

PEDIATRIC MASSIVE TRANSFUSION SAFETY STRATEGY

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ABSTRACT

Pediatric massive transfusion is a time-critical intervention in which uncontrolled hemorrhage may rapidly causing developmental hemostatic differences, dilutional coagulopathy, hypothermia, acidosis, and electrolyte disturbance, leading to substantial morbidity and mortality. In contrast to adult practice, pediatric transfusion management remains less standardized, and bedside decisions are still frequently influenced by extrapolated evidence, local protocols, and clinician judgment. This review aimed to summarize a practical, safety-oriented approach to pediatric massive transfusion, with emphasis on perioperative assessment, monitoring, activation criteria, transfusion protocols, and prevention of transfusion-related complications. We performed a narrative review of literature published between 2018 and 2026. Priority was given clinical practice guidelines, expert consensus documents, systematic reviews, and clinically relevant observational studies addressing pediatric major hemorrhage, trauma, cardiac surgery, extracorporeal support, viscoelastic testing, tranexamic acid, whole blood, and patient blood management. Evidence was selected for clinical relevance to perioperative anesthesia practice and synthesized theme. Safe pediatric massive transfusion requires early recognition of major bleeding, timely protocol activation, balanced and goal-directed blood product delivery, close hemodynamic and hemostatic reassessment, and active prevention of predictable metabolic and transfusion-related complications. Overall, the current literature supports a restrictive, physiology-guided approach while underscoring the need for stronger prospective pediatric evidence.

Keywords: Pediatric massive transfusion, hemorrhage, transfusion safety, blood management, viscoelastic testing.

1. INTRODUCTION

Pediatric massive transfusion remains one of the most demanding problems in perioperative and emergency care. Although it is most often discussed in major trauma, the same resuscitative challenge may arise during complex surgery, tumor resection, extracorporeal support, and other causes of life-threatening hemorrhage. The challenge is that pediatric massive transfusion remains both uncommon and inconsistently defined. As a result, protocol activation in many settings still depends heavily on clinician judgment rather than on a universally accepted pediatric criteria. That gap matters, because delayed recognition may postpone delivery of blood transfusion precisely when deterioration is the fastest.^{1,2}

The pediatric population also presents distinct physiological challenges. Transfusion practice spans a broad developmental spectrum, from preterm neonates to adolescents, with important differences. These differences become even more relevant during major bleeding, when children are especially vulnerable to dilutional coagulopathy, hypothermia, acidosis, and rapid loss of physiological reserve. In the perioperative setting, especially during cardiopulmonary bypass or extracorporeal support, these problems are intensified by anticoagulation, circuit-related hemodilution, platelet dysfunction, and ongoing activation of coagulation and inflammation, all of which increase both bleeding risk and transfusion complexity.³⁻⁶

Transfusion itself is a therapy with meaningful short-term and long-term implications. Blood transfusion should be approached as a therapy with meaningful risks, rather than as an automatic response to abnormal laboratory values alone. Plasma and platelet transfusions are frequently given prophylactically despite limited pediatric evidence supporting many thresholds and practices. Transfusion-related complications, including acute lung injury, circulatory overload, hemolytic reactions, and metabolic disturbances, remain highly relevant in younger and critically ill children. This has driven a broader movement toward restrictive, physiology-guided, and safety transfusion strategies in pediatric practice.^{4,7,8}

Patient blood management now seen as a central role in pediatric transfusion safety. Its scope includes early identification of anemia, minimization of avoidable blood loss, rational use of antifibrinolytics and conservation measures, and more selective transfusion practice. Pre-operative anemia remains common in children, including those presenting for elective procedures, while real-world practice in resource-limited settings may still often practice liberal transfusion because of delayed laboratory access, cost barriers, or limited infrastructure. These observations suggest that transfusion safety begins before hemorrhage occurs and depends as much on preparation as on the resuscitation itself.⁹⁻¹¹

Recent pediatric trauma literature has further emphasized the need for earlier recognition of children at risk of transfusion. Although the pediatric evidence remains limited, current data suggest that whole blood transfusion is feasible in selected children and may improve early outcomes in some high-risk trauma populations. While, growing interest in viscoelastic testing reflects the need for more dynamic assessment of clot formation, clot strength, and fibrinolysis

during active bleeding, even though pediatric validation and standardized thresholds remain incomplete.^{2,12-14}

A focused review of pediatric massive transfusion from a safety perspective is importantly needed. The key issue is no longer just whether blood products can be delivered quickly, but how they can be delivered safely, appropriately, and aligned with pediatric physiology. This literature review discusses the physiological characteristics of pediatric massive blood loss, perioperative assessment of bleeding risk, intraoperative hemodynamic and hemostatic monitoring, indications for massive transfusion, transfusion protocols, and practical strategies to reduce transfusion-related harm while supporting effective resuscitation.

2. METHODS

A structured literature search was conducted through online databases PubMed/MEDLINE, Scopus, ScienceDirect, and SpringerLink. Search terms were combined using Boolean operators. Combination of key terms as search strategy were: (pediatric OR pediatric OR child OR neonate OR infant OR adolescent) AND (“massive transfusion” OR “major hemorrhage” OR “hemorrhage” OR “hemorrhagic shock” OR trauma OR “perioperative bleeding”) AND (“viscoelastic testing” OR “tranexamic acid” OR “whole blood” OR “patient blood management” OR “cardiac surgery”).

Articles were eligible if they were published in English between 2018 and 2026 and addressed one or more clinically relevant aspects of pediatric massive transfusion safety. These included: physiological responses to major blood loss, perioperative predictors of transfusion need, patient blood management, intraoperative hemodynamic or

hemostatic monitoring, viscoelastic-guided transfusion, massive transfusion protocols, component therapy or whole blood, and transfusion-related complications. Studies involving neonates, infants, children, or adolescents were considered eligible when their findings were applicable to the review question. Priority was given to clinical practice guidelines, expert consensus statements, systematic reviews, meta-analyses, and multicenter observational studies. Adult-only studies, case reports, conference abstracts, and studies without accessible full text were excluded.

3. DISCUSSION

3.1. Physiological Characteristics in Pediatric Massive Blood Loss

Pediatric massive blood loss cannot be approached as a scale-down version of adult hemorrhage. The pediatric population spans a wide developmental range, from preterm neonates to adolescents, and the response to bleeding varies accordingly. Circulating blood volume, anemia tolerance, metabolic demand, and hemostatic function all change with age. The same absolute blood loss may be tolerated very differently by an adolescent and by a neonate. In practice, this means that severe shock may develop after a comparatively small absolute volume loss in younger children, particularly in neonates and infants, whose margin for physiological compensation is narrow from the outset.^{1,3}

One of the central features of pediatric hemorrhage is the importance of developmental stage. Evangelista *et al.* note that neonates may meet criteria for massive transfusion after relatively small absolute volumes of blood loss because their total blood volume is so limited. The same review also emphasizes that the children who undergo massive transfusion tend to be more severely injured, more hypothermic, and physiologically more unstable than

transfused children who do not meet massive transfusion criteria. This is clinically relevant because the early course of pediatric hemorrhage is often defined less by a single laboratory threshold than by the interaction between blood loss, temperature, tissue perfusion, and evolving coagulopathy. The physiology deteriorates as a system, not as isolated compartments.¹

A second feature is developmental hemostasis. Hemostatic pathways in neonates and young children are not just the immature, they are differently in quantitative and function from those of older children and adults. Differences in coagulation testing is age-dependent, particularly in neonates and young children, complicate interpretation of some blood test such as activated partial thromboplastin time (aPTT) and anti-factor Xa.¹⁵ Cholette *et al.* reported that developmental differences in the neonatal and infant coagulation system, combined with the small blood volume of these patients, increase both bleeding and thrombotic risk. In major hemorrhage, these developmental characteristics make children especially vulnerable to rapid progression from blood loss to dilutional coagulopathy, particularly when transfusion and resuscitation are initiated before the underlying hemostatic defect has been fully characterized.^{5,15}

The physiological becomes more complex when hemorrhage is accompanied by traumatic brain injury or extracorporeal support. In children with acute brain injury, several coagulopathic patterns, including abnormalities in clot strength, fibrinolysis, and clotting factor depletion, all of which have been associated with mortality and disability. In Extracorporeal Membrane Oxygenation (ECMO) and Ventricular Assist Device (VAD) populations, effective anticoagulation is particularly

difficult because of developmental hemostasis, turbulent flow, and ongoing interaction between blood and artificial surfaces. These children therefore exist in a unstable balance between hemorrhage and thrombosis, and that balance may shift quickly during major bleeding or aggressive transfusion support.^{1,15}

Massive blood loss in children is also characterized by a predictable metabolic and hematologic cascade. Among the most important consequences are dilutional coagulopathy, hypothermia, acidosis, and electrolyte disturbance. Hypocalcemia as the most common metabolic complication of transfusion, driven by citrate chelation of calcium, and this problem is particularly relevant in neonates because citrate metabolism is less efficient in this age group. Hyperkalemia also a major concern, especially with stored blood, because extracellular potassium rises over time and has been implicated in serious arrhythmias. These features are not peripheral complications, but they are part of the physiology of pediatric massive transfusion itself and help explain why children may worsen even after blood transfusion delivery has begun if resuscitation is not closely controlled.¹

In perioperative hemorrhage, particularly during pediatric cardiac surgery, hemodilution is often a dominant physiological challenge. Sebastian and Ahmed reported that cardiopulmonary bypass in children may produce marked hemodilution because the priming volume of the circuit is large relative to the patient's circulating volume. In neonatal patients, this imbalance may be a major determinant of the metabolic response to surgery. Immature hemostatic systems, smaller relative size, higher oxygen requirements, and longer bypass times all contribute to the unusually high transfusion burden seen in this group.⁴ Cholette *et al.* found that the discrepancy between patient blood volume and circuit volume in small children increases both

bleeding and thrombotic risk. This means that in pediatric massive blood loss, the physiology is not shaped by hemorrhage alone, but also by the resuscitation environment in which that hemorrhage occurs.⁵

The clinically important factors are not only the volume of blood loss, but also the child's developmental stage, total circulating volume, hemostatic phenotype, metabolic reserve, and the presence of aggravating factors such as hypothermia, anticoagulation, extracorporeal circulation, or traumatic brain injury. This combination helps explain both the speed which children may decompensate and the difficulty of defining a single universal threshold for intervention. A safe transfusion strategy has to begin with highlighting these physiological differences rather than with adult-derived assumptions applied to smaller bodies.

2. Perioperative Assessment: Evaluation Risk of Bleeding, Patient Preparation, Prophylactic Strategy

Safe pediatric massive transfusion begins before hemorrhage occurs. The perioperative objectives are to identify children at increased risk of major bleeding early, optimize reversible risk factors, and prepare a resuscitation plan that is balanced to the anticipate physiologic stress. In children, this assessment should not rely on diagnosis alone. Age, body size, baseline hemoglobin, urgency of surgery, expected blood loss, cardiopulmonary bypass exposure, extracorporeal support, and the presence of cyanotic heart disease or comorbidity all influence bleeding risk and transfusion requirement. Recent pediatric cardiac data also show that perioperative transfusion risk is higher in younger, low body weight patients, in those with lower preoperative hemoglobin, cyanotic congenital heart disease, longer cardiopulmonary bypass (CPB)

duration, larger priming volume, and lower intraoperative temperature, supporting a more individualized preoperative risk classification rather than a uniform approach for all children.^{4,16}

In trauma, early bedside recognition is especially important because major bleeding may occur before full laboratory result available. In a large pediatric trauma cohort, penetrating injury, abdominal injury, polytrauma, Glasgow Coma Scale (GCS), tracheal intubation, and cardiopulmonary resuscitation were all associated with increased probability of early transfusion. These are clinically useful warning signs because they are usually available in the prehospital or very early in-hospital phase. The same principle applies in non-trauma surgery, where in pediatric intracranial tumor surgery, younger age and prolonged operative duration were associated with intraoperative transfusion, while emergency procedures and comorbidity were linked to greater transfusion requirement. These findings support a perioperative assessment strategy that integrates patient factors, disease severity, and procedure-related bleeding risk rather than waiting for instability to occurs first.^{2,17}

Effective preparation needs an objective assessment of patient's current conditions. In low-resource settings, delayed laboratory access, cost barriers, and limited perioperative infrastructure may push practice toward liberal preoperative transfusion based largely on clinical suspicion. A study found that many children in a resource-limited surgical center were getting transfusion without prior laboratory confirmation of anemia, addressing the operational limitations in real-world practice rather than evidence-based threshold values. A safe strategy to do is building applicable systems for earlier anemia detection and perioperative planning, including point-of-care screening where available, rather

than normalizing empiric transfusion as a substitute for assessment.¹¹

Any of the following criteria define severe bleeding:

- Bleeding that leads to at least one organ dysfunction, using Pediatric Logistic Organ Dysfunction (PELOD)-2 score criteria of organ dysfunction, within 24 hours of the previous assessment (if there is no previous assessment, the baseline results are presumed to be normal). The organ dysfunction should be associated with the bleeding, in absence of other causes.
- Bleeding that leads to hemodynamic instability, defined as an increase in heart rate (HR) by > 20% from baseline or a decrease in blood pressure (BP) by > 20% from baseline. The hemodynamic instability should be associated with the bleeding, in absence of other causes.
- Bleeding leading to a drop in hemoglobin (Hb) >20% within 24 hours. The drop in Hb should be associated with the bleeding, in absence of other causes.
- Quantifiable bleeding ≥ 5 ml/kg/hr for ≥ 1 hour (eg. chest tube, drain).
- Intraspinal bleeding leading to loss of neurologic function below the lesion, non-traumatic intra-articular bleeding leading to decreased range of movement, or intraocular bleeding leading to impaired vision.

All of the following criteria must be present to define moderate bleeding:

- Bleeding more than minimal bleeding but without criteria for severe bleeding.
- Bleeding not leading to organ dysfunction, as measured by the PELOD-2 score.
- Bleeding not leading to hemodynamic instability, i.e. change in HR > 20% or drop of BP < 20% from baseline.
- Bleeding leading to a drop in Hb $\leq 20\%$.
- Quantifiable bleeding ≥ 1 ml/kg/hr but < 5 ml/kg/hr (eg. chest tube, drain).

Any of the following criteria define minimal bleeding:

- Streaks of blood in endotracheal tube (ETT) or during suctioning only.
- Streaks of blood in nasogastric (NG) tube.
- Macroscopic hematuria, or less than or equal to 1+ ($\leq 1+$) red blood cells present on urine dipstick if available.
- Subcutaneous bleeding (including hematoma and petechiae) < 5 cm (2 inches) in diameter.
- Quantifiable bleeding < 1 ml/kg/hr (eg. chest tube, drain).
- Bloody dressings required to be changed no less than each 6 hours, or weighing no more than 1 mL/kg/hr if weighed, due to slow saturation.

Figure 1. Bleeding Assessment Scale in Critically Ill Children (BASIC)⁷

The prophylactic strategy should be equally selective. Current pediatric research suggests that unless a patient is actively bleeding, abnormal laboratory values shouldn't be automatically treated with plasma or platelets. Transfusion and Anemia Expertise Initiative-Control/Avoidance of Bleeding (TAXI-CAB) guidelines prioritize clinical context over laboratory values, emphasizing that preventative transfusions are often unnecessary for patients with only mild coagulopathy or low platelet counts. In non-cardiac procedures and invasive interventions, decisions should consider procedure type, bleeding severity, and the overall hemostatic picture rather than isolated numerical thresholds. This is particularly relevant in perioperative care, where overcorrection may expose children

to transfusion-related harm without clear benefit.^{7,18,19}

Among pharmacologic prophylactic therapy, tranexamic acid (TXA) is the most consistently supported adjunctive agent. A systematic review and meta-analysis across pediatric surgeries showed that TXA reduced perioperative blood loss and transfusion requirements, including erythrocyte and plasma transfusion. For perioperative planning, the practical implication is that TXA should be considered early in children at significant risk of major blood loss, but within a strategy that remains procedure-specific and attentive to safety rather than dose escalation.²⁰⁻²²

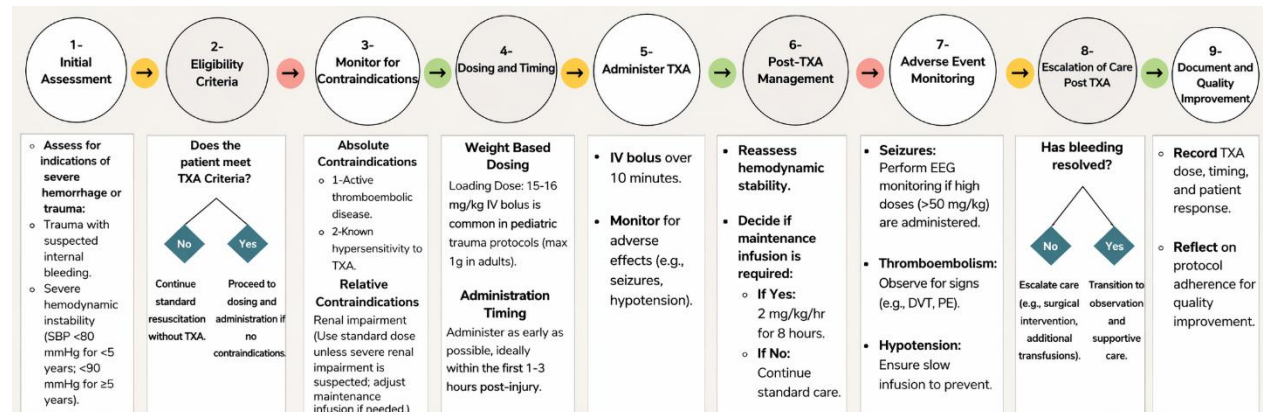


Figure 2. TXA Administration Protocol for Pediatric Trauma and Severe Hemorrhage in Pediatric Emergency Settings²²

The perioperative preparation should include advance planning for blood product availability and blood conservation. In pediatric cardiac surgery, contemporary blood conservation programs have shown that structured preoperative and intraoperative planning that can reduce blood product exposure without obvious worsening of early outcomes. These programs combine restrictive transfusion consideration with miniaturized circuits, ultrafiltration, cell salvage, autologous priming, and closer multidisciplinary coordination. The core principle is children at high risk of major bleeding should enter the operating room with a documented transfusion plan, a monitoring strategy, and predefined intensified pathways. In pediatric massive blood loss is part of the resuscitation itself.^{3,16,23}

Strategies targeting the three core pillars of pediatric patient blood management			
1. Optimization of red cell mass	- Definition and detection of anemia according to age - Placental transfusion - Delayed cord clamping - Iron supplementation - Prophylactic iron in preterm and term infants - Nutritional deficiency: dietary recommendations and treatment - Detection and management of preoperative anemia (oral/parenteral) - Other types of nutritional anemia (e.g., B12, folate deficiency) - Use of ESAs - Reducing the need for exchange transfusion in neonatal jaundice - Use of IVIG if necessary - Intensive phototherapy		
	2. Minimization of blood loss Blood conservation strategies - Minimizing blood loss from phlebotomy - Use of non-invasive techniques and point-of-care testing devices - Autologous blood donation - ANH - Cell salvage	Optimization of coagulation/hemostasis - Preoperative planning for patients with known bleeding disorders - Use of hemostatic agents (antifibrinolytic agents, platelets, FFP, cryoprecipitate, fibrinogen, PCC, rFVIIa) in the prevention of bleeding	Surgical and anesthesia techniques - Appropriate surgical technique - Avoiding hypothermia - Viscoelastic testing - Use of topical hemostatic agents
3. Enhancement of the patient's physiological tolerance to anemia and optimization of transfusion practices	- Use of age-appropriate hematological parameters for neonates, infants, and children - Transfusion decisions based not only on hemoglobin levels but also on the patient's clinical status and underlying condition - Restrictive transfusion strategy - Maintaining a single-unit transfusion policy - Maintaining normothermia - Ensuring acid-base balance		

ESAs: Erythropoietin-stimulating agents; IVIG: intravenous immunoglobulin; ANH: acute normovolemic hemodilution; FFP: fresh frozen plasma; PCC: prothrombin complex concentrate; rFVIIa: recombinant factor VIIa.

Figure 3. Strategies of Pediatric Patient Blood Management⁹

3.3. Intraoperative Hemodynamic Monitoring and Safety Strategy, and Hemostatic

If a major bleeding is suspected or occurring, intraoperative management

should move quickly from simple volume replacement to physiology-guided resuscitation. In children, hemodynamic stability cannot be judged by hemoglobin alone. Acute blood loss

may surpass the laboratory result confirmation, and an acceptable hemoglobin value does not exclude inadequate oxygen delivery. In practice, the more useful approach is serial assessment of heart rate, blood pressure, perfusion, acid-base status, lactate, urine output, and the overall condition progression of the child during bleeding and resuscitation. This is very important in smaller children, whose compensatory reserve is limited and whose deterioration may be sudden rather than gradual.^{24,25}

Temperature and metabolic control are equally important to intraoperative safety. Hypothermia, acidosis, and dilution all worsen coagulopathy and reduce the effectiveness of hemostatic resuscitation. Focus on keeping the patient warm and using heated infusions (including warm blood transfusion), while restricting crystalloids is a smart transfusion strategy, and frequent reassessment of calcium and acid-base status should be treated as main intraoperative management rather than secondary treatment. This principle is especially relevant in pediatric cardiac surgery and other prolonged procedures, where hemodilution, anticoagulation, platelet dysfunction, and inflammatory activation may intensify bleeding even when surgical control is adequate.^{1,4}

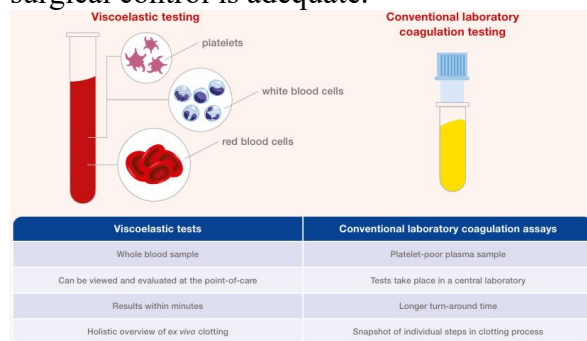


Figure 4. Advantages Of Viscoelastic Testing Compared with Conventional Coagulation Testing¹⁴

Hemostatic monitoring should be structured but practical. Conventional tests such as prothrombin time (PT), aPTT, platelet count, and fibrinogen are useful, but they provide only a partial and delayed picture during active hemorrhage.

Viscoelastic testing (VET) offers a more dynamic whole-blood assessment of clot initiation, clot strength, and fibrinolysis, which explains its growing use in trauma, cardiac surgery, and extracorporeal support. Current pediatric evidence supports VET as an adjunctive, not a stand-alone trigger. Recent guideline suggest that it may help guide plasma and platelet transfusion in selected high-risk settings, particularly trauma, CPB, and ECMO, but interpretation still has to be integrated with clinical findings and conventional laboratory results rather than treated as a replacement for them.^{5,14,15}

It is also important to recognize the implementation gap. Pediatric trauma studies of viscoelastic monitoring have shown that even when the technology is available, use may remain inconsistent, often because it is reserved for the sickest patients or because teams lack confidence in interpretation. Emerging platforms such as Quantra may improve speed, standardization, and workflow integration, but pediatric-specific validation is still incomplete. Current evidence shows that viscoelastic testing is a useful clinical tool for selected cases, provided it is integrated with traditional coagulation tests and real-time physiological assessment.^{26,27}

Intraoperative safety in pediatric massive blood loss depends on anticipating instability before collapse occurs. This requires continuous reassessment of perfusion and oxygen delivery, deliberate prevention of hypothermia and metabolic deterioration, and a hemostatic monitoring strategy that is both timely and interpretable. Current evidence recommends a multimodal approach based in real-time patient status, which clinicians should follow trends and treat the specific underlying, instead of only correcting laboratory result values alone.

3.4. Massive Blood Transfusion Indication

Pediatric massive transfusion remains difficult to define uniformly. Commonly used definitions by literatures include transfusion of ≥ 40 mL/kg of blood products within 24 hours, replacement of $\geq 50\%$ of blood volume within 3 hours, or replacement of one circulating blood volume within 24 hours. Although these criteria are useful for research classification, they are less useful for real-time activation because they are fundamentally retrospective and may delay intervention. Using volume-based criteria risks a delayed response, potentially missing the window for intervention until the patient has progressed to shock or coagulopathy.^{1,3}

In clinical practice, the indication for massive transfusion should therefore be based on ongoing or anticipated life-threatening hemorrhage with a high probability of repeated blood transfusion requirement, rather than on hemoglobin concentration or volume thresholds alone. Current pediatric literature indicates that physician's clinical judgment remains the predominant factor for protocol activation, because reliable pediatric prediction tools remain limited. In addition, during acute hemorrhage, transfusion decisions may need to be made before laboratory result value can be obtained, and children should not be transfused based on hemoglobin value alone. Because in practice, what matters more is the pattern of ongoing blood loss, the speed of deterioration, and whether the child is likely to require repeated or escalating blood product replacement to maintain hemodynamic stability and tissue perfusion.¹

The clearest specific indications are seen in trauma. Massive transfusion should be strongly considered in critically injured children with hemorrhagic shock, particularly in the presence of penetrating injury, abdominal injury, polytrauma, severe neurologic impairment, endotracheal intubation, or cardiopulmonary resuscitation, all of which have been associated with increased odds of early transfusion. Early

balanced resuscitation becomes relevant, and protocol activation should be driven by the clinical state rather than by a single universal formula.^{1,25}

Massive transfusion should be considered when there is active major bleeding that cannot be controlled with initial resuscitation and is expected to require ongoing transfusion support. In trauma, the strongest early indicators of transfusion need include penetrating injury, abdominal injury, polytrauma, GCS ≤ 8 , endotracheal intubation, and cardiopulmonary resuscitation. In the Trauma Register DGU® analysis, these variables were independently associated with markedly increased odds of early transfusion, with adjusted odds ratios of 4.32 for penetrating trauma, 4.18 for abdominal injury, 4.18 for polytrauma, 2.49 for GCS 3–8, 2.51 for intubation, and 2.46 for CPR. These are therefore clinically useful triggers for early activation of a massive transfusion pathway, particularly when bleeding is ongoing and definitive hemorrhage control is not yet secured.²

The same principle applies in perioperative bleeding. Massive transfusion should be activated when blood loss becomes rapid, persistent, and hemodynamically consequential, especially if the child is already requiring repeated red cell replacement or is showing evidence of evolving shock, worsening perfusion, metabolic acidosis, or coagulopathy. In this setting, the indication is dynamic. It rests on the pattern of hemorrhage and physiologic deterioration, not on a single laboratory threshold. Pediatric guidelines favor a proactive trigger, which is if it's clear a child won't stay stable without massive blood support, the protocol should be activated immediately, rather than waiting to check off every formal criteria box.²⁴

A focused bedside indication can be as follows: pediatric massive transfusion should be considered when there is

active life-threatening bleeding together with either hemorrhagic shock, major injury patterns strongly associated with transfusion need, or a clinical settings suggesting that the child will require ongoing, repeated blood transfusion support in a short time frame. This formulation is more consistent with the available pediatric literature than reliance on volume-based definitions alone.

3.5. Transfusion Protocol

A pediatric massive transfusion protocol should function as a coordinated delivery system, not simply as a list of blood products. Its purpose is to ensure that red cells, plasma, platelets, and adjunctive therapies can be delivered rapidly, in a reproducible sequence, while hemorrhage control and physiologic monitoring continue in parallel. Establishing a uniform framework is critical, as it bridges the gap between varying center practices and prevents the delays and communication breakdowns that occur during rapidly evolving hemorrhage. Study by Evangelista *et al.* reported that pediatric protocols remain heterogeneous, with differences in activation thresholds, product availability, and first-pack composition, while Russell *et al.* reported that high-quality pediatric evidence remains limited and that protocol design still relies partly on expert consensus.^{1,25}

The standard for component therapy in pediatric trauma is now based in balanced resuscitation, ensuring all blood products are delivered in a coordinated model. Russell *et al.* state that in critically injured children with hemorrhagic shock following trauma, resuscitation with red blood cells, plasma, and platelets in ratios between 2:1:1 and 1:1:1 may be considered.²⁵ This recommendation is clinically important because it moves pediatric practice away from red-cell-dominant replacement and toward earlier correction of trauma-induced coagulopathy. In more general pediatric transfusion guidance, Mokhtar *et al.* recommend a therapeutic FFP dose of 10–15 mL/kg, repeated according to clinical and

laboratory response during acute bleeding, and advise use of ABO-identical plasma whenever possible.³ These data support a protocol built around early balanced component delivery rather than delayed plasma or platelet supplementation after large-volume red cell transfusion has already occurred.

An alternative protocol pathway is whole blood. This has gained increasing attention because it provides red cells, plasma, and platelets in a single product and may reduce dilution from multiple additives. Evangelista *et al.* reported that early pediatric trauma experience suggests that up to 20 mL/kg of warm whole blood as the initial transfusion can be delivered safely and efficiently, without reported transfusion-related complications in initial series. More recent pediatric literature has continued to support the feasibility of low-titer group O whole blood, and observational trauma data suggest a possible reduction in early mortality in selected children, particularly those with traumatic brain injury. For protocol design, this means that institutions with access to low-titer group O whole blood may reasonably incorporate it into pediatric massive transfusion pathways, while centers without such access may continue to rely on balanced component therapy.^{1,12,13}

A complete protocol should also incorporate serial reassessment and adjunctive therapy. Massive transfusion in children is rarely a one-time product decision. It is a repeating cycle of blood product delivery, monitoring, hemorrhage control, and protocol adjustment. Russell *et al.* recommend serial monitoring of blood volume and coagulation status while active resuscitation is ongoing, and allow consideration of viscoelastic testing as an adjunct to guide decisions. Evangelista *et al.* further argue that TXA should be considered in the severely bleeding child, given the role of hyperfibrinolysis in acute traumatic

coagulopathy and the emerging pediatric trauma data supporting TXA use. The most credible pediatric transfusion protocol is one that combines early activation, balanced component therapy or whole blood, repeated reassessment, and timely use of adjuncts, rather than a fixed-volume formula applied without physiologic feedback.^{1,25}

3.6. Safety Strategy

A safe pediatric transfusion strategy is defined not only by rapid blood product delivery, but by appropriate transfusion, timely reassessment, and avoidance of unnecessary exposure. This principle is especially important in children because transfusion-related harm is clinically relevant, while the evidence supporting many prophylactic transfusion practices remains limited. In critically ill children, plasma and platelet transfusions are often administered in the absence of active major bleeding, despite weak pediatric evidence for many thresholds and indications. Contemporary pediatric guidance therefore favors a more restrictive and context-based approach, particularly outside life-threatening hemorrhage.^{8,18,19}

The first safeguard is to avoid treating laboratory values abnormalities individually. In non-cardiac procedures and other non-hemorrhagic settings, recent consensus statements do not support routine prophylactic correction of mild coagulopathy or thrombocytopenia without clinically significant bleeding. Similarly, in liver disease, sepsis, oncology, and other critically ill pediatric populations, restrictive plasma and platelet transfusion strategies are favored, with emphasis on the child's overall hemostatic status rather than on INR, aPTT, or platelet count alone. This is important to safety because it reduces unnecessary transfusion without withholding support from children who are truly unstable or actively bleeding.^{18,19}

A broad pediatric transfusion framework also supports this safety-oriented view. Wittenmeier, Piekarski and Steinbicker emphasize that transfusion decisions in children should be

individualized according to hemorrhagic status, physiologic stability, and underlying disease, rather than determined by hemoglobin concentration alone. In life-threatening hemorrhage, balanced transfusion is appropriate. However, in many non-hemorrhagic critical care settings, a restrictive strategy or no transfusion is recommended. The same framework also highlights that specific populations, children with severe cardiopulmonary disease, severe PARDS, ECMO/VAD support, or myocardial dysfunction, may require individualized decisions guided by oxygen delivery and overall clinical status. This reinforces an essential safety principle, which is pediatric transfusion practice is safest when blood is given selectively and withheld deliberately when benefit is uncertain.⁸

The second safeguard is standardization of practice. Institution-specific algorithms, predefined escalation pathways, and multidisciplinary communication make transfusion more consistent during rapidly evolving hemorrhage. In pediatric cardiac settings, structured blood conservation and transfusion programs have reduced red cell and plasma exposure without clear worsening of early outcomes, and some studies have reported lower rates of complications such as acute kidney injury or liver injury after implementation of coordinated blood management strategies. Although these data arise mainly from cardiac surgery, standardized pathways reduce variation, improve readiness, and make transfusion decisions less dependent on improvised bedside judgment alone.^{5,16,23}

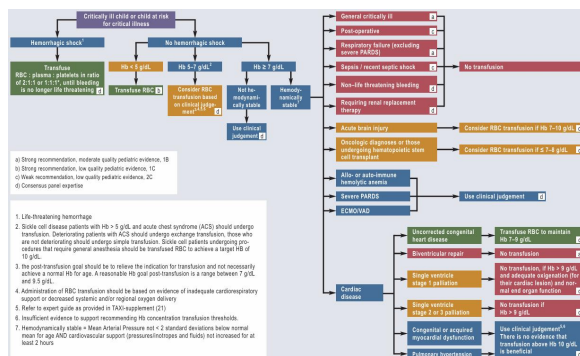


Figure 5. Pediatric Transfusion Decision Framework in Critical Illness⁸

The third safeguard is serial physiologic and hemostatic reassessment. Conventional coagulation tests remain useful, but they are limited during active bleeding. Viscoelastic testing offers a more dynamic assessment of clot initiation, clot strength, and fibrinolysis, and pediatric literature supports its use as an adjunct in selected high-risk settings such as trauma, cardiac surgery, and extracorporeal support. No single test should determine transfusion on its own. Safe practice depends on integrating bleeding pattern, temperature, perfusion, acid-base status, calcium balance, and laboratory trends, while maintaining awareness that clinical

4. CONCLUSION

Pediatric massive transfusion should be regarded as a physiology-guided, safety-centered process, rather than as rapid blood replacement alone. The current literature supports early recognition of life-threatening hemorrhage, prompt activation of coordinated transfusion pathways,

balanced and goal-directed blood transfusion, close hemodynamic and hemostatic reassessment, and active prevention of predictable complications such as hypothermia, dilutional coagulopathy, electrolyte disturbance, and acidosis. In children, the safest transfusion decisions are those based on the overall clinical state, bleeding pattern, and evolving physiologic response, not on hemoglobin concentration or retrospective volume thresholds alone.

deterioration may precede definitive laboratory confirmation.^{14,15,25}

A safety strategy must actively prevent the predictable complications of major transfusion. Pediatric massive transfusion is vulnerable to hypothermia, dilutional coagulopathy, hypocalcemia, hyperkalemia, and acidosis, each of which can worsen hemorrhage or impair organ perfusion if recognized late. Active warming, careful monitoring of ionized calcium and potassium, cautious fluid administration, and early correction of metabolic derangement should therefore be treated as routine components of resuscitation. At the same time, patient blood management measures, including preoperative anemia optimization, tranexamic acid, cell salvage, minimization of phlebotomy, and reduced priming volume where relevant, help lower transfusion burden before complications accumulate. In this sense, pediatric transfusion safety is not a single intervention, but a chain of preventive decisions that begins before bleeding and continues throughout resuscitation.^{1,4,9,20}

The pediatric evidence-based literatures continue to favor a restrictive and on going clinical progression-specific approach outside life-threatening bleeding, highlighting that unnecessary transfusion may itself contribute to morbidity. Safe practice therefore depends on multidisciplinary planning, standardized institutional protocols, and repeated bedside reassessment throughout resuscitation. Further prospective pediatric studies are still needed to refine activation criteria, optimal component or whole-blood strategies, and monitoring thresholds for different pediatric subgroups.

REFERENCES

Evangelista ME, Gaffley M, Neff LP. Massive transfusion protocols for pediatric patients: Current perspectives. Journal of Blood Medicine. Dove Medical Press Ltd;

2020. p. 163–72.
doi:10.2147/JBM.S205132
2. Schneider NRE, Kraus R, Lefering R, Hemm F, Uzun DD, Heiss C, et al. Indicators of early transfusion in paediatric trauma: a retrospective analysis of 11,849 cases from the TraumaRegister DGU®. *Scand J Trauma Resusc Emerg Med*. 2025 Dec 1;33(1). doi:10.1186/s13049-025-01516-x PubMed PMID: 41299591.
3. Mokhtar G, Adly A, Baky AA, Ezzat D, Hakeem GA, Hassab H, et al. Transfusion of blood components in pediatric age groups: an evidence-based clinical practice guideline adapted for the use in Egypt using ‘Adapted ADAPTE.’ *Ann Hematol*. 2024 Apr 1;103(4):1373–88. doi:10.1007/s00277-024-05657-4 PubMed PMID: 38388746.
4. Sebastian R, Ahmed MI. Blood Conservation and Hemostasis Management in Pediatric Cardiac Surgery. *Frontiers in Cardiovascular Medicine*. Frontiers Media SA; 2021. doi:10.3389/fcvm.2021.689623
5. Cholette JM, Muszynski JA, Ibla JC, Emani S, Steiner ME, Vogel AM, et al. Plasma and Platelet Transfusions Strategies in Neonates and Children Undergoing Cardiac Surgery With Cardiopulmonary Bypass or Neonates and Children Supported by Extracorporeal Membrane Oxygenation: From the Transfusion and Anemia EXpertise Initiative-Control/Avoidance of Bleeding. *Pediatric Critical Care Medicine*. 2022 Jan 1;23:E25–36. doi:10.1097/PCC.0000000000002856 PubMed PMID: 34989703.
6. Deschmann E, Dame C, Sola-Visner MC, Fustolo-Gunnink SF, Guyatt GH, Patel RM, et al. Clinical Practice Guideline for Red Blood Cell Transfusion Thresholds in Very Preterm Neonates. *JAMA Network Open*. American Medical Association; 2024. p. e2417431. doi:10.1001/jamanetworkopen.2024.17431 PubMed PMID: 38874929.
7. Nellis ME, Remy KE, Lacroix J, Cholette JM, Bembea MM, Russell RT, et al. Research Priorities for Plasma and Platelet Transfusion Strategies in Critically Ill Children: From the Transfusion and Anemia EXpertise Initiative-Control/Avoidance of Bleeding. *Pediatric Critical Care Medicine*. 2022 Jan 1;23:E63–73. doi:10.1097/PCC.0000000000002859 PubMed PMID: 34989706.
- Wittenmeier E, Piekarski F, Steinbicker AU. Blood Product Transfusions for Children in the Perioperative Period and for Critically Ill Children. *Dtsch Arztebl Int*. 2024 Jan 26;121(2):58–65. doi:10.3238/arztebl.m2023.0243 PubMed PMID: 38051160.
- Acar SO, Gürocak ÖT. Patient Blood Management in Pediatric Patients: Current Strategies and Future Perspectives. *Turkish Journal of Hematology*. Turkish Society of Hematology; 2025. p. 170–80. doi:10.4274/tjh.galenos.2025.2025.0301 PubMed PMID: 40790922.
- du Plessis A, Lee CA, Jooma Z. The prevalence of anaemia in children presenting for elective surgical and diagnostic procedures requiring sedation or general anaesthesia at two tertiary hospitals in Johannesburg. *BJA Open*. 2026 Mar;100524. doi:10.1016/j.bjao.2025.100524
- Charuvila S, Aziz TT, Davidson SE, Naznin U, Sinha S, Ahmed S, et al. An Observational Study of Paediatric Preoperative Transfusion Practice in a Resource-Limited Setting. *World J Surg*. 2022 Mar 1;46(3):709–17. doi:10.1007/s00268-021-06402-y PubMed PMID: 35006324.
- Abou Khalil E, Morgan KM, Gaines BA, Spinella PC, Leeper CM. Use of whole blood in pediatric trauma: a narrative review. *Trauma Surgery and Acute Care Open*. BMJ Publishing Group; 2024. doi:10.1136/tsaco-2023-001127 PubMed PMID: 38196932.
- Painter R, Nahmias J, Nguyen PD, Guner Y, Goodman LF, Chen PM, et al. Whole blood transfusion in pediatric trauma patients with traumatic brain injury may decrease the risk of early death. *Pediatr*

- Surg Int. 2025 Dec 1;41(1). doi:10.1007/s00383-025-06175-8 PubMed PMID: 40864239.
14. Hartmann J, Hermelin D, Levy JH. Viscoelastic testing: an illustrated review of technology and clinical applications. Research and Practice in Thrombosis and Haemostasis. Elsevier B.V.; 2023. doi:10.1016/j.rpth.2022.100031
15. Regling K, Saini A, Cashen K. Viscoelastic Testing in Pediatric Mechanical Circulatory Support. Frontiers in Medicine. Frontiers Media S.A.; 2022. doi:10.3389/fmed.2022.854258
16. Wang W, Wang H, Liu J, Jin Y, Liu J. Quality management of comprehensive blood conservation strategies during cardiopulmonary bypass in pediatric cardiac surgery. BMC Anesthesiol. 2026 Mar 30.
17. Söner HT, Oygen Ö, Güvenç B, Türkan RT, Şener F, Söner S, et al. Blood transfusion in pediatric intracranial tumor surgery. BMC Anesthesiol. 2024 Dec 1;24(1). doi:10.1186/s12871-024-02748-7 PubMed PMID: 39402508.
18. Tucci M, Crighton G, Goobie SM, Russell RT, Parker RI, Haas T, et al. Plasma and Platelet Transfusion Strategies in Critically Ill Children Following Noncardiac Surgery and Critically Ill Children Undergoing Invasive Procedures Outside the Operating Room: From the Transfusion and Anemia EXpertise Initiative-Control/Avoidance of Bleeding. Pediatric Critical Care Medicine. 2022 Jan 1;23:E50–62. doi:10.1097/PCC.0000000000002858 PubMed PMID: 34989705.
19. Lieberman L, Karam O, Stanworth SJ, Goobie SM, Crighton G, Goel R, et al. Plasma and Platelet Transfusion Strategies in Critically Ill Children With Malignancy, Acute Liver Failure and/or Liver Transplantation, or Sepsis: From the Transfusion and Anemia EXpertise Initiative-Control/Avoidance of Bleeding. Pediatric Critical Care Medicine. 2022 Jan 1;23:E37–49. doi:10.1097/PCC.0000000000002857 PubMed PMID: 34989704.
- Wei Y, Zhang Y, Jin T, Wang H, Li J, Zhang D. Effects of Tranexamic Acid on Bleeding in Pediatric Surgeries: A Systematic Review and Meta-Analysis. Front Surg. 2021 Oct 13;8. doi:10.3389/fsurg.2021.759937
- O'Donnell DB, Vazquez S, Greisman JD, Uddin A, Graifman G, Dominguez JF, et al. Tranexamic Acid Dosing in Craniosynostosis Surgery: A Systematic Review with Meta-analysis. Plast Reconstr Surg Glob Open. 2022 Oct 17;10(10):E4526. doi:10.1097/GOX.0000000000004526
- Alsabri M, Fahmy K, Zayed A. Tranexamic Acid in Pediatric Care: A Comprehensive Overview. Journal of Pediatric Pharmacology and Therapeutics. Pediatric Pharmacy Advocacy Group, Inc.; 2026. p. 18–29. doi:10.5863/JPPT-25-00027
- Bohuta L, Chan T, Charette K, Latham G, Greene CL, Mauchley D, et al. Significant reduction in blood product usage, same early outcomes: Blood conservation in infants undergoing open heart surgery. In: JTCVS Open. Elsevier B.V.; 2024. p. 450–7. doi:10.1016/j.xjon.2024.10.006
- Warner LL, Thalji L, Hunter Guevara LR, Warner MA, Kor DJ, Warner DO, et al. Transfusion targets and adverse events in pediatric perioperative acute Anemia. J Clin Anesth. 2024 Jun 1;94. doi:10.1016/j.jclinane.2024.111405 PubMed PMID: 38309132.
- Russell R, Bauer DF, Goobie SM, Haas T, Nellis ME, Nishijima DK, et al. Plasma and Platelet Transfusion Strategies in Critically Ill Children Following Severe Trauma, Traumatic Brain Injury, and/or Intracranial Hemorrhage: From the Transfusion and Anemia EXpertise Initiative-Control/Avoidance of Bleeding. Pediatric Critical Care Medicine. 2022 Jan 1;23:E14–24. doi:10.1097/PCC.0000000000002855 PubMed PMID: 34989702.
- Aladegbami B, Choi P, Keller M, Vogel A. A pilot study of viscoelastic monitoring in pediatric trauma: Outcomes and lessons

learned. J Emerg Trauma Shock.
2018;11(2):98.
doi:10.4103/jets.jets_150_16 PubMed
PMID: 29937638.

27. Deskins C, Smith S, Bonasso PC, Jones WS, Bower RI, Bowers M, et al. Quantra® Viscoelastic Testing in Pediatric Trauma: A Review of Emerging Evidence and Clinical Integration. Cureus. 2025 Dec 13. doi:10.7759/cureus.99134