Transfusion-Related Acute Lung Injury (TRALI) n=1

17a

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Definition:

Transfusion-related acute lung injury (TRALI) is defined as acute dyspnoea with hypoxia and bilateral pulmonary infiltrates during or within 6 hours of transfusion, in the absence of circulatory overload or other likely causes, or in the presence of human leucocyte antigen (HLA) or human neutrophil antigen (HNA) antibodies cognate with the recipient.

There was 1 confirmed case of TRALI this year, with a further 11 cases reported as suspected TRALI. Of these, 3 cases were transferred to transfusion-associated dyspnoea (TAD), 2 cases to transfusion-associated circulatory overload (TACO) and 4 cases were withdrawn. The final 2 cases have been deferred to the next Annual SHOT Report as serology results are in progress. The 1 confirmed case was transferred to TRALI from TAD.

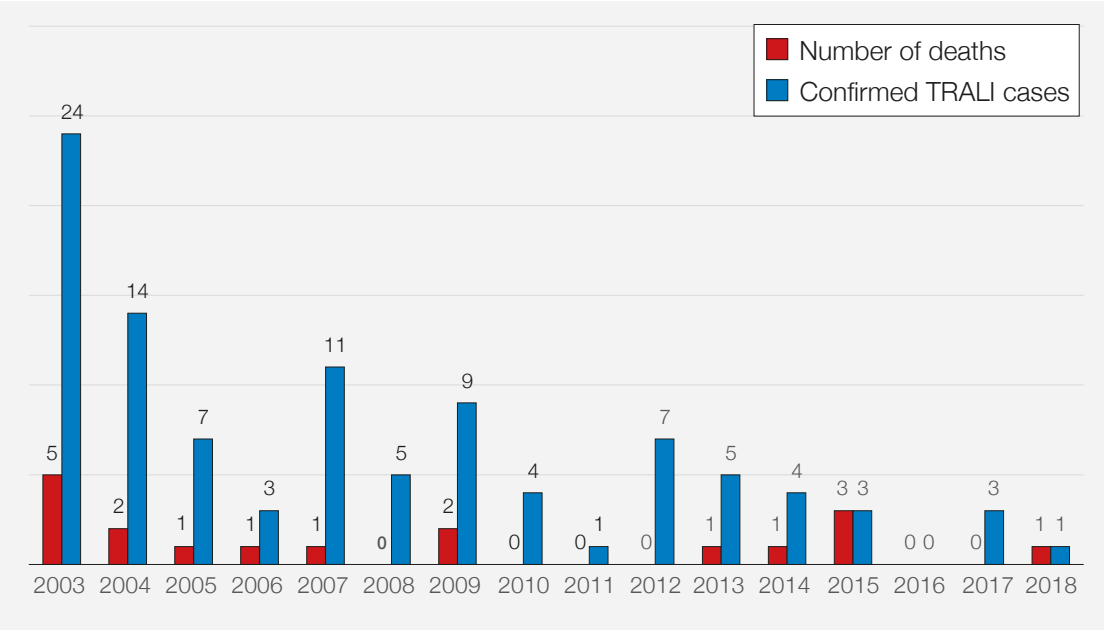

Figure 17a.1: Number of confirmed TRALI cases and deaths at least possibly related to TRALI by year of report

TRALI=transfusion-related acute lung injury

Figure 17a.1 shows TRALI cases from 2003-2018, classified using the criteria introduced in the 2016 Annual SHOT Report. The use of male donors only for fresh frozen plasma (FFP) was implemented in 2003. Cases are recorded as deaths if the death was at least 'possibly' related to the transfusion (imputability 1 or greater).

Assessment of TRALI

The classification criteria are outlined in Table 17a.1 below. A mapping of how the revised criteria compare to the widely used Canadian Consensus definitions for TRALI is given in Table 17a.3, in order to help international comparison.

Table 17a.1: Revised SHOT criteria for assessment of TRALI cases

Classification	Definition	Mapping to Canadian Consensus definition
Highly likely	Cases with a convincing clinical picture and positive serology	TRALI +positive serology
Probable	Cases with positive serology but other coexisting morbidity which could independently cause acute lung injury or fluid overload	Possible TRALI (pTRALI) +positive serology
Equivocal	Cases with positive serology in the clear presence of lung injury due to other causes or fluid overload	Not TRALI [excluded because of other morbidity but meets positive criteria]+positive serology
Antibody-negative TRALI	Cases with a convincing clinical picture where serology is not available or negative	TRALI + absent or negative serology
Unlikely - reclassify as TAD	Cases where the picture and serology was not supportive of the diagnosis. These cases are transferred to TAD	pTRALI or not TRALI + negative or absent serology

Table 17a.2: TRALI case probability (SHOT criteria) - 2018 cases

Probability	Number of cases
Highly likely	0
Probable	0
Equivocal	0
Antibody-negative	1
Unlikely-transferred to TAD/TACO	5

Table 17a.2 includes notified cases which have been transferred to other categories but not cases which have been withdrawn or deferred.

Table 17a.3: Classification using Canadian Consensus definitions

Canadian Consensus classification	Number of cases
TRALI	0
Possible TRALI	1
Not TRALI	0

Table 17a.3 includes only cases classified as TRALI, withdrawn or transferred cases would by definition be classified as 'Not TRALI'.

Deaths n=1

Case 17a.1: Antibody-negative TRALI - post mortem diagnosis without serology

A male patient in his late 60s, with recent diagnoses of advanced myelodysplasia and prostate cancer presented to the emergency department (ED) with abdominal pain, hypotension and a platelet count of 6. He had a raised C-reactive protein, metabolic acidosis with raised lactate, low albumin and renal impairment prior to transfusion and received two units of red cells and a unit of platelets on the day of admission uneventfully. Over 24 hours later, 10 minutes after starting a platelet transfusion, he became acutely breathless and hypoxic with a further fall in blood pressure and deterioration in renal function. In view of his underlying diagnoses, a decision was made not to escalate care further and he suffered a cardiac arrest shortly afterwards.

Post-mortem findings showed pleural effusions and gross pulmonary oedema, with no evidence of infection, infarction or injury, and the coroner gave 'transfusion lung injury' as the primary cause of death. Serological investigations were not performed as the National Health Service Blood and Transplant (NHSBT) expert panel felt that the picture was one of terminal decline rather than a transfusion reaction.

The case was initially reported to SHOT as TAD, however we have included the case as 'antibody-negative TRALI' in view of the coronial diagnosis. We considered imputability as 'death probably due to transfusion' as the transfusion does appear to have been a major contributor even though the patient was clearly very unwell before the transfusion.

Cumulative serological data

Since 1996, 207 of 328 reported cases have had full laboratory investigation for TRALI. Concordant antibodies were identified in 118/207 (57.0%) of these. The most frequently identified antibody specificities (either alone or in combination with other concordant antibodies) have been HLA-DR4 (22/118 cases, 18.6%), HLA-DR52 (17/118, 14.4%) and HLA-A2 (19/118, 16.1%). All other HLA antibody specificities have been identified in less than 10% of cases. Concordant HNA specific antibodies, alone or in combination, have been found as follows: HNA-1a (10/118 cases, 8.5%); HNA-2 (2/118, 1.7%); HNA-3a (2/118, 1.7%).

Analysis of reports of 187 complete TRALI investigations between 2001 and 2018 inclusive has shown that the specificities of concordant antibodies were as follows:

HLA class I alone	HLA class II alone	Both HLA class I and HLA class II	Granulocyte specific antibody (+/- HLA antibodies)	None identified
21/187 (11.2%)	36/187(19.3%)	27/187 (14.4%)	19/187(10.2%)	84/187 (44.9%)

Table 17a.4: Concordant donor antibodies 2001 to 2018 inclusive

Commentary

Numbers of confirmed and reported TRALI cases are similar to previous years. The confirmed case this year was difficult to classify. It would not strictly meet SHOT TRALI definitions as there are other plausible explanations for the reaction (as was considered by the NHSBT expert panel), and there is no serological evidence; nevertheless the case was included as TRALI as the death certificate has recorded this as the cause of death. The case highlights the difficulty in making decisions on whether to investigate serologically, especially as recalling donors for investigation does have an associated harm in terms of donor anxiety and temporary deferral. Cases in England are reviewed by an expert panel of intensivists independent of NHSBT and cases are investigated if they meet criteria of timing, hypoxia and lack of alternative diagnoses; however, the basis for the decision is not available to SHOT when reviewing. It is probably prudent to have a lower threshold for investigating donors where there is a patient death or long term harm which appears attributable to transfusion, even though other pulmonary complications may be more likely.

An updated international consensus definition of TRALI has recently been accepted for publication (Vlaar et al. 2019). This is intended to update the earlier Canadian Consensus definition and was produced using a Delphi consultation methodology between international experts, including a representative from SHOT. The new classification remains based on clinical features and takes account of updated criteria for acute respiratory distress syndrome (ARDS). It will become clearer how the new definition changes the understanding of pulmonary complications of transfusion and also how it interacts with updated definitions for TACO as the new classification becomes more widely used internationally. As a haemovigilance organisation, we consider that it remains important to distinguish antibody mediated cases in order to monitor preventative strategies. It is therefore proposed that from 2019 we will continue to classify cases according to the SHOT definition but provide a parallel classification using the new scheme for international comparison.

Reference

Vlaar APJ, Toy T, Fung M et al. (2019) A consensus redefinition of transfusion-related acute lung injury. *Transfusion* 2019 doi.org/10.1111/trf.15311.