Komplikationsmanagement auf der Intensivstation: Transfusionen und assoziierte Probleme

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Clotting-Guide
vom Labor zur Diagnose
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Erklärungen

Der Vortragende hat Honorare für Beratertätigkeiten und Vorträge sowie Forschungs- und Reisekostenunterstützungen von Ablynx/Sanofi, Alexion, Biotest, CSL-Behring, Novo Nordisk, Roche, Takeda und Technoclone erhalten.

Er ist Mitglied der Steuerungsgruppen von mehreren klinischen Studien.

Alle Begriffe in diesem Vortrag sind als geschlechtsneutral zu verstehen.

Transfusionen und Indikationen:

Transfusion	Therapeutische Indikation	Prophylaxe
Erythrozytenkonzentrate	manifeste Anämie (je nach Hämoglobin-Wert und Klinik)	bei erwartetem und manifestem Blutverlust
Thrombozytenkonzentrate	Thrombopenie und aktive Blutung	zur Verhinderung von Blutungen (je nach Thrombozytenzahl und Klinik)
Plasma	Aktive Blutung bei Gerinnungsfaktor-mangel (V, XI) Akutes Leberversagen	Verhinderung von Blutungen in Risikosituationen bei Faktormangel oder Leberversagen
Vollblut	keine	keine
Granulozytenkonzentrate	schwerste Infektionen bei schwerer Neutropenie	Verhinderung von Infektionen bei Risikopatienten mit anhaltender Neutropenie
Plasma-Komponenten (Albumin, Immunglobuline)	Ig Substitution bei Infekten Albumin-Substitution bei Mangel	Infektionsprophylaxe bei Ig-Mangel

Zahlen:

EUROPEAN COMMISSION
DIRECTORATE-GENERAL FOR HEALTH AND FOOD SAFETY

Medical Products and Innovation
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Summary of the 2023 Annual Reporting of Serious Adverse Reactions and Events for Blood and Blood Components

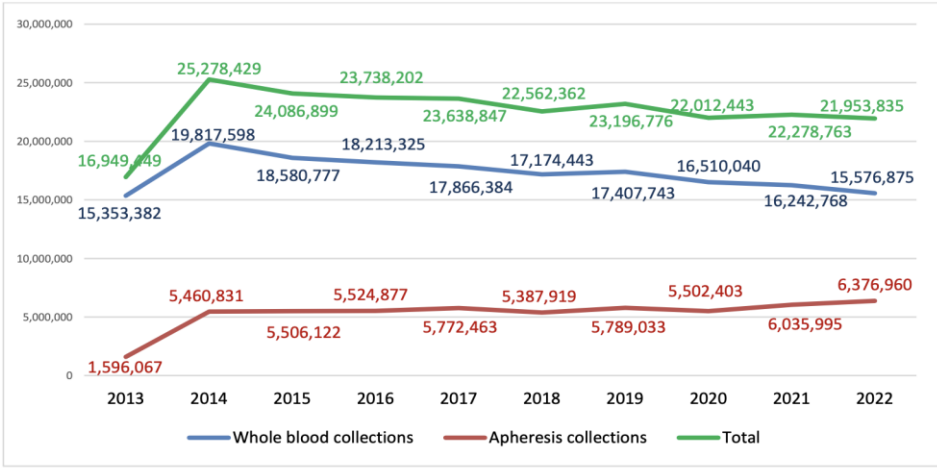

Figure 1. Whole blood, apheresis and total number of collections: 2013 – 2022 comparative data

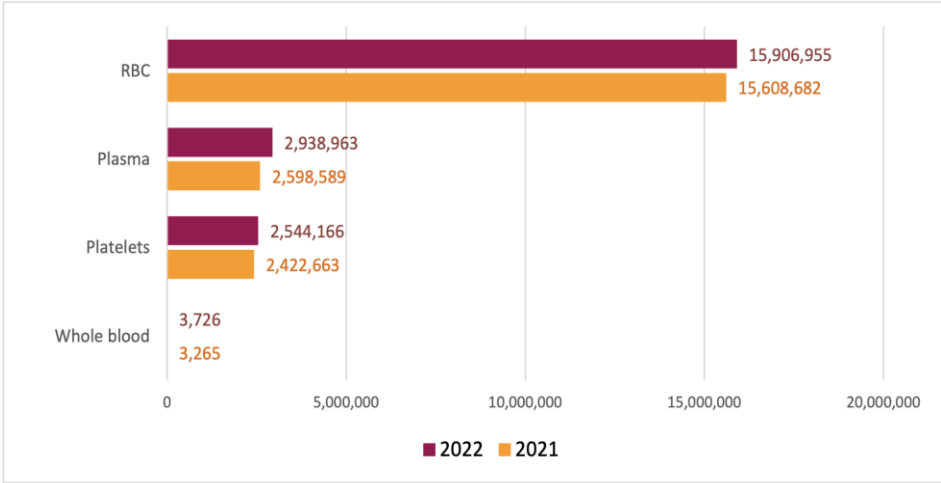

Figure 2. Units issued per blood component type; 2021 – 2022 comparative data

Mögliche Komplikationen von Transfusionen:

Infektiöse Komplikationen:

- Keimübertragung über Spender
- Kontamination bei Produktion
- Kontamination vor und während Transfusion

Nicht-Infektiöse Komplikationen:

Akute Reaktionen (<24h)

- febrile, nicht-hämolytische Reaktionen
- Allergische Reaktionen, Urtikaria, Anaphylaxie
- Transfusions-bedingte Kreislaufüberladung (TACO)
- Hypotension
- TRALI, Dyspnoe
- Akute Hämolyse (AB0 oder nicht-AB0 vermittelt, immunologisch oder nicht-immunologisch)

Verzögerte Reaktionen (>24h)

- verzögerte Serumreaktion, verzögerte hämolytische Reaktion
- Immunisierung, posttransfusionelle Purpura (Thrombopenie)
- Graft-versus-Host Reaktion

Sonstiges

- Eisenüberladung
- Übertragung von Mikropartikeln bzw. Substanzen aus den Kunststoff-Beuteln

Table 1. Temporal relationship between transfusions and noninfectious adverse outcomes and their rate per components transfused based on National Blood Collection and Utilization Surveys, 2011 to 2015

Name	Temporal relationship to transfusion	Severity	Reaction rate in 2015*
Allergic/urticarial	0-4 h	Mild-moderate	1:1 200
Acute hemolytic (ABO related)	0-24 h	Severe	1:200 000
Acute hemolytic (non-ABO related)	0-24 h	Mild-severe	1:105 000
Anaphylactic	0-1 h	Severe	1:30 000
Delayed serologic	1-28 d	Mild	1:5 400
Delayed hemolytic	1-28 d	Mild-moderate	1:22 000
Febrile nonhemolytic	0-4 h	Mild	1:900
Hypotensive	0-1 h	Mild-moderate	1:11 000
Posttransfusion purpura	2-14 d	Severe	1:57 000
TACO	0-6 h	Mild-severe	1:9 000
TRALI	0-6 h	Mild-severe	1:60 000
Transfusion-associated dyspnea	0-24 h	Mild	1:14 000
Transfusion-associated graft-versus-host disease	4-30 d	Severe (often fatal)	1:13 000 000

*Numbers are approximated to the nearest 100s, 1000s, 10 000s, and 100 000s.

Goel R, Tobian AAR, Shaz BH. Noninfectious transfusion-associated adverse events and their mitigation strategies. Blood. 2019;133(17):1831-1839. doi: 10.1182/blood-2018-10-833988.

Inzidenzen (EU):

EUROPEAN COMMISSION
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Medical Products and Innovation
Medical Products: Quality, Safety, Innovation

Inzidenzen (pro 10^5 transfundierten Einheiten)

Type	SAR 2021	SAR 2022	Fatal 2021	Fatal 2022
RBC	5,4	6,4	0,14	0,11
PLT	17,3	19,8	0,18	0,16
Plasma	7,2	9,1	0	0,11
total	**7,3**	**8,3**	**0,14**	**0,13**

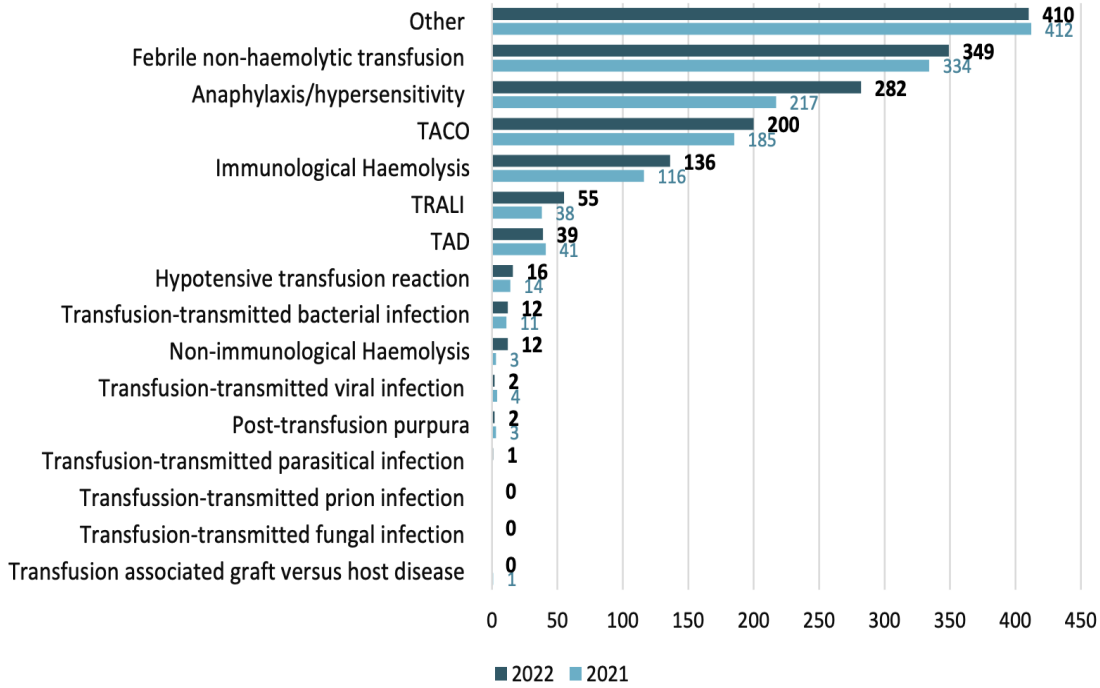
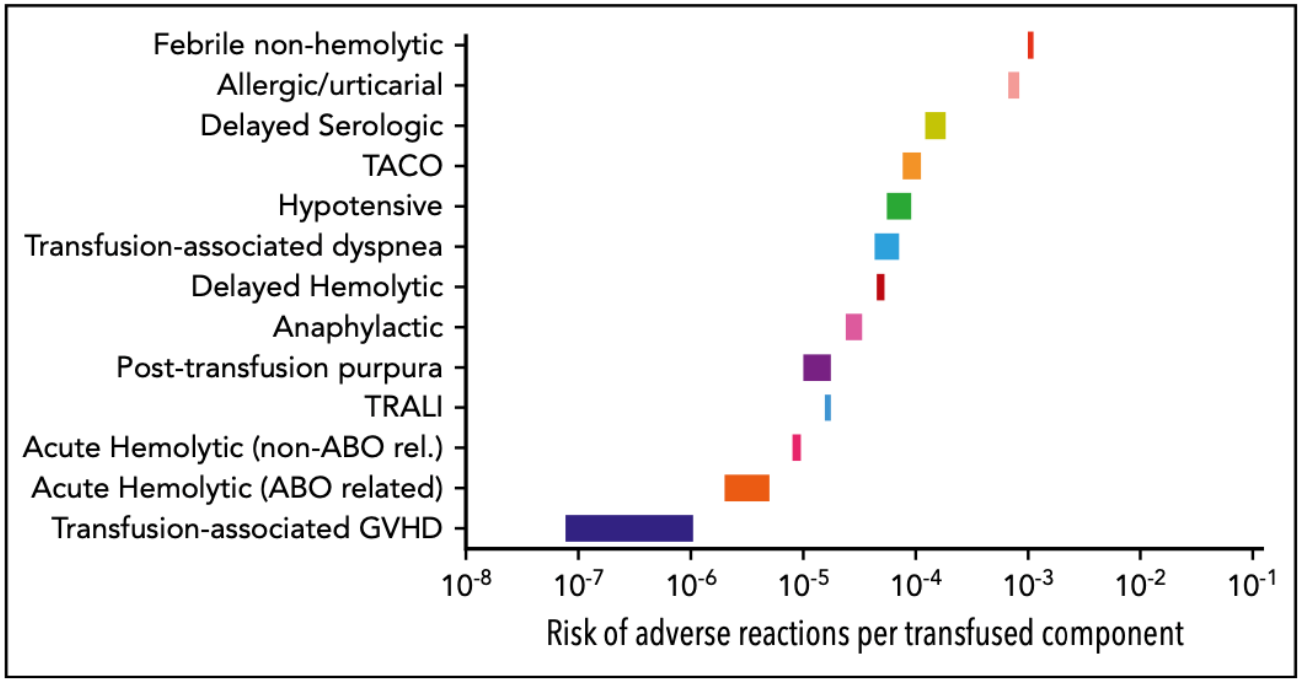


Figure 12. Distribution of SAR by type of reaction; 2021 – 2022 comparative data

Inzidenzen (US-Daten):

FIGURE 1. Noninfectious adverse outcome rates per component transfused based on National Blood Collection and Utilization Surveys, 2011 to 2015.



Goel R, Tobian AAR, Shaz BH. Noninfectious transfusion-associated adverse events and their mitigation strategies. Blood. 2019;133(17):1831-1839. doi: 10.1182/blood-2018-10-833988.

Ursachen von SAEs:

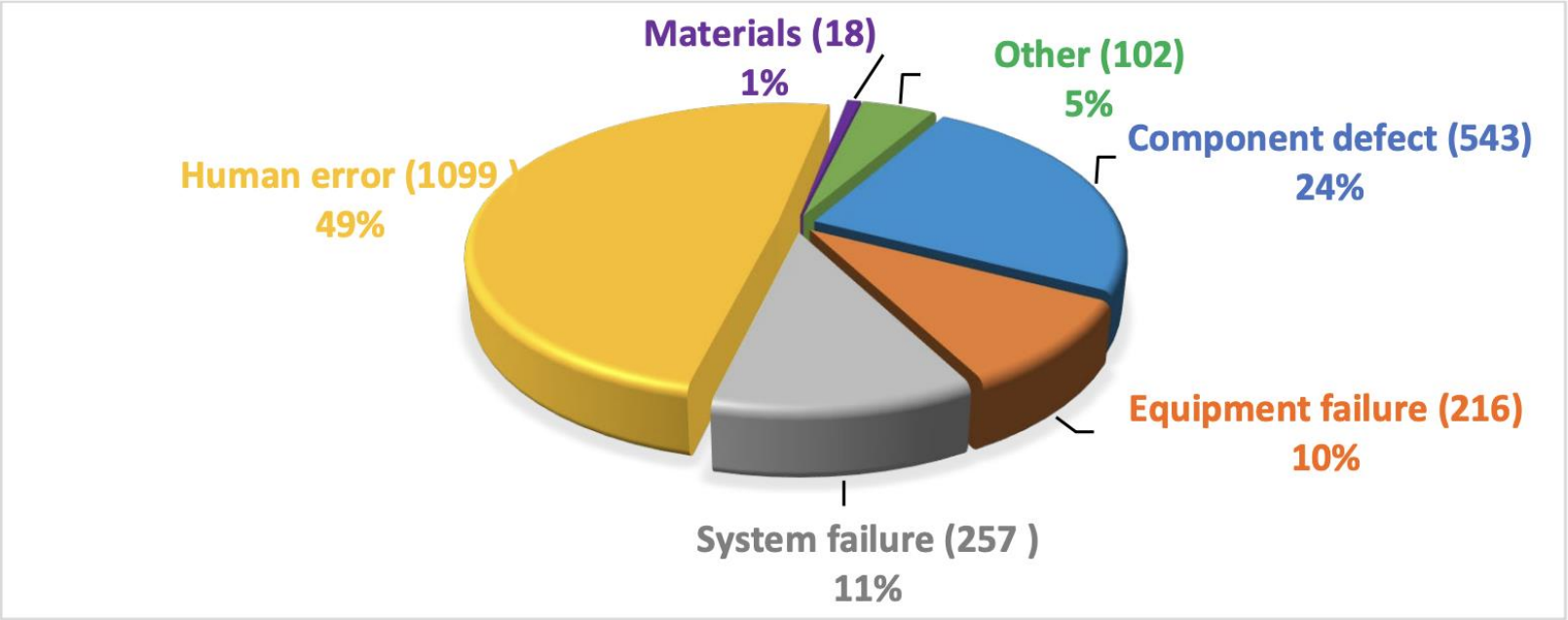


Figure 21. Distribution of SAE by type (absolute numbers and percentages); data 2022

Todesfälle per SAE:

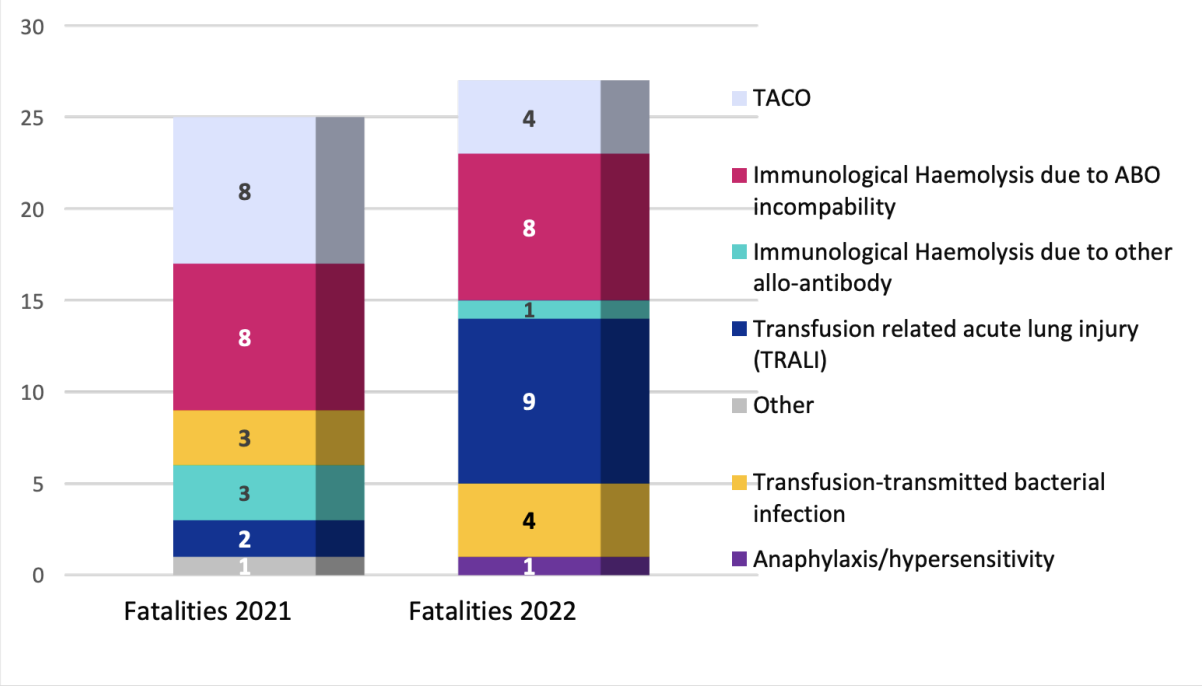


Figure 14. Fatalities by SAR type (imputability level 2-3); 2021 – 2022 comparative data

Transfusion-related Lung Injury (TRALI)

A consensus redefinition of transfusion-related acute lung injury

Alexander P.J. Vlaar,[1,2] Pearl Toy,[3] Mark Fung,[5] Mark R. Looney,[4] Nicole P. Juffermans,[1,2] Juergen Bux,[6] Paula Bolton-Maggs,[7] Anna L. Peters,[8] Christopher C. Silliman,[9] Daryl J. Kor,[10] and Steve Kleinman[11]

- Akute respiratorische Veschlechterung in zeitlichem Zusammenhang mit einer Transfusion
- **Neue Definition 2019:**

TRALI Typ 1:

- akutes Auftreten <6h nach der Transfusion
- Hypoxie (P/F<300 oder SO_2<90% bei Raumluft)
- beidseitiges Lungenödem im C/P Röntgen
- kein Nachweis einer linksatrialen Belastung (ECHO)
- keine sonstigen ARDS-Risikofaktoren

TRALI Typ 2:

- Pat. mit bekannten ARDS Risikofaktoren oder sich verschlechterndes ARDS
- Stabiler Zustand in den letzten 12 h vor der Transfusion
- akutes Auftreten <6h nach der Transfusion
- Hypoxie (P/F<300 oder SO_2<90% bei Raumluft)
- beidseitiges Lungenödem im C/P Röntgen
- kein Nachweis einer linksatrialen Belastung (ECHO)

Vlaar APJ, et al. A consensus redefinition of transfusion-related acute lung injury. Transfusion. 2019 Jul;59(7):2465-2476. doi: 10.1111/trf.15311.

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TABLE 6. Transfusion risk factors for TRALI

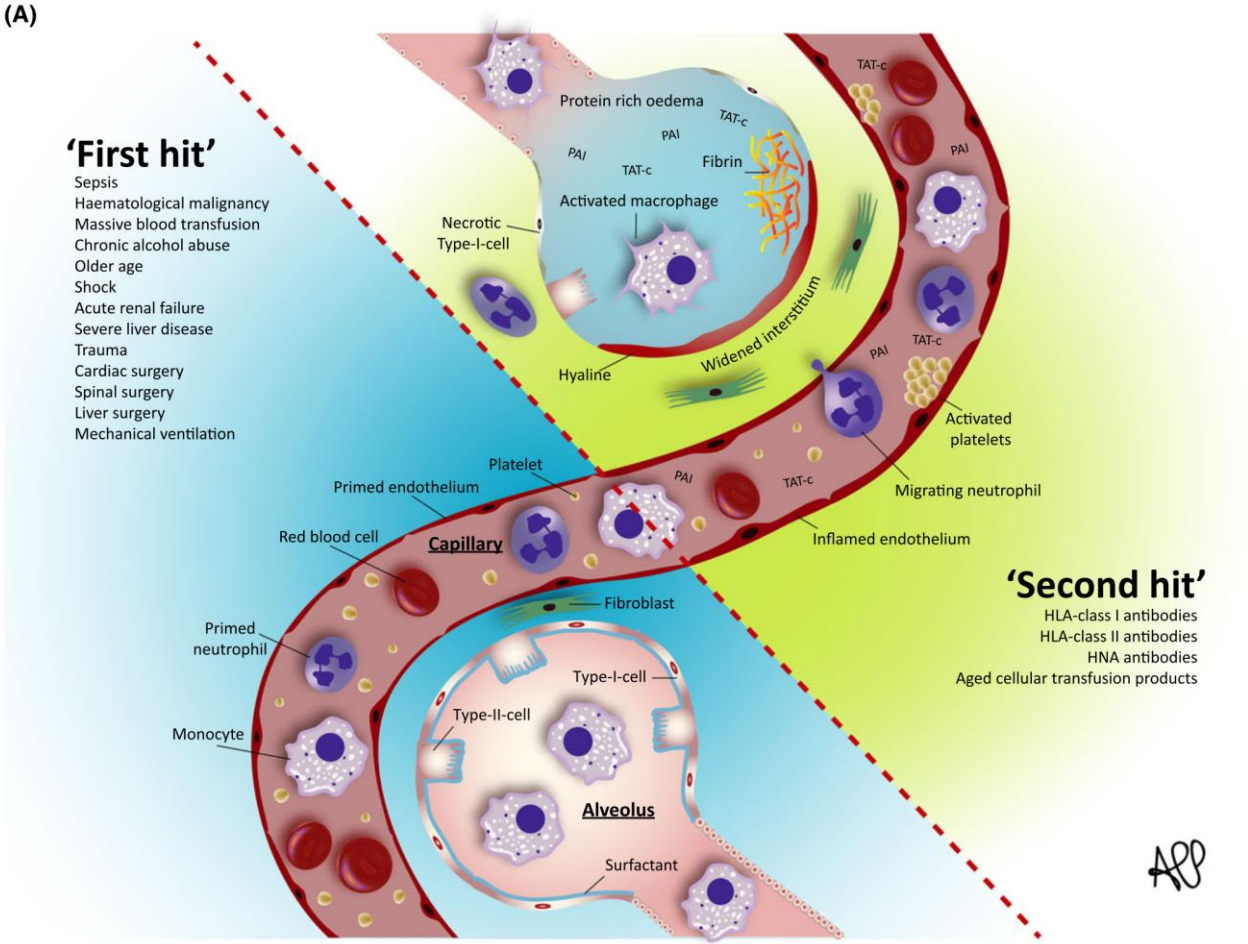
- Cognate HLA Class II antibody[39,42,48,53,71]
- Cognate HNA antibody[30]
- Granulocyte antibody positive by GIFT[39]
- Cognate anti-HLA Class I that activates cells as shown, for example, by granulocyte aggregation in vitro[71] or at least by a positive by GIFT result
- Higher volume of female plasma[39]

Vlaar APJ, et al. A consensus redefinition of transfusion-related acute lung injury. Transfusion. 2019 Jul;59(7):2465-2476. doi: 10.1111/trf.15311.

TABLE 5. Conditions historically associated with TRALI and ARDS

I. Conditions historically associated with TRALI and pTRALI that are also major ARDS risk factors in the Berlin definition (Table 4)*
- Sepsis†
- Noncardiogenic shock‡
- Massive transfusion§

II. Conditions historically associated with TRALI (or both TRALI and ARDS) but not listed as major ARDS risk factors in the Berlin definition (Table 4)*
- Cardiac surgery[13,43]
- Increased pretransfusion plasma IL-8[39]
- Mechanical ventilation with peak airway pressure >30 cm H_2O[39]
- Chronic alcohol abuse[39]
- Current smoker[39]
- Positive fluid balance[39]
- Higher APACHE II score[14,16]
- Increased age[13]
- End-stage liver disease[15]
- Postpartum hemorrhage[44]
- Liver transplantation surgery[39,45]
- Thrombotic microangiopathy[44]
- Surgery requiring multiple transfusions[46]
- Hematologic malignancy[16,43,44]



Peters AL, Van Stein D, Vlaar AP. Antibody-mediated transfusion-related acute lung injury; from discovery to prevention. Br J Haematol. 2015 Sep;170(5):597-614. doi: 10.1111/bjh.13459.

Transfusion-associated circulatory overload and transfusion-related acute lung injury

John W. Semple,[1-5] Johan Rebetz,[1] and Rick Kapur[1]

[1]Division of Hematology and Transfusion Medicine, Lund University, Lund, Toronto, Canada; and [3]Department of Pharmacology, [4]Department of Me Toronto, Toronto, Canada

Table 2. Key diagnostic features differentiating TACO from TRALI

Key diagnostic feature	Specific diagnostic readout	TACO	TRALI
Acute onset of respiratory distress symptoms	Onset <6 h upon blood transfusion	Yes	Yes
Hypoxemia	SpO_2 < 90% or PaO_2/FiO_2 < 300 mm Hg on room air	Yes	Yes
Pulmonary edema	Bilateral infiltrates on chest radiograph	Yes	Yes
Alternative risk factors for ALI	eg, pneumonia, sepsis, aspiration, multiple trauma, acute pancreatitis	No	No
			Yes: possible TRALI
Hydrostatic pulmonary pressure increased	Pulmonary artery occlusion pressure >18 mm Hg	Yes	No
Protein-poor edema fluid	Edema or plasma protein concentration <0.65 at the onset of acute respiratory failure	Yes	No
Increased ventricular filling/myocardial stretching[32-34]	B-type natriuretic peptide (BNP) >250 or pre-/posttransfusion BNP ratio >1.5 or N-terminal pro-BNP >1000 pg/mL	Yes	Yes*/No
Response to diuretics	Rapid and significant improvement	Yes	No
Cardiogenic nonlaboratory evidence for circulatory overload	Systolic ejection fraction <45 and no severe valvular heart disease on echocardiography	Yes	No
	Systolic blood pressure >160		
	Vascular pedicle width >65 mm and cardiothoracic ratio >0.55 on chest radiograph		
Cardiac ischemia	New ischemic changes on electrocardiography or new troponin T levels of >0.05	No	No

Semple JW, Rebetz J, Kapur R. Transfusion-associated circulatory overload and transfusion-related acute lung injury. Blood. 2019 Apr 25;133(17):1840-1853. doi: 10.1182/blood-2018-10-860809.

Allgemein-Maßnahmen:

- Transfusion stoppen, Venenzugang offen halten, Kristalloide infundieren
- Vitalzeichen dokumentieren, Organfunktionen erfassen
- Symptomatische Therapie nach Bedarf (Steroide, Antihistaminika, Adrenalin, Vasopressoren, Antipyretika, Sauerstoff, Antihypertensiva, Diuretika)
- Konserven asservieren, inkl. Etiketten und Papiere
- Patientenidentifikation wiederholen
- Hämovigilanz-Meldung

Vlaar AP, Zwaginga JJ, Wiersum-Osselton JC. How I diagnose and treat cardiorespiratory complications of transfusion. Blood. 2024 Oct 7:blood.2023022899. doi: 10.1182/blood.2023022899.

Fieber

Transfusion reactions: prevention, diagnosis, and treatment

Meghan Delaney, Silvano Wendel, Rachel S Bercovitz, Joan Cid, Claudia Cohn, Nancy M Dunbar, Torunn O Apelseth, Mark Popovsky, Simon J Stanworth, Alan Tinmouth, Leo Van De Watering, Jonathan H Waters, Mark Yazer, Alyssa Ziman, for the Biomedical Excellence for Safer Transfusion (BEST) Collaborative

Lancet 2016; 388: 2825–36

All transfusions must be stopped when a patient is experiencing a reaction and assessed by a provider
Provide supportive therapy to support vital organ function (cardiac, pulmonary, renal)
For questions regarding transfusion reaction diagnosis or management, call the transfusion service, or other appropriate physician

Reaction	Symptoms	Interventions
Increase in temperature		
Possible febrile non-haemolytic reaction	Incremental increase <1°C above baseline and no other new symptoms	• Close observation, frequent vital signs • If stable and no other new symptoms then continue with transfusion
Possible bacterial contamination Possible haemolysis	Incremental increase ≥1°C above baseline, or incremental increase <1°C with any other new symptoms (chills or rigors, hypotension, nausea or vomiting)	• Stop transfusion, keep intravenous line open, assess patient, check patient ID and unit ID and compatibility • Antipyretic drug • Consider blood cultures (patient); empirical antibiotics if neutropenic • Do not resume transfusion • Strongly consider culturing blood product if ≥2°C increase in temperature or if high clinical suspicion of sepsis • Notify blood transfusion laboratory; return unit (with administration set) plus post-transfusion patient sample to blood transfusion laboratory
For consistently febrile patient due to underlying disease or treatment, when possible: • Avoid starting transfusion if patient's temperature is increasing • Treat fever with antipyretic drug before starting transfusion • If incremental increase in temperature ≥1°C above baseline treat as per above (stop and do not resume transfusion, cultures if indicated) • Notify blood transfusion laboratory, return unit (with administration set) plus post-transfusion patient sample to blood transfusion laboratory		

Delaney M, et al. Transfusion reactions: prevention, diagnosis, and treatment. Lancet. 2016;388(10061):2825-2836. doi: 10.1016/S0140-6736(15)01313-6.

Allergie

Transfusion reactions: prevention, diagnosis, and treatment

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Reaction	Symptoms	Interventions
Allergic symptoms		
Urticaria	Mild hives, rash, or skin itching only	• Stop transfusion, keep intravenous line open, and assess patient • Antihistamines • Notify patient clinician and blood transfusion laboratory; sample not required • If symptoms resolve, then can resume transfusion • If symptoms do not improve or worsen or recur then discontinue transfusion; return unit (with administration set) to blood transfusion laboratory
Possible allergic reaction	Hives, rash, itching, and or any other new symptoms (throat, eye, and tongue swelling, etc)	• Stop transfusion, keep intravenous line open, assess patient, check patient ID and unit ID and compatibility • Antihistamines • Do not resume transfusion • Notify blood transfusion laboratory; return unit (with administration set) plus post-transfusion patient sample to blood transfusion laboratory

Delaney M, et al. Transfusion reactions: prevention, diagnosis, and treatment. Lancet. 2016;388(10061):2825-2836. doi: 10.1016/S0140-6736(15)01313-6.

Dyspnoe

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Reaction	Symptoms	Interventions
Respiratory symptoms		
Possible anaphylaxis, transfusion-associated circulatory overload, septic transfusion reaction, or transfusion-related acute lung injury	Bronchospasm, dyspnoea, tachypnoea and hypoxaemia, copious frothy pink-tinged fluid (from endotrachel tube)	• Stop transfusion, keep intravenous line open, assess patient, check patient ID and unit ID and patient compatibility • Treat symptoms as indicated (adrenaline, antihistamines, steroids; oxygen and respiratory support, diuretics; fluid, blood pressure, and renal support) • Chest radiograph for presence of bilateral interstitial infiltrate, if suggestive of transfusion-related acute lung injury • Blood cultures (patient and product), if high clinical suspicion of sepsis • Do not resume transfusion • Notify blood transfusion laboratory; return unit with administration set, plus post-transfusion patient sample. Associated products can be quaratined

Delaney M, et al. Transfusion reactions: prevention, diagnosis, and treatment. Lancet. 2016;388(10061):2825-2836. doi: 10.1016/S0140-6736(15)01313-6.

Sonstiges

Transfusion reactions: prevention, diagnosis, and treatment

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Reaction	Symptoms	Interventions
All other symptoms		
Possible anaphylaxis, haemolytic transfusion reaction, fluid overload, or transfusion-related acute lung injury	Chills, rigors, hypotension, nausea or vomiting, feeling of impending doom, back or chest pain, intravenous site pain, cough, dyspnoea, hypoxia	• Stop transfusion, keep intravenous line open, assess unit, check patient ID and unit ID and patient compatibility • Treat symptoms as indicated (adrenaline, antihistamines, steroids; oxygen and respiratory support, diuretics; fluid, blood pressure, and renal support) • Blood cultures (patient and product) if high clinical suspicion of sepsis • Do not resume transfusion • Notify blood transfusion laboratory; return unit with administration set, plus post-transfusion patient sample. Associated products can be quaratined

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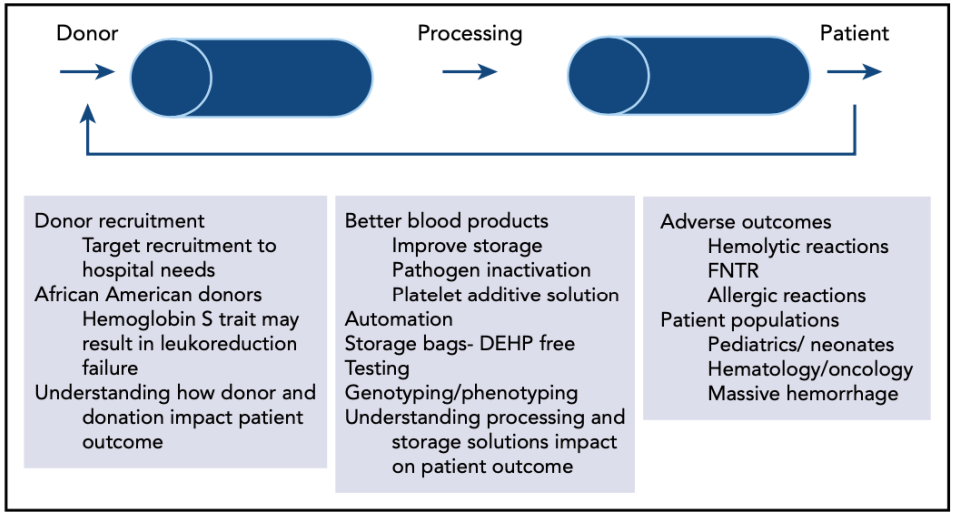
Interventionen zur Reduktion der Transfusions-bedingten AE

- Reduktion der Transfusions-Rate, konservative Transfusions-Trigger
- Patient Blood Management
- Awareness für TAEs
- bessere technische Methoden
- Strikte Hämovigilanz und Patientenidentifikation
- Pathogen-Reduktionsmaßnahmen
- Spender-Auswahl, Spender-Screening



- Leukozytendepletion von Erythrozyten und Thrombozytenkonzentraten
- Verwendung von Einzelspender-Produkten vorzugsweise von männlichen Spendern oder von Spenderinnen ohne vorhergehende Schwangerschaft und ohne Leukozyten-Antikörper

Semple JW, Rebetz J, Kapur R. Transfusion-associated circulatory overload and transfusion-related acute lung injury. Blood. 2019 Apr 25;133(17):1840-1853. doi: 10.1182/blood-2018-10-860809.

Übertragbare Erreger:

Spenderscreening:

- Hepatitis A, B, C, E
- HIV, (HTLV)
- Lues
- West-Nil Virus
- Bakterien
- Trypanosoma Cruzi
- Cytomegalie-Virus
- Parvovirus B19
- (Malaria)

kein Spenderscreening:

- Dengue Fieber
- Babesien
- Plasmodien
- Leishmanien
  Brucella
- Prionen (JCD)
- Zika-Virus
- etc.

Übertragbare Erreger ohne Krankheitswert:

- TTV, HGV

Zusammenfassung

- Schwerwiegende Transfusionsreaktionen sind selten
- Unterschiedliche Manifestationen möglich
- Eine Keimübertragung durch Transfusionen ist extrem unwahrscheinlich
- Allgemeine (intensiv)medizinische Maßnahmen sind meist ausreichend
- Hämovigilanz-Meldung und Dokumentation
- Rationale Transfusionspolitik mit restriktiver Indikationsstellung für alle Blutprodukte