Medical and Surgical Management of Colorectal Cancer Patients Presenting with Haemostatic Disorders

15

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15.1 Introduction

Haemostasis is a complex process whose function is to limit blood loss from an injured vessel and to maintain normal blood flow in the circulation [1].

Maintaining haemostasis during surgery is essential [2] to preserve physiologic functions for the patient, provide the surgeon with the ability to see the operative field and promote successful wound management and patient outcomes. In addition, effective surgical haemostasis also results in fewer blood transfusions, decreased operating time and reduced morbidity and mortality for patients.

Proper haemostasis is a function of balance between procoagulant systems (platelets, coagulation cascade) and anticoagulant systems (APC/protein S, fibrinolysis). If haemostasis is out of balance due to a defect in one of these systems, then either thrombosis or bleeding may occur [3]. The coagulation system is exquisitely regulated: in addition to clot formation that must occur to prevent bleeding at the time of vascular injury, two related processes must exist to prevent propagation of the clot beyond the site of injury. First, there is a feedback inhibition on the coagulation cascade, which deactivates the enzyme complexes leading to thrombin formation. Second, mechanisms of fibrinolysis allow for breakdown of the fibrin clot and subsequent repair of the injured vessel with deposition of connective tissue [4].

Normal coagulation pathway represents a balance between the procoagulant pathway that is responsible for clot formation and the mechanisms that inhibit the same beyond the injury site. Imbalance of the coagulation system may occur in the perioperative period or during critical illness, which may be secondary to numerous factors leading to a tendency of either thrombosis or bleeding [5].

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Bleeding disorders are characterized by defects in haemostasis that lead to an increased susceptibility to bleeding. They are caused either by platelet disorders (primary haemostasis defect), coagulation defects (secondary haemostasis defect), or a combination of both. In people with congenital or acquired bleeding disorders undergoing surgical interventions, haemostatic treatment is needed in order to correct the underlying coagulation abnormalities and minimize the bleeding risk. This treatment varies according to the specific haemostatic defect, its severity and the type of surgical procedure. Ideally, surgical interventions in patients with bleeding disorders should be performed as elective procedures, following careful pre-, intra- and postoperative planning. Unfortunately, not uncommonly patients with diagnosed bleeding disorders or on anticoagulation therapy present with acute surgical conditions requiring emergency surgery. A multidisciplinary approach is essential, and the surgical team must closely liaise with the haematology and anaesthetic team. The need for massive transfusion should be anticipated, and guidelines should be in place to provide the simultaneous administration of blood, plasma, and platelets.

A basic understanding of haemostasis is necessary for properly interpreting laboratory studies in order to accurately diagnose the disorder and ensure appropriate treatment.

15.2 Physiology of Haemostasis

Haemostasis is the physiological process that stops bleeding at the site of an injury while maintaining normal blood flow elsewhere in the circulation. The endothelium in blood vessels maintains an anticoagulant surface that serves to maintain blood in its fluid state, but if the blood vessel is damaged, components of the subendothelial matrix are exposed to the blood [6].

There are two main components of haemostasis. Primary haemostasis refers to platelet aggregation and platelet plug formation. Platelets are activated in a multi-faceted process, and as a result they adhere to the site of injury and to each other [7], plugging the injury. Secondary haemostasis refers to the deposition of insoluble fibrin, which is generated by the proteolytic coagulation cascade [8]. This insoluble fibrin forms a mesh that is incorporated into and around the platelet plug. This mesh serves to strengthen and stabilize the blood clot.

Under physiologic conditions, haemostasis is accomplished by a complex sequence of interactions between platelets, the endothelium, and multiple circulating or membrane-bound coagulation factors. Four major physiologic events participate in the haemostatic process: vascular constriction, platelet plug formation, fibrin formation, and fibrinolysis [9]. Although each tends to be activated in order, the four processes are interrelated so that there is a continuum and multiple reinforcements (Table 15.1).

Table 15.1 Schematically, after a loss of vascular integrity (e.g. an injury to a vessel), four major events occur in the following sequence

1. Vasoconstriction This is the initial response to vessel injury which limits the flow of blood to the area. Vasoconstriction is subsequently linked to platelet plug formation. Thromboxane A2 (TXA2) is produced locally at the site of injury via the release of arachidonic acid from platelet membranes and is a potent constrictor of smooth muscle. Similarly, endothelin synthesized by injured endothelium and serotonin (5-hydroxytryptamine) released during platelet aggregation are potent vasoconstrictors. The extent of vasoconstriction varies with the degree of vessel injury. A small artery with a lateral incision may remain open due to physical forces, whereas a similarly sized vessel that is completely transected may contract to the extent that bleeding ceases spontaneously.
2. Platelet plug formation Platelets have a pivotal role in haemostasis by forming the initial haemostatic plug that provides a surface for the assembly of activated coagulation factors leading to the formation of fibrin-stabilized platelet aggregates and subsequent clot retraction. In a healthy blood vessel, and under normal blood flow, platelets do not adhere to surfaces or aggregate with each other. However, in the event of injury, platelets are exposed to subendothelial matrix, and adhesion and activation of platelets begins. After vasoconstriction, platelets are activated by thrombin and aggregate at the site of injury to form a temporary, loose platelet plug. This clumping activity is stimulated by the protein fibrinogen and by platelets binding to collagen exposed following rupture of the endothelial lining of vessels when injured. This process requires von Willebrand's factor (VWF), a protein in the subendothelium which binds to glycoprotein I/IX/V on the platelet membrane. After adhesion, platelets initiate a release reaction that recruits other platelets from the circulating blood to seal the disrupted vessel; up to this point, this process is known as primary haemostasis.
3. Fibrin clot formation To stabilize the initially loose platelet plug, a fibrin clot or mesh forms to trap the plug. This process called secondary haemostasis consists of the cascade of coagulation serine proteases that culminates in cleavage of soluble fibrinogen by thrombin to form a crosslinked fibrin mesh at the site of an injury. Most of the clotting factors are proteins that are synthesized in the liver and circulate in an inactive form. Many of the proteins have protease capability, thereby allowing them to cleave their target beneath them in the cascade and activate it by exposing its own protease site. The elements of the coagulation cascade are designated by Roman numerals; an 'a' suffix denotes the active form of the factor. There are two pathways involved with the clotting cascade that meet at a certain point to become a common pathway. The intrinsic pathway is activated by damage directly to the blood vessel and the exposure of collagen to the circulating platelets within the blood. The extrinsic pathway is activated by tissue damage outside of the blood vessel, hypoxia, sepsis, malignancy and inflammation. The common point in both pathways is the activation of factor X to factor Xa. Factor Xa activates prothrombin (factor II) to thrombin (factor IIa). Thrombin, in turn, converts fibrinogen to fibrin. One convenient feature of depicting the coagulation cascade with two merging arms is that commonly used laboratory tests segregate abnormalities of clotting to one of the two arms. An elevated activated partial thromboplastin time (aPTT) is associated with abnormal function of the intrinsic arm of the cascade, whereas an elevated prothrombin time (PT) is associated with the extrinsic arm.

(continued)

Table 15.1 (continued)

4. Fibrinolysis
The role of the fibrinolytic system is to dissolve blood clots during the process of wound
healing and to prevent blood clots in healthy blood vessels. This occurs through the action of
plasmin.
The fibrinolytic system is a parallel system which is activated along with activation of
coagulation cascade and serves to limit the size of clot. Fibrinolysis is an enzymatic process
that dissolves the fibrin clot into fibrin degradation products (FDPs) by plasmin originating
from fibrin-bound plasminogen in the liver.

15.3 Clinical Assessment of Patients with Haemostatic Disorders

A good detailed comprehensive history is the best predictor of a bleeding problem [10]. Questions should be asked to assess the type and sites of bleeding, whether it involves the cutaneous and mucous membranes (i.e. petechiae, purpura bruises, epistaxis, gingival bleeding, menorrhagia and/or haematuria). Bleeding from skin and mucous membranes tends to occur with platelet disorders, while bleeding into deep tissue, joints and muscles suggest a coagulation factor defect.

Questions on whether the bleeding is spontaneous or follows trauma must also be asked. Any history of blood transfusion or other blood components is very important. Information on all surgeries including tooth extractions and any history of abnormal bleeding during or after surgery should be evaluated. Any patient who has had major surgery, a tonsillectomy or dental extractions, without unusual bleeding has had the best evaluation of their coagulation system possible [11].

Excessive bleeding in response to circumcision or from the umbilical stump is common in patients with haemophilia A or B [12]. Patients with vascular disorders secondary to connective tissue abnormalities such as Ehlers-Danlos syndrome may give a history of easily distensible skin or extraordinary ligament laxness. Drug history is of extreme importance since a wide variety of drugs affect haemostasis, and recent treatment with aspirin and antiaggregants, heparin, and oral anticoagulants should be noted.

Family history can be relevant in case of congenital disorders: haemophilia follows a pattern of X-linked recessive inheritance. However, up to 30% of case of haemophilia A are spontaneous mutations with no family history. Von Willebrand's disease is difficult to diagnose because of the variability in inheritance [13], autosomal dominant and recessive and the variability among patients in the level of von Willebrand factor present.

The history should include information on diseases and organs that may also affect haemostasis, such as liver and renal disease, essential thrombocythaemia, systemic lupus erythematosus, haematological malignancies, myeloproliferative disease and solid organ malignancies. Abnormal haemostasis should be anticipated in patients with short bowel or malabsorption syndromes, who may have impaired coagulation secondary to vitamin K deficiency. Surgical haemostasis may prove difficult in patients with vascular and connective tissue disorders, such as

Ehlers-Danlos syndrome, or in patients under chronic steroids treatment or with prior radiation therapy to the abdomen, in whom careful tissue handling is mandatory.

On physical examination one should look for signs of bleeding or their sequelae and for signs of a possible underlying disorder that can cause the haemostatic derangement. Careful examination of the skin is essential for the detection of petechiae and ecchymoses. These signs may be prominent on the legs, where the hydrostatic pressure is greatest. Hematomas, ecchymoses, and protracted oozing should be looked for at sites of venipunctures, injections and arterial and venous catheter insertion sites. Joint deformities and limited joint mobility are suggestive of severe deficiency of factor VII, VIII, IX or X or severe von Willebrand disease. Weight and body mass index must be measured.

The immediate clinical history of hospitalized patients should focus on recent surgeries, blood losses and blood products transfusions, the physiological status (vital parameters, temperature, and pH) and extent of previous resuscitation to suspect and identify the presence of a coagulopathy.

15.4   Laboratory Assessment

First-line investigations [14] can include a full blood count (FBC) to assess platelet count, peripheral blood smear examination, prothrombin time (PT), fibrinogen, activated partial thromboplastin time (APTT), a thrombin time (TT), bleeding time (BT) and D-dimer.

Platelets play an integral role in haemostasis by forming a haemostatic plug and by contributing to thrombin formation. The normal circulating number of platelets ranges from 150,000 to 450,000 platelets per microliter of blood, and if not consumed in a clotting reaction, platelets are normally removed by the spleen and have an average life span of 7–10 days.

The FBC will reveal abnormalities in platelet numbers, and the blood film will show platelet morphology, excluding the possibility of a systemic illness and other haematological disorders. The intrinsic pathway of coagulation is assessed by aPTT (normal value 25–38 s) so that any abnormalities are detected. Prothrombin time (normal value 10–14 s) assesses the extrinsic coagulation pathway and the generation of fibrin, detected by the thrombin time (normal value 15–19 s).

Other necessary blood tests include haemoglobin level and group and safe in case a transfusion of blood products is needed. Calcium, liver electrolytes and renal function tests are necessary not only to replace deficits but also to determine the appropriate dose of treatments in patients with acute or chronic kidney injury.

The activated partial thromboplastin time (aPTT) evaluates the function of fibrinogen, prothrombin and factors V, VIII, IX, X, XI and XII, and the normal range is 30–40 s. Prolonged aPTTs are associated with acquired or congenital bleeding disorders associated with coagulation factor deficiency, vitamin K deficiency, liver disease, DIC, von Willebrand disease, leukaemia, and haemophilia. The aPTT essentially measures the intrinsic clotting pathway and is particularly useful in monitoring heparin therapy.

Table 15.2 Screening test results in various bleeding disorders

Platelet count	PT	aPTT	Differential diagnosis
N	+	N	Factor VII deficiency (early liver disease, early vitamin K deficiency, early warfarin therapy) Dysfibrinogenemia Factor VII inhibitor Some cases of DIC
N	N	+	Factor VIII, IX, XI deficiency Inhibitors to factor VIII, IX, XI VWD Heparin Lupus inhibitor
N	+	+	Vitamin K deficiency Liver disease Warfarin Heparin Factor V, X deficiency
−	+	+	DIC Liver disease HIT
−	N	N	Increased platelet destruction Decreased platelet production Hypersplenism
+	N	N	Myeloproliferative disorders
N	N	N	Mild VWD Qualitative platelet defects Factor XIII deficiency

N = normal, − = decreased, + = increased

The prothrombin time (PT) is an assay designed to screen for defects in fibrinogen, prothrombin, and factors V, VII, and X and thus measures activities of the extrinsic pathway of coagulation. When any of these factors is deficient, then the PT is prolonged. A normal PT is 11.0–12.5 s. A PT greater than 20 s is indicative of coagulation deficit. The most common measure of PT is to divide the time of coagulation of a patient's blood by that of a known standard, and this value is referred to as the international normalized ratio (INR). The PT measures the vitamin K dependant clotting pathways (extrinsic pathway) and is therefore of particular use in measuring the effect of warfarin therapy (warfarin is a vitamin K antagonist).

Evaluation of further specific coagulation factors must be guided by these screening tests and should be discussed with the haematology team (Table 15.2).

15.5 Bleeding Disorders

Because of the complex nature of haemostasis, potential interference in the process can occur at many levels [15]. Platelet number or function can be insufficient to adequately support coagulation. Alternatively, abnormalities in the clotting factors may underlie an abnormality of haemostasis, either from an intrinsic defect in one of the factors or as the result of pharmacotherapy.

15.5.1 Platelet Disorders

A normal platelet count is $150–400 \times 10^9$/L. Thrombocytopenia can be congenital, due to impaired bone marrow production, i.e. aplastic anaemia, megaloblastic anaemia and bone marrow infiltration, or a result of increased platelet destruction/consumption. Examples include immune-related conditions like autoimmune thrombocytopenia (ITP), systemic lupus erythematosus and drugs and non-immune conditions such as disseminated intravascular coagulation (DIC), thrombotic thrombocytopenic purpura (TTP) and hypersplenism (splenic sequestration).

Bleeding disorders can also be due to abnormal platelet function in inherited conditions (Glanzmann's thrombasthenia, Bernard-Soulier syndrome and von Willebrand's disease) or acquired (e.g. uraemia and in myeloproliferative disorders). Antiplatelets medications such as aspirin and nonsteroidal anti-inflammatory drugs can often be continued perioperatively, but clopidogrel should be discontinued. Liasing with the cardiology team is essential in patients on dual antiplatelets therapy for recent coronary artery surgery.

15.5.2 Inherited Coagulation Disorders

The main bleeding disorders are genetically inherited. Haemophilia results from defects in secondary haemostasis. Haemophilia A is due to deficiency of factor VIII, and haemophilia B is due to deficiency of factor IX [16]. Deficiency in either of these proteins causes a very similar bleeding phenotype characterized by excess bruising and spontaneous bleeding into the joints, muscles, internal organs and brain. Factor VIII and factor IX are both X-linked genes. Thus haemophilia is primarily expressed in males, with haemophilia A present in about 1 in 5000 males and haemophilia B present in about 1 in 20,000 males. Depending on the mutation, haemophilia can be severe (<1% function), moderate (1–5%), or mild (5–20%). Haemophilia A and haemophilia B are treated mainly by infusion of recombinant factor VIII or factor IX, respectively.

Von Willebrand disease (VWD) is a bleeding disorder caused by deficiency or defect in von Willebrand factor (VWF). VWF is involved in platelet aggregation and is also a carrier for factor VIII. VWF is an autosomal gene, so the disease is present equally in men and women. The severity of the different types of VWD varies, and various therapies are available and preferred for different forms of the disease. Recommendations for factor replacement and duration of perioperative therapy vary according to disease severity and the magnitude of the surgical procedure.

The main drug used for treatment is desmopressin (DDAVP), which is a vasopressin analogue that stimulates release of VWF from endothelial cells and therefore temporarily increases the concentration of VWF in the blood. Type 3 VWD is more severe, and it is treated by infusion with pasteurized plasma-derived pure VWF/factor VIII concentrate. Both of these drugs can also be supplemented with the antifibrinolytic tranexamic acid.

15.5.3 Acquired Bleeding Disorders

These commonly include liver disease, trauma, hypothermia, vitamin K deficiency, DIC, and anticoagulant therapy. Disorders of vessels and supporting tissues may

also account for bleeding disorders, and the weakening of the supportive tissues and blood vessel abnormalities as occurs in the ageing process or corticosteroid usage should not be overlooked.

15.5.3.1 Liver Disease

Majority of clotting factors are synthesized in the liver; therefore, severe liver disease is associated with coagulopathy. The most common coagulation abnormalities associated with liver dysfunction are thrombocytopenia and coagulation function manifested as prolongation of the PT.

Thrombocytopenia in patients with liver disease typically is related to hypersplenism, reduced production of thrombopoietin, and immune-mediated destruction of platelets. Platelet transfusions are the mainstay of therapy; however, the effect typically lasts only several hours. Decreased production or increased destruction of coagulation factors as well as a vitamin K deficiency can contribute to a prolonged PT and increased INR in patients with liver disease. Coagulopathy caused by liver disease is most often treated with FFP.

Since the liver is also involved in the clearance of activated clotting factors and fibrinolytic products, it may predispose to DIC.

15.5.3.2 Coagulopathy of Trauma and Hypothermia

Traditionally recognized causes of traumatic coagulopathy include acidosis, hypothermia, and dilution of coagulation factors. However, a significant proportion of trauma patients arrive at the emergency department coagulopathic, and this early coagulopathy is associated with a significant increase in mortality.

Hypothermia must be prevented as is also associated with anticoagulatory effects, which are more pronounced in the presence of acidosis. The effects may result from platelet dysfunction in mild hypothermia (below 35 °C) to decreased synthesis of clotting enzymes and plasminogen activator inhibitors when temperatures is <33 °C.

15.5.3.3 Disseminated Intravascular Coagulation

Disseminated intravascular coagulation (DIC) is characterized by systemic activation of blood coagulation [17], which results in generation and deposition of fibrin, leading to microvascular thrombi in various organs and contributing to multiple organ dysfunction syndrome (MODS).

DIC occurs because of aberrant activation of the clotting cascade, leading to fibrin deposition in small vessels, combined with activation of fibrinolytic mechanisms, leading to bleeding. DIC is usually a common final haemostatic disorder caused by other conditions such as sepsis, pancreatitis, liver disease, pregnancy complications, burns, or trauma. Because they are consumed by the ongoing prothrombotic and fibrinolytic processes, coagulation proteins and platelets can become depleted, leading to bleeding. Thus, in DIC, haemorrhage and thrombosis can occur simultaneously.

In acutely ill hospitalized patients, DIC usually presents with prolongation of the PT and aPTT along with decreased fibrinogen and platelets; systemic bleeding may or may not be present. Typically, bleeding manifests as ecchymoses, purpura and

petechiae; it also occurs at surgical incisions or insertion sites of vascular access catheters. Mucosal and urinary bleeding are common.

Thrombocytopenia; prolongation of the PT, aPTT and thrombin time; and hypo-fibrinogenaemia are characteristic. Because DIC tends to be secondary to other disorders, addressing the underlying disorder is the mainstay of treatment. Therapy is otherwise supportive.

15.5.3.4   Patients on Anticoagulation Therapy

The perioperative management of patients receiving long-term oral anticoagulation therapy is an increasingly common problem. Firm evidence-based guidelines regarding which patients require perioperative 'bridging' anticoagulation are needed. Bridging anticoagulation involves discontinuation of oral anticoagulation before surgery and the use of IV or SC agents for several days before and (sometimes) after surgery. Most studies have shown that preoperative bridging is associated with an acceptably low postoperative bleeding rate [18]. It is essential to consider the estimated procedural bleeding and the thromboembolic risk of the patient in order to determine the timing of anticoagulant interruption and the need for bridging anticoagulation, which is dependant on the anticoagulation agent used and on the clinical indication.

Spontaneous bleeding can be a complication of anticoagulant therapy with either heparin, warfarin, low molecular weight heparins, or factor Xa inhibitors. Examples include haematuria, soft tissue bleeding, intracerebral bleeding, skin necrosis, and abdominal bleeding. Bleeding into the abdominal cavity is by far the most common complication of warfarin therapy and may be intraperitoneal, extraperitoneal, or retroperitoneal. Bleeding secondary to anticoagulation therapy is also not an uncommon cause of rectus sheath hematomas. In most of these cases, reversal of anticoagulation is the only treatment that is necessary. Lastly, it is important to remember that one of the first symptoms of an underlying tumour may be bleeding in a patient who is receiving anticoagulation therapy.

Surgical intervention may prove necessary in patients receiving anticoagulation therapy. When the aPTT is <1.3 times the control value in a patient receiving heparin or when the INR is <1.5 in a patient taking warfarin, reversal of anticoagulation therapy may not be necessary. However, meticulous surgical technique is mandatory, and the patient must be observed closely throughout the postoperative period [19]. There remain two major risk groups who will require conversion to IV unfractionated heparin in the perioperative period to maintain therapeutic anticoagulation in the absence of postoperative bleeding. These are patients with mechanical cardiac valve prostheses and those with a history of acute venous thromboembolism within the previous 4 weeks or during a current pregnancy. The heparin must be stopped 6 h before the operation and restart 12 h after operation, and oral warfarin should be reintroduced as soon as possible thereafter. Epidural anaesthesia is best avoided for those on therapeutic heparin. The newer direct oral anticoagulants (eg, direct thrombin inhibitor dabigatran, factor Xa inhibitors rivaroxiban, apixaban, edoxaban) have shorter half-lives, making them easier to discontinue and resume rapidly, but lack an approved drug-specific antidote, raising concenrns on management of bleeding in patients requiring urgent surgery.

For more rapid reversal of anticoagulation, vitamin K can be administered in patients having warfarin, while use of protamine sulphate is effective in patients receiving IV heparin. However, significant adverse reactions may be encountered when administering protamine, especially in patients with severe fish allergies. Symptoms include hypotension, flushing, bradycardia, nausea, and vomiting. Rapid reversal of anticoagulation can be accomplished with FFP in an emergent situation. Liaison with the haematology team is essential [20] and institutional guidelines are strongly recommended.

Parenteral administration of vitamin K also is indicated in elective surgical treatment of patients with biliary obstruction or malabsorption who may be vitamin K deficient. However, if low levels of factors II, VII, IX, and X (vitamin K-dependent factors) are a result of hepatocellular dysfunction, vitamin K administration is ineffective. For patients who were taking warfarin preoperatively and are at high risk for thrombosis, low molecular weight heparin should be administered, while the INR is decreasing and should be restarted at prophylactic dosages as soon as possible after surgery.

15.6   Thrombotic Disorders

The constitutive or acquired disorders of thrombosis are termed as thrombophilia and are presented in Table 15.3.

There are a number of factors that are associated with the hypercoagulable states. In addition to the genetic and hereditary disorders that predispose to thrombosis [21], several risk factors such as smoking, obesity, pregnancy, immobility, malignancy, surgery and females on oral contraceptives may also contribute to its development. Disorders of ATIII deficiency and reduced protein C and protein S are inherited in autosomal dominant fashion and are associated with increased risk of thrombosis [22]. Acquired protein C and protein S deficiency may be observed in vitamin K deficiency, warfarin therapy, pregnancy, liver cirrhosis, and sepsis. The risk of thromboembolism in the perioperative period is well recognized. Therefore,

Table 15.3 Hereditary and acquired bleeding and thrombotic disorders

Hereditary	Acquired
Bleeding disorders	
Haemophilia A, B, C	Consumptive coagulopathies
Factor V, VII, X, XII deficiency	DIC
Prothrombin deficiency	Liver disease
Afibrinogenaemia	Vitamin K deficiency
	Microangiopathic haemolytic anaemias
Thrombotic disorders	
Antithrombin III deficiency	Antiphospholipid antibody syndrome
Protein C deficiency	Increased levels of factors VIII, IX, XI, fibrinogen
Protein S deficiency	Homozygous homocystinuria
Factor V Leiden	
Prothrombin mutation	

patients with hereditary thrombophilia should be given thromboprophylaxis in consultation with the haematology team. Even in the absence of any known thrombophilia markers, surgical patients are at increased risk of venous thromboembolism as a result of their immobility and the postoperative inflammatory response [23]. All should be assessed for their individual risk in relation to the procedure planned and advised about the importance of leg exercise and early mobilization. Appropriate antiembolism hosiery should be fitted, and anticoagulant prophylaxis with subcutaneous low molecular weight heparin must be ensured [24], and 28 days postoperative treatment must be considered after major colorectal surgery [25].

15.7   Technical Considerations in Colorectal Surgery

Excessive bleeding during or after a surgical procedure may be the result of ineffective haemostasis, blood transfusion, undetected haemostatic defect, consumptive coagulopathy and/or fibrinolysis. Excessive bleeding from the operative field not associated with bleeding from other sites usually suggests inadequate mechanical haemostasis.

Preoperative anaemia is common in colorectal cancer patients [26] and must be corrected [27], as it is a recognised risk factor for postoperative complications. Minimally invasive surgery reduces surgical trauma [28] and reduces blood loss compared to laparotomy [29]. Nevertheless, application of laparoscopic surgery in the emergency setting has a steep learning curve [30] and must be reserved to highly trained colorectal surgeons to minimize conversions and morbidity [31].

New vessel sealing devices and topical haemostatic agents play an important role in common or complex general surgical procedures [32]. These are not a substitute for meticulous surgical technique. The advantages and disadvantages of each agent must be weighed in selecting the correct agent to control bleeding. In general, the minimum amount of each topical haemostatic agent should be used to minimize toxic effects and adverse reactions, interference with wound healing and procedural cost, and surgeons must be familiar with them [33].

Patients with inflammatory conditions such as diverticulitis, peritonitis and inflammatory bowel disease are at significant risk of intraoperative bleeding, due to oedematous tissue planes and a thickened bowel mesentery. Inappropriate and excessive traction must be avoided, as catastrophic bleedings may occur, for example from the spleen or the gastrocolic common trunk of Henle, during mobilisation of the splenic and hepatic flexure of the colon, respectively. Presacral venous bleeding is a technically challenging and potentially life-threatening complication of rectal surgery. Rapid control is important to prevent a fatal outcome. The first temporary manoeuvre is direct pressure at the point of bleeding together with aspiration of the accumulated blood. Conventional haemostatic methods often fail and may occasionally further shear the delicate veins, extend the area of active haemorrhage and significantly worsen the problem. Pelvic packing controls presacral bleeding effectively and may be lifesaving [34]. Alternative methods of packing without the need for reoperation have been also described [35]. Metallic thumbtacks [36] can be used

to control presacral bleeding, omental or muscle fragment welding [37] and bone wax use are also very effective techniques. It is imperative to consider the stability of the patient when using potentially time-consuming techniques to control intraoperative haemorrhage. When a patient begins developing the lethal triad of acidosis, coagulopathy and hypothermia, the surgeon must always consider packing to rapidly control haemorrhage and prevent further deterioration [38]. Resuscitation with large volumes of crystalloids and blood products may exacerbate hemodilution, thrombocytopenia and abnormal coagulations, and surgeons must promptly proceed to damage control in cases of severe intraoperative bleeding unresponsive to conventional measures. Anastomotic bleeding is also a not uncommon complication in patients on anticoagulants treatment in the perioperative period and while minor haemorrhage can be treated conservatively under close observation, unstable patients require return to theatre where experienced endoscopic support should be available. If an ileocolic anastomosis is performed, a hand-sewn technique should be considered to minimise the risk of staple line bleeding [39]. Postoperative intraabdominal haemorrhage often occurs as diffuse bleeding from raw surfaces and requires correction of underlying coagulopathy and abdominal packing if adequate haemostasis cannot be achieved [40].

15.8 Conclusions

Patients with inherited bleeding disorders represent a higher-risk population in the perioperative setting. Although surgery in this group of patients will continue to be challenging, careful perioperative planning, coordinated by an experienced haematology team, should ensure a successful outcome in most cases. Therapeutic anticoagulation preoperatively and postoperatively is becoming increasingly more common. The patient's risk of intraoperative and postoperative bleeding and the estimated thromboembolic risk should guide the need for reversal of anticoagulation therapy preoperatively and the timing of its reinstatement postoperatively.

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