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ORIGINAL ARTICLE

Focus on perioperative management of anticoagulants and antiplatelet agents in spine surgery

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Summary Perioperative management of anticoagulants and antiplatelet agents is based on a compromise between the risk of hemorrhage induced by maintaining (or substituting for) them and the risk of thrombosis if they are discontinued. The hemorrhage risk in major spinal surgery is clear (50—81% incidence of transfusion), and the incidence of postoperative symptomatic spinal hematoma varies between 0.4% and 0.2% depending on whether low-molecular-weight heparin (LMWH) is prescribed postoperatively. The French Health Authority, in 2008, published guidelines on the management of patients treated with vitamin K antagonists. Treatment may be stopped without preoperative replacement in certain cases of atrial fibrillation or venous thromboembolic disease; otherwise, preoperative replacement by curative dose unfractionated heparin (UFH) or LMWH is recommended, with withdrawal early enough to avoid peroperative bleeding. Postoperative care should take account of hemorrhagic risk following surgery. The management of patients treated with antiplatelets is delicate, as maintenance is preferable in most of the situations in which they are prescribed (bare or active stenting, or secondary prevention of myocardial infarction, stroke or peripheral ischemia), although they are liable to increase the risk of perioperative hemorrhage, especially when associated to antithrombotic prophylaxis. If surgery cannot be performed under treatment continuation, the interruption should be as short as possible. New guidelines are presently being drawn up under the auspices of the French Health Authority. In both types of treatment, the strategy should be jointly determined by surgeon, anesthesiologist and cardiologist, to optimize individualized care taking account of each party's requirements, with the patient in the central role. The selected strategy should be clearly stated in the patient's file.
Level of evidence: V.

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Introduction

Perioperative management of anticoagulants and antiplatelet agents is a concern shared by anesthesiology and surgery teams. The latter face the risk of hemorrhage induced by an aggressive procedure and enhanced by maintenance of treatment and by the risk of arterial or venous thrombosis associated with perioperative withdrawal. Spinal surgery covers a wide variety of procedures, with varying associated hemorrhage risk precluding any single solution. The considerations discussed in the present article focus on these various aspects with a view to recommending rational attitudes guided by the association of surgical and patient-based risks.

Hemorrhage and thrombosis risk in spine surgery

Hemorrhage risk

The hemorrhage risk specific to spinal surgery seems not to be clearly assessed in the various attempted stratifications of surgical specialties. Orthopedic and neurologic surgeries are respectively classified as moderate and high risk, but spine surgery is not given a classification [1].

Hemorrhage risk depends partly of the degree of blood loss, but also on the postoperative location of hemorrhage (spinal hemorrhage).

Blood loss ranged from 650 to 2839 mL in 900 patients undergoing arthrodesis surgery without preventive strategies for bleeding [2]; the transfusion rate ranged from 50% to 81%. Most cases involved instrumentation, recognized in previous studies as a factor of increased bleeding and need for transfusion [3]. Postoperative hemorrhage in 2507 patients undergoing spine surgery with antithrombotic prophylaxis ranged from 0 to 4.3% depending on the study [4]. Four independent factors were identified as predictive of transfusion in 230 patients undergoing scheduled thoracolumbar surgery [5]: age superior than 50 years, preoperative hemoglobin concentration inferior than 12 g/dL, superior than two levels of arthrodesis, and transpedicular osteotomy. By weighting each of these factors, the authors were able to draw up a predictive score perfectly correlated with the number of erythrocyte concentrates actually delivered.

Spinal hematoma is a major postoperative hemorrhagic complication. A meta-analysis of 493 articles published between 1966 and 2007 [6] found 16 studies identifying risk of symptomatic hematoma with ($n = 6$) or without ($n = 10$) associated antithrombotic prophylaxis. Incidence varied between 0.4% and 0.2% depending on whether low-molecular-weight heparin (LMWH) was prescribed or not. These figures are very low compared to those for asymptomatic postoperative hematoma detected on MRI [7,8]. These findings are comparable to those of Cheng et al. [4], who reported 10 hematomas in 2507 patients operated on. This rate is comparable to that observed in anesthesiologic practice providing epidural analgesia with concomitant treatment affecting [9]. It clearly raises the problem of adapted postoperative anticoagulant and antiplatelet management.

Thrombosis risk

The 2005 French Anesthesiology and Intensive Care Society (*Société française d'anesthésie réanimation* [SFAR]) recommendations for antithrombotic prophylaxis [10] in spine surgery identify three risk categories, with prevention strategies adapted to the surgical procedure and patient status (Table 1).

The 2008 American guidelines [11] recommend no prophylaxis in moderate risk surgery, LMWH, unfractionated heparin (UFH) or intermittent pneumatic compression (IPC) in case of minor associated risk factors, and combined phar-

Table 1 Prevention of deep venous thrombosis: French Anesthesiology and Intensive Care Society (SFAR) 2005 recommendations.

Head, neck and spine surgery			
Surgical risk	Patient-related risk	Recommendations	Grade
Low			
ENT	–	Nothing or GCS	D
Discal hernia			
1 or 2 level cervical laminectomy	+	LMWH	D
Moderate			
Extensive cervical laminectomy	–	UFH ± GCS	D
Dorsolumbar laminectomy		LMWH ± GCS	D
Spinal osteosynthesis	+	IPC	D
		LMWH	D
High			
Intracranial neurosurgery		LMWH/UFH	A/B
		+ GCS or IPC	C
Medullary trauma		LMWH or UFH	B
		+ GCS or IPC	C

LMWH: low-molecular-weight heparin; UFH: unfractionated heparin; GCS: graduated compression stocking; IPC: intermittent pneumatic compression.

macologic and mechanical prophylaxis in case of major thrombosis risk factors. In case of major postoperative hemorrhage risk (multiple trauma), priority should be given to IPC, with medical prophylaxis as a bridge or complement during phase-out.

The most recent reports argue for overall reduction of postoperative thrombosis risk [4]. In absence of prophylaxis, the risk of documented (phlebography, Doppler, ultrasound or fibrinogen test) deep venous thrombosis (DVT) in a population of 1,619 patients was 6% in trauma without medullary involvement, 5.3% in deformity and 2.3% in degenerative damage; risk of pulmonary embolism (PE) in the same indications was respectively 2%, 2.7% and 0.4%. Incidence of DVT and PE respectively ranged from 0 to 0.6% and 0 to 0.2% in case of antithrombotic prophylaxis. Another meta-analysis [12] reported overall prevalence of 1.09% for DVT and 0.06% for PE (total of 4383 patients). In absence of prophylaxis, incidence of DVT was 5.8%. Operative level (cervical vs. thoracolumbar) and type of pathology did not impact DVT prevalence.

Perioperative management of anticoagulants and antiplatelets

Patients under vitamin K agonists (VKA)

Vitamin K agonists treatment is basically indicated in patients equipped with a mechanical cardiac valve or subject to atrial fibrillation or venous thromboembolic disease. In 77% of cases, the drug prescribed in France is fluindione (Préviscan®). The hemorrhage risk associated with surgery depends on the international normalized ratio (INR), an index of anticoagulant level. Target INR in most procedures is inferior than 1.5; it should be inferior than 1.2 in neurosurgery, and likewise probably in spinal surgery involving a risk of postoperative spinal hematoma. Table 2 shows thrombosis risk associated with withdrawal of treatment.

Perioperative management of VKA was the subject of the 2008 French Health Authority (*Haute Autorité de la santé* [HAS]) recommendations [13]. In situations of moderate risk, treatment is withdrawn preoperatively (last dose, D-5), without bridging. In case of elevated thrombosis risk, VKAs are bridged by preoperative heparin (iv UFH to obtain ACT = 2—3 × control; subcutaneous UFH, 400 IU/kg per two injections; curative dose LMWH in two injections per day in case of mechanical valves or AF). Iv UFH, subcutaneous UFH and LMWH are terminated respectively 4—6, 8—12 and 24 hours before surgery. The HAS website presents bridging proposals.

If the eve of surgery INR is greater than 1.5, addition of 5 mg per os vitamin K is recommended. Surgery should be scheduled for the morning, to optimize postoperative management.

In emergency, with less than 12 hours to surgery, administration of 25 IU/kg (= 1 ml/kg) iv PPSB (coagulation factors II, VII, IX and X) and 5 mg per os vitamin K is recommended, with control INR 30 minutes after injection to check reversion.

Postoperative management is less straightforward, depending on the previously estimated thrombosis risk. In high-risk situations and in absence of major persistent hemorrhage risk, resumption of VKA is recommended within 24 hours or at least as soon as possible after surgery. Heparin should be administered at curative dose in the 6—48 hours postoperatively. When curative treatment cannot be implemented rapidly, antithrombotic prophylaxis is to be undertaken on the usual protocol. The attitude of spine surgeons, however, was reported to vary greatly in terms of the interval to initiation of antithrombotic prophylaxis [14], which is generally at 24—48 hours post-surgery, on subjective criteria of personal experience.

In low thrombosis risk situations, rapid resumption of VKA and initiation of antithrombotic prophylaxis are recommended.

These standardized management protocols are likely to be brought into question by the advent of new oral anticoagulants (dabigatran, rivaroxaban, apixaban, etc.). Their field of action can be extended well beyond their present indications, for antithrombotic prophylaxis after total hip or knee replacement. Large scale trials have been run, particularly in the cardiovascular field (AF, DVT, acute coronary syndrome [ACS]) with a long-term view to replacing VKAs. This strategy would mean revisiting perioperative management as a whole, as their action time is much shorter (shorter preoperative withdrawal?) but their effect much faster (what postoperative resumption strategy?).

Patient under antiplatelets

Long-course antiplatelets are prescribed to prevent arterial thrombosis. They comprise acetylsalicylic acid (aspirin) and thienopyridines (clopidogrel [Plavix®] or ticlopidine [Ticlid®]), prescribed in isolation or in association. While acting on different specific targets, their effect is an irreversible 7—10 days inhibition of platelet function.

Table 2 Thrombosis risk on termination of vitamin K agonists (VKA) according to indications.

	Mechanical valve	AF	VTED
Moderate risk		All other patients	Other DVT or PE
High risk	Any mechanical valve	S, IS, systemic embolism	PE < 3 months Proximal DVT < 3 months Recurrent VTED

AF: atrial fibrillation; VTED: venous thromboembolic disease; S: stroke; IS: ischemic stroke; PE: pulmonary embolism; DVT: deep venous thrombosis.

Treatment-termination thrombosis risk depends on the type of underlying pathology. It is considered major in ACS of less than 1 month and for bare or active stents implanted respectively for less than 6 weeks or 1 year [15,16], and intermediate in secondary prevention of MI, stroke or lower limb arteriopathy. Several studies have spotlighted preoperative interruption of antiplatelet therapy as an independent risk factor for perioperative arterial thrombotic accident (MI, ischemic stroke [IS]) [15].

Current antiplatelet management guidelines therefore tend to recommend perioperative maintenance if compatible with the surgical procedure and its associated hemorrhage risk [15—17]. Risk assessment has not been evaluated in the spinal surgery literature [18]. A Chinese study of 138 procedures for narrow lumbar canal found significantly elevated bleeding associated with aspirin therapy [19]. A survey of practice among German neurosurgeons found that they interrupted antiplatelet therapy for a mean of 7 days [20].

What proposals can be made in practice, awaiting the guidelines currently being drawn up by the HAS and due to be published late 2011 or in 2012? Treatment should be maintained in case of low hemorrhage risk. Otherwise, at least aspirin should be maintained (with the possibility, if not contraindicated, of temporary conversion from clopidogrel to aspirin). Recent bare or active stenting requires delaying non-emergency surgery to after 6 weeks or 1 year, respectively; this long delay following active stenting means the cardiologist needs to be informed in advance if surgery is liable to be scheduled within the year following stenting, in which case a bare stent may be preferred.

In case of clear per- and postoperative hemorrhage risk (including risk of maintaining aspirin associated with possible postoperative antithrombotic prophylaxis), temporary preoperative interruption is preferable. Five days interruption is recommended for clopidogrel; for aspirin, it could be shorter, a recent study having demonstrated platelet function recovery after 3 days interruption in 58 patients on long-course treatment with 100 mg per day [21].

Non-steroid anti-inflammatory (NSAI) or LMWH substitution has not proved its efficacy. Early postoperative resumption is vital in order to avoid major thrombotic events (MI, stroke).

In emergency surgery for patients under antiplatelets, platelet transfusion is indicated in case of hemorrhage. It is not, however, indicated preventively according to the French health-products safety agency (*Agence française de sécurité sanitaire des produits de santé* [Afssaps]). Adjuvant bleeding control methods (normothermia, correction of anemia, tranexamic acid, posture, etc.) help limit blood loss [2,22,23].

The arrival on the market of new antiplatelet agents (prasugrel, ticagrelor) will lead to a review of the management principles outlined above. They have the advantage of being more effective against thrombosis (but also on bleeding), more fast-acting and, in the case of ticagrelor, reversible. These pharmacologic specificities will require adapting pre- and postoperative strategy, as with the new anticoagulants.

In conclusion, perioperative management of drugs impacting hemostasis requires real case-by-case assessment of the risk/benefit ratio: on one hand, the hemorrhage risk entailed by maintaining treatment and, on the other, the thrombosis risk entailed by perioperative withdrawal. Dialog between the various physicians (surgeon, anesthesiologist, cardiologist) is a prerequisite. The strategy decided on should be recorded in the patient's file.

Disclosure of interest

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