



# Intraoperative Massive Hemorrhage and Management in Thoracic Surgery

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## ABSTRACT

Massive hemorrhage (MH) is most commonly seen in acute trauma, complex cardiac surgery, obstetric hemorrhage, and coagulopathic patients. However, it can also occur during any intraoperative event and remains one of the greatest challenges for anesthesiologists. Major intraoperative bleeding is less common in thoracic surgery than in the past. The use of minimally invasive surgical techniques and the widespread implementation of patient blood management strategies starting from the preoperative period can be considered among the contributing factors. Although the incidence of MH in thoracic surgery is low, its mortality rate is high. Massive airway bleeding (hemoptysis) and major vascular injuries have been identified as conditions with a high risk of MH. In thoracic surgery, MH is a rare but life-threatening condition. Effective communication between the operating room team and the blood bank, along with a well-organized approach, is crucial. Ensuring adequate intravenous access during MH is a priority. Additionally, patient positioning should be carefully managed to increase preload and cerebral perfusion. Intraoperative MH is a rare but highly fatal condition in thoracic surgery.

**Keywords:** Blood transfusion, massive hemorrhage, thoracic surgery

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## Massive Hemorrhage

Massive bleeding is most commonly seen in acute trauma, complex cardiac surgery, obstetric hemorrhage, and coagulopathic patients. However, it can also occur during any intraoperative event and remains one of the greatest challenges for anesthesiologists. In predictable situations, it can be successfully managed with proper preparation and an organized approach, whereas in unpredictable cases, it may initially lead to a chaotic environment.

There is no universally accepted international definition of massive hemorrhage (MH). MH is defined as the loss of more than one blood volume within 24 hours, the loss of 50% of the patient's total blood volume in less than 3 hours, bleeding exceeding 150 ml/min, or the need for  $\geq 10$  units of packed red blood cells (RBCs) within 24 hours (10/24),  $\geq 6$  units of RBCs within 6 hours (6/6), or  $\geq 5$  units of RBCs within 4 hours (5/4).<sup>[1,2]</sup>

Some guidelines have defined MH with a clinical focus, characterized by a systolic blood pressure below 90 mmHg and a heart rate exceeding 110 bpm.<sup>[3]</sup> However, it should be noted that rapid blood loss can lead to paradoxical bradycardia; therefore, the absence of tachycardia does not rule out significant blood loss.<sup>[4]</sup>

In a review focused on the definition of MH and transfusion, with the majority of publications related to obstetrics and trauma, 15 different definitions of MH were identified.<sup>[5]</sup>

## Intraoperative Massive Hemorrhage

Intraoperative massive hemorrhage is the leading cause of cardiac arrest in the operating room, and its definition is even more challenging and complex.<sup>[6]</sup>

According to data from a study conducted in Japan using a survey method, between 2003 and 2005, life-threatening

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bleeding was reported in 1,011 out of 1,367,790 patients registered from 782 hospitals, with a reported mortality rate of 45.4% within the following seven days. This study noted that in surgery-related MH cases, 63% of patients lost a blood volume equivalent to their circulating blood volume, while 37% lost twice their circulating blood volume. Additionally, it was reported that 51% of patients experienced blood loss exceeding 120 ml/min, 31% exceeded 240 ml/min, but the maximum bleeding rate was not documented in 22% of cases.

During the intraoperative period, patients may experience life-threatening bleeding that does not strictly fit the general definition of MH. Regardless of the total blood loss, factors such as the patient's comorbidities, pre-existing anemia, and delays in blood transfusion can further exacerbate the severity of the bleeding.<sup>[6,7]</sup>

### Thoracic Surgery and Massive Bleeding

By the late 1990s, more than 17% of hospital deaths related to thoracic surgery were attributed to bleeding, and 28.6% of these cases occurred during the intraoperative period. In recent years, major intraoperative bleeding in thoracic surgery has been observed at a lower rate than in the past. This decline is attributed to the use of minimally invasive surgical techniques and the widespread adoption of patient blood management strategies starting from the preoperative period.<sup>[8]</sup>

In elective lung resections, the intraoperative erythrocyte suspension (ES) transfusion rate is low (7.1–7.4%), whereas it is higher in emergency cases, open surgeries, decortication procedures, pneumonectomies, and esophagectomies.<sup>[9,10]</sup>

A retrospective study involving 62,571 patients undergoing thoracic surgery examined perioperative adverse events, identifying 150 adverse events (0.2%), of which 33 (22%) were classified as critical incidents (CIs). Among these CI cases, 27 (81.8%) occurred during the intraoperative period, while six occurred in the postoperative anesthetic care unit. Out of 12 deaths, eight were attributed to critical incidents. CIs are significant causes of mortality that can be prevented through early detection and appropriate intervention by the surgeon.<sup>[11]</sup>

Although the incidence of CIs in thoracic surgery is low, their mortality rate is high. Massive airway bleeding (hemoptysis) and major vascular injuries have been identified as conditions associated with a high risk of CI.<sup>[12,13]</sup>

Hemoptysis can originate from either the upper or lower airways. Depending on the duration and volume of bleeding, it can range from mild hemoptysis to life-threatening hemoptysis. Airway bleeding exceeding 600 ml/24 hours is defined as massive hemoptysis,<sup>[14]</sup> while 200

ml/hour of airway bleeding is classified as life-threatening hemoptysis. In patients with chronic respiratory failure, even 50 ml/hour of bleeding is sufficient to be considered life-threatening hemoptysis.<sup>[15]</sup>

The definition of hemoptysis should consider the degree of hypoxemia, involvement of the contralateral lung, and the need for mechanical ventilation and transfusion.<sup>[16]</sup>

During massive hemoptysis, while the cardiovascular system combats hypovolemia, the respiratory system struggles with hypoxemia. In 90% of cases, massive hemoptysis originates from high-pressure bronchial circulation, while 5% arise from the aorta (ruptured aneurysms, aortobronchial fistulas) and 5% from pulmonary vessels. Massive blood transfusion (MBT) may not always be necessary in massive hemoptysis, as hypoxia—rather than the bleeding itself—exacerbates the severity of the crisis. Even a 150–200 ml bleed can be fatal in patients with restricted respiratory function due to respiratory failure. In some cases, blood loss severe enough to cause shock may occur.<sup>[16]</sup>

Due to the presence of numerous vital vascular networks, complex anatomy, and constant cardiorespiratory motion, procedures such as mediastinoscopy, lung resections, transhiatal-transthoracic esophagectomies, and thymectomies—whether performed via minimally invasive or open techniques—carry a risk of procedure-related major vascular injury.<sup>[13]</sup>

According to data from a retrospective study on the incidence of intraoperative bleeding during thoracic surgery, the incidence of severe bleeding was found to be 0.2% in mediastinoscopy, 4.7% in minimally invasive anatomical resections, and 5% in open surgery.<sup>[17]</sup>

Although major bleeding during mediastinoscopy is a rare event, it remains a potentially morbid and fatal complication. It can be prevented through a thorough understanding of the anatomical relationships in the mediastinum, careful dissection, and the operator's experience. If significant bleeding occurs, initial control can be achieved through tamponade. Successful management requires prompt and well-coordinated care.<sup>[18]</sup> Simple and accessible protocols should always be readily available.<sup>[19]</sup>

Although video-assisted thoracoscopic surgery (VATS) lobectomy has been shown to offer many advantages over the thoracotomy approach, life-threatening intraoperative bleeding can still occur. The incidence of such bleeding has been reported to range from 4.11% to 10.83%.<sup>[20–25]</sup>

In VATS, bleeding caused by pulmonary artery injury is the most dangerous due to the artery's relatively fragile structure and the very high volume of blood flow through it.<sup>[26]</sup> Severe pulmonary artery injury may necessitate unplanned extensive pulmonary resection, such as

pneumonectomy, and in serious cases, it can result in the patient's intraoperative death.<sup>[27]</sup> Although bleeding from the bronchial artery is common in thoracoscopic surgery, it can be successfully controlled with compression, electrocautery, ultrasonic energy devices, or hemostatic clips.<sup>[28]</sup>

Changes in the branching pattern of the pulmonary artery may sometimes occur, and if these variations are not detected beforehand, they can lead to bleeding. Although less common, venous abnormalities are also recognized as a potential cause of vascular complications. Preoperative imaging, particularly computed tomography (CT), provides a valuable opportunity to identify vascular anatomical variations and understand the tumor's location relative to major vascular structures. It is estimated that 95% to 98% of the vascular anatomy relevant to the surgical procedure can be accurately identified through preoperative CT.<sup>[29,30]</sup>

Understanding the anatomical topographic details, structure, course, and specific characteristics of the pulmonary vessels is crucial for the prevention and management of bleeding.<sup>[17]</sup> Life-threatening bleeding can also occur during the postoperative period in thoracic surgery, which is more dangerous and carries a higher mortality rate than intraoperative bleeding.<sup>[31,32]</sup>

In thoracic surgery, massive bleeding (MB) is rare but has a high mortality rate. Timely communication and an organized approach between the surgical team and the blood bank are crucial. Even with experienced and adequate personnel, some issues may be overlooked, or miscommunication may occur. Therefore, the use of pre-prepared cognitive aids and ongoing training through simulated scenarios is important.<sup>[12,33]</sup>

During MB, establishing adequate intravenous access is prioritized over arterial or central monitoring. Care should be taken with patient positioning to increase preload and cerebral perfusion. In cases of injuries to the superior vena cava or the arms, wide subdiaphragmatic venous access should be established.

## Massive Blood Transfusion

MBT requires immediate intervention and coordination among clinicians, nurses, other healthcare providers, laboratories, and blood banks, necessitating a multidisciplinary approach.<sup>[33]</sup>

Most of the literature on MBT decision-making is trauma-specific and has low sensitivity. Parameters influencing the decision for MBT can be affected by intraoperative drug use, general anesthesia, and the surgical procedure itself.<sup>[34]</sup>

Early diagnosis of blood loss, timely preparation of blood and blood products if they are not readily available, restoration of tissue perfusion and oxygenation with adequate blood

volume and hemoglobin levels, administration of appropriate blood components for coagulation, and prevention of unnecessary blood product replacement necessitate the implementation of massive transfusion protocols (MTP).<sup>[35]</sup>

During MBT, optimizing oxygenation, cardiac output, tissue perfusion, metabolic status, and hemostasis should be the primary goals. According to MTP, complete blood counts, coagulation studies, ionized calcium levels, and arterial blood gas analyses should be monitored every 30–60 minutes, either at the bedside or in the laboratory. The target parameters should include an arterial pressure between 60 and 65 mm Hg, hemoglobin levels between 7 and 9 g/dL, an international normalized ratio (INR) below 1.5, fibrinogen levels between 1.5 and 2 g/L, platelet counts above 50,000/ $\mu$ L, a pH between 7.35 and 7.45, and a core body temperature maintained above 35°C.<sup>[36,37]</sup>

In patients with ongoing bleeding and coagulopathy, erythrocyte suspension (ES) transfusion should continue until hemoglobin (Hb) levels reach  $\geq 10$  g/dL if the patient is stable and not actively bleeding, and  $\geq 7$  g/dL in other cases.<sup>[38]</sup> At the bedside, thromboelastography, thromboelastometry, and platelet function tests allow for targeted treatment of coagulopathy.<sup>[39]</sup>

For patients undergoing massive transfusion, as well as for most stable medical and surgical patients (excluding those with acute myocardial infarction), a restrictive transfusion strategy involves administering less blood, transfusing at lower hemoglobin levels (usually 7–9 g/dL), and setting lower target hemoglobin levels. This approach is based on multiple clinical trials, with specific thresholds determined by studies conducted in patient populations similar to the one being treated. Some patients may remain asymptomatic from anemia even when their hemoglobin levels are below the recommended thresholds, while in symptomatic patients, transfusion at higher hemoglobin levels is generally appropriate. However, there are certain conditions where exceptions to the restrictive transfusion strategy may apply, such as in patients with coronary vascular disease and symptomatic anemia, where higher hemoglobin thresholds may be warranted.<sup>[40]</sup>

During massive bleeding, various methods can be applied depending on the clinical situation, some of which remain controversial in the literature. The use of hemostatic agents is among these methods. However, there is no evidence that the prophylactic or therapeutic use of fresh frozen plasma (FFP) significantly reduces blood loss.<sup>[41]</sup> Therefore, its use to decrease blood loss or the need for blood products is not recommended.<sup>[42]</sup>

Other hemostatic agents include factor XIII (FXIII), a coagulation factor that acts at the end of the coagulation

cascade. However, there is no evidence that FXIII reduces bleeding, decreases the need for blood products, or lowers the requirement for reoperation due to bleeding.<sup>[43]</sup>

**Fibrinogen:** In patients with bleeding and fibrinogen levels below 1.5–2 g/L, fibrinogen replacement is considered appropriate.<sup>[44]</sup>

**Desmopressin** (1-deamino-8-D-arginine vasopressin; DDAVP) is a vasopressin analog that increases the release of von Willebrand factor (vWF) from endothelial cells. The prophylactic use of desmopressin to reduce blood loss is not recommended. However, in patients experiencing bleeding due to platelet dysfunction (whether inherited or acquired), the use of DDAVP may be considered to reduce blood loss and the need for transfusion.<sup>[45]</sup>

**Antifibrinolytics**, particularly tranexamic acid (TXA), deserve special mention. TXA is used to reduce blood loss and the need for blood transfusion.<sup>[46]</sup> A meta-analysis of studies showed that mortality rates were lower in critically bleeding trauma patients treated with TXA. However, this difference was not statistically significant, and no reduction was observed in the amount of transfused red blood cell concentrates.<sup>[47]</sup>

Finally, regarding fluid management during massive bleeding, debates on this topic are still ongoing. The primary goal of fluid management is to maintain adequate blood pressure, cardiac output, tissue perfusion, and oxygenation. Discussions continue regarding the choice between crystalloids and colloids. Crystalloid solutions are routinely used in cardiac surgery due to their lower cost and reduced risk of coagulopathy, infection, and anaphylaxis. However, it has been reported that high volumes of normal saline solution (0.9%) alter serum osmolarity, increase blood product usage, and lead to hyperchloremic acidosis and postoperative acute kidney injury.<sup>[48]</sup>

Among the most commonly used colloid solutions are hydroxyethyl starch (HES) solutions, albumin, and gelatin, which are more effective in expanding intravascular volume. However, the main disadvantages of these solutions include impaired kidney function, the need for renal replacement therapy, a tendency for bleeding, and an increased risk of mortality. The literature presents conflicting results on this subject, and no single consensus has been reached regarding the use of colloid solutions.<sup>[49,50]</sup>

The goal of fluid therapy in massive bleeding is to achieve hemodynamic stability through volume therapy during the perioperative period.<sup>[51]</sup> To minimize bleeding and reduce the need for blood transfusion, hemodilution should be avoided during fluid resuscitation.<sup>[52]</sup>

In conclusion, intraoperative massive bleeding (MB) in thoracic surgery is a rare but highly fatal condition. Anticipating conditions that could lead to MB, identifying

vascular anatomical variations through preoperative CT, and determining the relationship of the tumor with major vascular structures can help prevent potentially fatal hemorrhages. During massive transfusion, optimizing intravascular volume and tissue oxygenation, maintaining coagulation, and correcting electrolyte imbalances should be integral to each institution's massive transfusion protocol (MTP), along with pre-prepared cognitive aids for crisis situations.

## Disclosures

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