Pulmonary Complications of Transfusion: Non-TACO (n=30)

17b

Authors: Tom Latham and Shruthi Narayan

Acknowledgements: All members of the pulmonary WEG

Definition:

Cases where there was respiratory deterioration temporally related to transfusion which may not be due to the patient's condition and which do not meet SHOT surveillance criteria for TACO.

Abbreviations used in this chapter

AF	Atrial fibrillation
ARDS	Acute respiratory distress syndrome
ATD	Adult therapeutic dose
ATRA	All-trans-retinoic acid
BNP	B-type natriuretic peptide
CCU	Critical care unit
CLL	Chronic lymphocytic leukaemia
COPD	Chronic obstructive pulmonary disease
CXR	Chest X-ray
FAHR	Febrile, allergic and hypotensive reactions
FFP	Fresh frozen plasma
GI	Gastrointestinal
Hb	Haemoglobin
HDU	High dependency unit
ISBT	International Society of Blood Transfusion
ICU	Intensive care unit
IV	Intravenous
RC	Revised consensus (TRALI criteria)
TACO	Transfusion-associated circulatory overload
TAD	Transfusion-associated dyspnoea
TRALI	Transfusion-related acute lung injury
UCT	Uncommon complications of transfusion
WEG	Working expert group

Key SHOT message

- The understanding and nomenclature of pulmonary complications is evolving. Cases submitted are reviewed by the SHOT pulmonary WEG (which includes pulmonologists) to assess the reports for imputability, causality and categorisation.
- Regardless of final categorisation, preventable risk factors for established causes such as fluid overload are identifiable in many cases

Recommendations

- Patients who develop respiratory distress during or up to 24 hours following transfusion, where transfusion is suspected to be the cause, must be reported to SHOT with as much detail (clinical and laboratory aspects) as possible

Action: All staff involved in transfusion

- A structured incident review should be undertaken for all cases of respiratory deterioration after transfusion. This will ensure optimum organisational and individual patient safety measures are in place to protect patients from TACO as far as possible

Action: Trust/Health Board governance and clinical risk departments, all staff investigating transfusion incidents

Introduction

As noted in the overview chapter, all pulmonary complication reports which do not meet the ISBT TACO criteria have been consolidated into a single chapter this year. Categorisation of pulmonary complications following transfusion remains a complex area with ongoing international collaboration for validation of definitions and data collection. Often, the interpretation of the cases submitted is limited by the available clinical information including results of relevant investigations. Transfers of cases submitted between categories (FAHR, TACO, TRALI, UCT etc.) reflect the challenges involved in interpreting these real-life cases. By consolidating cases together, it is hoped that preventable factors can be identified regardless of the final classification, which will always to some extent be arbitrary.

The SHOT pulmonary WEG continues to attempt applying the new proposed RC TRALI definitions to those cases reported under TAD to see if it helps categorise these reactions (Table 17b.1). As there are have been few cases with positive leukocyte antibodies for many years, these cases have been reported as 'antibody-positive' in addition to the RC classification. There was 1 case classified as TRALI type II with risk factors for ARDS and 1 case with worsening respiratory status in the 12 hours prior to transfusion, categorised as transfused ARDS.

Cases classified as TAD represent cases which do not fit TRALI or TACO criteria, either because clinical features do not meet criteria or because there was insufficient information to classify. As in the previous years, cases included under TAD have been subdivided based on adequacy of the clinical information available. TAD-C (those with complete or adequate clinical information) and TAD-IC (those with insufficient clinical information).

Figure 17b.1 summarises the categorisation and transfers of pulmonary complication cases submitted this year.

Table 17b.1 Summary of classification using the revised consensus criteria

Table 7 Comparison table to assist with pulmonary reaction classification

	TRALI Type I	TRALI Type II	ARDS	TRALI/TACO	TACO	TAD
Hypoxemia	Present	Present	Present	Present	May be present but not required	May be present but not required
Imaging evidence of pulmonary edema	Documented	Documented	Documented	Documented	May be present but not required	May be present but not required
Onset within 6 hr	Yes	Yes	Yes	Yes	Yes*	No*
ARDS risk factors	None	Yes—with stable or improving respiratory function in prior 12 hr	Yes—with worsening respiratory function in prior 12 hr	None, or if present, with stable or improving respiratory function in prior 12 hr	Not applicable	Not applicable
LAH†	None/mild	None/mild	None/mild	Present or not evaluable	Present	May be present but not required

*Some definitions of TACO allow onset up to 12 hours posttransfusion. However, our current recommendation is that 6 hours be used. If pulmonary edema occurs greater than 6 hours following the transfusion and is clinically suspicious for a temporal association with transfusion, the case should be classified as TAD as is currently done in many hemovigilance systems.

†LAH is difficult to assess. When LAH is suspected, we recommend using objective evaluation to determine if it is present. Objective criteria include imaging (e.g., echocardiography) or invasive measurement (e.g., pulmonary artery catheter pressure measurement). However, clinical judgment is often required and, if this is needed, should be used for case classification as follows: TRALI and/or TACO = respiratory insufficiency at least partially explained by hydrostatic lung edema resulting from cardiac failure or fluid overload or unable to fully assess the contribution of hydrostatic lung edema resulting from cardiac failure or fluid overload; TACO = respiratory insufficiency explained by hydrostatic lung edema resulting from cardiac failure or fluid overload.

Reproduced from Vlaar et al. 2019

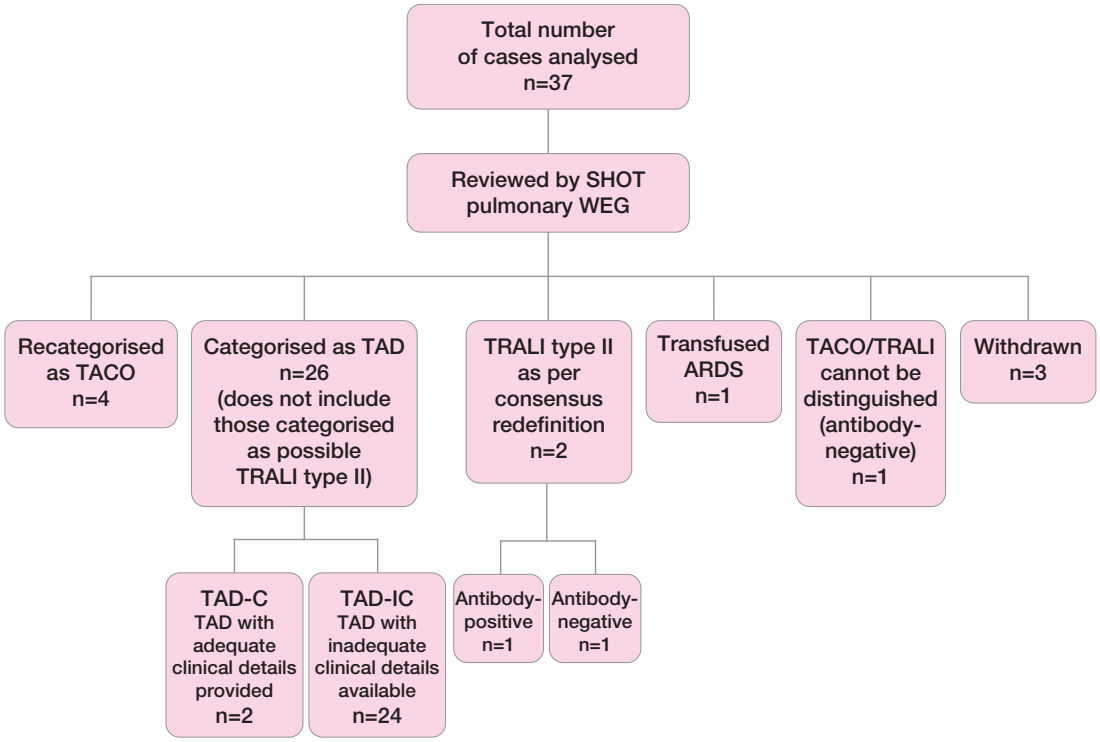


Figure 17b.1: Summary of transfers and categorisation of cases included under TAD

WEG=working expert group; TACO=transfusion-associated circulatory overload; TAD=transfusion-associated dyspnoea; TRALI=transfusion-related acute lung injury; ARDS=acute respiratory distress syndrome

Most cases included as TAD had incomplete clinical and laboratory information (TAD-IC). This could either be due to lack of availability or accessibility of the information when the reporter was submitting the case or that all the relevant investigations were not done as part of patient management.

Many cases had identifiable factors which could explain the respiratory deterioration. These are summarised in Figure 17b.2.

There was only 1 case of antibody-associated TRALI, which was considered as probably contributing to the patient's death.

There were 3 patients with COVID-19 pneumonitis. Interpretation of the clinical and radiological picture in patients with COVID-19 pneumonia who developed worsening respiratory status <24 hours after administration of any blood component continues to be a challenge. Multiple factors could contribute to the deterioration in these patients, ranging from worsening of the COVID-19 pneumonitis (sudden respiratory deterioration with ARDS is well recognised in these patients), to other factors such as thromboembolism and cardiac effects of COVID-19. Secondary bacterial infections and other rare events such as pneumothorax and pneumomediastinum can also cause respiratory deterioration (Pooni et al. 2020). Imputablity has been attributed as being 'possible' in these cases.

Figure 17b.2: Summary of possible explanatory factors for non-TACO pulmonary complications

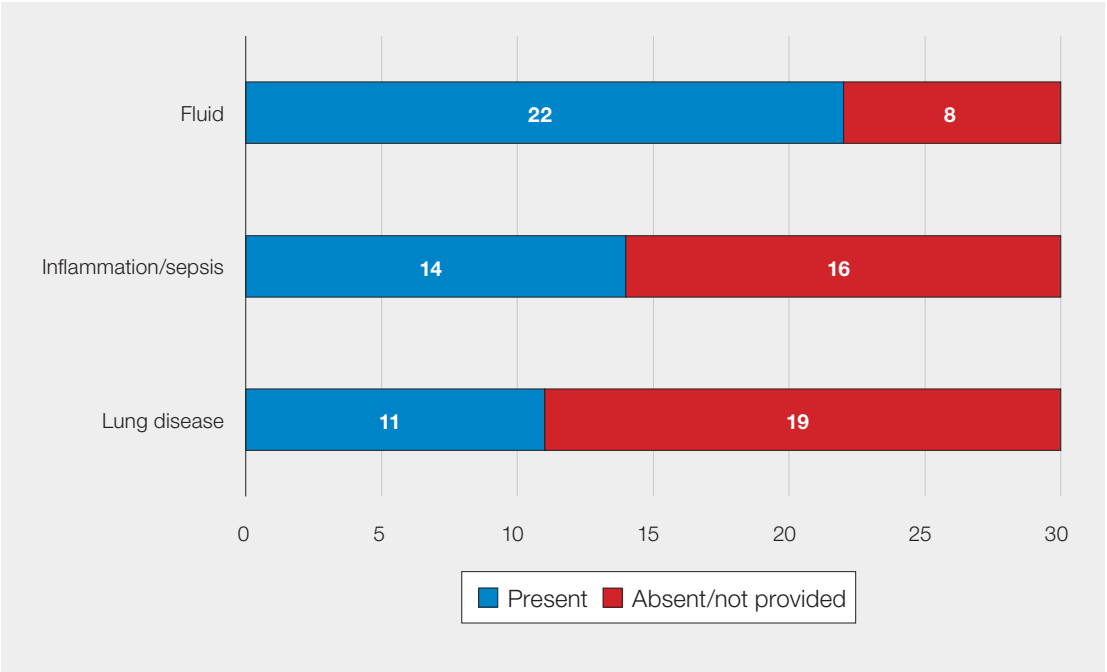
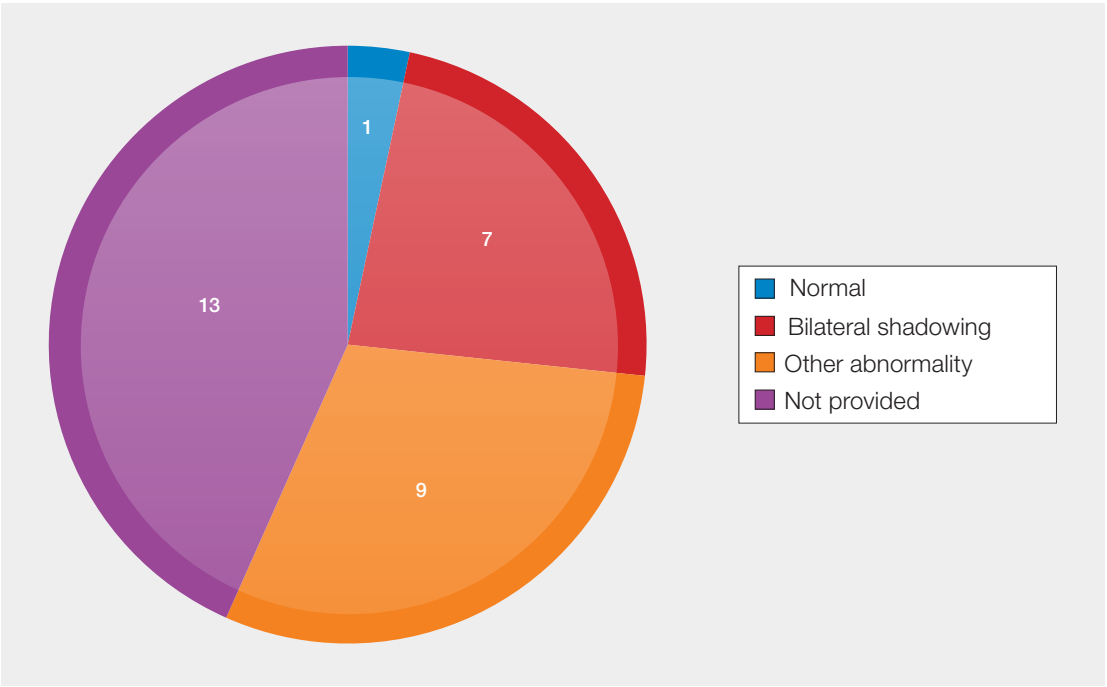


Figure 17b.3: Summary of imaging findings for non-TACO pulmonary complications



Deaths related to transfusion n=7

There were 7 transfusion-related deaths, 2 were categorised as having an imputability of probable, and the other 5 were all possibly related to the transfusion.

Pulmonary complications contribute significantly to transfusion-related deaths reported in the UK. Table 17b.2 summarises all pulmonary complication deaths this year. In particular, the table summarises features (pre-existing patient factors, aspects of the transfusion and features of the reaction) which could support fluid or the underlying disease causing a respiratory deterioration. The table also notes the challenges in applying definitions.

It is notable that in all cases where death occurred, patients had some risk factors for, or features of, fluid overload. In 3 cases, the patients had advanced liver disease. Pulmonary complications are common

in liver disease, with multiple underlying mechanisms, many of which, including fluid overload, may be exacerbated by transfusion.

A full narrative description of all cases which caused death can be found in the supplementary information on the SHOT website (https://www.shotuk.org/shot-reports/report-summary-and-supplement-2021/).

Table 17b.2: Summary of pulmonary complication deaths

Case	Category	Imputability	Blood components transfused	Feature or risks for fluid overload	Underlying disease	Imaging	Difficulty classifying
1	TACO/ TRALI antibody-negative	2	3 red cell units	Rise in BNP, heart failure on 200mg frusemide	Autoimmune haemolysis	Bilateral CXR changes	Imputability of heart disease, between RC and SHOT class
2	TRALI type II antibody-positive	2	2 red cell units, 4 FFP, 1 ATD platelet	Large volume transfusion over 3 hours	Myelodysplasia, sepsis	Bilateral CXR changes	Imputability of antibody
3	TRALI type II	1	1 red cell unit	Cirrhosis, anaemia Hb 47g/L	Cirrhosis, anaemia Hb 47g/L	Bilateral pulmonary oedema, effusions	Difference between SHOT and RC class
4	TAD-IC	1	1 red cell unit	History of AF, heart failure, cirrhosis	Cirrhosis, COPD	Perhilar consolidation	Does not fit TRALI/ TACO
5	TAD-IC	1	3 FFP	Alcoholic liver disease	COVID-19, GI bleed	Not supplied	Limited clinical detail
6	TAD-IC	1	1 red cell unit	Decompensated heart failure anaemia Hb 79g/L	COVID-19	Not supplied	Limited clinical detail
7	TAD-IC	1	1 red cell unit	Renal impairment, cardiac impairment, low albumin, positive fluid balance	GI bleed	Not supplied	Limited clinical detail

Major morbidity n=2

Both cases included here are those where patients needed admission to HDU/ICU/CCU following respiratory deterioration post transfusion. They subsequently recovered.

Table 17b.3: Summary of pulmonary complication major morbidity cases

Case	Category	Imputability	Blood components transfused	Features or risks for fluid overload	Underlying disease	Imaging	Difficulty classifying
1	TAD-C	1	2 ATD platelets, 1 red cell unit	Cardiac and renal impairment, IV fluid, response to diuretic	Lymphoma, sepsis	Unilateral consolidation	Does not meet TACO/ TRALI criteria
2	TAD-C	1	4 red cell units		GI bleed, CLL, COVID-19	Bilateral pulmonary oedema	Antibody-negative, definition of 'stable respiratory state'

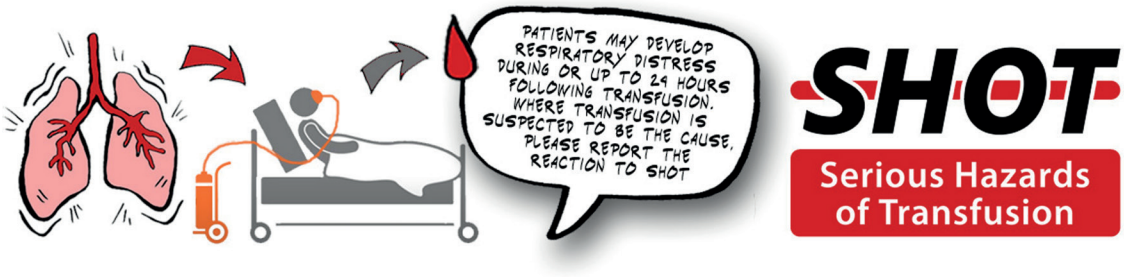
Learning point

- All cases with post-transfusion pulmonary complications must be reported to the Blood Service so that further investigation can be done as appropriate to help classify these cases. Regardless of final classification, many cases have identifiable risk factors which may have compromised the ability of the patient to tolerate the transfusion

Conclusion

As illustrated in the cases included here, most patients with pulmonary complications are very unwell with multiple ongoing issues and it is often difficult to establish whether the transfusion contributed to the deterioration or whether the deterioration was coincidental. Consolidation of cases into one chapter and incorporating the RC TRALI criteria has led to a proliferation of classes, which will be helpful for international comparison but there is not always a clear dividing line between cases assigned to different classifications.

There is still much work that needs to be done to understand pulmonary complications, and identify common themes which will inform future preventative and management strategies. Some of the uncertainty revolves around whether there may be undiscovered mediators in the transfusion which contributed to the reaction, which will always be impossible to rule out. What is apparent however is that there are often identifiable features, particularly for fluid overload that could indicate patients at higher risk of transfusion. These factors are identifiable across categories and it is probably more helpful to acknowledge that all factors coexist and interact rather than to make subjective decisions about which was the most important in order to assign cases to a single category. It is hoped that consolidating cases in to a single chapter will help to assess pulmonary complication cases holistically, and a retrospective review of cases is planned for this year.



References

Pooni R, Pandey G, Akbar S. Broadening the differential: pneumomediastinum and COVID-19 infection. *BMJ Case Rep.* 2020;**13(8)**:e237938. doi: 10.1136/bcr-2020-237938.

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