Arab Republic of Egypt
Egyptian Health Council
Egyptian Board of Anesthetics, Surgical Intensive Care and Pain Management

Guidelines for

Regional Anesthesia in the Patient Receiving Antithrombotic or Thrombolytic therapy

Prepared by

The "Guidelines Development Group" (GDG) of the Scientific Committee of the Egyptian Board of Anesthetics, Surgical Intensive Care and Pain Management.

Contents

Acknowledgements

The Guidelines for Regional anesthesia in the patient receiving antithrombotic or thrombolytic therapy - Edition 2026 - were prepared by the **Guidelines Development Group (GDG)** of the Egyptian Board of Anesthetics, Surgical Intensive Care and Pain Management group which reserves the right to determine the publication and distribution of the Guidelines. The Guidelines are subject to revision, and the updated versions will be published when needed, as warranted by the evolution of new-evidenced medical knowledge, new technology, and new practice trends. Although the Egyptian Board of Anesthetics, Surgical Intensive Care and Pain Management encourages Egyptian anesthesiologists to adhere to its practice guidelines to ensure high-quality patient care, we cannot guarantee any specific patient outcome. Anesthesiologists should exercise their own professional judgement in determining the proper course of action for any patient's circumstances. Egyptian Board of Anesthetics, Surgical Intensive Care and Pain Management assumes no responsibility or liability for any error or omission arising from the use of any information contained in its Guidelines to the Practice of Regional anesthesia in the patient receiving antithrombotic or thrombolytic therapy

These Guidelines are intended to apply to all anesthesiologists in Egypt. The independent practice of anesthesia is a specialized field of medicine, which should be practiced by physicians with appropriate training who continue their education in the practice of anesthetics, surgical intensive care, pain management, perioperative care, and resuscitation.
All physicians applying for privileges in anesthesia should show satisfactory completion of specialist postgraduate training in anesthesiology certified by either the Egyptian Board training or the standard training in University programs to be able to provide these services. International medical graduates approved for licensure by provincial regulatory bodies should show training equivalent to the Egyptian standard. The only route to specialist recognition in anesthesiology in Egypt is through the "certification process" of "Egyptian Health Council" (EHC).

We would like to acknowledge the Anesthesia **Guidelines Development Group (GDG)** of the Egyptian Board of Anesthetics, Surgical Intensive Care and Pain Management.

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Abbreviations

AAPM: American Academy of Pain Medicine
ACCP: American College of Clinical Pharmacy
ACOG: American College of Obstetricians and Gynecologists.
ADP: Adenosine diphosphate
AF: Atrial Fibrillation
AGREE II: Appraisal of Guidelines for Research and Evaluation II
aPCC: activated prothrombin complex concentrates
aPTT: Activated Partial Thromboplastin Time
ASA: American Society of Anesthesiologists.
ASRA: American Society of Regional Anesthesia
ASRA PM: American Society of Regional Anesthesia and Pain Medicine
aXa: anti-X activity
BID: twice daily
BMI: body mass index
CAD: Coronary artery disease
CrCI: Creatinine clearance
CT: Computed Tomography
CYP3A4: Cytochrome P450 3A4
CV: Cardiovascular
DOACs: Direct oral anticoagulants
DTI: direct thrombin inhibitor
DVT: Deep venous thrombosis
DXA: direct Xa antagonists
ECG: Electrocardiography
EHC: Egyptian Health Council
EHRA: European Heart Rhythm Association
ESA: European Society of Anaesthesiology
ESAIC: European Society of Anaesthesiology and Intensive Care**.**
ESRA: European Society of Regional Anaesthesia
FDA: Food and Drug Administration
FFP: Fresh Frozen Plasma
GDG: Guidelines Development Group
GP IIb/IIIa inhibitors: Glycoprotein IIb/IIIa inhibitors
GPS: Good Practice Statement.
GRADE: Grading of Recommendations Assessment, Development and Evaluation
HIT: Heparin-induced thrombocytopenia
ICU: intensive care unit
IMPROVE: International Medical Prevention Registry on Venous Thromboembolism
INR: international normalized ratio
IV: Intravenous
LA: Local Anesthetic
LMWH: Low molecular weight heparin
MI: Myocardial infarction
MRI: Magnetic Resonance Imaging
N/A: Not available
NIBP: Non-invasive Blood Pressure
NSAID: Nonsteroidal Anti-inflammatory Drug
NYSORA: New York School of Regional Anesthesia
NVAF: Non-valvular atrial fibrillation

PAD: Peripheral artery disease
PADUA: from University of Padua, Padova Italy
PAUSE: Perioperative Anticoagulation Use for Surgery Evaluation
P2Y12 inhibitors: P2Y12 receptor antagonists or blockers (A class of antiplatelet medications)
PCC: prothrombin complex concentrates
PDE: phosphodiesterase
PE: Pulmonary embolism
P-gp: P-glycoprotein
PT: Prothrombin Time
RCT: Randomized Controlled Trials
rFVIIa: recombinant activated factor VIIa
SC: Sub-cutaneous
SOAP: Society for Obstetric Anesthesia and Perinatology.
THA: Total hip arthroplasty
TIA: Transient ischemic attack
TID: three times daily
tPA: Tissue-type plasminogen activator
UFH: Unfractionated Heparin
UK: United kingdom
USA: United States of America
VKA: Vitamin K Antagonist
VTE: Venous thromboembolism
WHO: World Health Organization

Glossary

Basic Principles and Terminology

The following definitions are used For the purposes of these guidelines:

Anesthesiologist: the term anesthesiologist in this document is used to designate all licensed medical practitioners with privileges to administer anesthetics, surgical intensive care, pain management, perioperative care, and resuscitation.

Antithrombotic therapy: a medical approach using medications to prevent or treat blood clots (thrombosis) in arteries and veins, reducing risks of stroke, heart attack, and venous thromboembolism.
Autonomic Dysfunction: New-onset urinary retention or fecal incontinence.

Back Pain: Severe, localized back pain, often described as "stabbing" or radiating to the legs.

Hematoma: is a collection of blood that pools outside of blood vessels, usually caused by injury or trauma to veins or arteries.

Motor Deficit: New or progressive extremity weakness (unable to perform a straight leg raise).

Neuraxial anesthesia: is a regional anesthetic technique involving the injection of medication (local anesthetics, often with opioids) into the cerebrospinal fluid or epidural space to block nerve conduction at the spinal cord/nerve root levels.

Regional anesthesia: a pain management technique that uses injections of local anesthetics to block nerves, numbing a specific, large area of the body (e.g., limbs, abdomen, or lower body) while the patient remains conscious or sedated.
Sensory Deficit: New or worsening numbness or "heaviness" in a dermatomal distribution.
Thrombolytic therapy: an emergency medical procedure that uses special medication, known as "clot-busters" (e.g., tissue plasminogen activator or tPA), to dissolve dangerous, deep-seated blood clots.

t-PA formulations: Tissue-type plasminogen activator (tPA) formulations include recombinant, FDA-approved thrombolytic agents (alteplase, reteplase, tenecteplase) for ischemic stroke, myocardial infarction, and pulmonary embolism.

Traumatic Tap: is defined as the aspiration or spontaneous appearance of blood in the needle or catheter during the performance of a regional anesthetic technique.

Executive Summary

These Guidelines deal with the cornerstone recommendations of Regional anesthesia in the patient receiving antithrombotic or thrombolytic therapy.

1. Administration of thromboprophylaxis

1.1 For each of the antithrombotic agents, we suggest that clinicians follow the FDA-approved dosing guidelines (Conditional)

2. Direct Oral Anticoagulants (DOAC)

2.1 Management of neuraxial block or deep plexus/peripheral block in the patient receiving a High dose of Apixaban (Eliquis)

2.1.1 We suggest that a high dose of apixaban be discontinued at least 72 hours prior to neuraxial block or deep plexus/peripheral block. Consider checking apixaban or aXa plasma level if <72 hours (Conditional)

2.1.2 We suggest that a residual apixaban plasma level <30 ng/mL or a residual aXa activity plasma level ≤0.1 IU/mL is acceptable prior to neuraxial block or deep plexus/peripheral block (Conditional)

2.1.3 We suggest that needle placement/catheter removal occurs at least 24 hours prior to the first postoperative dose (Conditional)

2.2 Management of neuraxial block or deep plexus/peripheral block in the patient receiving a Low dose of Apixaban (Eliquis)

2.2.1 We suggest that a low dose of apixaban be discontinued for at least 36 hours prior to neuraxial block or deep plexus/peripheral block. Consider checking apixaban or aXa plasma level if <36 hours (Conditional)

2.2.2 We suggest that a residual apixaban plasma level <30 ng/mL or a residual aXa activity plasma level ≤0.1 IU/mL is acceptable prior to neuraxial block or deep plexus/peripheral block (Conditional)

2.2.3 We suggest that needle placement/catheter removal occurs at least 6 hours prior to the first postoperative dose (Conditional)

2.3 Management of neuraxial block or deep plexus/peripheral block in the patient receiving a high dose of edoxaban (Savaysa)

2.3.1 **We suggest that a high dose of edoxaban be discontinued for at least 72 hours prior to neuraxial block or deep plexus/peripheral block. Consider checking edoxaban or aXa activity plasma level if <72 hours (Conditional)**

2.3.2 **We suggest that a residual edoxaban plasma level <30 ng/mL or a residual aXa activity plasma level ≤0.1 IU/mL is acceptable prior to neuraxial block or deep plexus/peripheral block (Conditional)**

2.3.3 **We suggest that needle placement/catheter removal occurs at least 24 hours prior to the first (postoperative) dose (Conditional)**

2.4 Management of the patient receiving a Low dose of Edoxaban (Savaysa)

There is no FDA-approved medical indication for low-dose edoxaban.

2.5 Management of neuraxial block or deep plexus/peripheral block in the patient receiving High dose of Rivaroxaban (Xarelto)

2.5.1 **We suggest that a high dose of rivaroxaban be discontinued for at least 72 hours prior to neuraxial block or deep plexus/peripheral block. Consider checking rivaroxaban or aXa activity plasma level if <72 hours (Conditional)**

2.5.2 **We suggest that a residual rivaroxaban plasma level <30 ng/mL or a residual aXa activity plasma level ≤0.1 IU/mL is acceptable prior to neuraxial block or deep plexus/peripheral block (Conditional)**

2.5.3 **We suggest that needle placement/catheter removal occurs at least 24 hours prior to the first postoperative dose (Conditional)**

2.6 Management of neuraxial block or deep plexus/peripheral block in the patient receiving a Low dose of Rivaroxaban (Xarelto)

2.6.1 **We suggest that a low dose of rivaroxaban be discontinued for at least 24 hours (30 hours if CrCl <30 mL/min) prior to neuraxial block or deep plexus/peripheral block. Consider checking rivaroxaban or aXa activity plasma level if <24 hours (Conditional)**

2.6.2 **We suggest that a residual rivaroxaban plasma level <30 ng/mL or a residual aXa activity plasma level ≤0.1 IU/mL [1] is acceptable prior to neuraxial block or deep plexus/peripheral block (Conditional)**

2.6.3 **We suggest that needle placement/catheter removal occurs at least 6 hours prior to the first postoperative dose (Conditional)**

2.7 Management of neuraxial block or deep plexus/peripheral block in the patient receiving a High dose of Dabigatran (Pradaxa)

2.7.1 **We suggest that a high dose of dabigatran be discontinued for at least 72 hours in patients with a CrCl ≥50 mL/min prior to neuraxial block or deep plexus/peripheral block. Consider checking dabigatran plasma level if <72 hours (Conditional)**

2.7.2 **We suggest that a high dose of dabigatran be discontinued for 120 hours in patients with a CrCl 30–49 mL/min prior to neuraxial block or deep plexus/peripheral block. Consider checking dabigatran plasma level if <120 hours (Conditional)**

2.7.3 **We suggest against the performance of neuraxial or deep plexus/peripheral blocks in patients with a CrCl <30 mL/min unless a dabigatran plasma level is obtained and <30 ng/mL (Conditional)**

2.7.4 **Prior to neuraxial block or deep plexus/peripheral block we suggest that a residual dabigatran plasma level <30 ng/mL is acceptable (Conditional)**

2.7.5 **We suggest that needle placement/catheter removal occurs at least 24 hours prior to the first postoperative dose (Conditional)**

2.8 Management of neuraxial block or deep plexus/peripheral block in the patient receiving a Low dose of Dabigatran (Pradaxa)

2.8.1 **We suggest that a low dose of dabigatran be discontinued for at least 48 hours prior to neuraxial block or deep plexus/peripheral block. Consider checking dabigatran plasma level if <48 hours (Conditional)**

2.8.2 **We suggest that a residual dabigatran plasma level <30 ng/mL is acceptable prior to neuraxial block or deep plexus/peripheral block (Conditional)**

2.8.3 **We suggest against the performance of neuraxial or deep plexus/peripheral blocks in patients with a CrCl <30 mL/min unless a dabigatran plasma level is obtained and <30 ng/mL (Conditional)**

2.8.4 **We suggest that needle placement/catheter removal occurs at least 6 hours prior to the first postoperative dose (Conditional)**

3. Use of Direct oral anticoagulant (DOAC) antidotes to facilitate placement of neuraxial block or deep plexus/peripheral block

3.1 **Suggest *against* the use of idarucizumab, andexanet alfa, prothrombin complex concentrates (PCC), or activated prothrombin complex concentrates (aPCC) to reverse DOAC anticoagulant activity to enable the safe performance of a neuraxial intervention in routine patients (Conditional)**

4. Intravenous and Subcutaneous Unfractionated Heparin

Management of neuraxial block or deep plexus/peripheral block in the patient receiving Unfractionated Heparin

4.1 **We recommend daily review of the patient's medical record to determine the concurrent use of medications that affect other pathways of hemostasis. These medications include antiplatelet medications, LMWH, and oral anticoagulants (Strong)**

4.2 **Since heparin-induced thrombocytopenia may occur during heparin administration, we recommend that patients receiving intravenous or subcutaneous UFH for >4 days have a platelet count assessed (Strong)**

4.3 Intravenous heparin

4.3.1 **Discontinue Intravenous heparin infusion for a minimum of 4–6 hours and coagulation status be assessed and normal prior to neuraxial block or deep plexus/peripheral block (Strong)**

4.3.2 **Delay intravenous heparin administration for a minimum of 1 hour after needle placement (Strong)**

4.3.3 **It is not recommended to maintain neuraxial or deep plexus catheters in the setting of continuous intravenous heparin administration. In the event of unanticipated heparinization, we recommend monitoring the patient with an indwelling catheter to allow for early detection of motor deficits and consider use of minimal concentration of local anesthetics to enhance early detection of a neuraxial hematoma (Strong)**

4.3.4 **Although the occurrence of a bloody or difficult neuraxial needle placement may increase the risk of hematoma, there are no data to support mandatory cancellation of a case. Direct communication with the surgeon and a specific risk-benefit decision about proceeding in each case is recommended (Strong)**

Heparinization during cardiopulmonary bypass

4.3.5 **It is not recommended to maintain neuraxial or deep plexus/peripheral catheters in the setting of full anticoagulation during cardiac surgery. If unanticipated heparinization occurs, we suggest postoperative monitoring of neurological status and consider use of minimal concentration of local anesthetics to enhance early detection of neuraxial hematoma (Conditional)**

4.4 Subcutaneous heparin

4.4.1 Preoperative low-dose UFH for thromboprophylaxis (5000 U two times per day or three times per day). We suggest needle placement occur a minimum of 4–6 hours after heparin administration or coagulation status be assessed and normal (Conditional)

4.4.2 Preoperative high dose UFH

7500–10 000 U two times per day or a daily dose of ≤20 000 U

We suggest neuraxial block occur a minimum of 12 hours after subcutaneous heparin administration and confirmation of normal coagulation status (Conditional)

>10 000 U subcutaneously per dose, or >20 000 U total daily dose

We suggest neuraxial block occur a minimum of 24 hours after subcutaneous heparin administration and confirmation of normal coagulation status (Conditional)

4.4.3 Postoperative low-dose UFH

There is no contraindication to maintaining neuraxial catheters in the presence of low-dose UFH. We suggest catheter removal occurs a minimum of 4–6 hours after heparin administration. Subsequent heparin administration may occur immediately after catheter removal (Conditional)

4.4.4 Postoperative high-dose UFH

The safety of indwelling neuraxial catheters in patients receiving doses >5000 U at a time or >15 000 U of UFH daily has not been established. We suggest that the risk and benefits be assessed on an individual basis and that techniques to facilitate detection of new/progressive neurological deficits (eg, enhanced neurological monitoring occur and neuraxial solutions to minimize sensory and motor block) be applied (Conditional)

5. Low molecular weight heparin (LMWH)

5.1 Management of neuraxial block or deep plexus/peripheral block in the patient receiving low molecular weight heparin

5.1.1 The aXa level is Not predictive of the risk of bleeding, although it may be useful in monitoring efficacy of therapy with high-dose regimens. We recommend against the *routine* use of aXa level monitoring (Strong)

5.1.2 Heparin-induced thrombocytopenia may occur during LMWH administration; therefore, we recommend that patients receiving LMWH for >4 days have a platelet count assessed prior to needle placement (Strong)

5.1.3 The presence of blood during needle and catheter placement does not necessitate postponement of surgery. We suggest that initiation of LMWH therapy in this setting should be delayed for 24 hours postoperatively and that this consideration be discussed with the surgeon (Strong)

5.2 Preoperative LMWH

5.2.1 In patients receiving low-dose LMWH, we recommend delay of at least 12 hours prior to needle/catheter placement (Stong)

5.2.2 In patients receiving high (therapeutic) doses of LMWH, we recommend delay of at least 24 hours prior to needle/catheter placement (Stong)

5.3 Postoperative LMWH

5.3.1 We recommend against concomitant administration of medications affecting hemostasis, such as antiplatelet drugs, standard heparin, or dextran, regardless of LMWH dosing regimen when there is an indwelling neuraxial catheter (Strong)

5.3.2 Twice-daily low dose. We recommend the first dose of LMWH be administered the following day and at least 12 hours after needle/catheter placement. Indwelling

catheters should be removed *prior* to initiation of LMWH. Administration of LMWH should be delayed for 4 hours after catheter removal (Strong)

5.3.3 Single daily low dose. We recommend the first postoperative LMWH dose should be administered at least 12 hours after needle/catheter placement. Indwelling neuraxial catheters do not appear to represent increased risk and may be maintained. The catheter should be removed 12 hours after the last dose of LMWH. Subsequent LMWH dosing should occur at least 4 hours after catheter removal (Strong)

5.3.4 Single or twice-daily high (*therapeutic*) dosing. High-dose LMWH may be resumed 24 hours after non-high-bleeding-risk surgery and 48–72 hours after high-bleeding-risk surgery. We recommend that indwelling neuraxial catheters be removed 4 hours *prior* to the first postoperative dose and the first postoperative dose should be at least 24 hours after needle/catheter placement, whichever is greater (Strong)

6. Antiplatelet Medications

Management of neuraxial block or deep plexus/peripheral block in the patient taking NSAIDs

6.1 NSAIDs appear to represent no added risk for the development of major bleeding after regional anesthetic techniques. NSAIDs (including aspirin) do not create a level of risk that will interfere with the performance of neuraxial or deep plexus/peripheral blocks. In patients receiving these medications, we do not identify specific concerns as to the timing of single-injection or catheter techniques, postoperative monitoring, or the timing of neuraxial catheter removal. (Strong)

6.2 Management of neuraxial block or deep plexus/peripheral block in the patient taking Thienopyridines (Clopidogrel, Prasugrel)

6.2.1 Based on labeling and surgical/procedural experience, the suggested time interval between discontinuation of thienopyridine therapy and needle placement is 5–7 days for clopidogrel, and 7–10 days for prasugrel (Conditional)

6.2.2 Neuraxial and deep plexus/peripheral catheters should not be maintained with prasugrel due to the rapid onset. However, since the antiplatelet effect is not immediate with clopidogrel, they may be maintained for 1–2 days, provided a loading dose of the antiplatelet agent is not administered (Conditional)

6.2.3 Thienopyridine therapy may be resumed immediately after needle placement/catheter removal, provided a loading dose of the drugs is not administered. If a loading dose is administered, we suggest a time interval of 6 hours between catheter removal and administration (Conditional)

6.3 Management of neuraxial block or deep plexus/peripheral block in the patient taking Ticagrelor

6.3.1 Based on labeling and surgical/procedural experience, the recommended time interval between discontinuation of ticagrelor therapy and needle placement is 5 days (Conditional)

6.3.2 Neuraxial catheters should not be maintained with ticagrelor due to the rapid onset (Conditional)

6.3.3 Ticagrelor therapy may be resumed immediately after needle placement/catheter removal, provided a loading dose of the drug is not administered. If a loading dose is administered, we suggest a time interval of 6 hours between catheter removal and administration (Conditional)

6.4 Management of neuraxial block or deep plexus/peripheral block in the patient taking platelet GP IIb/IIa inhibitors

6.4.1 **The platelet GP IIb/IIIa inhibitors exert a profound effect on platelet aggregation. Following administration, the time to normal platelet aggregation is 24–48 hours for abciximab and 4–8 hours for eptifibatide and tirofiban. We recommend that needle placement should be avoided until platelet function—as impacted by the GP IIb/IIIa inhibitor—has recovered. Caution in patients on dual therapy who may still have residual NSAID effect (Strong)**

6.4.2 **Postoperative. Although GP IIb/IIIa antagonists are contraindicated within 4 weeks of surgery, should one be emergently administered in the postoperative period following a neuraxial or deep plexus/peripheral technique, we recommend the neuraxial infusion should be limited to drugs minimizing sensory and motor block to facilitate assessment of neurological function and that the patient be carefully monitored neurologically (Strong)**

6.4.3 **Timing of catheter removal is based on ongoing risk of thromboembolism and need for continued antithrombotic therapy and the potential for spinal bleeding during catheter maintenance and removal (Conditional)**

6.5 Management of neuraxial block or deep plexus/peripheral block in the patient taking Cilostazol

6.5.1 **The risk of serious bleeding in the presence of residual cilostazol effect is unknown. Based on the elimination half-life, we suggest that needle placement be avoided for 2 days after discontinuation of cilostazol (Conditional)**

6.5.2 **We suggest that neuraxial and deep plexus/peripheral catheters be removed prior to reinstitution of cilostazol therapy postoperatively (Conditional)**

6.5.3 **We suggest that the first postoperative dose of cilostazol be administered 6 hours after neuraxial or deep plexus/peripheral catheter removal (Conditional)**

6.6 Management of neuraxial block or deep plexus/peripheral block in the patient taking Cangrelor

6.6.1 **The risk of serious bleeding in the presence of residual cangrelor effect is unknown. Based on the elimination half-life, we suggest that needle placement be avoided for 3 hours after discontinuation of cangrelor (Conditional)**

6.6.2 **We suggest that neuraxial and deep plexus/peripheral catheters be removed prior to reinstitution of cangrelor therapy postoperatively (Conditional)**

6.6.3 **We suggest that the first postoperative dose of cangrelor be administered 8 hours after neuraxial or deep plexus/peripheral catheter removal (Conditional)**

7. Parenteral Direct Thrombin Inhibitors

Management of neuraxial block or deep plexus/peripheral block in the patient taking parenteral Thrombin inhibitors (Argatroban, Bivalirudin, and Desirudin)

7.1 **In patients receiving parenteral thrombin inhibitors, we suggest against the performance of neuraxial techniques (Conditional)**

Parenteral anti-Xa agents

7.2 Management of neuraxial block or deep plexus/peripheral block in the patient receiving Fondaparinux

Low-dose fondaparinux (2.5 mg once per day)

7.2.1 **We suggest holding low-dose fondaparinux (2.5 mg once per day) for 36 hours (young patients) to 42 hours (elderly patients) in healthy patients with normal renal function (Conditional)**

7.2.2 **We suggest holding fondaparinux for a minimum of 58 hours in patients with moderate renal insufficiency (CrCl 30–50 mL/min) (Conditional)**

7.2.3 **We suggest not performing neuraxial or deep plexus/peripheral blocks in patients with severe renal impairment (CrCl <30 mL/min) due to the 72 hours half-life (Conditional)**

7.2.4 **We suggest testing aXa activity calibrated to fondaparinux if placing the needle prior to these recommended times is considered (aXa ≤0.1 IU/mL) (Conditional)**

High-dose fondaparinux (5–10 mg once per day)

7.2.5 **We suggest holding high-dose fondaparinux (5-10 mg once per day) for a minimum of 70 hours (in young patients) and for a minimum of 105 hours (in elderly patients) with normal renal function (Conditional)**

7.2.6 **We suggest testing aXa activity calibrated to fondaparinux if placing needle prior to the recommended times is considered (aXa ≤0.1 IU/mL) (Conditional)**

7.2.7 **We suggest that neuraxial catheters be removed at least 6 hours *prior* to the first postoperative dose (Conditional)**

8. Fibrinolytic and Thrombolytic drugs

Management of neuraxial block or deep plexus/peripheral block in the patient receiving Thrombolytic therapy

8.1 **In patients scheduled to receive thrombolytic therapy, we recommend that the patient be queried, and the medical record reviewed for a recent history of lumbar puncture, spinal or epidural anesthesia, or epidural steroid injection to allow appropriate monitoring. Guidelines detailing original contraindications for thrombolytic drugs suggest avoidance of these drugs for 10 days following puncture of non-compressible vessels (Strong)**

8.2 **In patients who have received fibrinolytic and thrombolytic drugs, we recommend against needle placement for at least 48 hours. Documentation of normalization of clotting studies (including fibrinogen) is suggested (Strong)**

8.3 **In those patients who have received neuraxial blocks at or near the time of fibrinolytic and thrombolytic therapy, we recommend that frequent neurological monitoring (eg, every 2 hours) should be continued for at least 48 hours after the last dose. If neuraxial blocks have been combined with fibrinolytic and thrombolytic therapy and ongoing epidural catheter infusion, we recommend the infusion should be limited to drugs minimizing sensory and motor block to facilitate assessment of neurological function (Strong)**

9. Vitamin K antagonists (warfarin)

Management of neuraxial block or deep plexus/peripheral block in the patient on Warfarin

9.1 **We recommend that the anticoagulant therapy be stopped 5 days prior to the planned procedure, and the INR be measured and normalized (normal range of the local laboratory) prior to needle placement. (Strong)**

9.2 **In patients receiving an initial dose of warfarin prior to surgery, we suggest the INR should be checked prior to needle placement if the first dose was given >24 hours earlier, or if a second dose of oral anticoagulant has been administered (Conditional)**

9.3 **In patients receiving low-dose warfarin therapy during epidural analgesia, we suggest that their INR be monitored daily (Conditional)**

9.4 **We suggest that neuraxial catheters be removed when the INR is <1.5 (Conditional)**

9.5 **In patients with INR >1.5 but <3, the increased risk of maintaining a neuraxial catheter remains unknown. We suggest indwelling catheters may be maintained or removed with caution, closely following the INR and duration of warfarin therapy. (Conditional)**

9.6 **In patients with an INR >3, we recommend that the warfarin dose be held or reduced in patients with indwelling neuraxial catheters (Strong)**

9.7 **Neurological testing of sensory and motor function should be performed routinely during epidural analgesia for patients on warfarin therapy. To facilitate neurological evaluation, we recommend that the type of analgesic solution be tailored to minimize the degree of sensory and motor blockade (Strong)**

9.8 **We suggest that neurological assessment be continued for at least 48 hours following catheter removal (Conditional)**

10. Herbal medications

Management of neuraxial block or deep plexus/peripheral block in patients using Herbal therapy

10.1 **The use of herbal medications does not create a level of risk that will interfere with the performance of neuraxial blocks. We recommend against the mandatory discontinuation of these medications or avoidance of regional anesthetic techniques in patients on these medications (Strong)**

11. Management of neuraxial block in the anticoagulated parturient

11.1 **Given the limited pharmacological data on antithrombotic agents in pregnancy and in the absence of a large series of neuraxial techniques in the pregnant population receiving prophylaxis or treatment for venous thromboembolism, we suggest that the recommendations included in this document be applied to parturients (Conditional)**

11.2 **However, in circumstances involving select high-risk parturients receiving VTE prophylaxis, and requiring urgent interventions for maternal or fetal indications, the risk of general anesthesia may be greater than neuraxial anesthesia, and exceptions/modifications of these recommendations may be appropriate (Conditional)**

12. Antithrombotic therapy in pregnancy

Management of deep plexus/peripheral block in the anticoagulated patient

12.1 **For patients undergoing deep plexus or deep peripheral block, we recommend that guidelines for neuraxial block be similarly applied (Strong)**

12.2 **For patients undergoing other plexus or peripheral techniques, we suggest performance, catheter maintenance, and catheter removal be based on site compressibility, vascularity, and consequences of bleeding, should it occur (Conditional)**

Introduction

Hemorrhagic complications may occur after any neuraxial (spinal or epidural) or peripheral/plexus regional anesthetic technique. However, when the bleeding occurs within fixed, non-compressible, and/or concealed sites, such as the spinal canal or psoas compartment, the result may be catastrophic. The development and evolving status of standards for the prevention of perioperative venous thromboembolism (VTE), as well as the introduction of increasingly more potent antithrombotic medications, resulted in concerns regarding the heightened risk of neuraxial bleeding after neuraxial and deep plexus or deep peripheral blocks. In response to these ongoing patient safety issues, the American Society of Regional Anesthesia and Pain Medicine (ASRA PM) has published the fifth edition on 2025 **[1]** after four previous sets of evidence-based recommendations for the management of regional anesthesia in the patient receiving antithrombotic or thrombolytic therapy.

The previous European Society of Anaesthesiology (ESA) guidelines on 'regional anesthesia and antithrombotic agents' were published in 2010 **[2].** In the same year, ASRA also published its third edition of similar guidelines **[3].** The fourth edition of the ASRA guidelines in 2018 were the result of a collaboration with ESA to construct a single set of guidelines **[4].** As a result, the differences were only minimal. The most recent European guidelines were a collaborative effort of both the ESAIC and the ESRA and were published in February 2022 **[5].**

An understanding of the complexity of this issue is essential to patient management and these guidelines cannot be applied universally to the complex scenarios that may confront clinicians. Rather, the decision to perform spinal, epidural, or deep plexus/peripheral anesthesia/analgesia, as well as the timing of catheter removal in a patient receiving antithrombotic therapy, should be made on an individual basis.

The following recommendations are aimed at providing basic guidelines to anesthetic practice for Anesthesia for Regional anesthesia in the patient receiving antithrombotic or thrombolytic therapy. They are intended as a framework for reasonable and acceptable patient care and should be interpreted as such to allow for some degree of flexibility in different circumstances.

Purpose and Scope of the guidelines

The purpose of these guidelines is to assist anesthesiologists to enhance the quality of their anesthetic practice based on evidence for care of ***Regional anesthesia in the patient receiving antithrombotic or thrombolytic therapy***, leading to improve patient safety, improve in health indicators such as mortality and incidence and severity of regional anesthesia-related complications and to increase patient satisfaction.

These guidelines focus on the anesthetic management of ***Regional anesthesia in the patient receiving antithrombotic or thrombolytic therapy***

The intended patient population includes all patients **receiving *antithrombotic or thrombolytic therapy*** undergoing **neuraxial block or deep plexus/peripheral block.**

Target Audience

These guidelines are intended for use by healthcare professionals working as Anesthesiologists. They also may serve as a resource for healthcare professionals such as anesthesia Nurses,

perioperative care teams, policy makers, hospital managers, and other stakeholders who advise or care for patients who will receive regional anesthesia care .
All physicians applying for privileges in anesthesia should show satisfactory completion of specialist postgraduate training in anesthesiology, standard training in the Egyptian Board program, University programs or equivalent.

METHODOLOGY

A comprehensive search for guidelines was done to identify the most relevant ones to consider for adaptation. For the literature review, potentially relevant clinical studies were identified *via* electronic and manual searches of the literature. The updated searches covered a 10-year period from January 1, 2015, to December 31, 2025. The inclusion/exclusion criteria that were followed in the search and retrieval of guidelines are adapted.

We selected guidelines only if they are:

- Evidence-based guidelines.
- National and/or international guidelines.
- Guidelines published from 2015 to 2025.
- Peer reviewed publications.
- Guidelines written in English language.

We Excluded guidelines that are:

- Written by a single author not on behalf of an organization as guideline to be valid and comprehensive, ideally requires multidisciplinary input.
- Published without references as the panel needs to know whether a thorough literature review was conducted and whether the current evidence was used in the preparation of the recommendations.

All retrieved Guidelines were screened and appraised using AGREE II instrument (www.agreetrust.org) by at least three members of the GDG. The panel decided on a cut-off point or ranked the guidelines (any guideline scoring above 50% on the rigor dimension was retained).

Guidelines used in the Adaptation Process:

The basic elements of the international guidelines for the management of regional anesthesia in the patient receiving antithrombotic or thrombolytic therapy published by international societies can be successfully implemented in the practice of regional anesthesia worldwide. The Guidelines Development Group (GDG) for the Egyptian Board of Anesthetics, Surgical Intensive Care, and Pain Management has adopted with modification:

1. Kopp SL, Vandermeulen E, McBane RD, Perlas A, Leffert L, Horlocker T. Regional anesthesia in the patient receiving antithrombotic or thrombolytic therapy: American Society of Regional Anesthesia and Pain Medicine. Evidence-Based Guidelines (fifth edition). Regional Anesthesia & Pain medicine. 2025 http://orcid.org/0000-0003-2997-5445 **(Reference No. 1)**

2. Horlocker TT , Vandermeuelen E , Kopp SL , *et al*. Regional Anesthesia in the Patient Receiving Antithrombotic or Thrombolytic Therapy: American Society of Regional Anesthesia and Pain Medicine Evidence-Based

Guidelines (Fourth Edition). Reg Anesth Pain Med 2018;**43**:263–309. doi:10.1097/AAP.0000000000000763 **(Reference No. 4)**

3. Kietaibl S , Ferrandis R , Godier A , *et al* . Regional anaesthesia in patients on antithrombotic drugs: Joint ESAIC/ESRA guidelines. Eur J Anaesthesiol 2022;**39**:100-32. doi:10.1097/EJA.0000000000001600 **(Reference No. 5)**

4. Narouze S, Benzon HT, Provenzano D , *et al*. Interventional Spine and Pain Procedures in Patients on Antiplatelet and Anticoagulant Medications (Second Edition): Guidelines From the American Society of Regional Anesthesia and Pain Medicine, the European Society of Regional Anaesthesia and Pain Therapy, the American Academy of Pain Medicine, the International Neuromodulation Society, the North American Neuromodulation Society, and the World Institute of Pain. Reg Anesth Pain Med 2018;**43(3)**:225-262. doi:10.1097/AAP.0000000000000700 **(Reference No. 6)**

5. Benzon HT, Nelson AM, Patel AG , *et al*. Literature review of spinal hematoma case reports: causes and outcomes in pediatric, obstetric, neuraxial and pain medicine cases. Reg Anesth Pain Med 2024. doi:10.1136/rapm-2023-105161 **(Reference No. 7)**

6. Douxfils J , Ageno W , Samama C-M , *et al*. Laboratory testing in patients treated with direct oral anticoagulants: a practical guide for clinicians. J Thromb Haemost 2018;**16**:209–19. doi:10.1111/jth.13912 **(Reference No. 17)**

7. Douketis JD , Spyropoulos AC , Murad MH , *et al*. Executive Summary: Perioperative Management of Antithrombotic Therapy: An American College of Chest Physicians Clinical Practice Guideline. Chest 2022;**162**:1127–39. doi:10.1016/j.chest.2022.08.004 **(Reference No. 58)**

8. Leffert LR, Dubois HM, Butwick AJ , *et al*. Neuraxial Anesthesia in Obstetric Patients Receiving Thromboprophylaxis With Unfractionated or Low-Molecular-Weight Heparin: A Systematic Review of Spinal Epidural Hematoma. Anesth Analg 2017;**125**:223–31. doi:10.1213/ANE.0000000000002173 **(Reference No. 93)**

9. Tsui BCH, Kirkham K, Kwofie MK , *et al*. Practice advisory on the bleeding risks for peripheral nerve and interfascial plane blockade: evidence review and expert consensus. Can J Anaesth 2019;**66**:1356–84. doi:10.1007/s12630-019-01466-w **(Reference No. 100)**

Strength of Recommendations

The strength of a recommendation communicates the importance of adherence to the recommendation.

Strong Recommendations	The GDG found that the desirable effects of adherence to the recommendation outweigh the undesirable effects. This means that in most situations the recommendation can be adopted.
Conditional Recommendations	This means that the GDG found that there is: ▪ Greater uncertainty about the strength of evidence, or ▪ The recommendation may account for a greater variety in patient values and preferences, or ▪ The resource use makes the intervention suitable for some, but not for other locations. Conditional recommendations are still the best available evidence to date, and it can be adopted if it meets the conditions mentioned with it.
Good Practice Statement (GPS)	Statements based on expert opinion of respected authorities, and the guidelines development group.

Evidence level

Evidence Assessment

According to WHO Handbook for Guidelines, we used the GRADE (Grading of Recommendations, Assessment, Development and Evaluation) approach to assess the quality of a body of evidence, develop and report recommendations. GRADE methods are used by WHO because these represent internationally agreed standards for making transparent recommendations.

Detailed GRADE information is available on the following sites:

- GRADE working group: https://www.gradeworkinggroup.org/
- GRADE online training modules: http://cebgrade.mcmaster.ca/

Quality Definition Implications

Evidence is categorized as High, Moderate, Low and Very low.

Table 1: Quality and Significance of the Four Levels of Evidence in GRADE:

Quality	Definition	Implications
High	The guideline development group is very confident that the true effect lies close to that of the estimate of the effect.	Further research is very unlikely to change confidence in the estimate of effect
Moderate	The guideline development group is moderately confident in the effect estimate: the true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different.	Further research is likely to have an important impact on confidence in the estimate of effect and may change the estimate
Low	Confidence in the effect estimate is limited: the true effect may be substantially different from the estimate of the true effect.	Further research is very likely to have an important impact on confidence in the estimate of effect and is unlikely to change the estimate
Very low	The group has very little confidence in the effect estimate: the true effect is likely to be substantially different from the estimate of the effect.	Any estimate of effect is very uncertain

RECOMMENDATIONS

These Guidelines deal with the cornerstone steps of Regional anesthesia in the patient receiving antithrombotic or thrombolytic therapy.

The main source of these guidelines is : Regional anesthesia in the patient receiving antithrombotic or thrombolytic therapy: American Society of Regional Anesthesia and Pain Medicine (ASRA PM) Evidence-Based Guidelines (fifth edition) January 2025 [1].

1. Administration of thromboprophylaxis

1.1 For each of the antithrombotic agents, we suggest that clinicians follow the FDA-approved dosing guidelines. (Conditional, High evidence)

	For thromboprophylaxis follow the FDA-approved dosing guidelines
Strength	**Conditional**
Benefit of Direction	Beneficial, Favorable
Evidence	**High** evidence: FDA Drug Labeling for individual antithrombotic agents*, ASRA/ESRA/ AAPM consensus**
Remarks	Since an individualized approach to thromboprophylaxis is complex, most recommendations are group-specific, with modifications based on the presence/absence of additional risk factors.

***FDA** Drug Labeling for individual antithrombotic agents provides the primary evidence base for dosing safety and pharmacokinetics used by guideline panels. Following FDA-approved dosing reduces risk of excess anticoagulant effect, spinal/epidural hematoma and bleeding complications and also promotes standardized, evidence-based prescribing.
Narouze, et al. (ASRA/ESRA consensus) **[6] recommends adherence to FDA labeling when managing antithrombotics around neuraxial/interventional procedures. Horlocker, et al**.** **[4]** Emphasizes use of manufacturer/FDA dosing and timing due to bleeding risk with neuraxial techniques. On 2024, a literature review of 940 spinal hematoma cases finds that most are spontaneous across all populations, with some linked to anticoagulants, trauma, or neuraxial procedures **[7].**

The agent, dosing regimen, and duration of thromboprophylaxis is based on identification of risk factors, both individual (eg, age, gender, history of thromboembolism) and group-specific (eg, primary reason for hospitalization, surgery, medical illness) **[8].** (**Appendix, Table 1)** Depending on the risks of thromboembolism and bleeding, thromboprophylaxis may be achieved with intermittent compression devices, with medications, or a combination of both. A logical approach to VTE prophylaxis begins with individualized risk assessment. Several well-validated risk assessment tools are available for individualized patient-specific guidance including both medical and surgical indications. For patients hospitalized with a medical condition, the PADUA **[9]** and IMPROVE **[10]** risk tools provide a well-validated framework for assessing which patients will most benefit from VTE prophylaxis. **(Appendix, Table 2)** Similar risk assessment tools are available for the surgical patient population. The Caprini and Rogers tools assign risk based on a number of surgery-specific and other clinical variables **[11].**

2. Direct oral anticoagulants (DOAC)

2.1 Management of neuraxial block or deep plexus/peripheral block in the patient receiving a High dose of Apixaban (Eliquis)

2.1.1 **We suggest that a high dose of apixaban be discontinued at least 72 hours prior to neuraxial block or deep plexus/peripheral block. Consider checking apixaban or aXa plasma level if <72 hours. (Conditional, Low evidence)**

2.1.2 **We suggest that a residual apixaban plasma level <30 ng/mL or a residual aXa activity plasma level ≤0.1 IU/mL is acceptable prior to neuraxial block or deep plexus/peripheral block. (Conditional, Low evidence)**

2.1.3 **We suggest that needle placement/catheter removal occurs at least 24 hours prior to the first postoperative dose. (Conditional, Low evidence)**

2.2 Management of neuraxial block or deep plexus/peripheral block in the patient receiving a Low dose of Apixaban (Eliquis)

2.2.1 **We suggest that a low dose of apixaban be discontinued for at least 36 hours prior to neuraxial block or deep plexus/peripheral block. Consider checking apixaban or aXa plasma level if <36 hours. (Conditional, Low evidence)**

2.2.2 **We suggest that a residual apixaban plasma level <30 ng/mL or a residual aXa activity plasma level ≤0.1 IU/mL is acceptable prior to neuraxial block or deep plexus/peripheral block. (Conditional, Low evidence)**

2.2.3 **We suggest that needle placement/catheter removal occurs at least 6 hours prior to the first postoperative dose. (Conditional, Low evidence)**

2.3 Management of neuraxial block or deep plexus/peripheral block in the patient receiving a high dose of edoxaban (Savaysa)

We suggest that a high dose of edoxaban be discontinued for at least 72 hours prior to neuraxial block or deep plexus/peripheral block. Consider checking edoxaban or aXa activity plasma level if <72 hours. (Conditional, Low evidence)

2.3.1 **We suggest that a residual edoxaban plasma level <30 ng/mL or a residual aXa activity plasma level ≤0.1 IU/mL is acceptable prior to neuraxial block or deep plexus/peripheral block. (Conditional, Low evidence)**

2.3.2 **We suggest that needle placement/catheter removal occurs at least 24 hours prior to the first (postoperative) dose. (Conditional, Low evidence)**

2.4 Management of the patient receiving a Low dose of Edoxaban (Savaysa)

There is no FDA-approved medical indication for low-dose edoxaban.

2.5 Management of neuraxial block or deep plexus/peripheral block in the patient receiving High dose of Rivaroxaban (Xarelto)

2.5.1 **We suggest that a high dose of rivaroxaban be discontinued for at least 72 hours prior to neuraxial block or deep plexus/peripheral block. Consider checking rivaroxaban or aXa activity plasma level if <72 hours. (Conditional, Low evidence)**

2.5.2 **We suggest that a residual rivaroxaban plasma level <30 ng/mL or a residual aXa activity plasma level ≤0.1 IU/mL is acceptable prior to neuraxial block or deep plexus/peripheral block. (Conditional, Low evidence)**

2.5.3 **We suggest that needle placement/catheter removal occurs at least 24 hours prior to the first postoperative dose. (Conditional, Low evidence)**

2.6 Management of neuraxial block or deep plexus/peripheral block in the patient receiving a Low dose of Rivaroxaban (Xarelto)

2.6.1 **We suggest that a low dose of rivaroxaban be discontinued for at least 24 hours (30 hours if CrCl <30 mL/min) prior to neuraxial block or deep plexus/peripheral block. Consider checking rivaroxaban or aXa activity plasma level if <24 hours. (Conditional, Low evidence)**

2.6.2 **We suggest that a residual rivaroxaban plasma level <30 ng/mL or a residual aXa activity plasma level ≤0.1 IU/mL [1] is acceptable prior to neuraxial block or deep plexus/peripheral block. (Conditional, Low evidence)**

2.6.3 **We suggest that needle placement/catheter removal occurs at least 6 hours prior to the first postoperative dose. (Conditional, Low evidence)**

2.7 Management of neuraxial block or deep plexus/peripheral block in the patient receiving a High dose of Dabigatran (Pradaxa)

2.7.1 **We suggest that a high dose of dabigatran be discontinued for at least 72 hours in patients with a CrCl ≥50 mL/min prior to neuraxial block or deep plexus/ peripheral block. Consider checking dabigatran plasma level if <72 hours. (Conditional, Low evidence)**

2.7.2 **We suggest that a high dose of dabigatran be discontinued for 120 hours in patients with a CrCl 30–49 mL/min prior to neuraxial block or deep. plexus/peripheral block. Consider checking dabigatran plasma level if <120 hours.(Conditional, Low evidence)**

2.7.3 **We suggest against the performance of neuraxial or deep plexus/peripheral blocks in patients with a CrCl <30 mL/min unless a dabigatran plasma level is obtained and <30 ng/mL. (Conditional, Low evidence)**

2.7.4 **Prior to neuraxial block or deep plexus/peripheral block we suggest that a residual dabigatran plasma level <30 ng/mL is acceptable. (Conditional, Low evidence)**

2.7.5 **We suggest that needle placement/catheter removal occurs at least 24 hours prior to the first postoperative dose. (Conditional, Low evidence)**

2.8 Management of neuraxial block or deep plexus/peripheral block in the patient receiving a Low dose of Dabigatran (Pradaxa)

2.8.1 **We suggest that a low dose of dabigatran be discontinued for at least 48 hours prior to neuraxial block or deep plexus/peripheral block. Consider checking dabigatran plasma level if <48 hours. (Conditional, Low evidence)**

2.8.2 **We suggest that a residual dabigatran plasma level <30 ng/mL is acceptable prior to neuraxial block or deep plexus/peripheral block (Conditional, Low evidence)**

2.8.3 **We suggest against the performance of neuraxial or deep plexus/peripheral blocks in patients with a CrCl <30 mL/min unless a dabigatran plasma level is obtained and <30 ng/mL. (Conditional, Low evidence)**

2.8.4 **We suggest that needle placement/catheter removal occurs at least 6 hours prior to the first postoperative dose. (Conditional, Low evidence)**

	Guidelines for management of neuraxial block or deep plexus/peripheral block in the patient receiving current medications known as DOACs consist of the oral direct Xa antagonists (DXA) apixaban (Eliquis), edoxaban (Savaysa), and rivaroxaban (Xarelto). Dabigatran (Pradaxa) is an oral direct thrombin inhibitor (DTI).
Strength	**Conditional**
Benefit of Direction	Beneficial
Evidence	**Low:** ASRA PM, 2025*, Large international, multicenter the PAUSE trial**, ACCP and European Heart Rhythm Association (EHRA) ***, ACCP and the ESAIC†, European guidelines of the Joint ESAIC/ESRA guidelines,2022††
Remarks	The use of routine coagulation tests such as the prothrombin time (PT) or the activated partial thromboplastin time (aPTT) should not be used to assess the degree of anticoagulation produced by the DOACs, as there is a large variability in the sensitivity of the reagent used in the different tests.

*In previous versions of the guidelines, the anticoagulant doses were described as prophylactic and therapeutic. Recent guidelines **[1]** using '**low dose**' and '**high dose**,' allowed the authors to be consistent with other published guidelines and more accurately describe the dose in the setting of specific patient characteristics and indications. A table showing the 'low' and 'high' doses of the various DOACs and their indications are shown in the Appendix, Table 3.

** The recent large international, multicenter "The Perioperative Anticoagulation Use for Surgery Evaluation" (**PAUSE**) trial reported the residual DOAC plasma levels after high doses of apixaban, dabigatran, and rivaroxaban, in 3007 patients with Non-valvular atrial fibrillation (NVAF), immediately prior to an invasive procedure **[12].**

***Both the ACCP and European Heart Rhythm Association (EHRA) recommend that the postoperative resumption of DOAC therapy, irrespective of the dose used, be delayed for 24 hours after a procedure with a low/moderate bleeding risk, and for 48–72 hours after a procedure with high bleeding risk, and only to be administered when adequate surgical hemostasis has been accomplished **[1,13].** In the interim, a prophylactic/low-dose anticoagulant, such as LMWH or UFH, can be considered in patients at high thrombotic risk **[1,13].**

† The most recent guidelines on VTE prophylaxis from the ACCP **[1]** and the ESAIC **[14,15]** were helpful to recommend the timing to resume a DOAC treatment after a neuraxial intervention (ie, the removal of the neuraxial catheter). VTE prophylaxis (ie, low dose) should be resumed/started 6 hours postoperatively, while therapeutic anticoagulation should be restarted ≥24 hours postoperatively **[14,15].**
In 2007, Rosencher *et al* recommended that the next/first postoperative dose of an antithrombotic agent to be administered ≥6 hours; i.e., 8 hours (the time needed for an initial platelet plug to solidify) minus T_{max} (the onset time of a drug, which is 2–3 hours for the DOACs) after surgery **[16].** †† The most recent European guidelines were a collaborative effort of both the ESAIC and the ESRA and were published in February 2022 **[5].**

The anticoagulant effect of DXAs can be reliably measured using drug-specific, calibrated anti-X activity (aXa) assays **[12,17-19].** A non-detectable anticoagulant effect is defined as a drug-specific threshold plasma level <30 ng/mL **[12, 18].** If drug-specific calibrated aXa assays are not available, a clinically relevant DXA effect can be ruled out by the use of UFH-calibrated or LMWH-calibrated chromogenic aXa assays **[17,20].** In these cases, an aXa activity of 0.1 IU/mL or less is considered to be an undetectable anticoagulant effect **[12,17-19].** *The availability of these tests throughout the USA and the rest of the world is presently unreliable. We provide recommendations and threshold values with the hope that these tests become more routine and the results more immediate.*

Although never clinically validated **[17,18],** most experts and international anesthesiology societies consider a DOAC plasma level <30 ng/mL as a safe hemostatic threshold **[21]** to avoid bleeding. Recent prospective data have become available on the residual anticoagulant effect following a standardized preoperative interruption of high doses of DOACs.

In the previous guidelines, the pharmacokinetic properties and expert opinion were key elements to recommend therapy-free time intervals to enable the safe performance of a neuraxial or deep plexus intervention in patients treated with a DOAC. A neuraxial anesthetic intervention is considered a high bleeding risk procedure as bleeding would have important consequences not so much in terms of blood loss, but mainly in terms of a neurological deficit caused

by bleeding into a confined space **[13, 22].** It is therefore recommended that a complete return of normal hemostasis is required before any neuraxial or deep plexus/peripheral block is performed.

3. Use of Direct oral anticoagulant (DOAC) antidotes to facilitate placement of neuraxial block or deep plexus/peripheral block

3.1 Suggest *against* the use of idarucizumab, andexanet alfa, prothrombin complex concentrates (PCC), or activated prothrombin complex concentrates (aPCC) to reverse DOAC anticoagulant activity to enable the safe performance of a neuraxial intervention in routine patients (Conditional, Low evidence)

Guideline	Suggest against reversal of the DOAC anticoagulant activity to enable the safe performance of a neuraxial intervention in routine patients
Strength	**Conditional**
Benefit of Direction	Favors NOT using reversal agents routinely.
Evidence	**Low:** Based mainly on indirect evidence, pharmacologic reasoning*, FDA approval** and safety concerns rather than robust clinical trials. Observational studies*****,** ASRA PM, ESRA and Pain Therapy
Remarks	Routine pharmacologic reversal solely to permit neuraxial block is discouraged; follow recommended DOAC discontinuation intervals instead.

*Andexanet alfa (Andexxa) is a recombinant protein that is indicated in patients treated with rivaroxaban or apixaban, where reversal of anticoagulation is needed due to life-threatening or uncontrolled bleeding.
Whether or not the remaining plasma levels of aXa activity after andexanet alfa administration are predictive of the risk of a neuraxial bleeding still remains unclear. In addition, current commercial aXa assays are unsuitable for measuring the remaining factor Xa activity following administration of andexanet alfa **[23].** Finally, re-elevation or incomplete reversal of anticoagulant activity may occur because of andexanet alfa's short terminal half-life (ie, 5–7 hours) and its ability to displace DXAs from the extravascular to the intravascular compartment **[24].**

Idarucizumab (Praxbind) is a humanized monoclonal antibody fragment. In October 2015, idarucizumab was approved by the FDA to be used in adult patients treated with dabigatran, when rapid reversal of its anticoagulant effects is required in situations of emergency surgery/urgent procedures or life-threatening or uncontrolled bleeding **[25]. Also, there are no controlled investigations on the use of reversal agents specifically aimed at neuraxial anesthetic techniques.

***The use of procoagulant agents such as prothrombin complex concentrates (PCC) or activated prothrombin complex concentrates (aPCC) may be an option if specific antidotes for the reversal of the DOACs are not available or are too costly **[1, 13].** observational studies (some retrospective) have shown the efficacy of PPC or aPCC in DOAC-treated patients who were actively bleeding **[26].** There are no data evaluating the use of PCC or aPCC for reversal in patients treated with DOACs and planned for a neuraxial intervention. If surgery can be postponed allowing spontaneous recovery of normal hemostasis, discontinuation of the antithrombotic drug is the preferred strategy. If waiting is not an option and reversal is needed for the safe conduct of the surgery itself, regional anesthetic techniques may be considered after full dabigatran reversal by idarucizumab.

4. Intravenous and Subcutaneous Unfractionated Heparin

Management of neuraxial block or deep plexus/peripheral block in the patient receiving Unfractionated Heparin.

4.1 We recommend daily review of the patient's medical record to determine the concurrent use of medications that affect other pathways of hemostasis. These medications include antiplatelet medications, LMWH, and oral anticoagulants (Strong, Moderate evidence)

	Review of the concurrent use of patient's medications that may affect other pathways of hemostasis.
Strength	**Strong**
Benefit of Direction	Beneficial (risk reduction, Clear safety benefit with minimal downside)
Evidence	**Moderate:** ASRA PM evidence-based guidelines (5th edition)*, expert consenus primarily derived from pharmacodynamic knowledge, observational safety data and case reports of spinal/epidural hematoma**
Remarks	Detects additive or synergistic anticoagulant effects

*Supporting evidence cited by ASRA PM (Fifth edition) **[1]** included case series linking neuraxial hematoma to multiple hemostasis-altering drugs, pharmacologic data showing additive anticoagulant effects and National and international hematoma registries.

** This recommendation was based on expert consensus emphasizing patient safety and prevention of neuraxial hematoma. Three factors associated with the increased risk of hematoma were identified: <60 min time interval between the administration of heparin and lumbar puncture, traumatic needle placement, and concomitant use of aspirin. These risk factors have been verified in subsequent large reviews of case reports of hematomas associated with neuraxial procedures in the presence of Unfractionated Heparin (UFH) **[27,28]**.

4.2 Since heparin-induced thrombocytopenia (HIT) may occur during heparin administration, we recommend that patients receiving intravenous or subcutaneous UFH for >4 days have a platelet count assessed (Strong, Low evidence)

	Assessment of Platetlet count in patients receiving IV or SC UFH for >4 days.
Strength	**Strong**
Benefit of Direction	Beneficial: Early detection of HIT.
Evidence	**Low:** ASRA PM evidence-based guidelines (5th edition)*, based primarily on observational data, case reports, and known epidemiology of HIT rather than randomized trials**.
Remarks	Awareness of both rapid-onset and delayed-onset HIT may prevent adverse therapeutic outcomes.

*Platelet count monitoring is inexpensive and noninvasive → therefore ASRA PM **[1]** issued a strong recommendation despite low-quality evidence. HIT incidence with UFH ≈ **0.1–5%**, highest after day 4, And complication risk (thrombosis) can reach 30–50% if untreated.

There is a subset of patients who will develop heparin-induced thrombocytopenia (HIT) after being on heparin for >5 days, resulting in a decreased platelet count **[29]. For this reason, patients receiving intravenous or subcutaneous UFH for >4 days should have a platelet count assessed prior to neuraxial block or catheter removal. While the typical onset of HIT occurs within 5–14 days following heparin initiation, patients with a recent heparin exposure within the past 30 days may develop rapid-onset HIT on heparin re-exposure **[30,31].** Thrombocytopenia, on re-presentation, may be mild to moderate. Importantly, heparin re-exposure may worsen clinical outcomes.

4.3 Intravenous heparin

4.3.1 Discontinue Intravenous heparin infusion for a minimum of 4–6 hours and coagulation status be assessed and normal prior to neuraxial block or deep plexus/peripheral block (Strong, High evidence)

4.3.2 Delay intravenous heparin administration for a minimum of 1 hour after needle placement (Strong, High evidence)

4.3.3 It is not recommended to maintain neuraxial or deep plexus catheters in the setting of continuous intravenous heparin administration. In the event of unanticipated heparinization, we recommend monitoring the patient with an indwelling catheter to allow for early detection of motor deficits and consider use of minimal concentration of local anesthetics to enhance early detection of a neuraxial hematoma (Strong, High evidence)

4.3.4 Although the occurrence of a bloody or difficult neuraxial needle placement may increase the risk of hematoma, there are no data to support mandatory cancellation of a case. Direct communication with the surgeon and a specific risk-benefit decision about proceeding in each case is recommended (Strong, High evidence)

	Intravenous UFH management in patients undergoing neuraxial or deep plexus blocks.
Strength	**Strong**
Benefit of Direction	Beneficial: reduces the risk of spinal/epidural hematoma.
Evidence	**High:** ASRA PM guidelines (fifth edition)*. Case series and case reports**,epidemiological surveys, the ASA Closed Claims database, and Supporting pharmacologic and observational data on UFH half-life.
Remarks	IV UFH has a short but clinically significant anticoagulant effect. Waiting ≥4–6 hours allows clearance of heparin activity and normalization of aPTT/coagulation status

*Intraoperative heparinization typically involves injection of 5000–10 000 units of heparin IV during the operative period, particularly in the setting of vascular surgery to prevent coagulation during cross-clamping of arterial vessels**[32].** Neuraxial anesthetic techniques may be considered for these patients, but the increased risk of neuraxial hematoma, as demonstrated by case series, epidemiological surveys, and the ASA Closed Claims database needs to be considered **[33-35].**

* According to ASRA PM guidelines (fifth edition) **[1],** maintaining a minimum 1-hour interval between needle placement and heparinization, as well as avoiding other hemostasis-altering medications, decreases the risk of significant bleeding.

Heparinization may be continued into or initiated in the postoperative period. However, the removal of a neuraxial catheter in the presence of heparin therapy increases the risk of hematoma formation. In a series by Vandermeulen *et al*, half of the spinal hematomas associated with intravenous heparinization were detected at the time of catheter removal **[34]. The risk of hematoma resulting from catheter removal has led to the recommendation that in patients who have undergone systemic heparinization, the heparin should be discontinued for 4–6 hours and the coagulation status assessed prior to neuraxial catheter manipulation or removal **[3].**

Management of a traumatic neuraxial procedure must also be considered. Previous case reports suggest that presence of a bloody tap or a traumatic regional block was an associated factor in approximately 50% of spinal hematomas **[34]. Although some investigators have recommended cancellation of the surgical procedures if these events occur **[36],** there are no clinical data to support this recommendation **[37].** Direct communication with the surgeon and a specific risk-benefit decision about proceeding in each case is recommended.

Heparinization during cardiopulmonary bypass

4.3.5 It is not recommended to maintain neuraxial or deep plexus/peripheral catheters in the setting of full anticoagulation during cardiac surgery. If unanticipated heparinization occurs, we suggest postoperative monitoring of neurological status and consider use of minimal concentration of local

anesthetics to enhance early detection of neuraxial hematoma. (Conditional, Low)

	Heparinization during cardiopulmonary bypass surgery with neuraxial or deep plexus/peripheral catheters
Strength	**Conditional**
Benefit of Direction	Beneficial, Favors the recommendation (risk reduction)
Evidence	**Low:** Based mainly on case reports, observational data, and expert consensus*. No randomized trials due to ethical constraints.
Remarks	Enables earlier detection of neurologic compromise if anticoagulation occurs unexpectedly. Minimizes masking of neurologic deficits by dense local anesthetic block

*To date, there is a single case of spinal hematoma following the full heparinization associated with cardiopulmonary bypass **[38].** However, these series involve small numbers of patients. Using a mathematical analysis of the probability of predicting a rare event and based on the total of 4583 epidural and 10 840 spinal anesthetics reported without complications, Ho *et al* estimated the risk of hematoma to be approximately 1:1528 for epidural and 1:3610 for spinal technique **[39].** Thus, this analgesic technique remains controversial in that the risk appears too great for the perceived benefits. Neuraxial anesthetics are therefore not recommended in the setting of high-dose anticoagulation and cardiopulmonary bypass.

4.4 Subcutaneous heparin

4.4.1 Preoperative low-dose UFH for thromboprophylaxis (5000 U two times per day or three times per day). We suggest needle placement occur a minimum of 4–6 hours after heparin administration or coagulation status be assessed and normal. (Conditional, Low evidence)

4.4.2 Preoperative high dose UFH

7500–10 000 U two times per day or a daily dose of ≤20 000 U

We suggest neuraxial block occur a minimum of 12 hours after subcutaneous heparin administration and confirmation of normal coagulation status. (Conditional, Low evidence)

>10 000 U subcutaneously per dose, or >20 000 U total daily dose

We suggest neuraxial block occur a minimum of 24 hours after subcutaneous heparin administration and confirmation of normal coagulation status. (Conditional, Low evidence)

4.4.3 Postoperative low-dose UFH

There is no contraindication to maintaining neuraxial catheters in the presence of low-dose UFH. We suggest catheter removal occurs a minimum of 4–6 hours after heparin administration. Subsequent heparin administration may occur immediately after catheter removal. (Conditional, Low evidence)

4.4.4 Postoperative high-dose UFH

The safety of indwelling neuraxial catheters in patients receiving doses >5000 U at a time or >15 000 U of UFH daily has not been established. We suggest that the risk and benefits be assessed on an individual basis and that techniques to facilitate detection of new/progressive neurological deficits (eg, enhanced neurological

monitoring occur and neuraxial solutions to minimize sensory and motor block) be applied. (Conditional, Low evidence)

	Subcutaneous Heparin management in patients undergoing neuraxial or deep plexus blocks.
Strength	**Conditional**
Benefit of Direction	Benefit > Risk (minimizes neuraxial bleeding risk while avoids unnecessary delay of thromboprophylaxis)
Evidence	**Low:** Several published case series and observational reports *, ASRA PM guidelines (fifth edition)**, pharmacokinetic studies. No high-quality RCTs specifically define the safest interval.
Remarks	Current recommendations of perioperative thromboprophylaxis, are based on the pharmacology of a SC 5000-unit dose of UFH, which results in an onset of anticoagulant effect 1 hour after administration that persists for 4–6 hours. Checking coagulation when timing is uncertain adds an additional safety layer.

Administration of 5000 units of heparin subcutaneously 2 or 3 times daily has been used extensively and is effective for prophylaxis against DVT. However, approximately 15% of patients may develop measurable changes in coagulation, with the aPTT rarely exceeding 1.5 times the normal level and normalizing within 4–6 hours after administration **[40].**

*The widespread use of SC heparin and the paucity of complications suggest that there is little risk of spinal hematoma associated with this therapy. There are 10 published series totaling over 12 000 patients who have received this therapy without complications. Three series, with a combined total of over 7000 patients who received epidural analgesia in the presence of 5000 units of heparin three times a day, reported no spinal hematomas **[41-43].** There are only five case reports of neuraxial hematomas: four epidural **[34, 44],** and one spinal **[45],** during neuraxial block with the use of subcutaneous heparin.

The safety of high-dose subcutaneous UFH (doses >5000 units or total daily dose >15 000 units) remains controversial due to the marked variability in patient response to these dosing regimens. According to ASRA PM guidelines (fifth edition) **[1] timing of assessment of coagulation status for residual heparin effect is based on dose and frequency of dosing. For example, for individual heparin dose of 7500–10 000 U two times per day or a daily dose of ≤20 000 U, it is suggested neuraxial block occur 12 hours after subcutaneous heparin administration *and* assessment of coagulation status with a normal aPTT. Likewise, for individual heparin dose >10 000 U subcutaneously per dose, or >20 000 U total daily dose, it is suggested neuraxial block occurs 24 hours after subcutaneous heparin administration *and* assessment of coagulation status with a normal aPTT **[3].**

5. Low Molecular Weight Heparin (LMWH)

5.1 Management of neuraxial block or deep plexus/peripheral block in the patient receiving low molecular weight heparin

5.1.1 The aXa level is Not predictive of the risk of bleeding, although it may be useful in monitoring efficacy of therapy with high-dose regimens. We recommend against the *routine* use of aXa level monitoring. (Strong, Low evidence)

5.1.2 Heparin-induced thrombocytopenia may occur during LMWH administration; therefore, we recommend that patients receiving LMWH for >4 days have a platelet count assessed prior to needle placement. (Strong, Low evidence)

5.1.3 The presence of blood during needle and catheter placement does not necessitate postponement of surgery. We suggest that initiation of LMWH therapy in this setting should be delayed for 24 hours postoperatively and that this consideration be discussed with the surgeon. (Strong, Low evidence)

	Management of neuraxial block or deep plexus/peripheral block in the patient receiving LMWH
Strength	**Strong**
Benefit of Direction	Benefit > Risk
Evidence	**Low:** ASRA PM guidelines (fifth edition) based mainly on many observational data, case reports, and extrapolation from UFH-associated HIT risk rather than randomized trials*.
Remarks	Platelet count is useful because of the possibility of Heparin-induced thrombocytopenia with the use of LMWH.

*The anticoagulant effect of LMWH is most readily assessed by the aXa activity. Because of reduced protamine binding to LMWH fractions, only the anti-IIa activity of LMWH is completely reversed; the aXa activity is not fully neutralized. Both anti-IIa and aXa activity may return up to 3 hours after protamine reversal **[46].** The aXa level above which is associated with significant bleeding risk remains unknown. An aXa level of ≤0.1 IU/mL is considered an undetectable anticoagulant effect **[17-19].**

5.2 Preoperative LMWH

5.2.1 In patients receiving low-dose LMWH, we recommend delay of at least 12 hours prior to needle/catheter placement. (Stong, Low evidence)

5.2.2 In patients receiving high (therapeutic) doses of LMWH, we recommend delay of at least 24 hours prior to needle/catheter placement. (Stong, Low evidence)

	Management of patients on Low-dose/High-dose LMWH with needle/catheter placement
Strength	**Strong**
Benefit of Direction	Benefit > Risk
Evidence	**Low:** expert consensus from ASRA, Pharmacokinetic data, Large observational series, FDA safety data, Consistent expert consensus
Remarks	**Low-dose LMWH**: enoxaparin 40 mg/day, enoxaparin 30 mg every 12 hours, dalteparin 5000 IU daily. **High-dose LMWH**: enoxaparin 1 mg/kg every 12 hours, enoxaparin 1.5 mg/kg daily, dalteparin 120 IU/kg every 12 hours, dalteparin 200 IU/kg daily, or tinzaparin 175 IU/kg daily.

*Consistent expert consensus from ASRA **[1]** and ESAIC/European Society of Anesthesiology (ESA), Pharmacokinetic data, Large observational series and FDA safety data. The 12 hours (for prophylactic dose corresponds to decline of anti-Xa activity to safer levels while the 24 hours **(**therapeutic dosing) produces higher and more sustained anti-Xa levels. With high-dose LMWH, it is recommended that the last dose should occur at least 24 hours preoperatively and the last dose should be halved in patients with moderate (CrCl 30–49 mL/min) to severe (CrCl <30 mL/min) renal insufficiency to avoid an exaggerated or prolonged response **[47].**

5.3 Postoperative LMWH

5.3.1 We recommend against concomitant administration of medications affecting hemostasis, such as antiplatelet drugs, standard heparin, or dextran, regardless of LMWH dosing regimen when there is an indwelling neuraxial catheter. (Strong, High evidence)

	Against concomitant administration of medications affecting hemostasis with postoperative LMWH with an indwelling neuraxial catheter
Strength	**Strong**
Benefit of Direction	Benefit > Risk

Evidence	**High:** ASRA PM guidelines (fifth edition)*. High-quality evidence based on clinical data, pharmacologic rationale, and observational reports**
Remarks	Recommendation applies regardless of LMWH dosing regimen because risk is additive rather than dose-dependent alone.

*ASRA PM guidelines (fifth edition) **[1]** states that antiplatelet or oral anticoagulant medications administered in combination with LMWH increases the risk of neuraxial hematoma and recommends against concomitant administration of medications affecting hemostasis, such as antiplatelet drugs, standard heparin, or dextran, regardless of LMWH dosing regimen when there is an indwelling neuraxial catheter.

High-quality evidence based on accumulated clinical data, pharmacologic rationale, and observational reports of increased neuraxial hematoma risk with combined anticoagulant/antiplatelet therapy. The additive, if not synergistic effect of multiple hemostasis-altering medications cannot be overstated and may elevate the risk of hematoma in once-daily LMWH dosing to that of twice-daily dosing **[33].

5.3.2 Twice-daily low dose. We recommend the first dose of LMWH be administered the following day and at least 12 hours after needle/catheter placement. Indwelling catheters should be removed *prior* to initiation of LMWH. Administration of LMWH should be delayed for 4 hours after catheter removal. (Strong, Low evidence)

5.3.3 Single daily low dose. We recommend the first postoperative LMWH dose should be administered at least 12 hours after needle/catheter placement. Indwelling neuraxial catheters do not appear to represent increased risk and may be maintained. The catheter should be removed 12 hours after the last dose of LMWH. Subsequent LMWH dosing should occur at least 4 hours after catheter removal. (Strong, Low evidence)

5.3.4 Single or twice-daily high (*therapeutic*) dosing. High-dose LMWH may be resumed 24 hours after non-high-bleeding-risk surgery and 48–72 hours after high-bleeding-risk surgery. We recommend that indwelling neuraxial catheters be removed 4 hours *prior* to the first postoperative dose and the first postoperative dose should be at least 24 hours after needle/catheter placement, whichever is greater. (Strong, Low evidence)

	Needle/catheter placement & Neuraxial catheter removal with Postoperative LMWH
Strength	**Strong**
Benefit of Direction	Beneficial. Reduces spinal/epidural hematoma risk.
Evidence	**Low:** Consistent expert consensus (ASRA) Observational studies*, North American recommendations, ESAIC/ (ESA)**, FDA data, Pharmacokinetic/pharmacodynamic profile of LMWH, Prospective observational trial (2023).
Remarks	These recommendations aim at maintaining effective thromboprophylaxis while markedly reducing the incidence of spinal/epidural hematoma risk.

*Some observational studies indicate that a significant number of patients will have detectable aXa levels (>0.1 IU/mL) and some may have levels in the prophylactic and possibly therapeutic ranges. It is difficult to know whether this correlates with an increased risk of neuraxial hematoma. North American recommendations have drawn on the extensive European experience in the development of practice guidelines for the management of patients undergoing spinal and epidural blocks while receiving perioperative LMWH. A small quality improvement publication involving 19 patients found that almost 60% of patients taking high-dose enoxaparin still have higher than

expected aXa levels a minimum of 24 hours after the last dose. They also suggested that patients with lower CrCl and increased age may be at particular risk **[48].** Finally, a 2023 prospective observational trial of 103 patients concluded that the time from the last high-dose administration until the aXa level fell below 0.2 IU/mL was 31.5 hours **[49].**

The ESAIC/European Society of Anesthesiology (ESA) recommend that with either low-dose or high-dose LMWH, the time interval be doubled between last dose of LMWH or the dose halved in the presence of severe renal insufficiency (CrCl <30 mL/min) **[5]. Although the recommendation is against *routine* testing, assessment of residual aXa activity may be considered in patients who are elderly, morbidly obese **[50],** or patients with severe renal insufficiency, noting that the acceptable level of residual aXa level for performance of neuraxial block remains undetermined and therefore a level ≤0.1 IU/mL is suggested.

6. Antiplatelet medications

Management of neuraxial block or deep plexus/peripheral block in the patient taking NSAIDs

6.1 NSAIDs appear to represent no added risk for the development of major bleeding after regional anesthetic techniques. NSAIDs (including aspirin) do not create a level of risk that will interfere with the performance of neuraxial or deep plexus/peripheral blocks. In patients receiving these medications, we do not identify specific concerns as to the timing of single-injection or catheter techniques, postoperative monitoring, or the timing of neuraxial catheter removal (Strong, Low evidence)

	Neuraxial block or deep plexus/peripheral block in the patient taking NSAIDs
Strength	**Strong**
Benefit of Direction	Beneficial. No increased incidence of spinal epidural hematoma with NSAIDs alone.
Evidence	**Low:** ASRA PM, (Fifth edition)*, several large studies**, extensive clinical experience, observational studies, pharmacologic data and literature review.
Remarks	No mandatory hold time for NSAIDs or aspirin & No special timing for needle placement or catheter removal. Caution only when combined with other anticoagulants or coagulopathy.

*ASRA PM (fifth ed.) **[1]** uses strong language indicating clinicians can proceed with neuraxial and deep plexus/peripheral blocks in patients taking NSAIDs (including aspirin).

Several large studies have demonstrated the relative safety of central neural blockade in combination with NSAID therapy, although the total number of patients in this combined series is only 4714 **[51]. If low-dose aspirin creates the greatest impact on platelet function, patients receiving 60–325 mg aspirin would theoretically represent the greatest risk of significant bleeding. However, this is not noted in the literature **[52].** An exception to this are patients undergoing invasive pain procedures **[6,53].**

NSAIDs inhibit platelet cyclooxygenase and prevent the synthesis of thromboxane A2. Platelet cyclooxygenase is inhibited by low-dose aspirin (60–325 mg/day) while larger doses (1.5–2 g/day) will also inhibit the production of prostacyclin (a potent vasodilator and platelet aggregation inhibitor) by vascular endothelial cells and thus result in a paradoxical thrombogenic effect **[54].** As a result, low-dose aspirin (81–325 mg/day) is *theoretically* a greater risk factor for bleeding than higher doses. There is consensus that the optimal dose of aspirin for prevention of myocardial infarction, stroke, or vascular death lies within the narrow range of 75–160 mg/day **[55].**

Platelet function is affected for the life of the platelet following aspirin ingestion; other non-steroidal analgesics (naproxen, piroxicam, ibuprofen) produce a short-term defect, which normalizes within 3 days **[56].** Celecoxib

(Celebrex) is an anti-inflammatory agent that primarily inhibits cyclooxygenase-2, an inducible enzyme which is not expressed in platelets, and thus does not cause platelet dysfunction **[57].**

6.2 Management of neuraxial block or deep plexus/peripheral block in the patient taking Thienopyridines (Clopidogrel, Prasugrel)

6.2.1 Based on labeling and surgical/procedural experience, the suggested time interval between discontinuation of thienopyridine therapy and needle placement is 5–7 days for clopidogrel, and 7–10 days for prasugrel. (Conditional, Low evidence)

6.2.2 Neuraxial and deep plexus/peripheral catheters should not be maintained with prasugrel due to the rapid onset. However, since the antiplatelet effect is not immediate with clopidogrel, they may be maintained for 1–2 days, provided a loading dose of the antiplatelet agent is not administered. (Conditional, Low evidence)

6.2.3 Thienopyridine therapy may be resumed immediately after needle placement/catheter removal, provided a loading dose of the drugs is not administered. If a loading dose is administered, we suggest a time interval of 6 hours between catheter removal and administration. (Conditional, Low evidence)

	Neuraxial block or deep plexus/peripheral block in the patient taking Thienopyridines: Clopidogrel (Plavix), and Prasugrel (Efient)
Strength	**Conditional**
Benefit of Direction	Beneficial. To reduce the risk of spinal/epidural hematoma
Evidence	**Low:** ASRA PM and the ACCP* expert opinion, the ESAIC/ERSA, and European labeling**, Retrospective studies but No prospective studies.
Remarks	Waiting 5–7 days (clopidogrel) and 7–10 days (prasugrel) allows sufficient generation of new functional platelets (~10% per day). The time intervals reflect labeling and pharmacological findings that the majority of patients may have a significant (though partial) recovery of platelet function at the shorter time. However, patients at high risk for bleeding require longer time intervals for complete recovery.

The antiplatelet effect of the thienopyridine derivatives, clopidogrel (Plavix) and prasugrel (Efient) results from inhibition of ADP-induced platelet aggregation. Thienopyridine derivatives demonstrate both time-dependent and dose-dependent effects.

*No prospective studies have evaluated perioperative management of clopidogrel, prasugrel, or ticagrelor in patients undergoing *non-cardiac* surgery. Retrospective studies suggest an increased risk of bleeding with clopidogrel continued perioperatively **[58].** Based on expert opinion (recommendation made with 'very low certainty of evidence') the ACCP **[58]** recommends that if a patient is to undergo an elective procedure and an antiplatelet effect is not desired, therapy with clopidogrel should be interrupted 'for 5 days prior to surgery **[59]** and prasugrel discontinued at least 7 days prior to any surgery **[60].**

However, these time intervals are not sufficient to have a return to baseline activity in all patients who displayed residual effects beyond these intervals and a longer time interval, such as 7 days for clopidogrel and 9 days for prasugrel may be desirable to further mitigate any potential bleeding risk **[61].** Based on European labeling, the ESAIC/ERSA recommends 5–7 days for clopidogrel and 7 days for prasugrel **[5].**

6.3 Management of neuraxial block or deep plexus/peripheral block in the patient taking Ticagrelor

6.3.1 Based on labeling and surgical/procedural experience, the recommended time interval between discontinuation of ticagrelor therapy and needle placement is 5 days. (Conditional, Low evidence)

6.3.2 Neuraxial catheters should not be maintained with ticagrelor due to the rapid onset. (Conditional, Low evidence)

6.3.3 Ticagrelor therapy may be resumed immediately after needle placement/catheter removal, provided a loading dose of the drug is not administered. If a loading dose is administered, we suggest a time interval of 6 hours between catheter removal and administration. (Conditional, Low evidence)

	Neuraxial block or deep plexus/peripheral block in the patient taking Ticagrelor
Strength	**Conditional**
Benefit of Direction	Beneficial. Reduces the risk of spinal/epidural hematoma
Evidence	**Low:** ACCP, ESAIC/ESRA based on European labeling* and surgical/procedural experience. Limited clinical experience rather than randomized trials
Remarks	Recommendation is precautionary due to the potentially catastrophic consequence of neuraxial bleeding.

*Based on expert opinion (recommendation made with 'very low certainty of evidence'), the ACCP **[1]** recommends that ticagrelor be discontinued 3–5 days prior to surgery, while the ESAIC/ESRA based on European labeling recommends a 5-day interval **[5].**

Ticagrelor (Brilinta) represents a new class of non-thienopyridine platelet inhibitors Ticagrelor completely *reversibly* inhibits ADP-induced platelet activation, unlike the thienopyridines. Ticagrelor also acts directly on the P2Y12 receptor and does not require cytochrome P450 biotransformation. After a loading dose of Ticagrelor, an antiplatelet effect is observed within 30 min, while maximum effect is achieved within 2 hours. After discontinuation, platelet function recovers 70% in 3 days and to baseline in 5 days **[62,63].** Labeling recommends to interrupt therapy with ticagrelor for 5 days prior to surgery that has a major risk of bleeding **[64].**

6.4 Management of neuraxial block or deep plexus/peripheral block in the patient taking platelet GP IIb/IIa inhibitors

6.4.1 The platelet GP IIb/IIIa inhibitors exert a profound effect on platelet aggregation. Following administration, the time to normal platelet aggregation is 24–48 hours for abciximab and 4–8 hours for eptifibatide and tirofiban. We recommend that needle placement should be avoided until platelet function - as impacted by the GP IIb/IIIa inhibitor - has recovered. Caution in patients on dual therapy who may still have residual NSAID effect. (Strong, Low evidence)

6.4.2 Postoperative. Although GP IIb/IIIa antagonists are contraindicated within 4 weeks of surgery, should one be emergently administered in the postoperative period following a neuraxial or deep plexus/peripheral technique, we recommend the neuraxial infusion should be limited to drugs minimizing sensory and motor block to facilitate assessment of neurological function and that the patient be carefully monitored neurologically. (Strong, Low evidence)

6.4.3 Timing of catheter removal is based on ongoing risk of thromboembolism and need for continued antithrombotic therapy and the potential for spinal bleeding during catheter maintenance and removal (Conditional, Low evidence)

	Neuraxial block or deep plexus/peripheral block in the patient taking Platelet GP IIb/IIa inhibitors including abciximab (Reopro), eptifibatide (Integrilin), and tirofiban (Aggrastat).
Strength	**Strong**
Benefit of Direction	Beneficial. Reduce risk of spinal/epidural hematoma**:**
Evidence	**Low:** ASRA PM (fifth edition)*, expert consensus, Pharmacology, Surgical/interventional cardiology experience. Lack of direct neuraxial outcome trials. ACCP & ESAIC/ESRA did not include recommendations.
Remarks	Additional caution is advised with dual antiplatelet/NSAID therapy**,** which may compound bleeding risk

Platelet GP IIb/IIIa receptor antagonists, inhibit platelet aggregation by interfering with platelet-fibrinogen and platelet-von Willebrand factor binding. The majority of clinical trials involving the GP IIb/IIIa antagonists have evaluated their use in the treatment of acute coronary syndrome, and thus the GP IIb/IIIa antagonists are typically administered in combination with aspirin and heparin. Contraindications include a history of surgery within 4–6 weeks **[65].** Time to normal platelet aggregation following discontinuation of therapy ranges from 8 hours (eptifibatide, tirofiban) to 24–48 hours (abciximab**) [55].** Thrombocytopenia is a known side effect **[55].**

* ASRA PM (fifth edition) expert consensus, included these recommendations**,** but ACCP and ESAIC/ESRA did not include recommendations for platelet GP IIb/IIIa because these medications are rarely administered to patients undergoing regional anesthesia/surgery **[5, 58].**

6.5 Management of neuraxial block or deep plexus/peripheral block in the patient taking Cilostazol

6.5.1 The risk of serious bleeding in the presence of residual cilostazol effect is unknown. Based on the elimination half-life, we suggest that needle placement be avoided for 2 days after discontinuation of cilostazol. (Conditional, Low evidence)

6.5.2 We suggest that neuraxial and deep plexus/peripheral catheters be removed prior to reinstitution of cilostazol therapy postoperatively. (Conditional, Low evidence)

6.5.3 We suggest that the first postoperative dose of cilostazol be administered 6 hours after neuraxial or deep plexus/peripheral catheter removal. (Conditional, Low evidence)

	Neuraxial block or deep plexus/peripheral block in the patient taking Cilostazol
Strength	**Conditional**
Benefit of Direction	Beneficial. Provides a safety margin based on drug elimination
Evidence	**Low:** ASRA review expert consenus*, mainly from pharmacokinetic data. Limited clinical outcome data. Absence of large prospective studies. ACCP and ESAIC/ESRA did not include recommendations.
Remarks	Platelet inhibition is reversible but persists for several half-lives after discontinuation.

* Small perioperative observational data sets cited in ASRA review expert consensus for these recommendations, but ACCP and ESAIC/ESRA did not include recommendations for cilostazol because the medication is rarely administered to patients undergoing regional anesthesia/surgery **[5, 58].**

Cilostazol produces a selective inhibition of phosphodiesterase (PDE) IIIA resulting in a weak, reversible inhibition of platelet aggregation. It has a half-life of 11 hours, which is prolonged in patients with severe renal impairment**[55].** The terminal half-life and the active metabolite is 21 hours. There are limited data on perioperative administration of cilostazol. However, a single case report of spinal hematoma following epidural catheter removal in the presence of cilostazol therapy has been reported **[66].**

6.6 Management of neuraxial block or deep plexus/peripheral block in the patient taking Cangrelor

6.6.1 The risk of serious bleeding in the presence of residual cangrelor effect is unknown. Based on the elimination half-life, we suggest that needle placement be avoided for 3 hours after discontinuation of cangrelor. (Conditional, Low evidence)

6.6.2 We suggest that neuraxial and deep plexus/peripheral catheters be removed prior to reinstitution of cangrelor therapy postoperatively. (Conditional, Low evidence)

6.6.3 We suggest that the first postoperative dose of cangrelor be administered 8 hours after neuraxial or deep plexus/peripheral catheter removal. (Conditional, Low evidence)

	Neuraxial block or deep plexus/peripheral block in the patient taking Cangrelor (Kengreal)
Strength	**Conditional**
Benefit of Direction	Beneficial. Particularly important in patients receiving multiple antithrombotic agents.
Evidence	**Low:** ASRA review expert consenus based primarily on pharmacokinetics and pharmacodynamics*. Very limited clinical experience with neuraxial techniques. Absence of large prospective safety trials. ACCP and ESAIC/ESRA did not include recommendations
Remarks	Cangrelor is an **intravenous**, **reversible** P2Y12 inhibitor. Because neuraxial bleeding risk data are lacking, the guideline uses a conservative safety margin of 3 hours (≈ many half-lives).

* ASRA MD (fifth edition) review expert consenus is based primarily on pharmacokinetics and pharmacodynamics. Very limited clinical experience with neuraxial techniques and absence of large prospective safety trials. ACCP and ESAIC/ESRA did not include recommendations for cangrelor because the medication is rarely administered to patients undergoing regional anesthesia/surgery **[5, 58].**

Cangrelor (Kengreal) is a direct and reversible intravenous P2Y12 inhibitor. The dosage of the drug is 30 µg/kg bolus followed by a 4 µg/kg/min infusion. Its antiplatelet effect is seen within 2 min of administration and inhibits platelet aggregation by 95%–100%. Its plasma half-life is 3–6 min and platelet recovery is rapid; 80% and 90% of the samples recover in 60 and 90 min, respectively **[67].**
The oral P2Y12 inhibitors are discontinued for 5–10 days before surgery. Cangrelor can therefore be used as a bridge therapy in these situations. It is possible that perioperative anesthesiologists will encounter this scenario more often in the future. In these cases, a 3-hour interval minimum, and preferably longer should be observed.

7. Parenteral Direct Thrombin Inhibitors

7.1 Management of neuraxial block or deep plexus/peripheral block in the patient taking parenteral thrombin inhibitors (Argatroban, Bivalirudin, and Desirudin)

In patients receiving parenteral thrombin inhibitors, we suggest against the performance of neuraxial techniques. (Conditional, Low evidence)

	Direct Thrombin inhibitors are: Argatroban (Acova), bivalirudin (Angiomax) and desirudin (Revasc)
Strength	**Conditional**
Benefit of Direction	Beneficial. To reduce the risk of spinal epidural hematoma, which may cause permanent neurologic injury.
Evidence	**Low:** ASRA guidelines (fifth edition)*, Based mainly on Pharmacokinetic and pharmacodynamic data, case reports, and expert consensus rather than randomized trials. Lack of prospective safety studies for neuraxial techniques during therapy.
Remarks	No well-established reversal strategy. Extremely limited safety data for neuraxial procedures

*Recommendation of ASRA is conservative due to very limited evidence **[1].** ASRA advises avoidance as the high potential harm (catastrophic neurologic injury) greatly outweighs the unproven benefit of neuraxial anesthesia in this setting.

**Although there are no case reports of spinal hematoma related to neuraxial anesthesia among patients who have received an intravenous thrombin inhibitor, spontaneous intracranial bleeding has been reported. The lack of information available and the approved applications of these agents (typically patients with HIT who will need therapeutic levels of anticoagulation) make patients receiving these medications poor candidates for neuraxial blockade.

Recombinant hirudin derivatives, including bivalirudin (Angiomax), and desirudin (Revasc) inhibit both free and clot-bound thrombin. Argatroban (Acova), an L-arginine derivative, has a similar mechanism of action. These medications are indicated for the treatment and prevention of thrombosis in patients with HIT and as an adjunct to angioplasty procedures **[68,69].** Desirudin is approved for prevention of VTE/PE following hip replacement **[70].** The anticoagulant effect of thrombin inhibitors is monitored by the aPTT, and is present for 1–3 hours after intravenous administration. Hemorrhagic complications, particularly when combined with thrombolytic or antiplatelet agents, may be life threatening. There is no 'antidote'; therefore, the antithrombin effect cannot be reversed pharmacologically.

Parenteral anti-Xa agents

7.2 Management of neuraxial block or deep plexus/peripheral block in the patient receiving fondaparinux

Low-dose fondaparinux (2.5 mg once per day)

7.2.1 We suggest holding low-dose fondaparinux (2.5 mg once per day) for 36 hours (young patients) to 42 hours (elderly patients) in healthy patients with normal renal function. (Conditional, Low evidence)

7.2.2 We suggest holding fondaparinux for a minimum of 58 hours in patients with moderate renal insufficiency (CrCl 30–50 mL/min). (Conditional, Low evidence)

7.2.3 We suggest not performing neuraxial or deep plexus/peripheral blocks in patients with severe renal impairment (CrCl <30 mL/min) due to the 72 hours half-life. (Conditional, Low evidence)

7.2.4 We suggest testing aXa activity calibrated to fondaparinux if placing the needle prior to these recommended times is considered (aXa ≤0.1 IU/mL). (Conditional, Low evidence)

High-dose fondaparinux (5–10 mg once per day)

7.2.5 We suggest holding high-dose fondaparinux (5-10 mg once per day) for a minimum of 70 hours (in young patients) and for a minimum of 105 hours (in elderly patients) with normal renal function. (Conditional, Low evidence)

7.2.6 We suggest testing aXa activity calibrated to fondaparinux if placing needle prior to the recommended times is considered (aXa ≤0.1 IU/mL). (Conditional, Low evidence)

7.2.7 We suggest that neuraxial catheters be removed at least 6 hours *prior* to the first postoperative dose. (Conditional, Low evidence)

	Management of neuraxial block or deep plexus/peripheral block in the patient receiving fondaparinux
Strength	**Conditional**
Benefit of Direction	Beneficial. Minimize the risk of spinal epidural hematoma, which is rare but catastrophic.
Evidence	**Low:** ASRA guidelines (fifth edition)* Evidence is based on expert consensus, pharmacokinetic data, FDA data, dose-ranging study, **. Limited clinical trial experience. No robust randomized safety trials.
Remarks	Pharmacology studies demonstrating: long half-life (~17–21 h), Irreversible anti-Xa activity and lack of specific reversal agent.

*Recommendations of ASRA **[1]** are based on the long half-life, the irreversible anti-Xa activity and the lack of specific reversal agent. There are no robust randomized safety trials of neuraxial anesthesia with fondaparinux.

One spinal hematoma was reported in the initial dose-ranging study, at a dose that was determined to be twice that required for thromboprophylaxis[71,72].** A series of 1631 patients undergoing continuous neuraxial or deep peripheral block reported no serious hemorrhagic complications. However, the catheters were removed 36 hours after the last dose of fondaparinux and subsequent dosing was delayed for 12 hours after catheter removal **[73].**

The FDA released fondaparinux with a black box warning about neuraxial anesthesia like that of the LMWHs and heparinoids. Fondaparinux produces its antithrombotic effect through factor Xa inhibition and is used when patients are intolerant to LMWH. Advantages of fondaparinux include: 100% bioavailability subcutaneously, instant onset of action, long half-life, and direct renal excretion **[74].** This drug is contraindicated in patients with severe renal impairment (CrCl <30 mL/min) and in patients weighing <50 kg. It should be used with caution in patients with moderate renal impairment (CrCl 30–50 mL/min). The plasma half-life of fondaparinux is 17–21 hours (17 hours in healthy, young patients and 21 hours in healthy, elderly patients), allowing for single daily dosing, with the first low (prophylactic) dose administered 6–8 hours postoperatively **[71].** The half-life in patients with moderate renal insufficiency (CrCl 30–50 mL/min) was found to be 29 hours, and 72 hours in patients with severe renal impairment (CrCl <30 mL/min). Routine coagulation tests such as PT and aPTT are relatively insensitive measures of fondaparinux and are unsuitable for monitoring. The aXa activity can be measured by aXa assay using the appropriate calibrator (fondaparinux). It is important to note that protamine would not be an effective reversal strategy. There is a paucity of prospective data and the studies that are published included such strict parameters that it is difficult to use them to develop recommendations.

8. Management of neuraxial block or deep plexus/peripheral block in the patient receiving Thrombolytic therapy

8.1 In patients scheduled to receive thrombolytic therapy, we recommend that the patient be queried, and the medical record reviewed for a recent history of lumbar puncture, spinal or epidural anesthesia, or epidural steroid injection to allow appropriate monitoring. Guidelines detailing original contraindications for thrombolytic drugs suggest avoidance of these drugs for 10 days following puncture of non-compressible vessels. (Strong, High evidence)

8.2 In patients who have received fibrinolytic and thrombolytic drugs, we recommend against needle placement for at least 48 hours. Documentation of normalization of clotting studies (including fibrinogen) is suggested. (Strong, High evidence)

	Thrombolytic and Fibrinolytic therapy in patients receiving neuraxial block or deep plexus/peripheral block.
Strength	**Strong**
Benefit of Direction	Beneficial. Reduces risk of catastrophic neuraxial hematoma.
Evidence	**High:** ASRA guidelines (fifth edition)*. Recommendations rely partly on pharmacological basis and case reports**.
Remarks	Fibrinolytics and thrombolytics are generally different names for the same class of emergency, clot-busting medications that activate plasminogen into plasmin to dissolve dangerous blood clots. They work by breaking down the fibrin mesh, which is why they are often referred to as fibrinolytic agents.

* Strong recommendation in the current ASRA PM (5th edition) wording **[1]** emphasizes the high hemorrhagic risk in these patients, especially when combined with other anticoagulants. Patients receiving fibrinolytic/ thrombolytic medications are at risk of serious hemorrhagic events, particularly those who have undergone an invasive procedure. Recommendations are based on the profound effect on hemostasis, the use of concomitant heparin and/or antiplatelet agents (which further increase the risk of bleeding), and the potential for *sponaneous* neuraxial bleeding with these medications.

The fibrinolytic system dissolves intravascular clots as a result of the action of plasmin which is a non-specific protease capable of dissolving fibrin clots and other plasma proteins, including several coagulation factors. Exogenous plasminogen activators, such as streptokinase and urokinase, dissolve thrombus and affect circulating plasminogen as well. Pharmacological t-PA formulations (Alteplase, Tenecteplase) are more fibrin-selective and have less effect on circulating plasminogen. Clot lysis leads to elevation of fibrin degradation products, which themselves have an anticoagulant antithrombotic effect by inhibiting platelet aggregation. Given the nature of the underlying thrombotic medical conditions being treated, patients who receive fibrinolytic therapy frequently receive intravenous heparin to maintain an aPTT of 1.5–2 times normal. Often an antiplatelet agent such as aspirin or clopidogrel is also added. While the plasma half-life of thrombolytic drugs is only hours, it may take days for the thrombolytic effect to resolve. Fibrinogen and plasminogen are maximally depressed at 5 hours after thrombolytic therapy and remain significantly depressed at 27 hours **[75]. Importantly, original contraindications to thrombolytic therapy included surgery or puncture of non-compressible vessels within 10 days **[76].**

8.3 In those patients who have received neuraxial blocks at or near the time of fibrinolytic and thrombolytic therapy, we recommend that frequent neurological monitoring (eg, every 2 hours) should be continued for at least 48 hours after the last dose. If neuraxial blocks have been combined with fibrinolytic and thrombolytic therapy and ongoing epidural catheter infusion, we recommend the infusion should be limited to drugs minimizing sensory and motor block to facilitate assessment of neurological function. (Strong, Low evidene)

	Frequent neurological monitoring and use of dilute drugs to facilitate assessment with fibrinolytic and thrombolytic therapy.
Strength	**Strong**
Benefit of Direction	Beneficial. Early detection and prevention of permanent neurologic injury.
Evidence	**Low:** ASRA guidelines (fifth edition)*, published reports, case reports and expert consensus **. There are no RTCs

Remarks	Neurologic recovery is strongly dependent on early recognition and decompression (ideally <8–12 hours). Frequent neurologic checks (every ~2 hours) increase the likelihood of detecting new motor weakness and sensory changes, and back pain. Using dilute epidural infusions that minimize motor block improves the sensitivity of neurologic assessment**.**

* Because the potential harm is severe and early monitoring is low risk, ASRA PM (5th edition) in the current guidelines **[1]** issued a strong recommendation despite low-quality evidence **(** primarily case reports, case series, and expert consensus**).** There are no RTCs; recommendations are based on the known catastrophic risk of spinal/epidural hematoma and pharmacologic effects of thrombolytics.
There are no large series addressing regional anesthesia in the patient receiving fibrinolytic/thrombolytic therapy. The majority of published reports involve *spontaneous* spinal or epidural hematomas after thrombolytic therapy **[37, 77-79]. Recent cases involve thrombolysis for myocardial infarction and bleeding has been reported at all spinal levels - cervical, thoracic, and lumbar **[80,81].**

9. Vitamin K antagonists (Warfarin)

Management of neuraxial block or deep plexus/peripheral block in the patient on Warfarin

9.1 We recommend that the anticoagulant therapy be stopped 5 days prior to the planned procedure, and the INR be measured and normalized (normal range of the local laboratory) prior to needle placement. (Strong, Moderate evidence)

	Management of neuraxial block or deep plexus/peripheral block in the patient on warfarin
Strength	**Strong**
Benefit of Direction	Beneficial. Reduces risk of catastrophic neuraxial hematoma.
Evidence	**Moderate:** ASRA PM (5th edition) and ESAIC/ESRA guidelines*. Based on pharmacokinetics, observational safety data, long clinical experience, case series, and case reports**
Remarks	The international normalized ratio (INR) is most sensitive to clotting factors VII and X and is slightly prolonged when factor VII is reduced to approximately 55% of baseline.

Warfarin exerts its anticoagulant effect by interfering with the synthesis of the vitamin K-dependent clotting factors VII, IX, X, and II (thrombin). The effects of warfarin are dependent on clotting factor half-lives and the anticoagulant effect is not apparent until there is a significant amount of biologically inactive clotting factors **[82].**
* ASRA PM (5th edition) in the current guidelines are consistent with ESAIC/ESRA guidelines **[5]** that warfarin should be discontinued for at least 5 days and the INR should be measured and normalized (per local laboratory) prior to performance of a neuraxial block. **Recommendations are based on warfarin pharmacology, the clinical relevance of vitamin K coagulation factor levels/deficiencies, long clinical experience, observational safety data case series, and case reports of spinal hematoma among these patients. Websites are available to assist clinicians with warfarin dosing **[83].**

9.2 In patients receiving an initial dose of warfarin prior to surgery, we suggest the INR should be checked prior to needle placement if the first dose was given >24 hours earlier, or if a second dose of oral anticoagulant has been administered. (Conditional, Low evidence)

9.3 In patients receiving low-dose warfarin therapy during epidural analgesia, we suggest that their INR be monitored daily. (Conditional, Low evidence)

9.4 We suggest that neuraxial catheters be removed when the INR is <1.5. (Conditional, Low evidence)

9.5 In patients with INR >1.5 but <3, the increased risk of maintaining a neuraxial catheter remains unknown. We suggest indwelling catheters may be maintained or removed with caution, closely following the INR and duration of warfarin therapy. (Conditional, Low evidence)

	Checking of INR prior to needle placement, for monitoring and for neuraxial catheter removal.
Strength	**Conditional**
Benefit of Direction	Beneficial. Reduces risk of catastrophic neuraxial hematoma.
Evidence	**Low:** ASRA PM (5th edition) consistent with ESAIC/ESRA guidelines*, based on large observational studies, long clinical experience, large case series**
Remarks	Daily INR monitoring allows early detection of excessive anticoagulation, facilitates timely catheter management and reduces risk of epidural hematoma.

*ASRA PM (5th edition) in the current guidelines are consistent with ESAIC/ESRA guidelines **[5]** that neuraxial injections and removal of epidural catheters appear to be safe when done within 24 hours after warfarin is initiated. This was documented by Parvizi *et al* **[84]**. who noted the absence of spinal hematoma in over 12 000 patients in whom they removed the epidural catheters within 24–48 hours of initiation of warfarin therapy. The safety of removing epidural catheters was also documented by other investigators **[85, 86].** No spinal hematoma occurred after removal of catheters 12–14 hours after warfarin therapy, even in the patients with INRs of 1.5–1.9. The mean (±SD) factor VII levels 12 hours after warfarin initiation were noted to be normal in the patients with INRs ≤1.4 and acceptable in the patients with INRs of 1.5–1.9 [**87].** Another group of investigators showed no spinal hematoma in 4365 patients when epidural catheters were removed while on warfarin; the mean duration of warfarin treatment was 2.1±0.6 days and the INRs at the time of removal was 1.9±0.4 (range 1.5–7.1) [**86].**

9.6 In patients with an INR >3, we recommend that the warfarin dose be held or reduced in patients with indwelling neuraxial catheters. (Strong, Low evidence)

9.7 Neurological testing of sensory and motor function should be performed routinely during epidural analgesia for patients on warfarin therapy. To facilitate neurological evaluation, we recommend that the type of analgesic solution be tailored to minimize the degree of sensory and motor blockade. (Strong, Low evidence)

9.8 We suggest that neurological assessment be continued for at least 48 hours following catheter removal. (Conditional, Low evidence)

	Warafrin dose in patients with an INR >3 in patients with indwelling neuraxial catheters. Neurological assessment during epidural and following catheter removal
Strength	**Strong**
Benefit of Direction	Beneficial. Early detection and prevention of catastrophic neurologic injury.
Evidence	**Low:** ASRA PM (5th edition) consistent with (ESAIC/ESRA guidelines, based primarily on high consensus among experts*).
Remarks	Reducing or holding the dose of warfarin maintains safer coagulation status while catheter remains in situ. - INR ≤3: catheter may remain with caution and monitoring.

	- INR >3: hold or reduce warfarin while catheter is in place. - Continue close neurologic monitoring until INR returns to safer range.

* ASRA PM (5th edition) guidelines are consistent with the ESAIC/ESRA guidelines **[5].** This recommendation is strong despite low evidence due to the high consensus among experts as spinal/epidural hematoma is rare but catastrophic and early neurological detection is critical for outcome.
When there is an elevated INR without major bleeding, the warfarin can be reversed with oral vitamin K. Intravenous vitamin K can be administered when there is active bleeding **[82].** When there is life-threatening bleeding, recombinant activated factor VIIa (rFVIIa), three-factor PCC which contain factors II, IX, and X, or four-factor PCC, containing factors II, VII, IX, and X, can be given. Activated rFVIIa and PCCs are better than FFP in reversing warfarin **[88].**

10. Herbal medications

Management of neuraxial block or deep plexus/peripheral block in patients using Herbal therapy

10.1 The use of herbal medications does not create a level of risk that will interfere with the performance of neuraxial blocks. We recommend against the mandatory discontinuation of these medications or avoidance of regional anesthetic techniques in patients on these medications (Strong, Low evidence)

	Management of neuraxial block or deep plexus/peripheral block in patients using herbal therapy. Common herbs evaluated: garlic, ginkgo, and ginseng.
Strength	**Strong**
Benefit of Direction	Beneficial
Evidence	**Low.** ASRA PM*, Case reports, Pharmacologic studies, Expert consensus, no high-quality RCT***
Remarks	Potential harms considered minimal when herbs are used alone (without concurrent anticoagulants, Known coagulopathy and traumatic needle placement).

*According to recommendations of ASRA PM **[1]** herbal medications alone do not significantly increase spinal hematoma risk and Routine discontinuation is not recommended. Caution only when combined with anticoagulants or in patients with bleeding disorders. Morbidity and mortality associated with herbal use may be more likely in the perioperative period because of the polypharmacy and physiological alterations that occur. Such complications include bleeding from garlic, ginkgo, and ginseng, and potential interaction between ginseng-warfarin **(Appendix, Table 4).**

Despite the widespread use of herbal medications, there are few controlled clinical trials of the efficacy (or adverse effects) and few outcome studies of the effects of herbal medications on surgical patients; a prospective study including over 600 patients found no differences in surgical outcomes, including bleeding, in patients reporting recent herbal therapy **[89]. However, while overall there does not appear to be a clinically significant increase in surgical bleeding or spinal hematoma in patients receiving herbal medications, data on the combination of herbal therapy with other forms of anticoagulation are lacking. The concurrent use of other medications affecting clotting mechanisms, such as oral anticoagulants or heparin, may increase the risk of bleeding complications in these patients. Thus, it is often recommended that these medications be discontinued in anticipation of surgery, but there is no reason for cancellation of the procedure if patients have not done so **[90].**

11. Antithrombotic therapy in pregnancy

Management of neuraxial block in the anticoagulated parturient

11.1 Given the limited pharmacological data on antithrombotic agents in pregnancy and in the absence of a large series of neuraxial techniques in the pregnant population

receiving prophylaxis or treatment for venous thromboembolism, we suggest that the recommendations included in this document be applied to parturients (Conditional, Low evidence)

11.2 However, in circumstances involving select high-risk parturients receiving VTE prophylaxis, and requiring urgent interventions for maternal or fetal indications, the risk of general anesthesia may be greater than neuraxial anesthesia, and exceptions/ modifications of these recommendations may be appropriate. (Conditional, Low evidence)

	Management of neuraxial block in the anticoagulated parturient.
Strength	**Conditional**
Benefit of Direction	Beneficial: Primarily consensus- and safety-driven.
Evidence	**Low:** ASRA PM (fifth ed.), based largely on pharmacologic principles, limited obstetric-specific neuraxial safety data, reliance on extrapolation from nonpregnant populations*, and a systematic review **
Remarks	Recommendation aims to minimize risk of spinal/epidural hematoma while allowing access to neuraxial analgesia.

*The primary guideline source is ASRA PM (fifth edition) **[1],** based largely on pharmacologic principles, limited obstetric-specific neuraxial safety data, Reliance on extrapolation from nonpregnant populations due to lack of robust pregnancy-specific data.

The incidence of neuraxial hematoma after spinal or epidural blockade in the obstetric population is difficult to determine, although it is widely reported that these patients have a significantly lower incidence of this complication than older populations **[33].** Bateman *et al* [**91**] confirmed the substantially lower risk of neuraxial hematoma in obstetric patients documenting seven epidural hematomas among 142 287 patients undergoing epidural anesthesia/analgesia (1:20 326). These findings are particularly notable since bloody taps, a reputed risk factor for neuraxial hematoma, are more common in the obstetric than in the general surgical population **[92].**

** A systematic review of English language publications (1952–2016) revealed no cases of neuraxial hematoma *due to neuraxial anesthesia and low dose (thromboprophylaxis) in obstetric patients*, although the denominator (total number of cases) was unknown **[93].** A subsequent publication reported the development of a neuraxial hematoma after spinal anesthesia for cesarean delivery when a larger dose of LMWH was administered post partum, earlier than the time interval recommended by ASRA guidelines **[94].** Potential explanations for the lower incidence of neuraxial hematoma in obstetric compared with older, orthopedic patients include the hypercoagulable state and a more compliant epidural space, unimpeded by osteoporotic deformities, which can accommodate larger volumes of blood before symptomatic neural compression occurs **[33,95].**

The peripartum management of the obstetric patient that receives anticoagulant medications presents a significant clinical challenge [**96,97**]. ACOG and the SOAP recommendations support every labor unit having a protocol for when anticoagulants should be stopped, and if short-term strategies such as converting to UFH, due to its shorter half-life, in anticipation of delivery should be considered [**97].** In the event of unforeseen labor or urgent cesarean delivery, the choice of analgesia and/or anesthesia should balance the risks of general anesthesia and benefits of neuraxial anesthesia given the anticoagulant, dose, time of administration, and pertinent laboratory values. The plan for reinitiating anticoagulation post partum must also incorporate the anesthetic management and hemostasis after delivery.

12. Plexus and peripheral blockade in the anticoagulated patient

Management of deep plexus/peripheral block in the anticoagulated patient

12.1 For patients undergoing deep plexus or deep peripheral block, we recommend that guidelines for neuraxial block be similarly applied. (Strong, Low evidence)

	Management of deep plexus/peripheral block in the anticoagulated patient
Strength	**Strong**
Benefit of Direction	Beneficial: Provides a conservative safety margin in anticoagulated patients.
Evidence	**Low:** ASRA PM based primarily on case reports and case series, pharmacologic reasoning and Expert consensus*. No randomized trials
Remarks	Deep plexus blocks occur in noncompressible spaces**,** similar to neuraxial techniques where bleeding in these locations can be occult and delayed and cause major neurologic injury.

12.2 For patients undergoing other plexus or peripheral techniques, we suggest performance, catheter maintenance, and catheter removal be based on site compressibility, vascularity, and consequences of bleeding, should it occur. (Conditional, Low evidence)

	Management of other plexus or peripheral techniques in the anticoagulated patient.
Strength	**Conditional**
Benefit of Direction	Beneficial
Evidence	**Low:** ASRA PM (fifth edition) based primarily on observational studies, case reports and case series, pharmacologic reasoning and Expert consensus*. No randomized controlled trials.
Remarks	Avoids unnecessarily strict neuraxial-type restrictions for low-risk blocks

*As per ASRA PM **[1]** evidence-based guidelines are based primarily on case reports and case series of bleeding complications, pharmacologic reasoning regarding noncompressible vascular spaces and expert consensus. Deep plexus blocks (e.g., lumbar plexus, paravertebral) occur in noncompressible spaces**,** similar to neuraxial techniques. Bleeding in these locations can be occult and delayed and cause major neurologic injury. Unlike neuraxial and deep plexus blocks, most peripheral nerve blocks occur in compressible locations**,** so risk varies widely by site. ASRA therefore recommends individual risk assessment based on three key factors: site compressibility, vascularity of the region and consequences of bleeding e.g., potential for nerve compression.

Unfortunately, there continues to be a lack of investigations examining the frequency and severity of hemorrhagic complications following plexus or peripheral blockade in anticoagulated patients. In addition, there continues to be case reports of significant morbidity related to hematomas following peripheral nerve blockade in coagulopathic patients **[98,99].**

In the practice advisory published by the Regional Anesthesia and Acute Pain Section of the Canadian Anesthesiologists Society sought to stratify the bleeding risk into 'low risk,' 'intermediate risk,' or 'high risk' for peripheral nerve blocks and interfascial plane blocks **[100].** Hemorrhagic complications following the deep plexus/deep peripheral techniques (including but not limited to those listed as high risk, eg, stellate ganglion, infraclavicular, lumbar sympathetic, lumbar plexus, and paravertebral), particularly in the presence of antithrombotic therapy, are often serious and a source of major patient morbidity **[100].** These cases continue to suggest that significant blood loss, rather than neural deficits, may be the most serious complication.

Implementation Considerations

<u>Before starting</u> the placement of the neuraxial intervention or deep plexus/peripheral block, do the following for the safe performance of the procedure:

- Check the regional block equipment before starting.
- Check the anesthetic machine first thing in morning.
- Check the airway management equipment.

- An Anesthetic assistant should be available.
- Emergency drugs must be instantly available.
- Monitoring equipment should be available (ECG, NIBP, Pulse oximeter) prior to start.
- WHO Checklist must be done.

Postoperative Monitoring & Clinical Red Flags:
Patients who have experienced a traumatic tap require **enhanced neurological monitoring** for at least 24 hours following the procedure or until the first dose of anticoagulation has been safely tolerated.

The 2-hour Audit: When indicated with neuroxial block, perform a focused neurological exam every 2 hours, assessing for:

- **Motor Deficit:** New or progressive lower extremity weakness (unable to perform a straight leg raise).
- **Sensory Deficit:** New or worsening numbness or "heaviness" in a dermatomal distribution.
- **Back Pain:** Severe, localized back pain, often described as "stabbing" or radiating to the legs.
- **Autonomic Dysfunction:** New-onset urinary retention or fecal incontinence.

Emergency Response: If any of the above "Red Flags" are identified:

- **STAT MRI:** Immediate neuroimaging (MRI is the gold standard; CT Myelogram is second line).
- **Neurosurgical Consult:** Immediate notification of the spine or neurosurgical team for potential emergency decompression.
- **Reverse Anticoagulation:** If the patient has received an anticoagulant dose, initiate reversal protocols; e.g. Protamine for Heparin, Idarucizumab for Dabigatran, or prothrombin complex concentrates (PCC) for Factor Xa inhibitors.

Research Gaps

Literature review shows insufficient research data that need further studies for:

- The pharmacologic reversal of the Direct oral anticoagulant (DOAC) effect by using their antidotes to facilitate placement of neuraxial block or deep plexus/peripheral block.
- The safety of indwelling neuraxial catheters in patients receiving postoperative high-dose UFH has not been established. Definition of the safest interval needs to be defined.
- No well-established reversal strategy in patients receiving parenteral thrombin inhibitors. Research is needed for Antidotes to the antithrombin effect, so it can be reversed pharmacologically.
- Lack of specific reversal agent in the patient receiving fondaparinux for safe anagement of neuraxial block or deep plexus/peripheral block.
- Inspite of the widespread use of herbal medications, there are few controlled clinical trials of the efficacy/adverse effects and few outcome studies of the effects of herbal medications on surgical patients. Data on combination of herbal therapy with other forms of anticoagulation are lacking.

- Lack of investigations examining the frequency and severity of hemorrhagic complications following plexus or peripheral blockade in anticoagulated patients.

Clinical Indicators for Monitoring

- Percentage of cases of neuraxial hematoma reported due to neuraxial anesthesia in patients treated with the initial recommended dose-ranging:
  Numerator: Number of cases of neuraxial hematoma reported
  Denominator: denominator: total number of the studied cases)
- Incidence of spinal hematoma reported in patients undergoing continuous neuraxial or deep peripheral block:
  Numerator: Number of cases of spinal hematoma reported
  Denominator: total number of patients undergoing continuous neuraxial or deep peripheral block
- Incidence of spinal hematoma reported at the time of neuraxial catheter removal:
  Numerator: Number of cases of spinal hematoma reported at time of catheter removal
  Denominator: total number of patients undergoing continuous neuraxial block
- Relation of the time of catheter removal to the incidence of spinal hematoma.

Update of the Guideline

The Guidelines of this current version (Year 2026) are subject to revision, and the updated versions will be published when needed, as warranted by the evolution of new-evidenced medical knowledge, new technology, and new practice trends.

Guidelines Development Contributors and Participants

Contributors and Participants:
The Guidelines Development Group (GDG) of the Egyptian Board of Anesthesia, Surgical Intensive Care, and Pain Management.

Annexes

Annex I: Evidence-to-Decision Tables

1. Transition to "Low/High Dose" Terminology and Conservative Timing

Recommendation: Replace "prophylactic/therapeutic" dosing with "low/high dose" and maintain a conservative "antihemorrhagic" approach for wait times.

Criterion	Evidence	Judgment	Remarks
Benefits	Standardizes dosing descriptions across international guidelines (ESAIC/ESRA).	Large	Reduces confusion regarding "therapeutic" doses used for prophylaxis in high-risk patients.
Risks	Hemorrhagic complications are rare but catastrophic (e.g., spinal hematoma).	Moderate–Large	Conservative timing (e.g., 72h for high-dose DOACs) prioritizes patient safety.
Values & Preferences	Patients and clinicians prioritize the avoidance of permanent neurologic injury.	High	An "antihemorrhagic" focus is preferred over shorter "antithrombotic" windows.
Acceptability	Alignment with FDA labeling and pharmacological half-lives.	High	More acceptable for risk-averse perioperative environments.
Feasibility	Requires clinician education on the new "Low/High" dose definitions.	Moderate	Ease of use is improved by consistent terminology across specialties.

2. Classification of Deep Plexus and Peripheral Blocks as "High Risk."

Recommendation: Apply the same stringent timing guidelines for neuraxial blocks to deep, non-compressible, or concealed peripheral blocks.

Criterion	Evidence	Judgment	Remarks
Benefits	Prevents significant morbidity from non-compressible bleeding (e.g., psoas or retroperitoneal hematoma).	Moderate	Essential for blocks like the lumbar plexus, paravertebral, and stellate ganglion.
Risks	Bleeding in these sites can lead to massive blood loss and neural deficit.	Large	Bleeding is often "concealed," delaying diagnosis compared to superficial sites.
Certainty of Evidence	Based on case reports and expert consensus (Level III).	Low–Moderate	Rarity of events prevents RCTs; expert opinion drives the safety mandate.
Resources	Requires access to emergency imaging (MRI/CT) if hematoma is suspected.	Moderate	Systems must have pathways for rapid diagnosis of deep bleeding.
Feasibility	Easily integrated into existing neuraxial safety checklists.	High	Simplifies decision-making by using a "one-rule" approach for high-risk sites.

3. Evidence-to-Decision Summary for Dosing and Timing

Criterion	Evidence & Judgment (ASRA 2025)	Remarks
Dosing Definition	Use "Low Dose" and "High Dose" based on actual milligrams administered.	Replaces the subjective "prophylactic/therapeutic" labels.
High-Risk Blocks	Include all neuraxial AND deep peripheral/plexus blocks.	Non-compressible sites carry similar risks to the epidural space.
Wait Times	Based on 5 half-lives for High Dose; 2-3 half-lives for Low Dose.	Ensures ≤ 5 - 10% residual drug activity before block.

4. Evidence-to-Decision Table of DOACs

Criterion	DOACs
Problem	DOACs complicate neuraxial anesthesia.
Benefit	Safe block if withheld 48–72 h.
Risk/Harm	High hematoma risk if too early.
Certainty of Evidence	Moderate.
Values & Preference	Clinicians prefer conservative timing.
Resource Use	Renal function testing required.
Equity	Limited in low-resource regions.
Acceptability	High if timing is respected.

5. Evidence-to-Decision Table of UFH

Criterion	UFH (Subcutaneous & Intravenous)
Problem	Patients on UFH require low or high anticoagulation, complicating neuraxial anesthesia**.**
Benefit	Safe neuraxial block is possible if timing and dose are respected.
Risk/Harm	Risk of spinal/epidural hematoma, especially with high-dose SC or continuous IV infusion.
Certainty of Evidence	Moderate for SC low-dose. Low for SC high-dose high for IV infusion.
Values& Preference	Clinicians prioritize patient safety and prefer clear timing rules.
Resource Use	Minimal cost; requires lab monitoring for IV UFH.
Equity	Widely available; monitoring may be limited in low-resource settings.
Acceptability	High for low-dose SC; moderate for high-dose SC; high for IV with monitoring.
Feasibility	Easy for SC low-dose; requires planning for SC high-dose and IV infusion.
Recommendation	SC UFH ≤ 5,000 units BID/TID: neuraxial block safe without delay. SC UFH > 10,000 units/day: delay ≥ 12 h. IV UFH infusion: stop 4–6 h before block and confirm normal coagulation.

6. Evidence-to-Decision Table of LMWH

Criterion	LMWH (Low & High-Dosing)
Problem	LMWH is widely used for surgical prophylaxis and therapeutic anticoagulation, complicating neuraxial anesthesia.
Benefit	Safe neuraxial block is possible if dosing intervals are respected.
Risk/Harm	Risk of spinal/epidural hematoma if block is performed too soon after dosing.
Certainty of Evidence	High for both low and high-dosing.
Values & Preference	Clinicians strongly prefer safety margins and clear timing guidance.
Resource Use	Minimal cost; routine monitoring not required.
Equity	Widely available; dosing schedules may vary globally.
Acceptability	High acceptability when timing rules are followed.
Feasibility	Easy to implement with clear scheduling.
Recommendation	Prophylactic LMWH: delay ≥ 12 h after last dose. Therapeutic LMWH: delay ≥ 24 h after last dose. Restart LMWH ≥ 4 h after catheter removal.

7. Evidence-to-Decision Table of Antiplatelets

Criterion	Aspirin / Clopidogrel / Ticagrelor / Prasugrel
Problem	Antiplatelets complicate neuraxial anesthesia.
Benefit	Safe block possible after discontinuation (except aspirin).
Risk/Harm	Hematoma risk if active.
Certainty of Evidence	High.
Values & Preference	Safety prioritized.
Resource Use	No monitoring available.
Equity	Widely available.
Acceptability	High if timing is respected.
Feasibility	Easy with discontinuation.
Recommendation	Aspirin: safe. Clopidogrel/ticagrelor: stop ≥ 5–7 d. Prasugrel: stop ≥ 7– 10 days.
Remarks	Restart only after catheter removal.

8. Evidence-to-Decision Table of Thrombolytics

Criterion	Thrombolytics (tPA formulations)
Problem	Used for acute MI, stroke, and PE.
Benefit	Life-saving in acute events.
Risk/Harm	Extremely high hematoma risk.
Certainty of Evidence	High.
Values & Preference	Safety prioritized; neuraxial avoided.
Resource Use	No safe monitoring strategy.
Equity	Limited in low-resource settings.
Acceptability	Low for neuraxial anesthesia.
Feasibility	Not feasible within 10 days.
Recommendation	Neuraxial block contraindicated within 10 days.

Remarks	Peripheral blocks may be considered with caution.

9. Evidence-to-Decision Table of Warfarin

Criterion	Warfarin (VKA; Vitamin K Antagonist)
Problem	INR elevation complicates neuraxial anesthesia.
Benefit	Safe block if INR ≤ 1.4.
Risk/Harm	High hematoma risk if INR is elevated.
Certainty of Evidence	High.
Values & Preference	INR confirmation is essential.
Resource Use	Requires INR testing.
Equity	Accessible in most systems.
Acceptability	High if INR ≤ 1.4.
Feasibility	Easy with routine INR monitoring.
Recommendation	Perform block only if INR ≤ 1.4.
Remarks	Resume warfarin after catheter removal.

Annex II: Timing Tables

1. Timing Table of LMWH:

Dosing	Pre-procedure Hold	Catheter Dwell	Removal	Resumption
Low	≥12 h	Caution	≥12 h after last dose	≥4 h post-removal
High	≥24 h	Avoid	≥24 h after last dose	Individualized, delay if bleeding risk.

2. Specific Drug Timing (Wait Times Before Block)

Drug Category	Low Dose (Wait Time)	High Dose (Wait Time)
UFH (Heparin)	4–6 hours	24 hours (check aPTT)
LMWH (Enoxaparin)	12 hours	24 hours
Apixaban / Rivaroxaban	24–30 hours	72 hours
Dabigatran	34–52 hours	72–110 hours (CrCl dependent)
Clopidogrel	5–7 days	5–7 days
Prasugrel	7–9 days	7–9 days

Annex III:
Traumatic (Bloody) Tap Management Protocol

- Definition and Identification: A **Traumatic Tap** is defined as the aspiration or spontaneous appearance of blood in the needle or catheter during the performance of a regional anesthetic technique. In the context of "high-risk" blocks, this indicates potential vessel injury in a non-compressible or concealed space (e.g., the epidural space or psoas compartment).

- Immediate Procedural Management:

- Aspiration Check**:** If blood is seen, the needle should be repositioned or the procedure aborted, depending on the clinical urgency and the degree of difficulty.
- Documentation**:** The occurrence of a traumatic tap **must** be clearly documented in the anesthetic record and the patient's medical chart to alert the postoperative care team.
- Surgical Communication**:** Inform the surgical team of the event, as it may influence the choice and timing of postoperative thromboprophylaxis.
- **Medication Management (Restart Delays):** To ensure the stability of the initial platelet plug and prevent the expansion of an occult hematoma, the administration of the first postoperative dose of anticoagulation must be delayed.

Medication	**Post-Traumatic Tap Restart Delay**	**Level of Evidence**
Apixaban	Delay 48 hours	Conditional / Manufacturer Recommendation
Rivaroxaban	Delay 24 hours	Conditional / Manufacturer Recommendation
LMWH (Enoxaparin)	Delay 24 hours	Strong / ASRA PM 2025
UFH (Heparin)	Delay 24 hours	Strong / ASRA PM 2025
Dabigatran / Edoxaban	Delay 24–48 hours*	Expert Opinion

*Note: While specific manufacturer recommendations are currently lacking for Dabigatran and Edoxaban, the ASRA 2025 "antihemorrhagic" philosophy suggests a conservative delay of at least 24 hours (or 48 hours if high-dose therapy is planned).

Appendix:

Table 1: Suggested risk stratification for patient-specific periprocedural thromboembolism*

Risk category	Mechanical heart valve	Atrial fibrillation	VTE
High (>10%/y risk of ATE or >10%/mo risk of VTE)	Mitral valve with major risk factors for stroke† Caged ball or tilting disc mitral valve in mitral/atric position Recent (<3 mo) stroke or TIA	$CHADS_2VASc$ score ≥7 or $CHADS_2$ score of 5 or 6; recent (<3 mo) stroke or TIA; rheumatic valvular heart disease	Recent (< 3 month and especially < 1 month) VTE Severe thrombophilia (deficiency of protein C, protein S, or antithrombin; homozygous factor V Leiden or prothrombin gene G20210A mutation or double heterozygous for each mutation, multiple thrombophilias) Antiphospholipid antibodies Active cancer associated with high VTE risk‡
Moderate (4%–10%/y risk of ATE or 4%–10%/mo risk of VTE)	Mitral valve without major risk factors for stroke Bileaflet AVR with major risk factors for stroke	$CHA2DS_2$ score of 5 or 6 or $CHADS_2$ score of 3 or 4	VTE within past 3–12 mo Recurrent VTE Non-severe thrombophilia (heterozygous factor V Leiden or prothrombin gene G20210A mutation) Active cancer or recent history of cancer
Low (<4%/y risk of ATE or <2%/mo risk of VTE)	Bileaflet AVR without major risk factors for stroke†	CHA_2DS_2 Vasc score of 1–4 or $CHADS_2$ score of 0–2 (and no prior stroke or TIA)	VTE >12 mo ago

*Empiric risk stratification that is a starting point for assessing perioperative thromboembolism risk; should be combined with clinical judgment that incorporates individual patient-related and surgery/procedure-related factors.
†Includes: AF, prior stroke/TIA during anticoagulant interruption or other prior stroke/TIA, prior valve thrombosis, rheumatic heart disease **[101].**

Table 2: VTE risk scoring tools: medical patients.

	Points	
Risk factor	**PADUA score [9]**	**IMPROVE score [10]**
Active cancer	3	2
Prior VTE	3	3
Reduced mobility	3	Limb paresis (2 points) Immobility ≥ 7 days (1 point)
Thrombophilia	3	2
Recent trauma/surgery (≤1 month)	2	–
Age ≥70 years	1	1 (age >60 years)
Heart or respiratory failure	1	–
Acute MI or ischemic stroke	1	ICU stay (1 point)
Acute infection/rheumatological disorder	1	–
Obesity (BMI >30)	1	–
Hormonal therapy	1	–
High thrombosis risk	≥4 points	≥4 points

BMI, body mass index; ICU, intensive care unit; IMPROVE, International Medical Prevention Registry on Venous Thromboembolism; MI, myocardial infarction; PADUA, University of Padua, Padova Italy; VTE, venous thromboembolism **[1].**

Table 3: Direct Oral Anticoagulants

	Apixaban (Eliquis) [102]	Edoxaban (Savaysa) [103]	Rivaroxaban (Xarelto) [104]	Dabigatran (Pradaxa) [105]
Low dose				
Indications and dosing	Reduction in the risk of recurrent DVT and PE following initial therapy: • 2.5 mg two times per day Prophylaxis of DVT following THA or TKA: • 2.5 mg two times per day	N/A	Reduction in the risk of recurrence of DVT and/or PE in patients at continued risk for DVT and/or PE • In patients with a CrCl >15 mL/min: 10 mg once per day • In patients with a CrCl <15 mL/min: avoid use Prophylaxis of DVT following THA or TKA: • In patients with a CrCl >15 mL/min: 10 mg once per day • In patients with a CrCl <15 mL/min: avoid use. Prophylaxis of VTE in ill medical patients at risk for thromboembolic complications, not at high risk of bleeding • In patients with a CrCl >15 mL/min: 10 mg once per day • In patients with a CrCl <15 mL/min: avoid use Reduction of risk of major cardiovascular events (CV death, MI, and stroke in CAD) • No dose adjustment needed based on CrCl • 2.5 mg two times per day plus aspirin (75–100 mg once per day) Reduction of risk of major thrombotic vascular events in PAD, including patients after recent lower extremity Revascularization due to symptomatic PAD	Prophylaxis of DVT and PE following THA: • In patients with CrCl >30 mL/min: 110 mg once per day first day, then 220 mg once per day • In patients with CrCl <50 mL/min and concomitant use of P-gp inhibitors (ie, dronedarone or systemic ketoconazole): avoid coadministration

			• No dose adjustment needed based on CrCl • 2.5 mg two times per day plus aspirin (75–100 mg once per day)	
High dose				
Indications and dosing	Reduction of risk of stroke and systemic embolism in NVAF: • 5 mg two times per day • In patients with at least two of the following characteristics: age ≥80 years, body weight <60 kg, or serum creatinine ≥1.5 mg/dL: • 2.5 mg two times per day Treatment of DVT and PE: • 10 mg two times per day for 7 days, followed by 5 mg two times per day • In patients receiving 5 mg or 10 mg two times per day and concomitant use of P-gp and strong CYP3A4 inhibitors (ie, ketoconazole, itraconazole, ritonavir): reduce the dose by 50%	Reduction of risk of stroke and systemic embolism in NVAF: • In patients with CrCl >50 to ≤95 mL/min: • 60 mg once per day • Do not use in patients with CrCl >95 mL/min • In patients with CrCl 15–50 mL/min: • 30 mg once per day Treatment of DVT and PE: • 60 mg once per day • In patients with one or more of the following clinical factors: CrCl 15–50 mL/min or body weight ≤60 kg, or the concomitant use of P-gp inhibitors: • 30 mg once per day	Reduction of risk of stroke and systemic embolism in NVAF: • In patients with CrCl >50 mL/min: • 20 mg once per day • In patients with CrCl 15–50 mL/min: • 15 mg once per day Treatment of DVT, PE, and reduction in the risk of recurrent DVT and of PE: • In patients with a CrCl >15 mL/min: • 15 mg two times per day for the first 21 days of the initial treatment • 20 mg once per day for the remaining treatment	Reduction of risk of stroke and systemic embolism in NVAF in adult patients: • In patients with CrCl >30 mL/min: • 150 mg two times per day • In patients with CrCl 30–50 mL/min and concomitant use of P-gp inhibitors (ie, dronedarone or systemic ketoconazole): • 75 mg two times per day • In patients with CrCl 15–30 ml min^{-1}: • 75 mg two times per day • In patients with CrCl <30 mL/min and concomitant use of P-gp inhibitors (ie, dronedarone or systemic ketoconazole): avoid coadministration Treatment of DVT and PE in adult patients: • In patients with CrCl >30 mL/min: 150 mg two times per day • Reduction in the risk of recurrent DVT and PE in adult patients: • In patients with CrCl >30 mL/min: 150 mg two times per day

CAD, coronary artery disease; CrCI, creatinine clearance; CV, cardiovascular; CYP3A4, cytochrome P450 3A4; DVT, deep venous thrombosis; MI, myocardial infarction; N/A, not available; NVAF, non-valvular atrial fibrillation; PAD, peripheral artery disease; PE, pulmonary embolism; P-gp, P-glycoprotein; THA, total hip arthroplasty; TIA, transient ischemic attack; VTE, venous thromboembolism.

Table 4: Three Herbal Medications with the greatest impact on hemostasis*

	Important effects	Perioperative concerns	Time to normal hemostasis after discontinuation
Garlic	Inhibition of platelet aggregation (may be irreversible) Increased fibrinolysis Equivocal antihypertensive activity	Potential to increase bleeding, especially when combined with other medications that inhibit platelet aggregation	7 days
Ginko	Inhibition of platelet-activating factor	Potential to increase bleeding, especially when combined with other medications that inhibit platelet aggregation	36 hours
Ginseng	Lowers blood glucose Increased prothrombin and activated partial prothrombin times in animals Other diverse effects	Hypoglycemia Potential to increase risk of bleeding Potential to decrease anticoagulant effect of warfarin	24 hours

Adapted from Horlocker* et al. *[3]
*At this time, it is not deemed necessary to discontinue herbal medications and allow resolution of their effects on hemostasis prior to surgery or anesthesia.

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