Care of the surgical patient: At a glance

Part 2: Oral Anticoagulants

- Introduce the readers to some of the additional risks associated with patients who are undergoing surgery and taking oral anticoagulants.
- Explore the use of vitamin K antagonists and heparin
- Discuss some of the management strategies and additional considerations that need to be addressed during the perioperative care continuum.

Introduction

As individuals are living longer with comorbidities and complex healthcare needs, some of the patients requiring surgical intervention can present with additional challenges for perioperative staff (Holt, 2012; Dhatariya, *et al.,* 2016; Keeling, Tait and Watson, 2016). It is imperative that these are addressed throughout the perioperative care continuum, in addition to the standard guidelines and care requirements for surgical patients (refer to article 'Care of the Surgical Patient: Part 1, Robertson and Ford, 2020), to reduce the risk of further complications. To demonstrate some of these challenges, this article provides some supplementary information regarding patients who are prescribed oral anticoagulants and are undergoing a surgical procedure.

Anticoagulation therapy

Anticoagulant therapy and its role within the treatment of cardiovascular disorders (people with atrial fibrillation and mechanical prosthetic heart valves) is well recognised (NICE, 2020a); however, there is now an increased awareness and acceptance of its use to treat and prevent against stroke and thromboembolism, all of which have implications for patients who are undergoing surgery (Pavord and Webster, 2015; Douketis and Lip, 2019). If prescribed anticoagulants are continued during surgery

or invasive procedures the risk of bleeding increases and additional potential harm may occur from the use of regional anaesthetics, including epidurals; however, if they are stopped, further thromboembolisms may develop (Keeling *et al.,* 2011). Therefore, for patients receiving anticoagulation therapy, perioperative management must be holistically tailored depending upon the patient's, current medication, International Normalised Ratio (INR), thromboembolism risk and the type of surgery/anaesthetic that the patient is scheduled to receive (Association of Anaesthetists of Great Britain and Ireland (AAGBI), 2016; Dubois *et al.,* 2017). With recent developments in pharmacology, there is now a range of direct oral anticoagulants (DOAC), such as Apixaban, Dabigatran, Edoxaban and Rivaroxaban, which have a fast onset of action; however, for the purpose of this article, we will focus on vitamin K antagonists and heparin, as these are the most commonly used (McIlmoyle and Tran, 2018).

Vitamin K Antagonists, as the name would suggest, inhibit several coagulation processes in which vitamin K is a co-factor (McIlmoyle and Tran, 2018). Namely, the conversion of glutamine acid to y-carboxyglutamic acid which is needed for the synthesis of prothrombin (coagulation factor ii), proconvertin (coagulation factor vii), plasma thromboplastin component (coagulation factor ix) and Stuart-Prower factor (coagulation factor x), and natural anticoagulants protein S and C (see figure 4) (Pavord and Webster, 2015). The most commonly used vitamin K antagonist is Warfarin (AAGBI, 2016). Warfarin is orally bioavailable and rapidly absorbed in the gastrointestinal tract; however, it has a varied half-life and causes many pharmacological interactions. These can decrease the effectiveness of the warfarin, increasing the risk of clot formation or the risk of bleeding and haemorrhage. Therefore, warfarin requires careful and close monitoring especially when administered alongside drugs that are known to interact with it, such as, paracetamol, ibuprofen, aspirin-based medication and antacids or laxatives (Pavord and Webster, 2015).

Heparins are sulphated glycosaminoglycans, which are isolated from porcine tissue (Martin and Hine, 2015). They are used for their ability to inhibit blood coagulation by binding to antithrombin and

enhancing its ability to inhibit thrombin production and fibrin clot formation, which are involved in the coagulation cascade process (see figure 4) (Pavord and Webster, 2015). The two main types of heparin are unfractured heparin (UFH) and low molecular weight heparin (LMWH); however, LMWH is usually preferred over (UFH) as LMWH due to its increased bioavailability and potential for reduced side effects (McIlmoyle and Tran, 2018; Douketis and Lip, 2019) (see figure 2).

International Normalised Ratio (INR)

International Normalised Ratio (INR) is a laboratory test used to check the anticoagulant effect of warfarin by using the outcome of the prothrombin time (PT) test, a measurement which monitors the time it takes blood to coagulate (Anderson, Wool and Madden, 2019). Target INR for those prescribed anticoagulants is ideally 2.5 (therapeutic range between 2-3), or 3.5 for individuals with recurrent VTE's (Keeling *et al.,* 2011; Pavord and Webster, 2015; AAGBI, 2016; NICE, 2020). If the patient's INR is 1.5 or above at the time of surgery, the balance of the risk of haemorrhage versus the urgency of undertaking the operation must be considered by the surgical team. INR should also be ideally measured the day before an operation in patients taking warfarin so that vitamin K can be administered if the INR is 1.5 or above, as this reverses warfarin's effect of inhibiting the synthesis of vitamin K dependent clotting factors, reducing the risk of bleeding and the possible need to cancel the surgery (Keeling *et al.,* 2011; NICE, 2020). If surgery is required urgently, to reverse warfarin anticoagulation, prothrombin complex concentrate can be used (Pavord and Webster, 2015) and to reverse the effects of heparin, protamine sulfate can be used to ensure the action of thrombin and fibrin in the coagulation cascade (AAGBI, 2016).

Thromboembolism risk

Venous Thromboembolism (VTE) is the overarching term used to describe deep vein thrombosis (DVT) and pulmonary embolism (PE) and is associated with the formation of a blood clot, known as a thrombus, in a vein. Thrombi has the potential to become dislodged, creating an embolism in another part of the body (Duff *et al.,* 2013; Rayt and Nasim, 2015). The thrombus usually develops in one of the larger and deeper veins of the body (most commonly the deep veins of the pelvis, thigh and lower leg). They are more prevalent in individuals whose blood is hypercoagulable and can also be caused by venous injury and venous stasis. As the body usually relies on movement and contraction of the lower limb muscles to assist with venous return, surgical patients, especially those undergoing a general anaesthetic and immobile, are therefore at higher risk of developing a thrombus. NICE (2018a) state that VTE has been attributed as being a major cause of death in hospitalised patients, with approximately 6500 annual deaths attributed to VTE in the UK, many of which can be avoidable. Consequently, VTE prevention has been recognised as a clinical priority for the NHS and completion of a VTE risk assessment is required for all patients admitted to hospital, just after admission or before the first consultant review (NICE, 2018a). This also has significance for surgical patients, as deaths due to post-operative strokes are substantially higher than fatalities because of bleeding (Keeling *et al.,* 2011; NICE, 2020). These risk assessments can be used to help determine and document if a patient is at increased risk of developing a thrombus as well as their risk of bleeding, both of which are taken into account when making decisions on whether anticoagulants are continued, stopped or if bridging therapy is required (Douketis, 2019) (see an example of general VTE risk assessment in figure 1).

Type of surgery

Another factor used when making a decision about treatment is also related to the surgery type, the surgical site and the individual patient's anatomy (Keeling, Tait and Watson, 2016). For example, if patients are undergoing procedures with a low risk of bleeding including cataract surgery, minor

dermatological surgery, a biopsy of a site that can be compressed to stop bleeding and joint aspiration/injection, anticoagulants may be continued (Keeling *et al.*, 2011; Dubois *et al.*, 2017). In contrast, for procedures with a high risk of bleeding, such as cardiovascular surgery, thoracic surgery, spinal surgery, liver and kidney biopsy, major abdominal surgery, cranial surgery and orthopaedic surgery, anticoagulants may need to be stopped (Lai *et al.*, 2014). Keeling, Tate and Watson (2016) suggest that while some surgeries can be considered at a lower or higher risk of bleeding, each case should be examined individually, and decisions to reduce, stop or replace anticoagulants should be made collaboratively between the operating team and patient. If it is necessary to stop warfarin before a procedure, individuals should be instructed to cease medication five days before the surgery, INR should be measured on the day before surgery, to allow administration of vitamin K if it is greater than or equal to 1.5 and re-checked on the morning of surgery if vitamin K has been administered (AAGBI, 2016).

Bridging therapy

Bridging therapy in the case of anticoagulant therapy refers to a pharmacological bridge that is created during a period when warfarin therapy is interrupted and when the INR is not within a therapeutic range. Medications that may be used for bridging therapy include UFH and LMWH e.g. tinzaparin (AAGBI, 2016). Bridging therapy may be required both preoperatively and postoperatively to balance the risk between a thromboembolism forming and major haemorrhage during the surgical intervention and patients will need to remain on this bridging therapy until they can resume their usual anticoagulant. If the patient has undergone surgery with a high risk of postoperative bleeding, it may be necessary to wait at least 48 hours before commencing bridging therapy (Keeling, Tait and Watson, 2016). However, bridging therapy should not be used routinely, as warfarin should never be interrupted for procedures of low bleeding risk or when patients are assessed as being at low risk of thromboembolism (Douketis and Lip, 2019). For patients who are at intermediate risk the decision for

perioperative use will depend upon the type of surgery and whether there is an increased risk of bleeding during or after the surgery and this will be patient-specific (McIlmoyle and Tran, 2018). For high-risk patients, bridging therapy should be considered and warfarin should be stopped 5 days before the surgery (see figure 3) (AAGBI, 2016).

Neuraxial and peripheral nerve blocks

It is recommended by AAGBI (2013) that for high-risk patients, regional anaesthesia should be utilised where possible due to the postoperative benefits of early mobility and the continuation of anticoagulant therapy. However, careful consideration must be undertaken with regards to the use, insertion and removal of epidurals or spinal anaesthesia/analgesia for patients who are receiving anticoagulant therapy, as clinically significant bleeding can cause neurological dysfunction (Horlocker, 2011; AAGBI, 2013). During insertion, coagulation status (INR) must be within therapeutic range and postoperative removal of indwelling catheters should never be undertaken if the patient has been recommenced on therapeutic anticoagulation therapy. Additionally, if the insertion is traumatic, the restarting of anticoagulant medication postoperatively may need to be delayed due to the risk of bleeding, haematoma formation and subsequent nerve damage (Horlocker, 2011). Epidural and spinal: In the postoperative period the patient must be monitored closely for any signs of neurological dysfunction as prompt interventions may be required (AAGBI, 2013). This observation should be taken by qualified, trained staff who are aware of the significance and the action required with any abnormal values. Epidural blockades are known to cause hypotension (low blood pressure), however, it is important to be mindful that postoperatively, hypotension can occur for various reasons, such as myocardial insufficiency, sepsis or dehydration, so these should be considered and excluded (AAGBI, 2013). Postoperatively, if haemostasis has been achieved, warfarin can usually be recommenced at the maintenance dose on the first evening or the following day (Keeling, Tait and Watson, 2016).

Conclusion

The increase of individuals living with complex needs and comorbidities means that the NHS is treating more and more surgical patients (National Patient Safety Agency, 2008; Holt, 2012; Dhatariya, *et al.*, 2016; Keeling, Tait and Watson, 2016). Patients who are undergoing continuous anticoagulant therapy are more at risk of several conditions, such as severe headaches, stomach pain and vision changes, but bleeding is a frequent issue that these individuals face. It is a responsibility of every healthcare professional to ensure that all patients are as safe as possible, so when these patients require surgical intervention, it is important that altered management strategies and associated risks are a part of healthcare education to ensure continued safety for these patients. With approximately eight million surgical interventions carried out every year by the NHS, the continued awareness of conditions and diseases, such as cardiovascular disorders (people with atrial fibrillation and mechanical prosthetic heart valves), that impact the care of the surgical patient is an important part of becoming a well-rounded and inclusive nurse or perioperative practitioner.

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Figure 1: Example of VTE Risk Assessment

BNJ: Please seek permission to use this table or use any VTE risk assessment that you may have on file.

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RISK ASSESSMENT FOR VENOUS THROMBOEMBOLISM (VTE)

Mobility – all patients (tick one box)	Tick		Tick		Tick
Surgical patient		Medical patient expected to have ongoing reduced mobility relative to normal state		Medical patient NOT expected to have significantly reduced mobility relative to normal state	
Assess for thrombosis and bleeding risk below				**Risk assessment now complete**	

Thrombosis risk			
Patient related	**Tick**	**Admission related**	**Tick**
Active cancer or cancer treatment		Significantly reduced mobility for 3 days or more	
Age > 60		Hip or knee replacement	
Dehydration		Hip fracture	
Known thrombophilias		Total anaesthetic + surgical time > 90 minutes	
Obesity (BMI >30 kg/m^2)		Surgery involving pelvis or lower limb with a total anaesthetic + surgical time > 60 minutes	
One or more significant medical comorbidities (eg heart disease;metabolic,endocrine or respiratory pathologies;acute infectious diseases; inflammatory conditions)		Acute surgical admission with inflammatory or intra-abdominal condition	
Personal history or first-degree relative with a history of VTE		Critical care admission	
Use of hormone replacement therapy		Surgery with significant reduction in mobility	
Use of oestrogen-containing contraceptive therapy			
Varicose veins with phlebitis			
Pregnancy or < 6 weeks post partum (see NICE guidance for specific risk factors)			

Bleeding risk			
Patient related	**Tick**	**Admission related**	**Tick**
Active bleeding		Neurosurgery, spinal surgery or eye surgery	
Acquired bleeding disorders (such as acute liver failure)		Other procedure with high bleeding risk	
Concurrent use of anticoagulants known to increase the risk of bleeding (such as warfarin with INR >2)		Lumbar puncture/epidural/spinal anaesthesia expected within the next 12 hours	
Acute stroke		Lumbar puncture/epidural/spinal anaesthesia within the previous 4 hours	
Thrombocytopaenia (platelets< 75x10^9/l)			
Uncontrolled systolic hypertension (230/120 mmHg or higher)			
Untreated inherited bleeding disorders (such as haemophilia and von Willebrand's disease)			

(NICE, 2018a)

301292 1p March 10

2

Figure 2: Comparisons between UFH and LMWH

Unfractured heparin	Low molecular weight heparin
• Increased half-life with increased concentration • Non-specific protein binding • <50% bioavailability (subcutaneously) • Hepatic and renal elimination • Risk of heparin-induced thrombocytopenia • Risk of osteoporosis with prolonged treatment	• More predictable dose response and stable half-life • Lower non-specific protein binding • >90% bioavailabilty (subcutaneously) • Renal elimination • Lower risk of heparin-induced thrombocytopenia • Lower risk of osteoporosis

(Pavour and Webster, 2015)

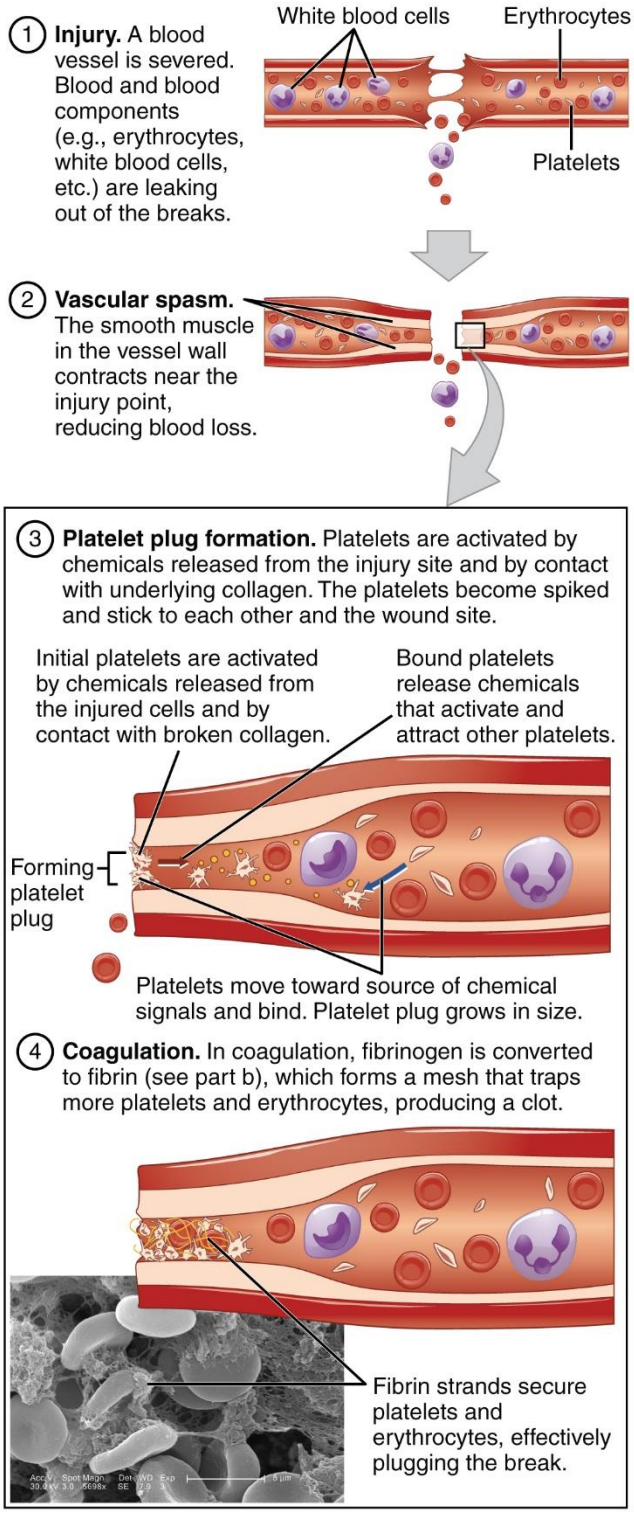
Figure3: Risk of thromboembolism and bridging anticoagulants

Risk Level ***Relevant comorbidities include previous surgery, trauma, immobility, malignancy, cancer therapy, older age, pregnancy, medical illness, cardiac or pulmonary failure, obesity and smoking**	**Patient Stratification**
Low	Minor surgery. Patients under 40 years old with no associated comorbidities. No bridging therapy required.
Moderate	Minor surgery. Patients have some relevant comorbidities OR are ages 40-60 years old without the associated risk factors. Bridging therapy conducted on an individual basis depending on the type and bleeding risk of the surgery.
High	• Major Surgery. • Patients over 60 years old. • Patients 40-60 years old with relevant comorbidities. Bridging therapy should be considered.
Highest	Major Surgery. Patients over 60 years old with multiple associated comorbidities. Bridging therapy should be considered and warfarin should be stopped 5 days before the surgery. Treatment dose of LMWH on days 4, 3 and 2 before surgery (if INR >2.5 give vitamin K). The day before surgery half treatment dose of LMWH. On the day of surgery, LMWH stopped and INR checked. Postoperatively LMWH administered until Warfarin commenced.

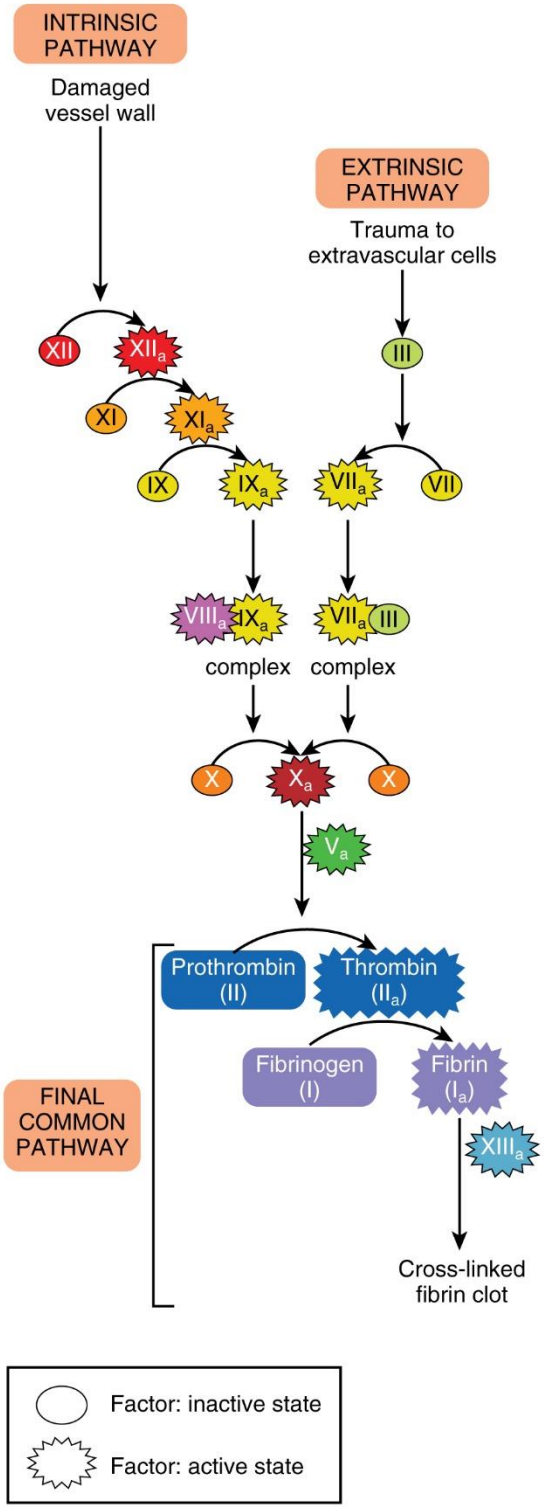
(AAGBI, 2016; McIlmoyle and Tran, 2018)

Figure 4 – Coagulation Cascade

BJN – PLEASE INSERT IMAGE OF COAGULATION CASCADE see figure below as an example



(a) The general steps of clotting



(b) Fibrin synthesis cascade

(https://commons.wikimedia.org/wiki/File:1909_Blood_Clotting.jpg)