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Anticoagulation Strategies After Spontaneous Retroperitoneal Hemorrhage in Patients Requiring Long-Term Anticoagulation

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Abstract

Patients undergoing pulmonary endarterectomy surgery require lifelong anticoagulation to prevent thromboembolic complications. However, spontaneous retroperitoneal hemorrhage (SRH) represents a rare but severe complication of long-term anticoagulation. There are controversies regarding the optimal timing and strategy for resuming anticoagulation. This review explores the current evidence on long-term anticoagulation management following spontaneous retroperitoneal hemorrhage. This review aims to analyze risks, diagnostic tests, therapeutic approaches, and clinical outcomes. We refer to a case report of SRH following pulmonary thromboembolectomy surgery, and we discuss conservative and interventional management strategies for the management of long-term anticoagulation after significant bleeding complications such as SRH.

Introduction

Life-long anticoagulation prevents thromboembolic events in patients after pulmonary thromboembolectomy surgery. The rationale of anticoagulation in chronic thromboembolic pulmonary hypertension is to avoid pulmonary arterial thrombosis and recurrence of deep venous thrombosis leading to embolism[1]. Current anticoagulant options for CTEPH include Vitamin K antagonists (VKAs) such as warfarin, which have been traditionally used due to their well-established efficacy. Recently, due to their favorable safety profiles, Direct Oral Anticoagulants (DOACs) such as rivaroxaban and apixaban have emerged as potential alternatives. However, evidence supporting the routine use of DOACs in CTEPH remains limited, and warfarin is still widely recommended[2].

Despite its benefits, anticoagulation is associated with significant bleeding risks. Spontaneous retroperitoneal hemorrhage (SRH) is a rare but potentially life-threatening condition. The clinical dilemma lies in determining the safest way and time to reinitiate anticoagulation after a serious bleed while minimizing the risk of recurrence and thromboembolic complications[3,4].

SRH results from vessel rupture within the retroperitoneal space, often exacerbated by anticoagulant use. Although the exact cause of this is unknown, certain risk factors, such as advanced age, renal impairment, high-dose anticoagulation, and concomitant use of antiplatelets, are known to exacerbate it. Several mechanisms contribute to SRH, including microvascular fragility, increased permeability of blood vessels, and reduced hemostatic capacity in patients on anticoagulation therapy. Additionally, comorbid

conditions such as hypertension, diabetes, and malignancies further exacerbate the risk[5,6]. Non-randomized trials have postulated that the use of direct oral anticoagulants (DOACs) versus vitamin K antagonists (VKAs) has a reduced incidence of bleeding. Also, suggesting that DOACs may have a lower risk of intracranial and retroperitoneal hemorrhage[1,7,8].

Clinical Presentation and Diagnosis

In our case report, a 73-year-old man underwent coronary artery bypass grafting and pulmonary thrombo-embolectomy surgery under deep hypothermic circulatory arrest (DHCA). Initially, the patient was started on low-molecular-weight heparin and aspirin. During the postoperative period, he developed acute generalized exanthematous pustulosis (AGEP), possibly secondary to penicillin or enoxaparin allergy. Hence, he was switched from subcutaneous enoxaparin to fondaparinux. While recovering from AGEP, on the 25th postoperative day, he developed severe abdominal pain and limb weakness. Although he was hemodynamically stable, his hemoglobin dropped significantly, prompting further investigation[9]. Patients with SRH typically present with abdominal pain, lower limb weakness, hypotension, and progressive anemia[10]. Depending on the severity of the hemorrhage, patients may exhibit hemodynamic instability requiring urgent intervention.

In our patient, contrast-enhanced computed tomography (CT) was performed, and it revealed a 13.9 cm retroperitoneal hematoma involving the left psoas muscle. Anticoagulation was paused, and the patient received tranexamic acid and blood transfusions. Serial imaging demonstrated hematoma stability, and gradual anticoagulation resumption with rivaroxaban was successfully implemented[4,9]. The gold standard for detecting retroperitoneal hemorrhage is computed tomography with contrast. This also helps in identifying active bleeding sources[3,11]. Additional imaging techniques, such as ultrasound and magnetic resonance imaging (MRI), may be utilized in specific scenarios, particularly for assessing hematoma evolution and ruling out underlying vascular abnormalities.

Laboratory findings often reveal acute blood loss anemia, elevated lactate levels (indicating hypoperfusion), abnormal coagulation profiles, prolonged INR for patients on warfarin, and low fibrinogen levels. Close monitoring of hemodynamic parameters and serial hemoglobin/hematocrit measurements are useful in guiding management.

Management Strategies for future anticoagulation

Managing anticoagulation for these patients is complicated as there needs to be a fine balance between maintaining adequate anticoagulation to prevent the risk of thrombosis and staying within the therapeutic window to prevent recurrent and possible life-threatening bleeding.

Once the patient has been diagnosed with retroperitoneal hemorrhage while on anticoagulation, the initial step is to stop anticoagulation therapy to prevent further blood loss. Adequate resuscitation is ensured through intravenous fluids and blood transfusions if required. In severe cases, administration of reversal agents such as prothrombin complex concentrate for warfarin or idarucizumab for dabigatran may be necessary to counteract excessive anticoagulation[6]. Continuous hemodynamic monitoring is important, as uncontrolled hemorrhage may necessitate rapid resuscitative and surgical or radiological interventions. Opioids and non-opioid analgesics may be required for pain control. However, nonsteroidal anti-inflammatory drugs (NSAIDs) should be avoided due to the risk of exacerbating the bleeding[7]. Laboratory markers should be monitored, including hemoglobin, platelet count, coagulation parameters, and renal function.

Imaging studies such as contrast-enhanced CT angiography are performed to evaluate the extent of hemorrhage and identify potential active bleeding sites. Most hemodynamically stable patients benefit from temporary cessation of anticoagulation, transfusions, and careful monitoring. Conservative management is particularly effective for small to moderate-sized hematomas without ongoing active bleeding. If ongoing hemorrhage is detected, interventions such as endovascular embolization can control bleeding. This effectively prevents hematoma expansion and reduces the need for surgical intervention. Surgical intervention is reserved for patients with persistent or expanding hematomas despite embolization. Open surgical evacuation is rarely required but may be necessary in cases of severe compartment syndrome or progressive neurological deficits due to hematoma compression.

Following hemorrhage control, an individualized risk-benefit assessment should guide the decision to resume anticoagulation. Balancing the risk of recurrent hemorrhage with the risk of thromboembolism is critical, particularly in patients with prior thromboembolic events[8]. A multidisciplinary approach is recommended. Risk stratification tools such as HAS-BLED and CHADSVa were originally designed for atrial fibrillation and are not specifically validated for CTEPH. The HAS-BLED score for bleeding risk and the CHADSVa score for stroke risk is sometimes used in clinical practice[12]. However, more research is needed to establish reliable scoring systems for patients with CTEPH. A stepwise approach is recommended, starting with low-dose anticoagulation before resuming full therapeutic doses. This strategy is supported by evidence suggesting that resumption within 7

to 14 days following stabilization reduces thromboembolic risk while minimizing recurrent bleeding[13]. Current evidence suggests that anticoagulation should typically be resumed within 7 to 14 days following stabilization. However, this timeline may be adjusted based on individual patient factors, including hematoma resolution on imaging and overall hemodynamic stability[2]. In cases where thromboembolic risk is exceptionally high, such as in patients with mechanical prosthetic valves or recent venous thromboembolism (VTE), temporary bridging with low-dose, low-molecular-weight heparin (LMWH) may be considered before transitioning to full-dose anticoagulation with close monitoring for any signs of rebleeding[13].

Direct oral anticoagulants (DOACs) are often favored over vitamin K antagonists (VKAs) due to their improved safety profile[1]. However, warfarin remains the gold standard for patients with mechanical heart valves due to its superior efficacy in preventing valve thrombosis[14]. Among the DOACs, apixaban and edoxaban are often preferred over rivaroxaban and dabigatran due to their lower rates of gastrointestinal bleeding[3]. Drug dose adjustment is necessary in patients with impaired renal function, liver disease, and frailty. In these patients, periodic monitoring is recommended to detect early signs of coagulopathy[15].

Long-term management of SRH focuses on preventing recurrence and optimizing anticoagulation therapy. Regular laboratory monitoring and modification of modifiable risk factors should be done to minimize future bleeding episodes[16]. Close follow-up is recommended with repeat imaging to check for hematoma resolution. Blood pressure control, renal function monitoring, and reassessment of the need for concomitant antiplatelet therapy should be considered to prevent further hemorrhagic events[6]. Additionally, patients should be educated about warning signs of recurrent hemorrhage and the importance of adherence to prescribed medications. Future research is needed to establish standardized guidelines on the optimal timing and strategy for anticoagulation resumption following major bleeding events such as SRH.

Conclusion

The management of anticoagulation after significant bleeding should be individualized as per the patient's needs. The emergence of DOACs with favorable safety profiles offers promising alternatives to VKAs[1]. Future clinical guidelines should incorporate risk-adapted strategies, emphasizing the role of early imaging, patient-specific risk assessment, and phased anticoagulation resumption to optimize outcomes[3,7]. Ongoing research is necessary to define standardized protocols for anticoagulation resumption and identify biomarkers predictive of recurrent hemorrhage risk[8].

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