

Executive Summary: Regional Anesthesia in the Patient Receiving Antithrombotic or Thrombolytic Therapy

American Society of Regional Anesthesia and Pain Medicine Evidence-Based Guidelines (Third Edition)

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Numerous studies have documented the safety of neuraxial anesthesia and analgesia in the anticoagulated patient. Patient management is based on appropriate timing of needle placement and catheter removal relative to the timing of anticoagulant drug administration. Familiarity with the pharmacology of hemostasis-altering drugs, the clinical studies involving patients undergoing neuraxial blockade while receiving these medications, as well as the case reports of spinal hematoma will guide the clinician in management decisions.

New challenges in the management of the anticoagulated patient undergoing neuraxial blockade have arisen as medical standards for the prevention of perioperative venous thromboembolism were established. Likewise, as more efficacious anticoagulants and antiplatelet agents have been introduced, patient management has become more complex. In response to these patient safety issues, the American Society of Regional Anesthesia and Pain Medicine (ASRA) convened its Third Consensus Conference on Regional Anesthesia and Anticoagulation. Portions of the material presented here were published as the proceedings of the 1997 and 2002 ASRA Consensus Conferences.^{1–6} The information has been updated to incorporate additional data available since the time of its publication. Variances from recommendations contained in this document may be acceptable based on the judgment of the responsible anesthesiologist. The consensus statements are designed to encourage safe and quality patient care but cannot guarantee a specific outcome. They are also subject to timely revision as justified by evolution of information and practice.

These recommendations focus on patients receiving neuraxial and peripheral techniques. The practice settings include inpatient (eg, operating rooms, intensive care units, postoperative surgical floors, labor and delivery settings, or hospital wards) and ambulatory facilities such as pain clinics. The recommendations are intended for use by anesthesiologists and other physicians and health care providers performing

neuraxial and peripheral regional anesthetic/analgesic blockade. However, these recommendations may also serve as a resource for other health care providers involved in the management of patients who have undergone similar procedures (eg, myelography, lumbar puncture).

The original article developed from the Consensus Conference held during the 32nd Annual Regional Anesthesia Meeting and Workshops held on April 19–22, 2007, in Vancouver, British Columbia, Canada, is published in this issue of *Regional Anesthesia and Pain Medicine* (*Reg Anesth Pain Med* 35: 64–101). The full-length document provides the necessary background to a more complete understanding of the clinical issues discussed at the Consensus Conference.

1.0 Administration of Antithrombotic Agents for the Prevention and Treatment of Venous Thromboembolism

- 1.1 In accordance with American College of Chest Physicians guidelines, for each of the antithrombotic agents, we recommend that clinicians follow the manufacturer-suggested dosing guidelines (Grade 1C).

2.0 Anesthetic Management of the Patient Receiving Thrombolytic Therapy

Patients receiving fibrinolytic/thrombolytic medications are at risk for 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 *spontaneous* neuraxial bleeding with these medications.

- 2.1 In patients scheduled to receive thrombolytic therapy, we recommend that the patient be queried and 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 after puncture of noncompressible vessels (Grade 1A).
- 2.2 In patients who have received fibrinolytic and thrombolytic drugs, we recommend against performance of spinal or epidural anesthetics except in highly unusual circumstances (Grade 1A). Data are not available to clearly outline the length of time neuraxial puncture should be avoided after discontinuation of these drugs.
- 2.3 In those patients who have received neuraxial blocks at or near the time of fibrinolytic and thrombolytic therapy, we recommend that neurologic monitoring

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should be continued for an appropriate interval. It may be that the interval of monitoring should not be more than 2 hrs between neurologic checks. 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 neurologic function (Grade 1C).

- 2.4 There is no definitive recommendation for removal of neuraxial catheters in patients who unexpectedly receive fibrinolytic and thrombolytic therapy during a neuraxial catheter infusion. We suggest the measurement of fibrinogen level (one of the last clotting factors to recover) to evaluate the presence of residual thrombolytic effect and appropriate timing of catheter removal (Grade 2C).

3.0 Anesthetic Management of the Patient Receiving Unfractionated Heparin (UFH)

Anesthetic management of the heparinized patient was established during 2 decades ago. Initial recommendations have been supported by in-depth reviews of case series, case reports of spinal hematoma, and the American Society of Anesthesiologists Closed Claims Project. Recent thromboprophylaxis guidelines identifying more patients as candidates for thrice-daily subcutaneous heparin and the potential for increased bleeding with this therapy have prompted a modification of the previous ASRA guidelines.

- 3.1 We recommend daily review of the patient's medical record to determine the concurrent use of medications that affect other components of the clotting mechanisms. These medications include antiplatelet medications, low-molecular weight heparin (LMWH) and oral anticoagulants (Grade 1B).
- 3.2 In patients receiving prophylaxis with subcutaneous UFH with dosing regimens of 5000 U twice daily, there is no contraindication to the use of neuraxial techniques. The risk of neuraxial bleeding may be reduced by delay of the heparin injection until after the block and may be increased in debilitated patients after prolonged therapy (Grade 1C).
- 3.3 The safety of neuraxial blockade in patients receiving doses greater than 10,000 U of UFH daily or more than twice-daily dosing of UFH has not been established. Although the use of thrice-daily UFH may lead to an increased risk of surgical-related bleeding, it is unclear whether there is an increased risk of spinal hematoma. We suggest that the risk and benefits of thrice-daily UFH be assessed on an individual basis and that techniques to facilitate detection of new/progressive neurodeficits (eg, enhanced neurologic monitoring occur and neuraxial solutions to minimize sensory and motor block) be applied (Grade 2C).
- 3.4 Because heparin-induced thrombocytopenia may occur during heparin administration, we recommend that patients receiving heparin for greater than 4 days have a platelet count assessed before neuraxial block and catheter removal (Grade 1C).
- 3.5 Combining neuraxial techniques with intraoperative anticoagulation with heparin during vascular surgery is acceptable with the following recommendations (Grade 1A):
- 3.5.1 Avoid the technique in patients with other coagulopathies.

3.5.2 Delay heparin administration for 1 hr after needle placement.

3.5.3 Remove indwelling neuraxial catheters 2 to 4 hrs after the last heparin dose and assess the patient's coagulation status; re-heparin 1 hr after catheter removal.

3.5.4 Monitor the patient postoperatively to provide early detection of motor blockade and consider use of minimal concentration of local anesthetics to enhance the early detection of a spinal hematoma.

3.5.5 Although the occurrence of a bloody or difficult neuraxial needle placement may increase risk, 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 warranted.

- 3.6 Currently, insufficient data and experience are available to determine if the risk of neuraxial hematoma is increased when combining neuraxial techniques with the full anticoagulation of cardiac surgery. We suggest postoperative monitoring of neurologic function and selection of neuraxial solutions that minimize sensory and motor block to facilitate detection of new/progressive neurodeficits (Grade 2C).

4.0 Anesthetic Management of the Patient Receiving LMWH

Anesthesiologists in North America can draw on the extensive European experience to develop practice guidelines for the management of patients undergoing spinal and epidural blocks while receiving perioperative LMWH. All consensus statements contained herein respect the labeled dosing regimens of LMWH as established by the Food and Drug Administration. Although it is impossible to devise recommendations that will completely eliminate the risk of spinal hematoma, previous consensus recommendations have seemed to improve outcome. Concern remains for higher-dose applications, where sustained therapeutic levels of anticoagulation are present.

4.1 The anti-Xa level is not predictive of the risk of bleeding. We recommend against the routine use of monitoring of the anti-Xa level (Grade 1A).

4.2 Antiplatelet or oral anticoagulant medications administered in combination with LMWH increase the risk of spinal hematoma. Education of the entire patient care team is necessary to avoid potentiation of the anticoagulant effects. We recommend against concomitant administration of medications affecting hemostasis, such as antiplatelet drugs, standard heparin, or dextran, regardless of LMWH dosing regimen (Grade 1A).

4.3 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 hrs postoperatively and that this consideration be discussed with the surgeon (Grade 2C).

4.4 Preoperative LMWH

4.4.1 Patients on preoperative LMWH thromboprophylaxis can be assumed to have altered coagulation. In these patients, we recommend that needle placement should occur at least 10 to 12 hrs after the LMWH dose (Grade 1C).

4.4.2 In patients receiving higher (treatment) dosages of LMWH, such as enoxaparin 1 mg/kg every 12 hrs, enoxaparin 1.5 mg/kg daily, dalteparin 120 U/kg every 12 hrs, dalteparin 200 U/kg

daily, or tinzaparin 175 U/kg daily, we recommend delay of at least 24 hrs to ensure normal hemostasis at the time of needle insertion (Grade 1C).

- 4.4.3 In patients administered a dose of LMWH 2 hrs preoperatively (general surgery patients), we recommend against a neuraxial techniques because needle placement would occur during peak anticoagulant activity (Grade 1A).

4.5 Postoperative LMWH

Patients with postoperative LMWH thromboprophylaxis may safely undergo single-injection and continuous catheter techniques. Management is based on total daily dose, timing of the first postoperative dose and dosing schedule (Grade 1C).

- 4.5.1 Twice-daily dosing. This dosage regimen is associated with an increased risk of spinal hematoma. The first dose of LMWH should be administered no earlier than 24 hrs postoperatively, regardless of anesthetic technique, and only in the presence of adequate (surgical) hemostasis. Indwelling catheters should be removed before initiation of LMWH thromboprophylaxis. If a continuous technique is selected, the epidural catheter may be left indwelling overnight but must be removed before the first dose of LMWH. Administration of LMWH should be delayed for 2 hrs after catheter removal.
- 4.5.2 Single-daily dosing. The first postoperative LMWH dose should be administered 6 to 8 hrs postoperatively. The second postoperative dose should occur no sooner than 24 hrs after the first dose. Indwelling neuraxial catheters may be safely maintained. However, the catheter should be removed a minimum of 10 to 12 hrs after the last dose of LMWH. Subsequent LMWH dosing should occur a minimum of 2 hrs after catheter removal. No additional hemostasis-altering medications should be administered owing to the additive effects.

5.0 Regional Anesthetic Management of the Patient on Oral Anticoagulants

The management of patients receiving warfarin perioperatively remains controversial. Recommendations are based on warfarin pharmacology, the clinical relevance of vitamin K coagulation factor levels/deficiencies, case series, and the case reports of spinal hematoma among these patients. Web sites are available to assist clinicians with warfarin dosing (www.WarfarinDosing.org).

- 5.1 Caution should be used when performing neuraxial techniques in patients recently discontinued from chronic warfarin therapy. In the first 1 to 3 days after discontinuation of warfarin therapy, the coagulation status (reflected primarily by factor II and X levels) may not be adequate for hemostasis despite a decrease in the international normalized ratio (INR; indicating a return of factor VII activity). Adequate levels of II, VII, IX, and X may not be present until the INR is within reference limits. We recommend that the anticoagulant therapy must be stopped (ideally 4–5 days before the planned procedure), and the INR measured before initiation of neuraxial block (Grade 1B).
- 5.2 We recommend against the concurrent use of medications that affect other components of the clotting

mechanisms and may increase the risk of bleeding complications for patients receiving oral anticoagulants and do so without influencing the INR. These medications include aspirin and other nonsteroidal anti-inflammatory drugs (NSAIDs), ticlopidine and clopidogrel, UFH, and LMWH (Grade 1A).

- 5.3 In patients who are likely to have an enhanced response to the drug, we recommend that a reduced dose be administered. Algorithms have been developed to guide physicians in the appropriate dosing of warfarin based on desired indication, patient factors, and surgical factors. These algorithms may be extremely useful in patients at risk for an enhanced response to warfarin (Grade 1B).
- 5.4 In patients receiving an initial dose of warfarin before surgery, we suggest the INR should be checked before neuraxial block if the first dose was administered more than 24 hrs earlier if or a second dose of oral anticoagulant has been administered (Grade 2C).
- 5.5 In patients receiving low-dose warfarin therapy during epidural analgesia, we suggest that their INR be monitored on a daily basis (Grade 2C).
- 5.6 Neurologic testing of sensory and motor function should be performed routinely during epidural analgesia for patients on warfarin therapy. To facilitate neurologic evaluation, we recommend that the type of analgesic solution be tailored to minimize the degree of sensory and motor blockade (Grade 1C).
- 5.7 As thromboprophylaxis with warfarin is initiated, we suggest that neuraxial catheters should be removed when the INR is less than 1.5. This value was derived from studies correlating hemostasis with clotting factor activity levels greater than 40%. We suggest that neurologic checks be continued for at least 24 hrs after catheter removal for these patients (Grade 2C).
- 5.8 In patients with INR greater than 1.5 but less than 3, we recommend that removal of indwelling catheters should be done with caution and the medication record reviewed for other medications that may influence hemostasis that may not effect the INR (eg, NSAIDs, clopidogrel, ticlopidine, UFH, LMWH) (Grade 2C). We also recommend that neurologic status be assessed before catheter removal and continued until the INR has stabilized at the desired prophylaxis level. (Grade 1C).
- 5.9 In patients with an INR greater than 3, we recommend that the warfarin dose be held or reduced in patients with indwelling neuraxial catheters (Grade 1A). We can make no definitive recommendation regarding the management to facilitate removal of neuraxial catheters in patients with therapeutic levels of anticoagulation during neuraxial catheter infusion (Grade 2C).

6.0 Anesthetic Management of the Patient Receiving Antiplatelet Medications

Antiplatelet medications, including NSAIDs, thienopyridine derivatives (ticlopidine and clopidogrel) and platelet glycoprotein (GP) IIb/IIIa antagonists (abciximab, eptifibatide, tirofiban) exert diverse effects on platelet function. The pharmacologic differences make it impossible to extrapolate between the groups of drugs regarding the practice of neuraxial techniques. There is no wholly accepted test, including the bleeding time, which will guide antiplatelet therapy. Careful preoperative assessment of the patient to identify alterations of health that might contribute to bleeding is crucial. These conditions include a

history of easy bruising/excessive bleeding, female sex, and increased age.

- 6.1 Nonsteroidal anti-inflammatory drugs seem to represent no added significant risk for the development of spinal hematoma in patients having epidural or spinal anesthesia. NSAIDs (including aspirin) do not create a level of risk that will interfere with the performance of neuraxial blocks. In patients receiving these medications, we do not identify specific concerns as to the timing of single-shot or catheter techniques in relationship to the dosing of NSAIDs, postoperative monitoring, or the timing of neuraxial catheter removal (Grade 1A).
- 6.2 In patients receiving NSAIDs, we recommend against the performance of neuraxial techniques if the concurrent use of other medications affecting clotting mechanisms, such as oral anticoagulants, UFH, and LMWH, is anticipated in the early postoperative period because of the increased risk of bleeding complications. Cyclooxygenase-2 inhibitors have minimal effect on platelet function and should be considered in patients who require anti-inflammatory therapy in the presence of anticoagulation (Grade 2C).
- 6.3 The actual risk of spinal hematoma with ticlopidine and clopidogrel and the GP IIb/IIIa antagonists is unknown. Management is based on labeling precautions and the surgical, interventional cardiology/radiology experience (Grade 1C).
 - 6.3.1 On the basis of labeling and surgical reviews, the suggested time interval between discontinuation of thienopyridine therapy and neuraxial blockade is 14 days for ticlopidine and 7 days for clopidogrel. If a neuraxial block is indicated between 5 and 7 days of discontinuation of clopidogrel, normalization of platelet function should be documented.
 - 6.3.2 Platelet GP IIb/IIIa inhibitors exert a profound effect on platelet aggregation. After administration, the time to normal platelet aggregation is 24 to 48 hrs for abciximab and 4 to 8 hrs for eptifibatid and tirofiban. Neuraxial techniques should be avoided until platelet function has recovered. Although GP IIb/IIIa antagonists are contraindicated within 4 weeks of surgery, should one be administered in the postoperative period (after a neuraxial technique), we recommend that the patient be carefully monitored neurologically.

7.0 Anesthetic Management of the Patient Receiving Herbal Therapy

Herbal drugs, by themselves, seem to represent no added significant risk for the development of spinal hematoma in patients having epidural or spinal anesthesia. This is an important observation because it is likely that a significant number of our surgical patients use alternative medications preoperatively and perhaps during their postoperative course.

- 7.1 The use of herbal medications does not create a level of risk that will interfere with the performance of neuraxial block. We recommend against mandatory discontinuation of these medications or avoidance of regional

anesthetic techniques in patients in whom these medications have been administered (Grade 1C).

8.0 Anesthetic Management of Patients Receiving Thrombin Inhibitors (Desirudin, Lepirudin, Bivalirudin, and Argatroban)

- 8.1 In patients receiving thrombin inhibitors, we recommend against the performance of neuraxial techniques (Grade 2C).

9.0 Anesthetic Management of the Patient Receiving Fondaparinux

The actual risk of spinal hematoma with fondaparinux is unknown. Consensus statements are based on the sustained and irreversible antithrombotic effect, early postoperative dosing, and the spinal hematoma reported during initial clinical trials. Close monitoring of the surgical literature for risk factors associated with surgical bleeding may be helpful in risk assessment and patient management.

- 9.1 Until further clinical experience is available, performance of neuraxial techniques should occur under conditions used in clinical trials (single-needle pass, atraumatic needle placement, avoidance of indwelling neuraxial catheters). If this is not feasible, an alternate method of prophylaxis should be considered.

10.0 Anesthetic management of the Anticoagulated Parturient

- 10.1 In the absence of a large series of neuraxial techniques in the pregnant population receiving prophylaxis or treatment of venous thromboembolism, we suggest that the ASRA guidelines (derived from mainly from surgical patients) be applied to parturients (Grade 2C).

11.0 Anesthetic Management of the Patient Undergoing Plexus or Peripheral Block

- 11.1 For patients undergoing deep plexus or peripheral block, we recommend that recommendations regarding neuraxial techniques be similarly applied (Grade 1C).

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