Egypt. J. Chem. Vol. 67, SI: M. R. Mahran, pp**. 1803 - 1811** (2024)

Egyptian Journal of Chemistry

http://ejchem.journals.ekb.eg/

Severe Bleeding in Preoperative Conditions: Emergent Interventions to Control Condition-An Updated Review

Laila Hassan Al Salman[1], Abdul Aziz Khaled Al-Zaaqi[2], Sultan Ibrahim Ahmed Almannaa[2], Salhah Yahya Alneami[2], Yahya Mahdi Abdullah Awaji[2], Emad Souleman Ebani[2], Alanoud Alharthi[2], Ghadah Altamimi[2], Nada Emad Al Sahhaf[2], Basel Hamid Almuabbadi[2], Hazzaa Alanazi[2], Reem N Albishi[2], Shatha Ahmed Alaryani[2], Nada Ahmad Alhejali[2], Maryam Salem Algarni[2], Khulood Abdu Hekoomi[2], Maha Mohammed Jafri[2], Zohoor Mahamaud Samtah[2], Haifa Abdulaziz Bin Nafesah[2], Shadia Maashi Alanazi[2]

[1]First Riyadh Health Cluster, Ministry of Health, Saudi Arabia
[2]King Saud Medical City, Saudi Arabia

Abstract

Background: Severe bleeding during preoperative and intraoperative conditions remains a major cause of morbidity and mortality. The risk of hemorrhage is heightened by factors such as trauma, anticoagulant therapies, and surgical complications. Effective preoperative management and timely interventions are crucial for controlling severe blood loss and minimizing the associated risks.

Aim: This review aims to provide an updated synthesis of interventions and strategies used to control severe bleeding in preoperative conditions, focusing on the mechanisms of hemorrhage, risk factors, and the management techniques employed to stabilize patients.

Methods: A comprehensive review of the existing literature was conducted, analyzing the underlying mechanisms of bleeding, including coagulopathy and the body's response to hemorrhagic shock. Clinical approaches such as fluid resuscitation, pharmaceutical interventions, and surgical techniques for managing severe bleeding were discussed.

Results: The review highlighted that hemorrhagic shock often occurs due to trauma-induced coagulopathy, shock, or the consumption of clotting factors. Fluid resuscitation strategies, including the use of crystalloids, colloids, and blood products, are essential in stabilizing patients. Additionally, medications such as inotropes and adrenergic agonists play a vital role in improving cardiac output and blood pressure. Effective interventions in managing hemorrhagic shock were found to rely heavily on rapid response, tailored treatments, and evidence-based guidelines.

Conclusion: Severe bleeding in preoperative conditions presents a complex challenge. Immediate intervention through appropriate fluid therapy, the use of pharmaceuticals, and surgical techniques are essential in controlling blood loss. The timely recognition and management of coagulopathy, hemorrhagic shock, and underlying health conditions are critical to improving patient outcomes and reducing mortality in these high-risk situations.

Keywords: severe bleeding, hemorrhagic shock, fluid resuscitation, anticoagulants, coagulopathy, trauma, surgical intervention..

.

1. Introduction

Bleeding in surgical patients can be attributed to various causes, including blood loss, haemodilution, acquired platelet dysfunction, the consumption of coagulation factors in extracorporeal circuits, activation of fibrinolytic and fibrinogenolytic pathways, inflammatory responses, and hypothermia [1]. Oral anticoagulants such as warfarin, dabigatran, rivaroxaban, apixaban, and edoxaban, along with platelet inhibitors like P2Y12 receptor inhibitors (e.g., clopidogrel, prasugrel, and ticagrelor), are common contributors to acquired haemostatic abnormalities in surgical patients. Consequently, haemostatic abnormalities—whether congenital or acquired—may predispose individuals to postoperative bleeding. While congenital bleeding disorders are rare, patients with such conditions undergoing surgery are typically under prior treatment. The ISTH bleeding questionnaire is as reliable as laboratory tests for predicting postoperative bleeding risk and can be integrated into preoperative assessments [2]. In most cases, bleeding is localized to the surgical site. Minimizing surgical bleeding in high-risk patients necessitates meticulous surgical technique, patience, and careful patient selection. An exhaustive examination of the wide array of topical haemostatic agents and devices available on the market exceeds the scope of this article [3].

Blood physiology is fundamental to sustaining life, as circulating blood plays a critical role in transporting oxygen, hormones, gases, and waste products throughout the body, while also contributing to significant immunological functions. Blood is crucial in regulating the homeostasis of pH, temperature, and other internal factors. Composed of plasma, erythrocytes, platelets, and leukocytes, blood supports numerous physiological processes that are vital to survival [4]. The adult human circulatory system typically carries between 4.5 and 5 liters of blood, with approximately 55% of this volume consisting of plasma, and the remaining 45% made up of

*Corresponding author e-mail: Lhalsalman@moh.gov.sa (Laila Hassan Al Salman)
Receive Date: 23 December 2024, Revise Date: 29 December 2024, Accept Date: 31 December 2024
DOI: 10.21608/ejchem.2024.346876.11031
©2024 National Information and Documentation Center (NIDOC)

cellular components. Blood volume in a healthy adult comprises around 7–8% of total body mass [5]. Haemorrhage refers to the rupture of a blood vessel, leading to blood leakage. This bleeding may range from minimal, such as petechiae and ecchymosis from superficial vessel injury, to more profound bleeding that alters vital signs and mental status [6]. Haemorrhage can be classified as either internal or external, with blood exiting the body through an orifice or wound. Clinical suspicion of internal bleeding necessitates a thorough history, physical examination, laboratory tests, imaging, and vigilant monitoring of vital signs. Particularly in trauma cases, haemorrhage remains a leading cause of preventable mortality [7].

Preoperative bleeding can be attributed to several factors, such as trauma. Haemorrhage is the leading cause of mortality in patients who survive to hospital admission after severe trauma, with the highest frequency occurring within the first three to four hours post-arrival. Major trauma, caused by events like car accidents, gunshot wounds, falls, or explosions, can lead to significant blood loss from ruptured organs (e.g., spleen) or substantial vascular injuries (e.g., brain bleeding). Such massive haemorrhaging often results in death prior to hospital arrival. Consequently, haemorrhage and haemorrhagic shock remain the predominant causes of mortality in traumatic injuries [8]. The risk associated with surgery is closely linked to the nature of the procedure. Studies consistently demonstrate that emergency surgeries carry a higher risk than elective procedures. Factors such as underlying illness and the stress induced by surgical treatment further heighten the risk. Cardiovascular surgery, in particular, is consistently ranked among the most hazardous operations, followed by vascular surgery, which is one of the riskiest surgeries outside of cardiac procedures. Notably, infra-inguinal surgeries are found to have similar cardiac morbidity rates to aortic reconstructive surgery [9]. Amputation is another high-risk vascular operation, as are abdominal, thoracic, and orthopedic surgeries [10].

Unusual clotting and bleeding can arise due to shock-induced coagulopathy. This condition is influenced by several factors, including the consumption of clotting factors, hemodilution due to excessive crystalloid infusion, acidosis, and hypothermia. The precise mechanism underlying coagulopathy remains undetermined, but it is postulated that thrombin and fibrin are formed in response to tissue factors released during trauma [11]. Additionally, trauma-induced hypoperfusion and ischemia are believed to trigger the production of activated protein C, leading to the consumption of plasminogen activator inhibitors, disruption of the clotting cascade, systemic anticoagulation, and hyperfibrinolysis. Acute traumatic coagulopathy is now managed with a high ratio of fresh frozen plasma to red blood cells [12]. In pregnancy, haemorrhage is a leading cause of maternal death, with significant bleeding occurring before, during, or after childbirth. Severe bleeding during labor is considered the primary cause of maternal mortality and morbidity globally [13]. The body's response to sudden blood loss is crucial in maintaining homeostasis, particularly in hemorrhagic shock, where inadequate blood volume results in insufficient tissue perfusion, leading to organ failure and widespread cellular damage [14].

In response to extreme blood loss, a cascade of stress reactions is initiated to prioritize blood flow to vital organs and mobilize stored energy. Hemorrhagic shock triggers baroreceptors in major thoracic arteries, stimulating adrenergic responses that involve both neuronal and hormonal components. These neurological effects occur almost instantaneously, while hormonal changes may take a bit longer to manifest. Sympathetic nervous system activation leads to vasoconstriction in peripheral arteries, with the heart also receiving sympathetic stimulation [15]. The endocrine response to hemorrhagic shock is governed by the hypothalamic-pituitary-adrenomedullary axis, which releases stress hormones such as adrenaline, norepinephrine, corticosteroids, renin, and glucagon. These hormones facilitate the breakdown of glycogen reserves and promote the release of glucose and fatty acids, which help sustain energy during shock [16]. Furthermore, lactate production from skeletal muscles due to anaerobic glycolysis is commonly observed in patients experiencing hemorrhagic shock. Elevated lactate levels are indicative of systemic hypoperfusion and normalize following appropriate resuscitation [17]. Factors such as age, overall health, body temperature (hypothermia or hyperthermia), and medications may influence the body's reaction to bleeding. Children and infants, for instance, compensate for blood loss primarily through increased heart rate, as opposed to blood pressure regulation, which places them at a higher risk of fatality when blood pressure drops [18].

In the assessment of hemorrhagic shock, early changes in arterial acid-base balance often precede drops in cardiac output. Even if pH and blood pressure appear unaffected, a decrease in bicarbonate levels and base deficit is an early indicator of bleeding [19]. Hemorrhagic shock can be differentiated from simple bleeding by identifying signs of widespread tissue hypoperfusion when the base deficit reaches a critical threshold. Symptoms such as tachycardia, a reduced base deficit, and poor urine output should raise suspicion for hemorrhagic shock [20]. When systemic oxygen delivery (DO2) falls below a critical threshold (DO2crit), tissues shift to anaerobic energy sources, marking the onset of compensated shock. If sufficient ATP is generated from both aerobic and anaerobic sources, cellular function can persist. However, some tissues, such as the liver, are more susceptible to irreversible damage from ischemia, while skeletal and smooth muscles are more resistant to hypoxia. The brain, on the other hand, is particularly vulnerable to even brief periods of oxygen deprivation [21]. The stomach and intestines are also highly sensitive to hypoperfusion, with signs of anaerobic metabolism appearing before significant declines in systemic oxygen levels. Once ATP reserves are depleted, cellular damage becomes irreversible, leading to cell membrane degradation and swelling due to failure of ion transport pumps critical for calcium and sodium regulation [22]. Energy depletion, acidosis, free radical production, and loss of adenine nucleotides collectively contribute to irreversible cellular damage during hypoxia [23].

Controlling Severe Blood Loss During Surgery

What Is Fluid Therapy?

Fluid resuscitation is designed to reduce blood loss, restore lost blood volume, and reinstate tissue perfusion and organ function. Clinical goals for systolic blood pressure (SBP) vary based on trauma type: 60–70 mmHg is suggested for penetrating trauma; 80–90 mmHg for blunt trauma without traumatic brain injury (TBI); and

100–110 mmHg for blunt trauma with TBI. Following evidence-based clinical guidelines and adjusting treatment according to local practices and the patient's unique condition enhances patient outcomes despite the inherent complexity and variability of clinical scenarios [24]. Fluid administration is deemed beneficial only if it induces an increase in stroke volume (SV) and, consequently, cardiac output. Patients who exhibit a minimum 10% increase in SV following a crystalloid fluid challenge of 500 mL are considered fluid-responsive. Key indicators of fluid responsiveness include pulse pressure variation, the passive leg-raising test, and variations in SV [25].

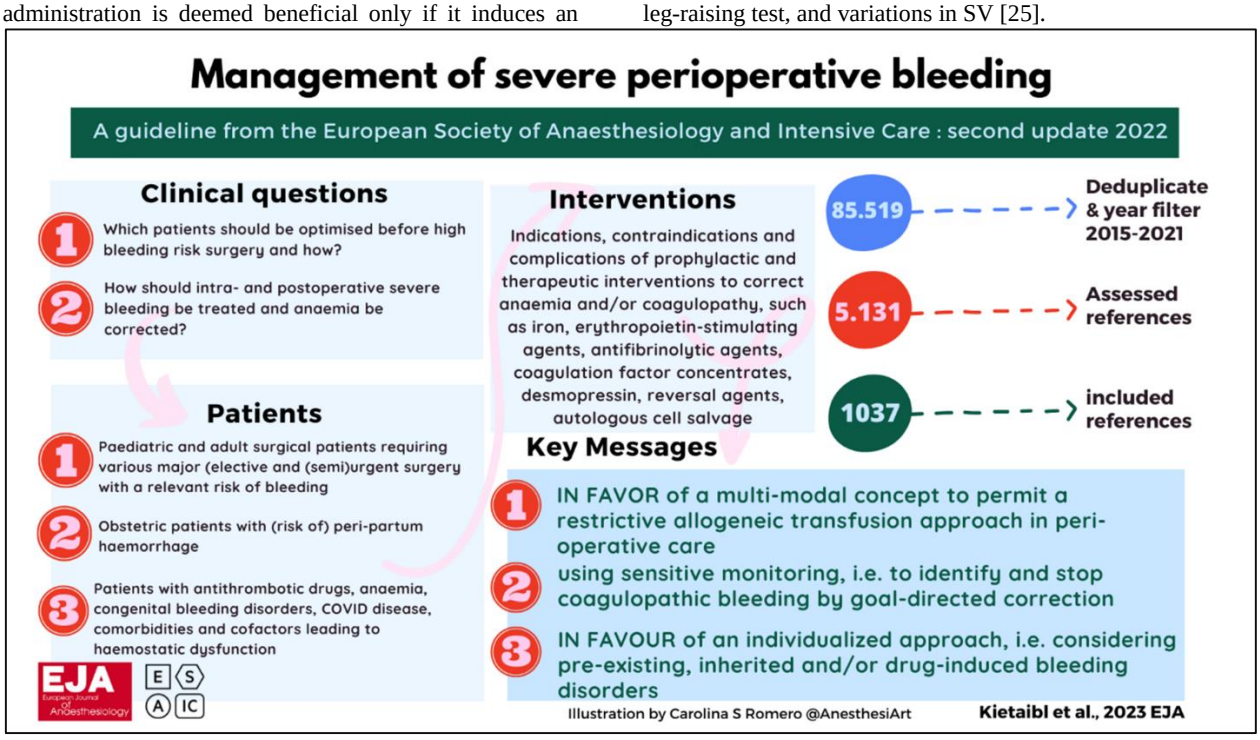

Figure 1: Management of Severe Preoperative Bleeding.

Examples of Infused Fluids:

The primary categories of fluids administered include crystalloids, colloids, and blood. Each fluid type has distinct benefits and clinical applications, with crystalloids and colloids being the primary focus of this discussion [26]. Crystalloids are electrolyte solutions used to replace fluids lost through respiration and urination. While crystalloids can temporarily enhance hemodynamics by increasing vascular volume, they are less effective than colloid solutions. Two major characteristics that distinguish crystalloids are their chemical composition and osmolality. For instance, normal saline (NS) and lactated Ringer's (LR) solutions are somewhat hypertonic (308 mOsm/l) and hypotonic (273 mOsm/l), respectively, when compared to plasma osmolality. In contrast, plasmacyte, with an osmolality of 294 mOsm/l, is the most neutral electrolyte solution available [27].

Colloid solutions, which are more likely to remain in the intravascular compartment, have been proposed for use in treating hemorrhagic shock. Examples of colloid solutions tested therapeutically include human albumin, hydroxyethyl starch (HES), and dextran. Colloid solutions require a smaller volume to achieve hemodynamic stability than crystalloids, as they are quickly resorbed into the intravascular space. However, colloids may further exacerbate extracellular fluid deficits, are more expensive, can bind and reduce serum ionized calcium levels, and may lower circulating immunoglobulin concentrations. Both crystalloid and colloid fluid resuscitation have been the subject of extensive clinical and experimental investigations [28]. Research suggests that a modest amount of hypertonic saline (5 ml/kg of 7.5% NaCl), with or without dextran, could serve as an effective initial resuscitation solution. Despite their hypertonicity, hypertonic solutions do not adversely affect immunological functions and have been demonstrated to improve microvascular flow, reduce intracranial pressure, and stabilize arterial pressure and cardiac output with minimal infusion volumes [29]. A 250 mL bolus of 7.5% saline delivered through a rapid infusion system is recommended for initial fluid resuscitation in hemorrhaging battlefield casualties. This approach is favored due to the safety and efficacy of hypertonic saline, its simplicity, the limited volume available for transport in military settings, and its cost-effectiveness. Systemic access may be achieved using either an intraosseous needle or an intravenous catheter. However, recent clinical trials have questioned this approach [30].

Pharmaceuticals for Resuscitation:

Inotropes are drugs that enhance myocardial contractility by altering the heart's contractile function. These agents include adrenergic agonists, phosphodiesterase III inhibitors, and calcium sensitizers [31]. Adrenergic agonists produce positive inotropic effects by stimulating beta-adrenergic receptors, increasing heart rate, stroke volume, and cardiac output. Based on their effects on blood pressure and heart rate, adrenergic agonists such as dobutamine, dopamine, norepinephrine, and epinephrine can be classified into subgroups of inopressors or inodilators. In the United States, the only available inodilators are milrinone and dobutamine [32]. Dopamine exerts its effects on the cardiovascular system through four receptors: dopaminergic type 1 and 2, and adrenergic alpha 1 and beta 1 receptors. At low doses (2.5 g/kg/min), dopamine causes vasodilation in coronary, renal, and splanchnic arteries. At moderate doses (3–5 g/kg/min), it

mediates significant inotropic and chronotropic effects through beta-1 receptors on cardiomyocytes. At higher doses (>5 g/kg/min), dopamine induces potent vasoconstriction via alpha-1 adrenergic receptors. Excessive dosages can result in severe hypertension and tachyarrhythmias. Dopamine, along with epinephrine, increases heart rate, blood pressure, and cardiac output through its potent beta-adrenergic actions. The optimal dose range for dopamine is 5 to 10 g/kg/min, with higher dosages resulting in more significant vasoconstriction. Dopamine has a half-life of less than two minutes, making dosage adjustments unnecessary in cases of renal failure [33]. Phosphodiesterase III inhibitors, such as milrinone, block the enzyme that degrades cyclic adenosine monophosphate (cAMP). Inhibition of this enzyme results in elevated cAMP levels, promoting calcium influx and enhancing myocardial contractility. Milrinone also induces peripheral vasodilation by inhibiting myosin light chain activation in smooth muscle cells of blood vessels. The half-life of milrinone is 2.3 to 2.4 hours in patients with heart failure or renal impairment. In cases where creatinine clearance is between 10 and 50 mL/min, milrinone should be initiated at doses lower than 0.0625 to 0.125 mcg/kg/min. Doses exceeding 0.5 g/kg/min may cause hypotension [34].

Levosimendan acts as a calcium sensitizer in cardiomyocytes, enhancing contractility by increasing the sensitivity of troponin C to intracellular calcium. Unlike milrinone, levosimendan does not rely on beta-adrenergic pathways, making it suitable for patients on beta-blockers. In addition to its positive inotropic effects, levosimendan also promotes peripheral vasodilation by activating ATP-sensitive potassium channels in vascular smooth muscle cells. The active metabolite of levosimendan has a prolonged half-life of 70–80 hours, which is extended in patients with renal dysfunction. Its extended half-life allows for pulse dosing, as the drug's effects persist even after 24 hours post-administration. Levosimendan is not available in the US market, and its prolonged renal clearance and half-life delay its steady-state effects [34]. Vasopressors, which induce peripheral vasoconstriction by increasing intracellular calcium in vascular myocytes, are used to increase systemic vascular resistance and mean arterial pressure (MAP). Catecholamines, considered a critical component of cardiogenic shock therapy, are employed in up to 90% of cardiogenic shock cases. The European Society of Cardiology classifies their use in cardiogenic shock as a class IIb/c recommendation [35]. Common catecholamine vasopressors, such as norepinephrine, epinephrine, dopamine, and phenylephrine, work by increasing blood vessel resistance and calcium levels within myocytes. These actions raise both systolic and diastolic blood pressure and elevate MAP by activating adrenergic receptors. However, due to the complexities involved, there is a lack of clinical data from randomized trials comparing inotropes with vasopressors. Consequently, current guidelines rely on meta-analysis, expert opinions, and review articles to guide the clinical application of these drugs [36].

Precautions During Surgery and Anaesthesia for Severe Bleeding Treatment:

Damage control surgery, a pivotal approach in managing severe trauma, involves an initial laparotomy with temporary abdominal closure, secondary resuscitation, and subsequent reoperation for definitive organ repair. This sequence requires a structured, coordinated strategy for success [37]. Once the decision to implement damage control is made, surgeons must act swiftly to complete the first laparotomy. The primary focus includes evacuation of hematomas and intraperitoneal contamination, followed by necessary organ repairs. Major vascular injuries may be controlled with clamps, sutures, or shunts, while temporary aortic occlusion may be required to manage bleeding during exploration and revascularization. Damage to hollow organs is typically addressed by suturing or stapling, offering temporary relief. When intestinal resections are performed, stapling the bowel ends can create discontinuities. Persistent bleeding may necessitate the use of laparotomy pads. To alleviate intra-abdominal pressure and preserve fascial integrity, temporary closure of the abdominal skin is achieved by approximating the skin margins with towel clips or sutures [38].

In cases of significant visceral edema due to fluid resuscitation, conventional closure of the abdomen may not be feasible. In such circumstances, options such as vacuum-assisted devices, X-ray cassette covers, sterile intravenous bags, and absorbable mesh are viable alternatives [39]. The second phase of damage control aims to restore normal physiological function and address underlying coagulopathy. Post-surgery, patients are transferred to the ICU for additional life-saving interventions. Methods such as radiant heat lighting, warming blankets, and chest tube insertion with warm saline pleural lavage are employed to rewarm the patient. A rapid infusion system is used to administer warm blood, plasma, or crystalloid solutions, while continuous monitoring and aggressive correction of electrolytes, hematology, and coagulation profiles are essential [40]. Following successful rewarming, correction of coagulopathy, and stabilization of fluid status and hemodynamics, the patient is returned to the operating theatre for final treatment. This second operation, typically performed within 24 to 72 hours of the first, involves the removal of laparotomy pads and a reassessment of the peritoneal contents for injury or nonviable intestines. Standard anastomosis techniques, including the formation of an endostomy when necessary, are employed to restore intestinal continuity. In cases where mechanical ventilation is anticipated for an extended period, an enteral feeding tube may be inserted. Upon completion of the procedure, the abdominal fascia is closed in the usual manner. If tension-free closure is not achievable, absorbable mesh or a vacuum-assisted closure device may be used [41]. Damage control surgery, though highly effective, is fraught with significant risks, including complications and even mortality. As such, it is imperative that only the most medically stable patients undergo this procedure. The common postoperative complications include wound infection, intra-abdominal abscess, wound dehiscence, bile leaks, entero-cutaneous fistulae, multiple organ failure, and abdominal compartment syndrome [39].

Management of Severe Perioperative Bleeding:

Special considerations are required during the anaesthesia of trauma patients, particularly when addressing the lethal triad of coagulopathy, acidosis, and hypothermia. A warmed intravenous (IV) line forced air warmer, and fast infuser with warming capabilities should be readily available. The operating room temperature must be raised above 30°C to mitigate the effects of hypothermia.

Pre-Induction

The presence of low body temperature as part of the deadly triad necessitates rapid intervention. Essential equipment checks—such as verification of the anaesthetic machine, airway instruments, and drugs—must be performed before induction to ensure life-saving tools are accessible [42]. Given that the patient may be exsanguinating, it is crucial to maintain continuous volume resuscitation to prevent fatal outcomes during induction. The interval between identifying the need for surgery and establishing vascular access, along with the placement of monitoring equipment (e.g., oxygen saturation, blood pressure, and ECG), is critical. Delaying anaesthesia induction to establish central access or initiate invasive monitoring is contraindicated. Simultaneously preparing the patient for surgery can reduce the time spent in these preparatory stages. Placing the patient in a supine position with the arms extended provides optimal surgical exposure and allows easy access during treatment. Pre-oxygenation, consisting of four full vital capacity breaths, is vital for maximizing oxygenation, particularly in obtunded patients. When pre-oxygenation is not possible, apneic oxygenation should be used [43].

Induction of Anaesthesia

Sedative-hypnotics are commonly used to induce anesthesia, but it is crucial to adjust the dosage to maintain hemodynamic stability. Ketamine (1 mg/kg) is preferred for its minimal effect on systemic vascular resistance compared to other hypnotics like propofol, which significantly reduces systemic vascular resistance. In cases of hypotension, a reduced dose of propofol (0.5-1 mg/kg) should be used, with continuous volume resuscitation to avoid vascular collapse [44]. For endotracheal intubation, succinylcholine (1 mg/kg) provides neuromuscular relaxation within 45 seconds. When succinylcholine is contraindicated, rocuronium (1-1.2 mg/kg) can serve as an effective alternative, achieving similar intubation conditions in about 60 seconds [45].

Maintaining the Airway

Post-induction, an endotracheal tube should be inserted promptly to prevent aspiration. Rapid sequence induction (RSI) with direct laryngoscopy is the preferred method for securing the airway in trauma patients. While there is debate over the necessity of cervical spine stabilization during RSI, minimizing unnecessary cervical spine movement is prudent. Direct laryngoscopy generally does not exacerbate spinal cord injuries [46]. Airway patency can be enhanced with adjuncts like the gum elastic bougie, a cost-effective and efficient tool. Video laryngoscopy, while offering better visualization of the vocal cords, does not guarantee first-attempt intubation success or reduce procedural time. It is essential to maintain a limited range of familiar airway tools and have backup plans in place, including surgical airway management tools [47]. Post-intubation, confirming correct tube placement and verifying end-tidal CO2 levels ensures an efficient surgical procedure. Insertion of an orogastric tube can also reduce the risk of aspiration at this stage [48].

Maintenance of Anaesthesia

During anaesthesia maintenance, both inhalational volatile agents and total intravenous anesthesia (TIVA) can be utilized. These agents must be carefully titrated according to the patient's hemodynamic status to ensure adequate sedation, hypnosis, and analgesia. The simultaneous administration of sedative-hypnotics (e.g., propofol, benzodiazepines) and analgesics (e.g., opioids) is crucial in minimizing awareness and the acute pain response. Dosage of morphine should be titrated to match the patient's hemodynamic condition. Establishing adequate intravenous access (e.g., large-bore peripheral IV, intraosseous) is essential, with additional access for continuous monitoring if necessary [49].

Resuscitation and Monitoring

As part of the resuscitation process, baseline laboratory tests, including coagulation studies and base excess measurements, should be sent immediately. Point-of-care testing (e.g., iSTAT) should be verified with traditional laboratory methods. Monitoring mean arterial pressure (MAP) is critical for directing both anaesthetic maintenance and resuscitation efforts. Research has shown that maintaining MAP above 55 mm Hg helps improve organ perfusion while reducing the risks associated with uncontrolled bleeding [50]. In trauma patients, isolated hypotensive episodes can significantly increase mortality, particularly in those with traumatic brain injury. Systolic blood pressure should be maintained at greater than 90 mm Hg in such patients [51].

Management of Hemorrhaging Ovarian Cysts:

Hemorrhaging ovarian cysts can lead to severe complications such as hemoperitoneum, impaired organ perfusion, and sepsis. Surgical intervention, including laparoscopic procedures to stop the bleeding or remove the cyst, is required for significant blood loss [51]. Laparoscopy is preferred in cases of ruptured hemorrhagic ovarian cysts due to its precision, fewer scars, reduced procedure time, and lower patient discomfort compared to open surgery [52].

Obstetric Haemorrhage

Severe obstetric hemorrhage remains a leading cause of maternal mortality and morbidity globally. According to the World Health Organization, between 25 and 30 percent of maternal deaths occur during or immediately after childbirth. While maternal mortality has decreased in industrialized nations due to advancements in antenatal and postpartum care, rates remain high in many developing countries. Postpartum hemorrhage is recognized as a major cause of maternal mortality, especially in low-income settings [53]. Massive obstetric hemorrhage has been extensively researched in terms of etiology, prevention, and treatment. While professional opinions may differ due to limited data, this article aims to provide a pragmatic approach to managing hemorrhage and the associated coagulopathy. Factors such as amniotic fluid presence and the potential for undetected bleeding complicate the accurate assessment of blood loss, with pregnancy-related physiological changes further obscuring the extent of hemorrhage [54]. Hemorrhaging can lead to severe medical complications, including acute respiratory distress syndrome (ARDS), coagulopathy, shock, infertility, and pituitary gland necrosis [55]. Given the rapid deterioration of obstetric patients experiencing significant bleeding, it is critical to involve senior anaesthesiologists and critical care teams promptly.

Excessive Use of Resuscitation

Circulatory overload resulting from transfusion is a well-documented clinical condition, primarily triggered by the rapid administration of blood or blood products. Individuals requiring substantial transfusions are particularly vulnerable to this condition, with heightened risks in the elderly, young children, and patients with diminished left ventricular function. Initial management of hemorrhagic shock typically involves the administration of crystalloids and colloids. However, when blood and blood

products become available and are transfused to patients, circulatory overload may occur [65]. Furthermore, abdominal compartment syndrome can arise from interstitial edema, which is a consequence of elevated hydrostatic pressure within the body.

Interventions for Severe Blood Loss

To manage severe blood loss, the following interventions are considered essential:

- Intravenous (IV) access should be established using large-bore peripheral IV cannulas, such as 14/16 gauge, or a wide-bore cannula with an insertion sheath. Placement of two such cannulas may be considered, particularly in the neck veins, with cannulation of the external jugular vein being a viable option in critical situations.
- Warming devices, such as surface and in-line fluid heaters, are employed to prevent hypothermia.
- Continuous monitoring of the patient's core temperature is crucial.
- Persistent invasive monitoring of arterial pressure is required to assess hemodynamic status.
- Adequate supplies of necessary fluids, including colloids (e.g., gelatins), crystalloids, infusion sets, and intravenous calcium preparations, must be ensured.
- Blood banks should be informed promptly about the impending need for blood products due to significant blood loss [65].
- Sufficient personnel should be available to transport samples for analysis and to collect blood and blood products when needed.
- Point-of-care tests, such as Arterial Blood Gas (ABG) analysis and Thromboelastography (TEG), are highly beneficial in critical care settings. Repeating the ABG on an hourly basis to assess hemoglobin (Hb), electrolytes, and lactate levels can assist in treatment decisions.
- Pressure bags or rapid infusion pumps should be available to facilitate the rapid administration of fluids.

Post-Surgical Intensive Care:

Post-surgical care in cases of substantial blood loss often involves managing circulatory overload and hemodynamic or biochemical instability. These complications commonly necessitate mechanical ventilation and continuous monitoring of vital signs [66].

Vital Sign Targets in Severe Blood Loss

In a healthy individual, the following values are considered standard: mean arterial pressure (MAP) should be around 60 mmHg, and systolic arterial pressure should be between 80-100 mmHg. For patients with hypertension, the MAP target may be set higher. Additionally, in cases of significant blood loss, the following lab values are considered critical: Hemoglobin (Hb) levels should range between 7-9 g/dl, International Normalized Ratio (INR) should be 1.5, and activated Partial Thromboplastin Time (PTT) should be around 42 seconds [67].

Conclusion:

Severe bleeding in preoperative conditions presents a significant challenge to patient care, requiring prompt and effective management strategies to mitigate the risks associated with blood loss and hemorrhagic shock. The mechanisms underlying severe bleeding involve a combination of coagulation abnormalities, hemodilution, trauma-induced coagulopathy, and the body's adaptive response to hemorrhage. Factors such as the use of anticoagulants, underlying health conditions, and the stress of surgery further complicate the management of bleeding during the perioperative period. The review emphasized the importance of early identification and intervention to control bleeding and improve outcomes. Fluid resuscitation plays a pivotal role in stabilizing the patient, with crystalloids and colloids being the primary fluids used. Crystalloids are generally more accessible and effective in increasing vascular volume, but colloids, which remain in the intravascular compartment, may be more appropriate in certain situations, especially in cases of hemorrhagic shock. Hypertonic saline has emerged as a promising option for initial resuscitation, providing rapid hemodynamic improvement with minimal volume infusion. The review also highlighted the use of blood products in managing significant blood loss, focusing on fresh frozen plasma, red blood cells, and platelets to restore normal hemostasis. Pharmaceutical interventions, particularly the use of inotropes and adrenergic agonists, are critical in managing patients with hemorrhagic shock. These agents enhance myocardial contractility and support vital organ perfusion. Adrenergic agonists, including dopamine, norepinephrine, and epinephrine, increase heart rate, blood pressure, and cardiac output, ensuring adequate tissue oxygenation during shock states. Other agents, such as milrinone, may also be used to improve cardiac performance and reduce vascular resistance. Timely and evidence-based management is essential for patients undergoing surgery, particularly those at high risk of severe bleeding. This includes not only fluid resuscitation and pharmacological treatments but also careful surgical techniques and patient selection. By recognizing early signs of coagulopathy and hemorrhagic shock, healthcare providers can improve patient survival rates and reduce postoperative complications. Enhanced preoperative assessment, including screening for bleeding disorders, remains a crucial step in identifying at-risk individuals and optimizing surgical outcomes. In conclusion, the management of severe bleeding in preoperative conditions is multifaceted and requires a coordinated approach involving prompt resuscitation, pharmacological intervention, and expert surgical care. Through comprehensive preoperative evaluation, vigilant monitoring, and timely interventions, patient outcomes can be significantly improved, reducing the burden of hemorrhagic complications and enhancing recovery in surgical settings.

References:

[1] R. M. Sniecinski and W. L. Chandler, "Activation of the hemostatic system during cardiopulmonary bypass," [in eng], *Anesth Analg*, vol. 113, no. 6, pp. 1319-33, Dec 2011, doi: 10.1213/ANE.0b013e3182354b7e.

[2] F. Rodeghiero *et al.*, "ISTH/SSC bleeding assessment tool: a standardized questionnaire and a proposal for a new bleeding score for inherited bleeding disorders," [in eng], *J Thromb Haemost*, vol. 8, no. 9, pp. 2063-5, Sep 2010, doi: 10.1111/j.1538-7836.2010.03975.x.

[3] H. E. Achneck, B. Sileshi, R. M. Jamiolkowski, D. M. Albala, M. L. Shapiro, and J. H. Lawson, "A comprehensive review of topical 1204 - 1229, 2022.

[5] K. Oakland, "Risk stratification in upper and upper and lower GI bleeding: Which scores should we use?," [in eng], *Best Pract Res Clin Gastroenterol,* vol. 42-43, p. 101613, Oct-Dec 2019, doi: 10.1016/j.bpg.2019.04.006.

[6] J. Magid-Bernstein *et al.*, "Cerebral Hemorrhage: Pathophysiology, Treatment, and Future Directions," [in eng], *Circ Res,* vol. 130, no. 8, pp. 1204-1229, Apr 15 2022, doi: 10.1161/circresaha.121.319949.

[7] K. Oakland, "Risk stratification in upper and upper and lower GI bleeding: Which scores should we use?," *Best Practice & Research Clinical Gastroenterology,* vol. 42, pp. 101613- 27, 2019.

[8] J. B. Holcomb *et al.*, "The prospective, observational, multicenter, major trauma transfusion [PROMMTT] study: comparative effectiveness of a timevarying treatment with competing risks," [in eng], *JAMA Surg,* vol. 148, no. 2, pp. 127-36, Feb 2013, doi: 10.1001/2013.jamasurg.387.

[9] C. K. Pandey *et al.*, "Intraoperative blood loss in orthotopic liver transplantation: The predictive factors," [in eng], *World J Gastrointest Surg,* vol. 7, no. 6, pp. 86-93, Jun 27 2015, doi: 10.4240/wjgs.v7.i6.86.

[10] D. M. Gualandro *et al.*, "Prediction of major cardiac events after vascular surgery," [in eng], *J Vasc Surg,* vol. 66, no. 6, pp. 1826-1835.e1, Dec 2017, doi: 10.1016/j.jvs.2017.05.100.

[11] S. Gando, "Disseminated intravascular coagulation in trauma patients," [in eng], *Semin Thromb Hemost,* vol. 27, no. 6, pp. 585-92, Dec 2001, doi: 10.1055/s-2001-18864.

[12] B. Mitra, P. A. Cameron, and R. L. Gruen, "Aggressive fresh frozen plasma [FFP] with massive blood transfusion in the absence of acute traumatic coagulopathy," [in eng], *Injury,* vol. 43, no. 1, pp. 33-7, Jan 2012, doi: 10.1016/j.injury.2011.10.011.

[13] R. Copotoiu, E. Cinca, O. Collange, F. Levy, and P. M. Mertes, "[Pathophysiology of hemorragic shock]," [in fre], *Transfus Clin Biol,* vol. 23, no. 4, pp. 222-228, Nov 2016, doi: 10.1016/j.tracli.2016.07.004. Physiopathologie du choc hémorragique.

[14] T. Jayakrishnan, D. Shah, and P. Mewawalla, "Hemophilia C: A Case Report With Updates on Diagnosis and Management of a Rare Bleeding Disorder," [in eng], *J Hematol,* vol. 8, no. 3, pp. 144-7, Sep 2019, doi: 10.14740/jh522.

[15] A. C. Nathwani, "Gene therapy for hemophilia," [in eng], *Hematology Am Soc Hematol Educ Program,* vol. 2019, no. 1, pp. 1-8, Dec 6 2019, doi: 10.1182/hematology.2019000007.

[16] M. Pai, "Acquired Hemophilia A," [in eng], *Hematol Oncol Clin North Am,* vol. 35, no. 6, pp. 1131-42, Dec 2021, doi: 10.1016/j.hoc.2021.07.007.

[17] C. Hermans and C. Lambert, "Therapeutic innovations for hemophilia," [in fre], *Rev Med Suisse,* vol. 16, no. 676-7, pp. 47-52, Jan 15 2020. Innovations thérapeutiques pour l'hémophilie.

[18] L. Scorrano *et al.*, "BAX and BAK regulation of endoplasmic reticulum Ca2+: a control point for apoptosis," [in eng], *Science,* vol. 300, no. 5616, pp. 135-9, Apr 4 2003, doi: 10.1126/science.1081208.

[19] C. S. Kase and D. F. Hanley, "Intracerebral Hemorrhage: Advances in Emergency Care," [in eng], *Neurol Clin,* vol. 39, no. 2, pp. 405-18, May 2021, doi: 10.1016/j.ncl.2021.02.002.

[20] S. J. Stanworth *et al.*, "Haematological management of major haemorrhage: a British Society for Haematology Guideline," [in eng], *Br J Haematol,* vol. 198, no. 4, pp. 654-67, Aug 2022, doi: 10.1111/bjh.18275.

[21] M. Erecińska and I. A. Silver, "Tissue oxygen tension and brain sensitivity to hypoxia," [in eng], *Respir Physiol,* vol. 128, no. 3, pp. 263-76, Nov 15 2001, doi: 10.1016/s0034-5687[01]00306-1.

[22] S. A. Oakes, J. T. Opferman, T. Pozzan, S. J. Korsmeyer, and L. Scorrano, "Regulation of endoplasmic reticulum Ca2+ dynamics by proapoptotic BCL-2 family members," [in eng], *Biochem Pharmacol,* vol. 66, no. 8, pp. 1335-40, Oct 15 2003, doi: 10.1016/s0006- 2952[03]00482-9.

[23] G. Gutierrez, H. D. Reines, and M. E. Wulf-Gutierrez, "Clinical review: hemorrhagic shock," [in eng], *Crit Care,* vol. 8, no. 5, pp. 373-81, Oct 2004, doi: 10.1186/cc2851.

[24] R. Rossaint *et al.*, "The European guideline on management of major bleeding and coagulopathy following trauma: fourth edition," [in eng], *Crit Care,* vol. 20, p. 100, Apr 12 2016, doi: 10.1186/s13054-016-1265-x.

[25] P. E. Marik, "Fluid Responsiveness and the Six Guiding Principles of Fluid Resuscitation," [in eng], *Crit Care Med,* vol. 44, no. 10, pp. 1920-2, Oct 2016, doi: 10.1097/ccm.0000000000001483.

[26] M. M. Krausz, "Initial resuscitation of hemorrhagic shock," [in eng], *World J Emerg Surg,* vol. 1, p. 14, Apr 27 2006, doi: 10.1186/1749-7922-1-14.

[27] "The Brain Trauma Foundation. The American Association of Neurological Surgeons. The Joint Section on Neurotrauma and Critical Care. Resuscitation of blood pressure and oxygenation," [in eng], *J Neurotrauma,* vol. 17, no. 6-7, pp. 471-8, Jun-Jul 2000, doi: 10.1089/neu.2000.17.471.

[28] T. T. Niemi, R. Miyashita, and M. Yamakage, "Colloid solutions: a clinical update," [in eng], *J Anesth,* vol. 24, no. 6, pp. 913-25, Dec 2010, doi: 10.1007/s00540-010-1034-y.

[29] C. Argyropoulos *et al.*, "Hypertonicity: Pathophysiologic Concept and Experimental Studies," [in eng], *Cureus,* vol. 8, no. 5, pp. e596-e596, 2016, doi: 10.7759/cureus.596.

[30] D. Burmeister, "Resuscitation Strategies for Burn Injuries Sustained in Austere Environments to Improve Renal Perfusion and Function," GENEVA FOUNDATION TACOMA WA TACOMA United States, 2019.

[31] E. Solomonov, M. Hirsh, A. Yahiya, and M. M. Krausz, "The effect of vigorous fluid resuscitation in uncontrolled hemorrhagic shock after massive splenic injury," [in eng], *Crit Care Med,* vol. 28, no. 3, pp. 749-54, Mar 2000, doi: 10.1097/00003246-200003000-00024.

[32] E. Polyzogopoulou, A. ArfarasMelainis, V. Bistola, and J. Parissis, "Inotropic agents in cardiogenic shock," [in eng], *Curr Opin Crit Care,* vol. 26, no. 4, pp. 403-410, Aug 2020, doi: 10.1097/mcc.0000000000000744.

[33] P. Le Corre, Y. Malledant, M. Tanguy, and R. Le Verge, "Steady-state pharmacokinetics of dopamine in adult patients," [in eng], *Crit Care Med,* vol. 21,

no. 11, pp. 1652-7, Nov 1993, doi: 10.1097/00003246-199311000-00013.

[34] L. Y. Z. Chong, K. Satya, B. Kim, and R. Berkowitz, "Milrinone Dosing and a Culture of Caution in Clinical Practice," [in eng], *Cardiol Rev*, vol. 26, no. 1, pp. 35-42, Jan/Feb 2018, doi: 10.1097/crd.0000000000000165.

[35] B. Ibánez *et al.*, "2017 ESC Guidelines for the management of acute myocardial infarction in patients presenting with ST-segment elevation," [in engspa], *Rev Esp Cardiol [Engl Ed]*, vol. 70, no. 12, p. 1082, Dec 2017, doi: 10.1016/j.rec.2017.11.010.

[36] J. C. Jentzer, J. C. Coons, C. B. Link, and M. Schmidhofer, "Pharmacotherapy update on the use of vasopressors and inotropes in the intensive care unit," [in eng], *J Cardiovasc Pharmacol Ther*, vol. 20, no. 3, pp. 249-60, May 2015, doi: 10.1177/1074248414559838.

[37] Y. Mizobata, "Damage control resuscitation: a practical approach for severely hemorrhagic patients and its effects on trauma surgery," [in eng], *J Intensive Care*, vol. 5, no. 1, p. 4, Jan 20 2017, doi: 10.1186/s40560-016-0197-5.

[38] D. Demetriades and A. Salim, "Management of the open abdomen," [in eng], *Surg Clin North Am*, vol. 94, no. 1, pp. 131-53, Feb 2014, doi: 10.1016/j.suc.2013.10.010.

[39] P. R. Miller *et al.*, "Prospective trial of angiography and embolization for all grade III to V blunt splenic injuries: nonoperative management success rate is significantly improved," [in eng], *J Am Coll Surg*, vol. 218, no. 4, pp. 644- 8, Apr 2014, doi: 10.1016/j.jamcollsurg.2014.01.040.

[40] J. Amado, P. Gago, W. Santos, J. Mimoso, and I. de Jesus, "Cardiogenic shock: Inotropes and vasopressors," [in eng por], *Rev Port Cardiol*, vol. 35, no. 12, pp. 681-695, Dec 2016, doi: 10.1016/j.repc.2016.08.004. Choque cardiogénico – fármacos inotrópicos e vasopressores.

[41] D. Bolliger, K. Görlinger, K. A. Tanaka, and D. S. Warner, "Pathophysiology and Treatment of Coagulopathy in Massive Hemorrhage and Hemodilution," *Anesthesiology*, vol. 113, no. 5, pp. 1205-1219, 2010, doi: 10.1097/ALN.0b013e3181f22b5a.

[42] N. A. Blondin, "Diagnosis andmanagement of periodic hypothermia," [in eng], *Neurol Clin Pract*, vol. 4, no. 1, pp. 26-33, Feb 2014, doi: 10.1212/01.CPJ.0000437350.47610.3a.

[43] N. M. Dave, "Premedication and Induction of Anaesthesia in paediatric patients," [in eng], *Indian J Anaesth*, vol. 63, no. 9, pp. 713-720, 2019, doi: 10.4103/ija.IJA_491_19.

[44] E. Halbeck, C. Dumps, and D. Bolkenius, "[Drugs for intravenous induction of anesthesia: ketamine, midazolam and synopsis of current hypnotics]," [in ger], *Anaesthesist*, vol. 67, no. 8, pp. 617-634, Aug 2018, doi: 10.1007/s00101-018-0469-7. Medikamente zur intravenösen Narkoseinduktion: Ketamin, Midazolam und Synopsis der gängigen Hypnotika.

[45] E. G. Johnson, A. Meier, A. Shirakbari, K. Weant, and S. Baker Justice, "Impact of Rocuronium and Succinylcholine on Sedation Initiation After Rapid Sequence Intubation," [in eng], *J Emerg Med*, vol. 49, no. 1, pp. 43-9, Jul 2015, doi: 10.1016/j.jemermed.2014.12.028.

[46] S. J. Sollid, H. M. Lossius, and E. Søreide, "Pre-hospital intubation by anaesthesiologists in patients with severe trauma: an audit of a Norwegian helicopter emergency medical service," [in eng], *Scand J Trauma Resusc Emerg Med*, vol. 18, p. 30, Jun 14 2010, doi: 10.1186/1757-7241-18-30.

[47] J. M. Tobin, "Usage and efficacy of airway adjuncts in an emergency intubation kit," [in eng], *Emerg Med Australas*, vol. 23, no. 4, pp. 514-5, Aug 2011, doi: 10.1111/j.1742- 6723.2011.01439.x.

[48] C. A. Marco and A. P. Marco, "Airway adjuncts," [in eng], *Emerg Med Clin North Am*, vol. 26, no. 4, pp. 1015-27, x, Nov 2008, doi: 10.1016/j.emc.2008.07.005.

[49] P. Barras, J. McMasters, K. Grathwohl, and L. H. Blackbourne, "Total intravenous anesthesia on the battlefield," WOMACK ARMY MEDICAL CENTER FORT BRAGG NC, 2005.

[50] M. Walsh *et al.*, "Relationship between intraoperative mean arterial pressure and clinical outcomes after noncardiac surgery: toward an empirical definition of hypotension," [in eng], *Anesthesiology*, vol. 119, no. 3, pp. 507- 15, Sep 2013, doi: 10.1097/ALN.0b013e3182a10e26.

[51] N. Carney *et al.*, "Guidelines for the Management of Severe Traumatic Brain Injury, Fourth Edition," [in eng], *Neurosurgery*, vol. 80, no. 1, pp. 6-15, Jan 1 2017, doi: 10.1227/neu.0000000000001432.

[52] C. Bottomley and T. Bourne, "Diagnosis and management of ovarian cyst accidents," [in eng], *Best Pract Res Clin Obstet Gynaecol*, vol. 23, no. 5, pp. 711- 24, Oct 2009, doi: 10.1016/j.bpobgyn.2009.02.001.

[53] T. Bansal, "Recombinant activated factor VII: A savior in management of postpartum hemorrhage," *Anaesthesia, Pain & Intensive Care*, pp. 227-229, 2019.

[54] A. Banks and A. Norris, "Massive haemorrhage in pregnancy," *Continuing Education in Anaesthesia Critical Care & Pain*, vol. 5, no. 6, pp. 195-198, 2005, doi: 10.1093/bjaceaccp/mki052.

[55] M. Walfish, A. Neuman, and D. Wlody, "Maternal haemorrhage," [in eng], *Br J Anaesth*, vol. 103 Suppl 1, pp. i47-56, Dec 2009, doi: 10.1093/bja/aep303.

[56] P. R. Rani and J. Begum, "Recent Advances in the Management of Major Postpartum Haemorrhage - A Review," [in eng], *J Clin Diagn Res*, vol. 11, no. 2, pp. Qe01-qe05, Feb 2017, doi: 10.7860/jcdr/2017/22659.9463.

[57] P. S. Ghodki and S. P. Sardesai, "Obstetric hemorrhage: anesthetic implications and management," *Anaesthesia, Pain & Intensive Care*, pp. 405-414, 2019.

[58] L. Ring and R. Landau, "Postpartum hemorrhage: Anesthesia management," in *Seminars in perinatology*, 2019, vol. 43, no. 1: Elsevier, pp. 35-43.

[59] N. Sehnke, K. Schwarz, and P. "cIONM in intrathoracic goiter–different decision of sternotomy," 2018.

[60] A. A. Klein *et al.*, "Association of Anaesthetists guidelines: cell salvage for peri-operative blood conservation 2018," [in eng], *Anaesthesia*, vol. 73,

no. 9, pp. 1141-1150, Sep 2018, doi: 10.1111/anae.14331.

[61] L. Kuppurao and M. Wee, "Perioperative cell salvage," *Continuing Education in Anaesthesia Critical Care & Pain*, vol. 10, no. 4, pp. 104-108, 2010, doi: 10.1093/bjaceaccp/mkq017.

[62] A. A. Klein *et al.*, "AAGBI guidelines: the use of blood components and their alternatives 2016," [in eng], *Anaesthesia*, vol. 71, no. 7, pp. 829-42, Jul 2016, doi: 10.1111/anae.13489.

[63] P. A. Carless, D. A. Henry, A. J. Moxey, L. O'Connell D, T. Brown, and D. A. Fergusson, "Cell salvage for minimising perioperative allogeneic blood transfusion," [in eng], *Cochrane Database Syst Rev*, no. 4, p. Cd001888, Oct 18 2006, doi: 10.1002/14651858.CD001888.pub2.

[64] V. Patil and M. Shetmahajan, "Massive transfusion and massive transfusion protocol," [in eng], *Indian J Anaesth*, vol. 58, no. 5, pp. 590-595, 2014/09// 2014, doi: 10.4103/0019-5049.144662.

[65] S. A. Esper and J. H. Waters, "Intraoperative cell salvage: a fresh look at the indications and contraindications," [in eng], *Blood Transfus*, vol. 9, no. 2, pp. 139-47, Apr 2011, doi: 10.2450/2011.0081-10.

[66] M. D. Neal *et al.*, "Massive transfusion: an evidence-based review of recent developments," [in eng], *Arch Surg*, vol. 147, no. 6, pp. 563-71, Jun 2012, doi: 10.1001/archsurg.2011.2212.

[67] A Elkady, W., Khalil, R., & H Abd Elrahman, M. (2023). Management of Severe Perioperative Bleeding. *Benha Journal of Applied Sciences*, *8*(3), 88-99.