKAs are restarted within 7 days of bleeding, and an increased risk of recurrent thromboembolism if VKAs are interrupted 14 days or more. Optimal timing of DOAC resumption following a GI bleed remains understudied.
Recurrent bleeding after resumption of OAC therapy is closely associated with patient-specific characteristics regardless of time to resumption; however, further studies are warranted to determine the optimal timing of re-initiation.
Providers should utilize a shared decision-making process which assesses indication, risk of thrombosis vs recurrent bleed, and other patient characteristics when deciding if/when to restart OAC. If OAC is restarted, strategies to reduce the risk of recurrent bleeding are imperative.
Thromboprophylaxis in COVID-19
THERAPEUTIC VS. STANDARD THROMBOPROPHYLAXIS WITH HEPARIN IN CRITICALLY AND NON-CRITICALLY ILL PATIENTS WITH COVID-19
The ACTIV-4a, REMAP-CAP, and ATTACC trials were part of an international, multiplatform, randomized clinical trial that combined data from these trials to compare therapeutic dose UFH or LMWH vs. standard pharmacologic thromboprophylaxis in critically and non-critically ill patients with COVID-19.
Rapid Takeaways:
Therapeutic dose UFH or LMWH in critically ill patients with COVID-19 does not appear to increase organ support-free days or survival to hospital discharge compared to usual care pharmacologic thromboprophylaxis (62.7% vs 64.5%, n=1,098). Similar findings were found in critically ill patients with COVID-19 treated with intermediate vs. standard dose LMWH in the INSPIRATION trial.
In contrast, in non-critically ill patients (defined as an absence of critical care–level organ support at enrollment), therapeutic dose UFH or LMWH appears to increase survival to hospital discharge without cardiovascular or respiratory organ support at 21 days (80.2% vs. 76.4%, n=2,219), but has an increased risk of major bleeding (1.9% vs 0.9%) and no clear impact on overall survival to hospital discharge (92.7% vs 91.8%) .
Absolute treatment benefit was more apparent in patients with d-dimer concentration two or more times the upper limit of normal. This differs from the ACTION trial in which therapeutic anticoagulation did not improve outcomes but increased bleeding in hospitalized COVID-19 patients with elevated d-dimer concentrations.
Additional information is needed to best define the risks and benefits of anticoagulation strategies in various cohorts of patients hospitalized with COVID-19.
N Engl J Med 2021 Apr 29;384(8):777-789.
Anticoagulation and Menstruation
ANTICOAGULATION IN MENSTRUATING WOMEN
Rapid Takeaways:
This illustrative review focuses on menstruation, anticoagulation, and contraception. Heavy menstrual bleeding (HMB) occurs in about 30% of all menstruating women, but 70% in menstruating women taking OAC.
Upon initiation of anticoagulation, menstruating women should be counseled about the risk, signs/symptoms, and potential management of HMB, and then regularly screened for heavy or abnormal bleeding and iron deficiency (e.g. CBC, ferritin assessment every 6 months).
Hormonal contraceptives may be safely continued in patients on therapeutic anticoagulation and may prevent HMB.
Rivaroxaban was associated with the highest rates of HMB followed by edoxaban. If appropriate, OAC therapy may be changed to an agent with lower risk of HMB, such as dabigatran or apixaban.
Treatment options from most preferred to least preferred include: progesterone only contraceptives, combined hormonal contraceptives, followed by procedural therapies or tranexamic acid.
Consequences of HMB:
Iron deficiency +/- anemia
Reduced quality of life
Missed work, school, or social obligations
Hysterectomy
Non-adherence leading to increased risk of thromboembolism
Signs and Symptoms of HMB:
Changing pad/tampon more than hourly or having to change overnight
Leaking/soaking through clothing
Period lasting >7 days
Passing clots >2.8cm (diameter of a quarter is 2.4cm)
Res Pract Thromb Haemost. 2021 Aug 1;5(5):e12570.
Comprehensive summaries of the most impactful articles from our biweekly literature updates. Includes a short overview and pub med link along with important takeaways from the article. Rapid Recaps are published monthly.
Authors: Bree Ballister, PharmD, Jessica Lucas, PharmD, Jessica Moore, PharmD, & David Parra, PharmD
Editorial Staff: Candace Bryant, PharmD & Bishoy Ragheb, PharmD
Excellence.ACForum.org
Anticoagulation Forum Literature Updates

- Literature update created 1st & 3rd Mondays, monthly
- Rapid Recap one month following by several editorial teams

Anticoagulation FORUM | Webinar Lunch & Learn

This webinar is brought to you, in part, by the support of the following companies: