# Ask the Experts

**Thursday | November 9, 2023 | 12:00pm ET**

Anticoagulation FORUM

# Presenters

**Arthur Allen, PharmD, CACP (moderator)**
Anticoagulation Program Manager
VA Salt Lake City Health Care System

**Geoff Barnes, MD, MSc**
Associate Professor of Internal Medicine
University of Michigan

**Adam Cuker, MD, MS**
Director, Penn Comprehensive and Hemophilia Thrombosis Program
Clinical Director, Penn Blood Disorders Center
Section Chief, Hematology
Associate Professor of Medicine, Hospital of the University of Pennsylvania
Associate Professor of Medicine in Pathology and Laboratory Medicine

**Andrea Van Beek, DNP, APRN, AGPCNP-BC, CACP (moderator)**
Nurse Practitioner, Anticoagulation and Thrombosis Service
Visalia Medical Clinic/Adventist Health Physicians Network

**Bishoy Ragheb, PharmD, BCACP, CACP**
Anticoagulation Clinical Pharmacist Practitioner Veterans Affairs Eastern Colorado Health Care System

**Sara Vazquez, PharmD, BCPS, CACP**
Clinical Pharmacist
University of Utah

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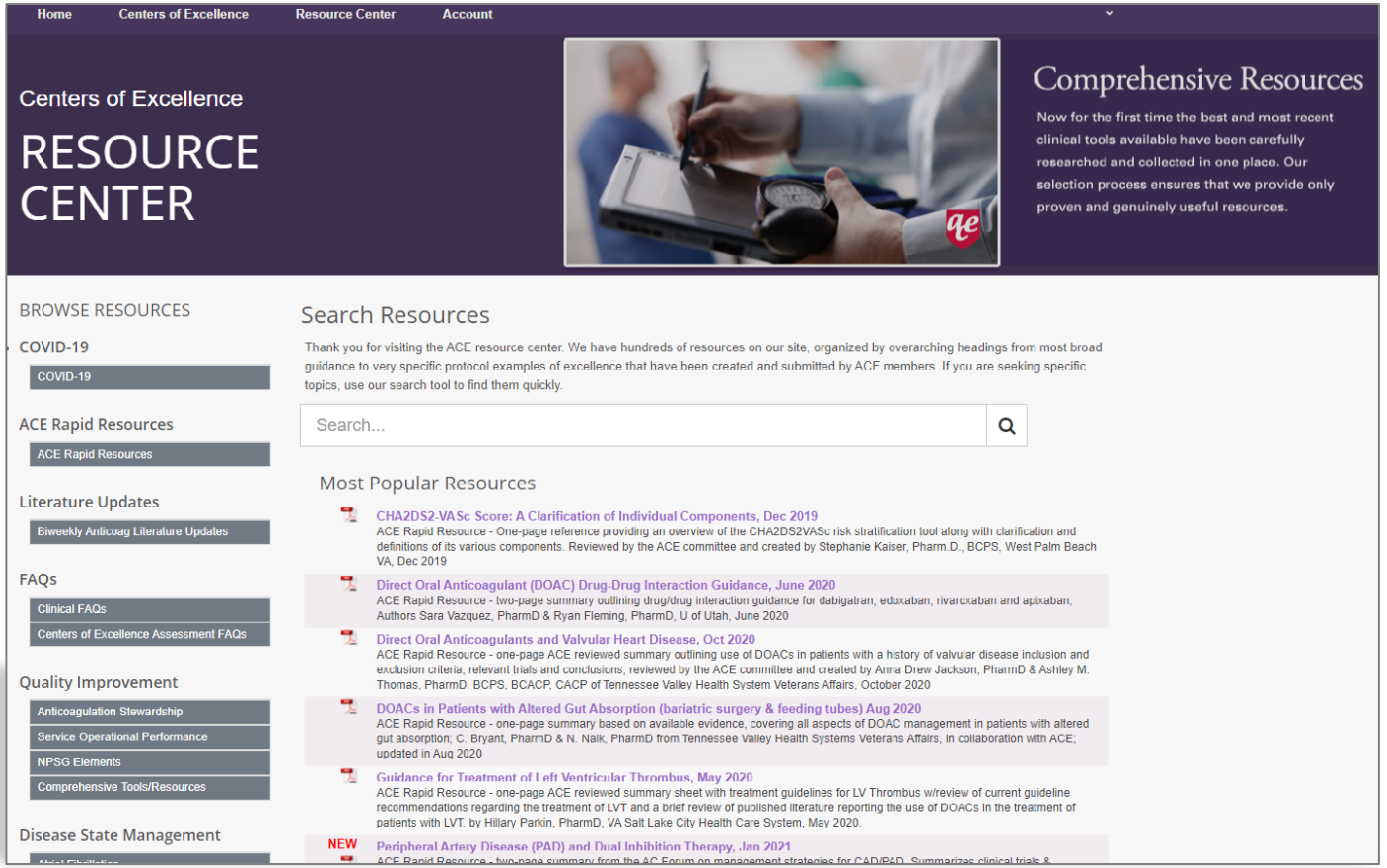


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Anticoagulation FORUM

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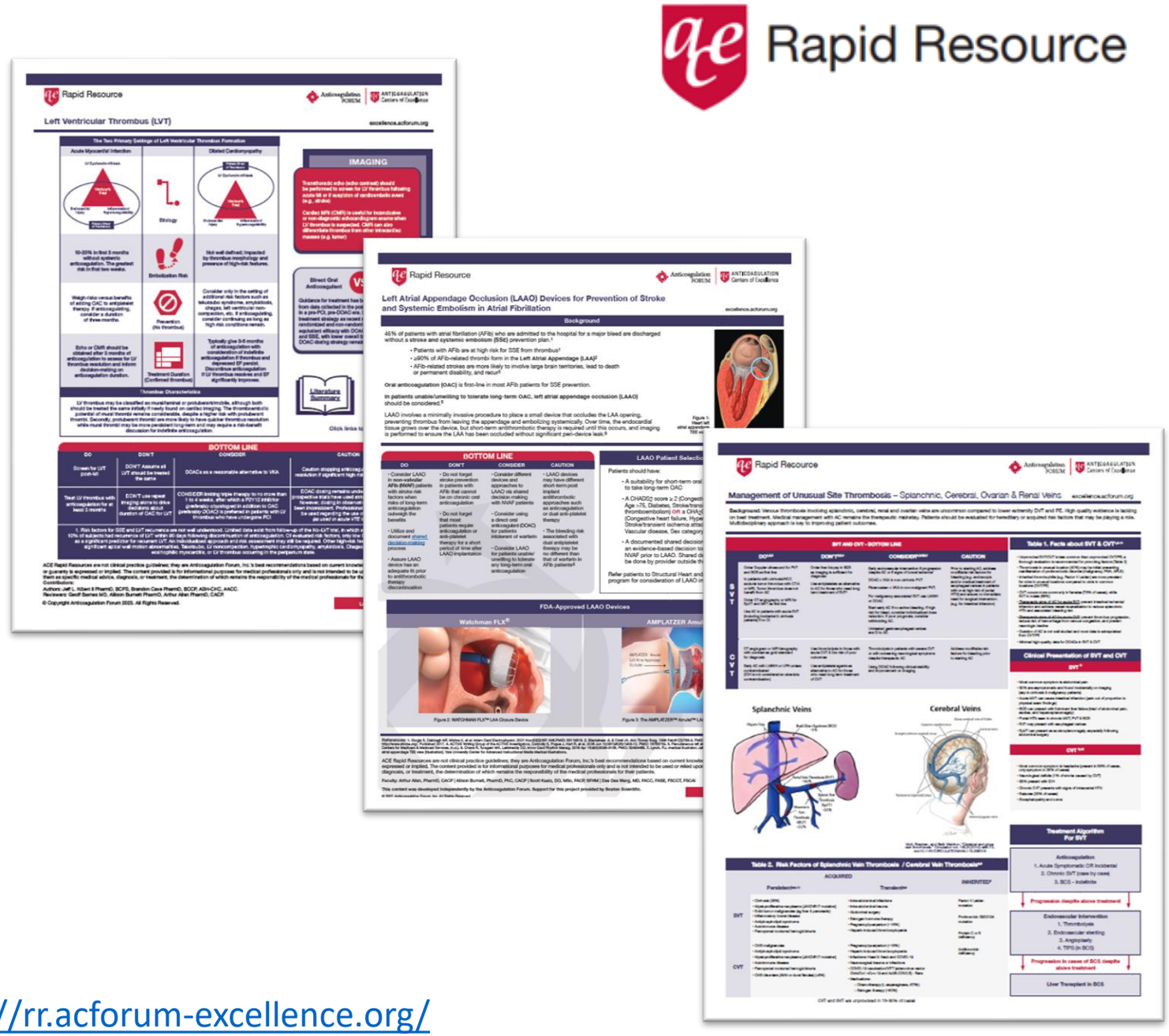


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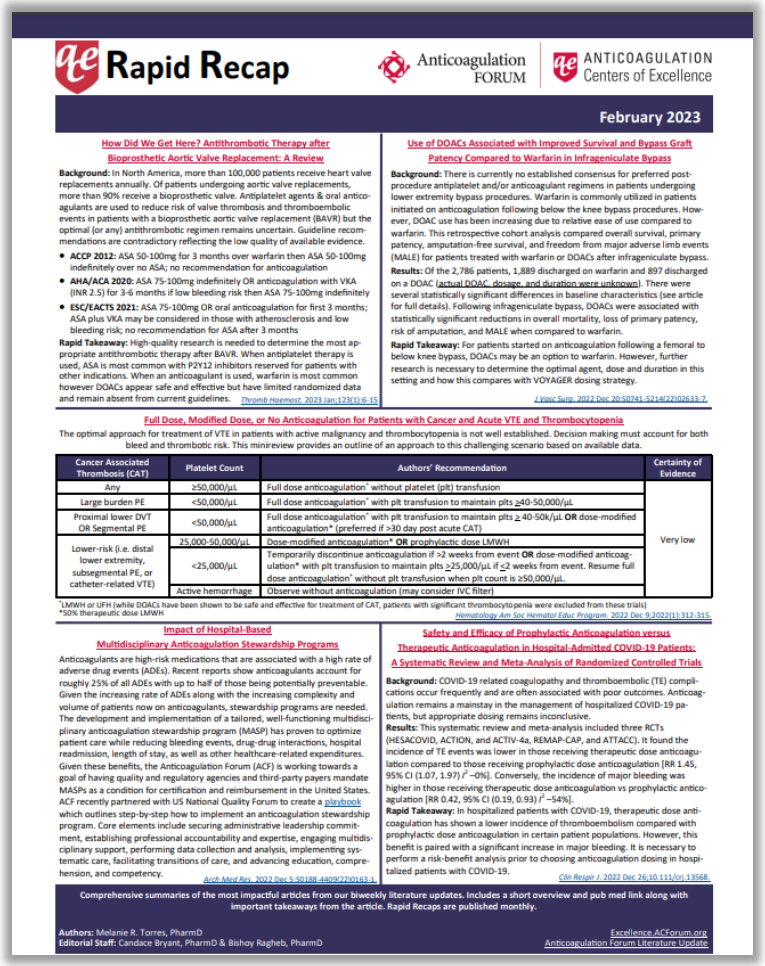
# Rapid Recap & Biannual Literature Review

Monthly summary of literature in bite-sized chunks!

Highlights the most important articles from our online literature search

Thank you to our editors for their dedication & skill



Rapid Recap | Anticoagulation FORUM | ANTICOAGULATION Centers of Excellence

February 2023

**How Did We Get Here? Antithrombotic Therapy after Bioprosthetic Aortic Valve Replacement: A Review**

**Background:** In North America, more than 100,000 patients receive heart valve replacements annually. Of patients undergoing aortic valve replacements, more than 90% receive a bioprosthetic valve. Antiplatelet agents & oral anticoagulants are used to reduce risk of valve thrombosis and thromboembolic events in patients with a bioprosthetic aortic valve replacement (BAVR) but the optimal (or any) antithrombotic regimen remains uncertain. Guideline recommendations are contradictory reflecting the low quality of available evidence.

- **ACCP 2012:** ASA 50-100mg for 3 months over warfarin then ASA 50-100mg indefinitely over no ASA; no recommendation for anticoagulation
- **AHA/ACA 2020:** ASA 75-100mg indefinitely OR anticoagulation with VKA (INR 2.5) for 3-6 months if low bleeding risk then ASA 75-100mg indefinitely
- **ESC/EACTS 2021:** ASA 75-100mg OR oral anticoagulation for first 3 months; ASA plus VKA may be considered in those with atherosclerosis and low bleeding risk; no recommendation for ASA after 3 months

**Rapid Takeaway:** High-quality research is needed to determine the most appropriate antithrombotic therapy after BAVR. When antiplatelet therapy is used, ASA is most common with P2Y12 inhibitors reserved for patients with other indications. When an anticoagulant is used, warfarin is most common however DOACs appear safe and effective but have limited randomized data and remain absent from current guidelines. *Thromb Haemost.* 2023 Jan;123(1):6-15

**Use of DOACs Associated with Improved Survival and Bypass Graft Patency Compared to Warfarin in Infragenicular Bypass**

**Background:** There is currently no established consensus for preferred post-procedure antiplatelet and/or anticoagulant regimens in patients undergoing lower extremity bypass procedures. Warfarin is commonly utilized in patients initiated on anticoagulation following below the knee bypass procedures. However, DOAC use has been increasing due to relative ease of use compared to warfarin. This retrospective cohort analysis compared overall survival, primary patency, amputation-free survival, and freedom from major adverse limb events (MALE) for patients treated with warfarin or DOACs after infragenicular bypass.

**Results:** Of the 2,786 patients, 1,889 discharged on warfarin and 897 discharged on a DOAC (actual DOAC, dosage, and duration were unknown). There were several statistically significant differences in baseline characteristics (see article for full details). Following infragenicular bypass, DOACs were associated with statistically significant reductions in overall mortality, loss of primary patency, risk of amputation, and MALE when compared to warfarin.

**Rapid Takeaway:** For patients started on anticoagulation following a femoral to below knee bypass, DOACs may be an option to warfarin. However, further research is necessary to determine the optimal agent, dose and duration in this setting and how this compares with VOYAGER dosing strategy.

*J Vasc Surg.* 2022 Dec 20:S0741-5214(22)02633-7.

**Full Dose, Modified Dose, or No Anticoagulation for Patients with Cancer and Acute VTE and Thrombocytopenia**

The optimal approach for treatment of VTE in patients with active malignancy and thrombocytopenia is not well established. Decision making must account for both bleed and thrombotic risk. This minireview provides an outline of an approach to this challenging scenario based on available data.

| Cancer Associated Thrombosis (CAT) | Platelet Count | Authors' Recommendation | Certainty of Evidence |
|---|---|---|---|
| Any | ≥50,000/μL | Full dose anticoagulation* without platelet (plt) transfusion | Very low |
| Large burden PE | <50,000/μL | Full dose anticoagulation* with plt transfusion to maintain plts ≥40-50,000/μL | |
| Proximal lower DVT OR Segmental PE | <50,000/μL | Full dose anticoagulation* with plt transfusion to maintain plts ≥ 40-50k/μL **OR** dose-modified anticoagulation* (preferred if >30 day post acute CAT) | |
| Lower-risk (i.e. distal lower extremity, subsegmental PE, or catheter-related VTE) | 25,000-50,000/μL | Dose-modified anticoagulation* **OR** prophylactic dose LMWH | |
| | <25,000/μL | Temporarily discontinue anticoagulation if >2 weeks from event **OR** dose-modified anticoagulation* with plt transfusion to maintain plts ≥25,000/μL if ≤2 weeks from event. Resume full dose anticoagulation* without plt transfusion when plt count is ≥50,000/μL. | |
| | Active hemorrhage | Observe without anticoagulation (may consider IVC filter) | |

*LMWH or UFH (while DOACs have been shown to be safe and effective for treatment of CAT, patients with significant thrombocytopenia were excluded from these trials)
*50% therapeutic dose LMWH

*Hematology Am Soc Hematol Educ Program.* 2022 Dec 9;2022(1):312-315.

**Impact of Hospital-Based Multidisciplinary Anticoagulation Stewardship Programs**

Anticoagulants are high-risk medications that are associated with a high rate of adverse drug events (ADEs). Recent reports show anticoagulants account for roughly 25% of all ADEs with up to half of those being potentially preventable. Given the increasing rate of ADEs along with the increasing complexity and volume of patients now on anticoagulants, stewardship programs are needed. The development and implementation of a tailored, well-functioning multidisciplinary anticoagulation stewardship program (MASP) has proven to optimize patient care while reducing bleeding events, drug-drug interactions, hospital readmission, length of stay, as well as other healthcare-related expenditures. Given these benefits, the Anticoagulation Forum (ACF) is working towards a goal of having quality and regulatory agencies and third-party payers mandate MASPs as a condition for certification and reimbursement in the United States. ACF recently partnered with US National Quality Forum to create a playbook which outlines step-by-step how to implement an anticoagulation stewardship program. Core elements include securing administrative leadership commitment, establishing professional accountability and expertise, engaging multidisciplinary support, performing data collection and analysis, implementing systematic care, facilitating transitions of care, and advancing education, comprehension, and competency. *Arch Med Res.* 2022 Dec 5:S0188-4409(22)01163-1.

**Safety and Efficacy of Prophylactic Anticoagulation versus Therapeutic Anticoagulation in Hospital-Admitted COVID-19 Patients: A Systematic Review and Meta-Analysis of Randomized Controlled Trials**

**Background:** COVID-19 related coagulopathy and thromboembolic (TE) complications occur frequently and are often associated with poor outcomes. Anticoagulation remains a mainstay in the management of hospitalized COVID-19 patients, but appropriate dosing remains inconclusive.

**Results:** This systematic review and meta-analysis included three RCTs (HESACOVID, ACTION, and ACTIV-4a, REMAP-CAP, and ATTACC). It found the incidence of TE events was lower in those receiving therapeutic dose anticoagulation compared to those receiving prophylactic dose anticoagulation [RR 1.45, 95% CI (1.07, 1.97) $I^2$ –0%]. Conversely, the incidence of major bleeding was higher in those receiving therapeutic dose anticoagulation vs prophylactic anticoagulation [RR 0.42, 95% CI (0.19, 0.93) $I^2$ –54%].

**Rapid Takeaway:** In hospitalized patients with COVID-19, therapeutic dose anticoagulation has shown a lower incidence of thromboembolism compared with prophylactic dose anticoagulation in certain patient populations. However, this benefit is paired with a significant increase in major bleeding. It is necessary to perform a risk-benefit analysis prior to choosing anticoagulation dosing in hospitalized patients with COVID-19. *Clin Respir J.* 2022 Dec 26;10.111/crj.13568.

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.

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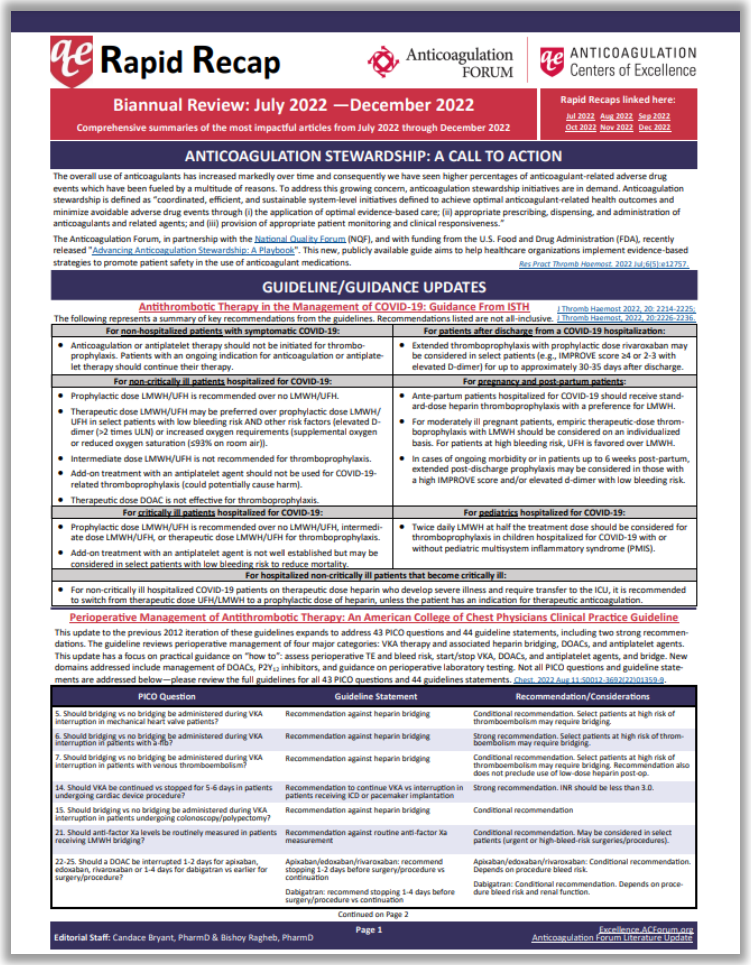
Anticoagulation Forum Literature Update



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**Biannual Review: July 2022 —December 2022**

Comprehensive summaries of the most impactful articles from July 2022 through December 2022

Rapid Recaps linked here:
Jul 2022 Aug 2022 Sep 2022
Oct 2022 Nov 2022 Dec 2022

## ANTICOAGULATION STEWARDSHIP: A CALL TO ACTION

The overall use of anticoagulants has increased markedly over time and consequently we have seen higher percentages of anticoagulant-related adverse drug events which have been fueled by a multitude of reasons. To address this growing concern, anticoagulation stewardship initiatives are in demand. Anticoagulation stewardship is defined as "coordinated, efficient, and sustainable system-level initiatives defined to achieve optimal anticoagulant-related health outcomes and minimize avoidable adverse drug events through (i) the application of optimal evidence-based care; (ii) appropriate prescribing, dispensing, and administration of anticoagulants and related agents; and (iii) provision of appropriate patient monitoring and clinical responsiveness."

The Anticoagulation Forum, in partnership with the National Quality Forum (NQF), and with funding from the U.S. Food and Drug Administration (FDA), recently released "Advancing Anticoagulation Stewardship: A Playbook". This new, publicly available guide aims to help healthcare organizations implement evidence-based strategies to promote patient safety in the use of anticoagulant medications. *Res Pract Thromb Haemost.* 2022 Jul;6(5):e13767.

## GUIDELINE/GUIDANCE UPDATES

**Antithrombotic Therapy in the Management of COVID-19: Guidance From ISTH** *J Thromb Haemost.* 2022; 20: 2214-2225. *J Thromb Haemost.* 2022; 20:2226-2236.

The following represents a summary of key recommendations from the guidelines. Recommendations listed are not all-inclusive.

**For non-hospitalized patients with symptomatic COVID-19:**

- Anticoagulation or antiplatelet therapy should not be initiated for thromboprophylaxis. Patients with an ongoing indication for anticoagulation or antiplatelet therapy should continue their therapy.

**For non-critically ill patients hospitalized for COVID-19:**

- Prophylactic dose LMWH/UFH is recommended over no LMWH/UFH.
- Therapeutic dose LMWH/UFH may be preferred over prophylactic dose LMWH/UFH in select patients with low bleeding risk AND other risk factors (elevated D-dimer (>2 times ULN) or increased oxygen requirements (supplemental oxygen or reduced oxygen saturation (≤93% on room air)).
- Intermediate dose LMWH/UFH is not recommended for thromboprophylaxis.
- Add-on treatment with an antiplatelet agent should not be used for COVID-19-related thromboprophylaxis (could potentially cause harm).
- Therapeutic dose DOAC is not effective for thromboprophylaxis.

**For critically ill patients hospitalized for COVID-19:**

- Prophylactic dose LMWH/UFH is recommended over no LMWH/UFH, intermediate dose LMWH/UFH, or therapeutic dose LMWH/UFH for thromboprophylaxis.
- Add-on treatment with an antiplatelet agent is not well established but may be considered in select patients with low bleeding risk to reduce mortality.

**For patients after discharge from a COVID-19 hospitalization:**

- Extended thromboprophylaxis with prophylactic dose rivaroxaban may be considered in select patients (e.g., IMPROVE score ≥4 or 2-3 with elevated D-dimer) for up to approximately 30-35 days after discharge.

**For pregnancy and post-partum patients:**

- Ante-partum patients hospitalized for COVID-19 should receive standard-dose heparin thromboprophylaxis with a preference for LMWH.
- For moderately ill pregnant patients, empiric therapeutic-dose thromboprophylaxis with LMWH should be considered on an individualized basis. For patients at high bleeding risk, UFH is favored over LMWH.
- In cases of ongoing morbidity or in patients up to 6 weeks post-partum, extended post-discharge prophylaxis may be considered in those with a high IMPROVE score and/or elevated d-dimer with low bleeding risk.

**For pediatrics hospitalized for COVID-19:**

- Twice daily LMWH at half the treatment dose should be considered for thromboprophylaxis in children hospitalized for COVID-19 with or without pediatric multisystem inflammatory syndrome (PMIS).

**For hospitalized non-critically ill patients that become critically ill:**

- For non-critically ill hospitalized COVID-19 patients on therapeutic dose heparin who develop severe illness and require transfer to the ICU, it is recommended to switch from therapeutic dose UFH/LMWH to a prophylactic dose of heparin, unless the patient has an indication for therapeutic anticoagulation.

**Perioperative Management of Antithrombotic Therapy: An American College of Chest Physicians Clinical Practice Guideline**

This update to the previous 2012 iteration of these guidelines expands to address 43 PICO questions and 44 guideline statements, including two strong recommendations. The guideline reviews perioperative management of four major categories: VKA therapy and associated heparin bridging, DOACs, and antiplatelet agents. This update has a focus on practical guidance on "how to": assess perioperative TE and bleed risk, start/stop VKA, DOACs, and antiplatelet agents, and bridge. New domains addressed include management of DOACs, $P2Y_{12}$ inhibitors, and guidance on perioperative laboratory testing. Not all PICO questions and guideline statements are addressed below—please review the full guidelines for all 43 PICO questions and 44 guidelines statements. *Chest.* 2022 Aug 11:S0012-3692(22)01359-9.

| PICO Question | Guideline Statement | Recommendation/Considerations |
|---|---|---|
| 5. Should bridging vs no bridging be administered during VKA interruption in mechanical heart valve patients? | Recommendation against heparin bridging | Conditional recommendation. Select patients at high risk of thromboembolism may require bridging. |
| 6. Should bridging vs no bridging be administered during VKA interruption in patients with a-fib? | Recommendation against heparin bridging | Strong recommendation. Select patients at high risk of thromboembolism may require bridging. |
| 7. Should bridging vs no bridging be administered during VKA interruption in patients with venous thromboembolism? | Recommendation against heparin bridging | Conditional recommendation. Select patients at high risk of thromboembolism may require bridging. Recommendation also does not preclude use of low-dose heparin post-op. |
| 14. Should VKA be continued vs stopped for 5-6 days in patients undergoing cardiac device procedure? | Recommendation to continue VKA vs interruption in patients receiving ICD or pacemaker implantation | Strong recommendation. INR should be less than 3.0. |
| 15. Should bridging vs no bridging be administered during VKA interruption in patients undergoing colonoscopy/polypectomy? | Recommendation against heparin bridging | Conditional recommendation |
| 21. Should anti-factor Xa levels be routinely measured in patients receiving LMWH bridging? | Recommendation against routine anti-factor Xa measurement | Conditional recommendation. May be considered in select patients (urgent or high-bleed-risk surgeries/procedures). |
| 22-25. Should a DOAC be interrupted 1-2 days for apixaban, edoxaban, rivaroxaban or 1-4 days for dabigatran vs earlier for surgery/procedure? | Apixaban/edoxaban/rivaroxaban: recommend stopping 1-2 days before surgery/procedure vs continuation<br>Dabigatran: recommend stopping 1-4 days before surgery/procedure vs continuation | Apixaban/edoxaban/rivaroxaban: Conditional recommendation. Depends on procedure bleed risk.<br>Dabigatran: Conditional recommendation. Depends on procedure bleed risk and renal function. |

Continued on Page 2



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Anticoagulation Forum Literature Update

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# Online Literature Update

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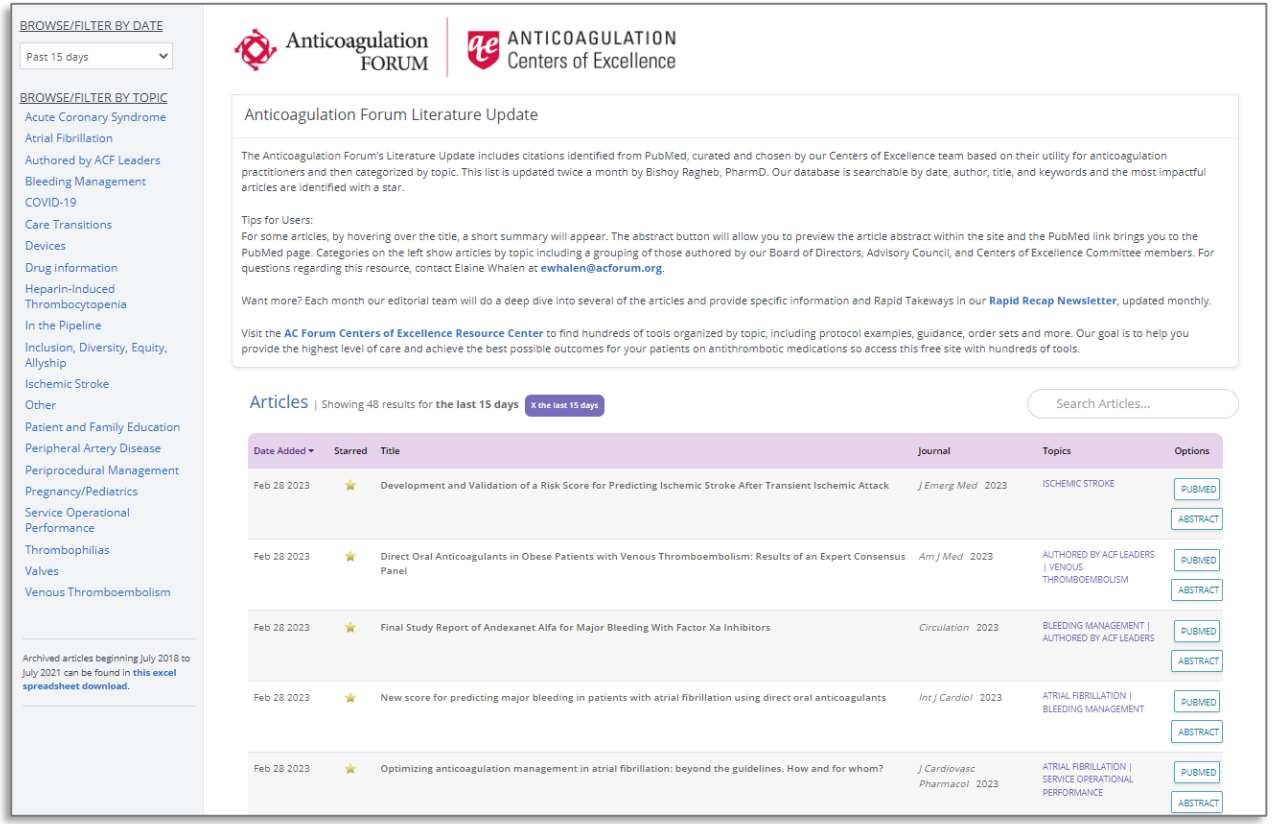


## Early Bird Pricing Ends Dec 3rd

The THSNA Summit is a collaboration of the 13 leading non-profit organizations in the fields of Thrombosis and Hemostasis. The Summit provides a focused forum for over 1,000 attendees with an interest in bleeding and clotting disorders to network, learn, and share across disciplines and disease states. The educational programming is organized in a series of plenary presentations, educational track sessions, oral abstract presentations and digital poster sessions.

**When you register, please note that you are associated with AC Forum!**

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