

# 18b Transfusion-Associated Circulatory Overload (TACO) n=92

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The reporting criteria for TACO have been revised by a joint working group from the International Society of Blood Transfusion (ISBT) haemovigilance working party, the International Haemovigilance Network (IHN) and American Association of Blood Banks (AABB) with wide international consultation. SHOT has continued to be a key contributor and collaborator in this work. Validation of the revised criteria took place throughout 2017.

An international consensus conference was the ultimate objective of the working party following validation of the reporting criteria. The working party recognised that the revised reporting criteria are an important improvement and will likely be further revised as research advances. The revision group is planning to finalise the validation and publish the criteria to make them available for use in due course. The validation process and expert discussions highlighted significant gaps in knowledge of TACO pathogenesis and diagnosis, and for this reason a consensus conference will be deferred until these issues can be more satisfactorily addressed. However, it was recognised that a workshop to appraise current and ongoing research would be valuable for future planning.

Experts agreed that delineating the current categories of pulmonary complications is problematic and there is likely considerable overlap. It is important this does not act as a barrier in reporting to SHOT. Transfusion-associated dyspnoea (TAD) is an essential category for capturing these cases.

## Key SHOT message

- Patients who develop respiratory distress during or up to 24 hours after transfusion where transfusion is suspected to be the cause must be reported to SHOT. The transfusion-associated circulatory overload (TACO) definition criteria can be used as guidance but this should not be restrictive. SHOT experts can transfer cases between categories

## Recommendation

- A formal pre-transfusion risk assessment for transfusion-associated circulatory overload (TACO) should be undertaken whenever possible, as TACO is the most commonly reported cause of transfusion-related mortality and major morbidity

**Action: All staff authorising transfusion**







TACO Checklist		Red cell transfusion for non-bleeding patients	If 'yes' to any of these questions	
	Does the patient have a diagnosis of 'heart failure' congestive cardiac failure (CCF), severe aortic stenosis, or moderate to severe left ventricular dysfunction? Is the patient on a regular diuretic?		<div style="text-align: center;">   <b>1</b> </div> <div style="text-align: center;">   <b>2</b> </div> <div style="text-align: center;">   <b>3</b> </div>	<ul style="list-style-type: none"> <li>Review the need for transfusion (do the benefits outweigh the risks)?</li> </ul>
	Is the patient known to have pulmonary oedema? Does the patient have respiratory symptoms of undiagnosed cause?			<ul style="list-style-type: none"> <li>Can the transfusion be safely deferred until the issue can be investigated, treated or resolved?</li> </ul>
	Is the fluid balance clinically significantly positive? Is the patient on concomitant fluids (or has been in the past 24 hours)? Is there any peripheral oedema? Does the patient have hypoalbuminaemia? Does the patient have significant renal impairment?			<ul style="list-style-type: none"> <li>Consider body weight dosing for red cells (especially if low body weight)</li> <li>Transfuse one unit (red cells) and review symptoms of anaemia</li> <li>Measure the fluid balance</li> <li>Consider giving a prophylactic diuretic</li> <li>Monitor the vital signs closely, including oxygen saturation</li> </ul>

Figure 18b.1: TACO pre-transfusion checklist

**Due to the differences in adult and neonatal physiology, babies may have a different risk for TACO. Calculate the dose by weight and observe the notes above.**

**Recommendation**

- Use weight-adjusted red cell dosing to guide the appropriate number of units required for all non-bleeding adult patients, ideally using tools which also highlight inappropriate transfusion (Grey et al. 2018)

**Action: All staff authorising transfusion**



### Deaths n=7

Two of the 7 deaths were clearly related to transfusion. One of these cases had major gastrointestinal haemorrhage while anticoagulated. Serial full blood counts showed the patient was overtransfused/over-resuscitated with red cells and died following development of pulmonary oedema. The patient in the other case had a history of left ventricular failure and received two units of red cells for symptomatic relief of anaemia. The patient developed pulmonary oedema during the second unit and died within an hour of transfusion. The remaining deaths were in patients who all had pre-existing comorbidities that are known risks for circulatory overload.

### Major morbidity n=20

Sixteen of the 20 cases of major morbidity had evidence of pre-existing fluid overload, pulmonary oedema, comorbidities predisposing to circulatory overload and/or were also receiving significant volumes of non-blood fluids and were therefore at risk of TACO. Two cases had no apparent risk factors for TACO but had received large volumes of blood components, and in 1 case there was evidence of over-estimation of haemorrhage. There were only 2 cases where TACO developed with no apparent risk factors reported.

## Demographic overview of cases

Table 18b.1:  
Demographics of  
reported TACO  
cases

Demographic	Number of reports
Deaths (imputability 3)	2
Deaths (imputability 2)	4
Deaths (imputability 1)	1
Major morbidity (serious sequelae)	0
Major morbidity (minor sequelae)	3
Major morbidity (signs and symptoms with risk to life with full resolution/unknown outcome)	17
Age	Range 3-97 years Median 77 years
Specialties	Haematology=18 Acute medicine=17 Intensive therapy unit (ITU)/anaesthetics=6 Adult surgical specialties=13 Other adult medical specialties=31 Paediatrics=1 Obstetrics=1 Other specialties/unknown=5
Bleeding patients (indication code R1 or 'massive bleeding' indicated)	15
Non-bleeding patients (other indication codes or not stated)	77

In agreement with previous years, the demographic analysis shows that TACO is more commonly reported in the older population and where transfusion is given for anaemia rather than bleeding. Haematology and adult medical specialties are again the most common specialties where TACO is reported.

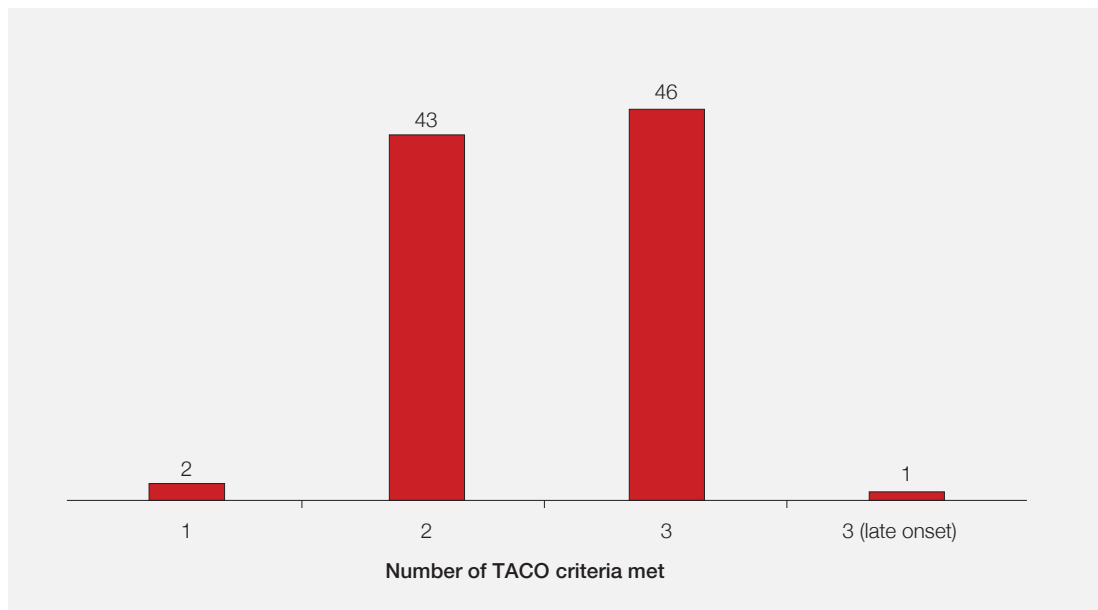
## Analysis by definition criteria

This year's data have been analysed using the draft TACO reporting criteria developed by the joint working group described in the introduction (ISBT 2017). These criteria are summarised below:

Patients classified as having TACO (surveillance diagnosis) should have acute or worsening respiratory compromise during or up to 12 hours after transfusion (SHOT accepts cases up to 24 hours after transfusion) and should exhibit two or more of the criteria below:

- Evidence of acute or worsening pulmonary oedema based on clinical physical examination and/or radiographic chest imaging and/or other non-invasive assessment of cardiac function e.g. echocardiogram
- Evidence of cardiovascular system changes not explained by the patient's underlying medical condition, including development of tachycardia, hypertension, jugular venous distension, enlarged cardiac silhouette and/or peripheral oedema
- Evidence of fluid overload including any of the following: a positive fluid balance; response to diuretic therapy combined with clinical improvement; and change in the patient's weight in the peri-transfusion period
- Elevation in B-type natriuretic peptide (BNP) levels (e.g. BNP or N-terminal (NT)-pro BNP) to greater than 1.5 times the pre-transfusion value. A normal post-transfusion BNP level is not consistent with a diagnosis of TACO; serial testing of BNP levels in the peri-transfusion period may be helpful in identifying TACO

These criteria establish a surveillance definition based on a complete description of an event, including information that becomes available well after onset. This is for reporting and tracking purposes and the criteria do not constitute clinical diagnosis for the purpose of real-time clinical interventions.



**Figure 18b.2:**  
Analysis of reports  
by the revised  
surveillance  
diagnosis criteria

TACO=transfusion-associated circulatory overload

Ninety-two reports were accepted into the TACO category. Eighty-nine (96.7%) met the revised surveillance criteria for TACO (89/92). In 1 of the 3 cases that did not strictly meet the criteria the timing of onset of symptoms was reported as 12-24 hours after transfusion. On review of the case the patient had received a large volume transfusion over a long period of time, which highlights the need for standardisation of the timing of symptom onset in relation to transfusion and is discussed further below. The 2 other cases scored only one criterion. One patient had pulmonary oedema following a large volume transfusion for haemorrhage, however due to lack of unanticipated cardiovascular parameter changes, no fluid balance record, no record of diuretic therapy and BNP not tested, only one criterion was met in an otherwise clinically compelling scenario. The other patient had received only a single unit of red cells and developed pulmonary oedema. In the absence of fluid balance measurement, lack of unanticipated cardiovascular parameter changes, failure to improve with diuretic therapy and BNP not tested, this case did not fully meet the new criteria. Although the patient had chronic underlying pulmonary pathology, the clinical scenario suggested that on balance the pulmonary oedema was probably precipitated by transfusion in this patient with risk factors for circulatory overload (renal impairment and requirement for regular diuretic medication).

The new criteria focus on the pathophysiology of circulatory overload based on the effects on cardiovascular and pulmonary systems. Pro-inflammatory features are being increasingly recognised in cases of pulmonary complications of transfusion. Whether these are purely circulatory overload, an overlapping syndrome or another unidentified entity is not understood. The two previous years' data have been analysed in the context of fever to explore this further.

## Fever in cases reported and categorised as TACO

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There is a recognised association between TACO and fever. The incidence was reported as 45/107 (42.1%) cases of TACO in a retrospective review (Parmar et al. 2017). Fever was defined as a temperature rise  $>1^{\circ}\text{C}$  to reach  $>38^{\circ}\text{C}$  and/or rigors or chills. Another study reported febrile or inflammatory symptoms in 65/97 (67.0%) cases of TACO (Andrzejewski et al. 2012).

A review of cases reported to SHOT in 2015 and 2016 showed that fever was a symptom in 34/164 (20.7%) cases reported as TACO. 'Fever' is not defined in the TACO questionnaire; it is a yes/no answer. In 15/34 (44.1%) cases with fever no alternative explanation for the fever was provided. In the cases where potential alternative explanations existed the patients were already on antibiotics or were being treated for infection prior to the transfusion.

If there are respiratory signs or symptoms suggestive of TACO, then the presence of fever does not exclude the diagnosis. This is reflected in the revised TACO surveillance diagnosis criteria (ISBT 2017). Research continues into the potential inflammatory processes involved in pulmonary oedema associated with transfusion.

## Timing of TACO symptoms

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TACO is generally considered to occur within 6 hours of transfusion, but SHOT has accepted cases within 24 hours of transfusion. Part of the revision work on the international surveillance criteria for TACO includes the timing of the reaction. The revised ISBT surveillance definition (ISBT 2017) is 'during or up to 12 hours after transfusion'.

All cases reported to SHOT between 2010 and 2016 where the timing of reaction was reported to be greater than 6 hours have been reviewed (Table 18b.2). A total of 83/555 (15.0%) of TACO cases were reported as being 6 hours or more after transfusion by the reporting organisation. Review of these shows that the 'time of transfusion' is often recorded as the time the first unit was started.

Certainly, in the case of multiple red cell transfusions, the total transfusion time will be more than 6 hours. Many of the cases analysed experienced a reaction during the transfusion or shortly after completion. Cases categorised as 'unclear' are where the data submitted were insufficient to reach a firm conclusion.

**Table 18b.2:**  
Timing of reported  
TACO cases

Time given for symptom onset by reporting hospital	Time of symptom onset from end of transfusion following review of the full data set				
	<6 hours	6-12 hours	12-24 hours	unclear	>24 hours
6-12 hours	<b>53</b>	31	16	6	
12-24 hours	<b>30</b>	10	4	8	5

A small number of patients experienced delayed reactions beyond 12 hours and 3 cases occurred beyond 24 hours, 2 of which were following outpatient transfusions and the timing of symptom onset was therefore potentially prior to the time of presentation to hospital.

The analysis demonstrates the need for an internationally agreed standard for the timing of the onset of TACO in relation to the transfusion episode.

## Illustrative cases

### Case 18b.1: An inappropriate transfusion leading to TACO and cancelled elective surgery

*A patient in their 90s was admitted for an elective total knee replacement. The patient's haemoglobin (Hb) was 95g/L and weight was 73kg. Two units of red cells were prescribed for preoperative Hb optimisation. A Hb check was not performed between units and a fluid balance chart was not in place. At the end of the second unit the patient had dyspnoea and was hypoxic, with hypertension and tachycardia. The chest X-ray was suggestive of pulmonary oedema and the post-transfusion Hb was 128g/L. The patient responded to diuretic therapy. The patient's surgery was cancelled due to TACO.*

Preoperative Hb optimisation should take place prior to admission where anaemia is identified, investigated and treated following surgical pre-assessment. Red cell transfusion is rarely appropriate except in occasional circumstances, for example where a patient has chronic bleeding or marrow impairment leading to anaemia that cannot be controlled medically.

Notwithstanding this, the patient in this case had a pre-transfusion Hb level that exceeded the trigger for transfusion and transfusion resulted in an excessive Hb level. The development of TACO then unfortunately led to the patient being discharged following recovery without having their surgery.

**Case 18b.2: Lack of attention to appropriate red cell dose leads to TACO**

*A patient in their 90s weighing 75kg with a newly diagnosed haematological condition was admitted with sepsis and a Hb level of 79g/L. The patient was known to have heart failure, renal impairment and peripheral oedema and therefore had risk factors for circulatory overload. Two units of red cells were prescribed with prophylactic diuretics. During transfusion of the second unit the patient became breathless, began coughing up frothy sputum, developed bilateral crackles, tachycardia and hypertension. The chest X-ray was consistent with pulmonary oedema.*

The root-cause analysis and preventive actions decided by the reporting hospital focused on future slow-rate transfusion, prophylactic diuretics and improved fluid balance measurement. Although these are important factors, the rate of transfusion in this case was not excessive (2-4 hours per unit) and diuretics were administered, suggesting TACO would not have been avoided in this scenario. However, the dose of red cells prescribed was not questioned as part of the root-cause analysis. Based upon a calculation of 0.4mL/kg raising the Hb level by 1g/L, this patient required less than a single unit of red cells to meet their target Hb. A weight-adjusted dose may have avoided TACO in this patient which developed during transfusion of the second unit.

**Case 18b.3: Inappropriate and excessive transfusion causing TACO in a patient without risk factors for circulatory overload**

*A patient in their 50s weighing 67kg was prescribed six units of red cells for iron deficiency anaemia after being admitted with Hb 37g/L. The patient had no risk factors for TACO except for profound anaemia. During the fifth unit the patient became dyspnoeic, hypoxic and hypertensive. The patient recovered after diuretic therapy and had a post-transfusion Hb level of 100g/L.*

Blood transfusion in iron deficiency anaemia is only appropriate as initial treatment if the patient is symptomatic. This patient was likely to be symptomatic with profound anaemia however the dose should have been limited to one or two units to resolve symptoms. The decision-making for this case appears to be aimed at a 'back to normal' Hb level with no attempt to treat the iron deficiency. Although a root-cause analysis was undertaken by the reporting hospital, much of the preventive action was focused on national education for junior medical staff and local implementation of the TACO checklist. Although these are important measures this case of TACO could have been avoided by a local policy of single unit or weight-adjusted red cell dosing. The transfusion laboratory has an important role in identifying and avoiding excessive and/or inappropriate transfusion.

## References

Andrzejewski C Jr, Popovsky M et al. Hemotherapy bedside biovigilance involving vital sign values and characteristics of patients with suspected transfusion reactions associated with fluid challenges: can some cases of transfusion-associated circulatory overload have pro-inflammatory aspects? *Transfusion* 2012;**52(11)**:2310-20.

Grey S, Farrar K et al. A web-App for weight-adjusted red cell dosing: post-development implementation and clinical effectiveness. *Br J Haematol* 2018;**181 Suppl 1**:146.

ISBT (2017). TACO reporting criteria (April 2017) draft for validation. [http://www.isbtweb.org/fileadmin/user\\_upload/TACO\\_reporting\\_criteria\\_April\\_2017\\_draft\\_for\\_validation.docx](http://www.isbtweb.org/fileadmin/user_upload/TACO_reporting_criteria_April_2017_draft_for_validation.docx) [accessed 4 January 2018].

Parmar N, Pendergrast J et al. The association of fever with transfusion-associated circulatory overload. *Vox Sang* 2017;**112(1)**:70-78.