10.1 Anticoagulation Therapy During Laparoscopic Surgery
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An invasive diagnostic or therapeutic urological procedure may be needed in patients receiving chronic oral anticoagulation therapy for complex medical problems that predispose to venous or arterial thromboembolism. However, the ability to control intraoperative bleeding and prevention of postoperative bleeding in such patients on anticoagulation therapy have to be safely balanced [1–3].

Recommendations for appropriate perioperative management of patients receiving long-term warfarin therapy remain debated. Anticoagulation therapy should be customized to patient risk factors and type of laparoscopic procedure planned. In this chapter we provide risk assessment and management guidelines for use of warfarin in patients undergoing laparoscopic surgery.

Synopsis of Anticoagulation Physiology

Oral anticoagulants (e.g., warfarin or Coumadin) inhibit vitamin K-dependent γ-carboxylation of the procoagulant factors II (prothrombin), VII, IX, and X, as well as the anticoagulant proteins C, S, and Z [4]. Factors VII, X, and II have a half-life of 4–6 h, 40–60 h, and 48–96 h, respectively. Four to 5 days are required for warfarin to achieve a full anticoagulant effect. After discontinuation of oral anticoagulants or vitamin K1 therapy, time for carboxylated coagulant factor restoration is proportional to their respective half-lives. The prothrombin time reflects plasma activities of factors II, VII, and X [5]. Heparin inhibits coagulation by enhancing antithrombin (AT) physiological regulation of hemostasis. Procoagulant enzymes such as thrombin, Xa, IXa, Xia, and TF/VII(a), are inhibited by AT. Unfractionated heparin (UFH) consists of highly sulfated glycosaminoglycans (porcine or bovine origin) of 3,000–30,000 Da. Low-molecular-weight heparin (LMWH, 1,000–10,000 Da) are prepared using chemical or enzymatic processes. UFH has both anti-Xa and anti-IIa activity, while LMWHs preferentially inactivate Xa [6].

The Anticoagulated Patient

Oral anticoagulants are commonly indicated for patients with mechanical prosthetic heart valves, chronic nonvalvular atrial fibrillation (AF), and venous thromboembolism (VTE). Other indications for chronic anticoagulation include mitral stenosis, left ventricular aneurysm, congestive heart failure with left ventricular dilation, severe coronary artery disease, presence of inferior vena cava filter, and synthetic peripheral arterial bypass graft [5].

Whenever a patient with these indications requires elective or emergency surgery, even temporary discontinuation of anticoagulants may lead to complications such as systemic emboli or occlusive thrombosis of mechanical heart valves, and increased risk of stroke in patients with AF [7, 8]. Further, the risk of recurrent VTE or pulmonary embolism (PE) within 3 months following acute deep vein thrombosis (DVT) is lower in patients receiving anticoagulation therapy (13% and 3% at 1 and 3 months, respectively) vs patients with no therapy (40% and 10% at 1 and 2 months, respectively) [9].
Patients with clotting and/or bleeding tendencies are challenging problems for surgeons. In fact, the surgical risk is increased in patients with congenital deficiencies in thrombosis inhibitors, (e.g., protein C, protein S, antithrombin III, dysfibrinogenemias, or dysfibrinolyis) or acquired (e.g., pregnancy, thrombo-cytemia, erythrocytemia, systemic lupus erythematosus) hypercoagulation conditions. By allowing early postoperative ambulation, laparoscopic surgery may decrease thrombogenic risks in such patients [10]. However, particularly during the initial learning phase of laparoscopic procedures, this benefit may be limited by longer duration of patient immobility. In addition, decreased central venous return secondary to CO2 pneumoperitoneum used during laparoscopy may potentially increase thrombogenic risks.

Bleeding related to anticoagulation may also develop as a result of therapy overdose, or drug interaction, which can interfere with normal hemostasis. Acetylsalicylic acid, some cephalosporins (cefamandole, cefmetazole, cefoperazone, and cefotetan), and NSAIDs interfere with warfarin metabolism and increase the risk of bleeding [11].

Appropriate and individualized management of such patients can be defined by quantifying the patient’s risk of thrombosis and bleeding associated with planned surgery, and the absolute indications for anticoagulant therapy. Surgical management options are strongly influenced by the location and extent of surgery, and the accessibility of compressive or physical means of bleeding control (i.e., packing, suturing, cautery, topical coagulant or antifibrinolytic) [12].

**Regimens for Reversing Oral Anticoagulation**

Vitamin K1 (phytonadione) is a specific pharmacological antagonist to warfarin and other anticoagulants. Therapeutic levels of oral anticoagulation can be reversed within 24–36 h by administering small doses of intravenous fat-soluble vitamin K1 (phytonadione), e.g., 1.5 mg over 60 min [13]. Alternatively, vitamin K can be administered orally. A similar result will likely be obtained with a 2.5-mg oral vitamin K1 dose [14]. Normal pancreatic and bowel function are required for absorption of vitamin K1 (fat-soluble). As such, patients with malabsorption who require an urgent procedure should be given intravenous vitamin K1. However, larger doses of vitamin K might markedly delay postoperative therapeutic oral anticoagulation recovery, and can cause anaphylactoid reactions. Subcutaneous vitamin K1 has erratic absorption, and intramuscular injection has increased risk of hematoma. Thus, these two administration routes should also be avoided [15].

Oral anticoagulation overdose without evidence of active bleeding can be managed with temporary discontinuation or dosage reduction of oral anticoagulants. Long-acting warfarin derivative overdose (INR > 4.5) can be partially antagonized using low doses of vitamin K1 (1–2 mg). In presence of minor bleeding, warfarin derivatives should be discontinued and 1–5 mg of vitamin K1 administered. Major bleeding treatment requires administration of vitamin K1 (10–20 mg) and prothrombin complex concentrates (PCC) at a dose of 1 IU PCC/kg body weight (with a loading dose of 30 IU PCC/kg bw) [16].

**Urgent Reversal of Chronic Oral Anticoagulation**

For life-threatening bleeding or urgent surgery, coagulation factor replacement therapy with fresh frozen plasma (FFP) is necessary [5]. As such, the required volume of transfused FFP units can be assessed by estimating the plasma volume (plasma volume [ml] = 40 × body weight [kg]) and the targeted net increase in plasma coagulant factor activity required. A typical FFP unit volume is 200–250 ml. In an average-sized individual, approximately six or seven units of FFP (15 or 16 ml/kg) will significantly reduce INR. However, factor VII’s plasma half-life is short (4–6 h); therefore several hours are needed following FFP transfusion for prothrombin time (PT) to prolong. Risk of intravascular volume overload, and transfusion transmitted infection are the most important limitations of FFP therapy. Virally inactivated prothrombin complex concentrate and restriction of such treatment to patients with life-threatening bleeding or urgent need for surgery minimizes risk of infection.

**Perioperative Anticoagulation Management**

The most common complication of oral anticoagulation is hematuria, followed by nasopharyngeal hemorrhages, and, less frequently, gastrointestinal, intracranial, and pulmonary bleeding [17–20]. Major and mi-