

17b Transfusion-Associated Circulatory Overload (TACO) n=110

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Key SHOT message

- 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. 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

Update

The surveillance definition for TACO has been revised by a joint working group from the International Society of Blood Transfusion (ISBT) haemovigilance working party, the International Haemovigilance Network (IHN) and AABB with wide international consultation. SHOT has been a key contributor and collaborator in this work. Validation of the revised definition took place throughout 2017 and a workshop for the revision group with other leading interested parties and experts in the field was held in October 2018 as part of the AABB annual meeting.

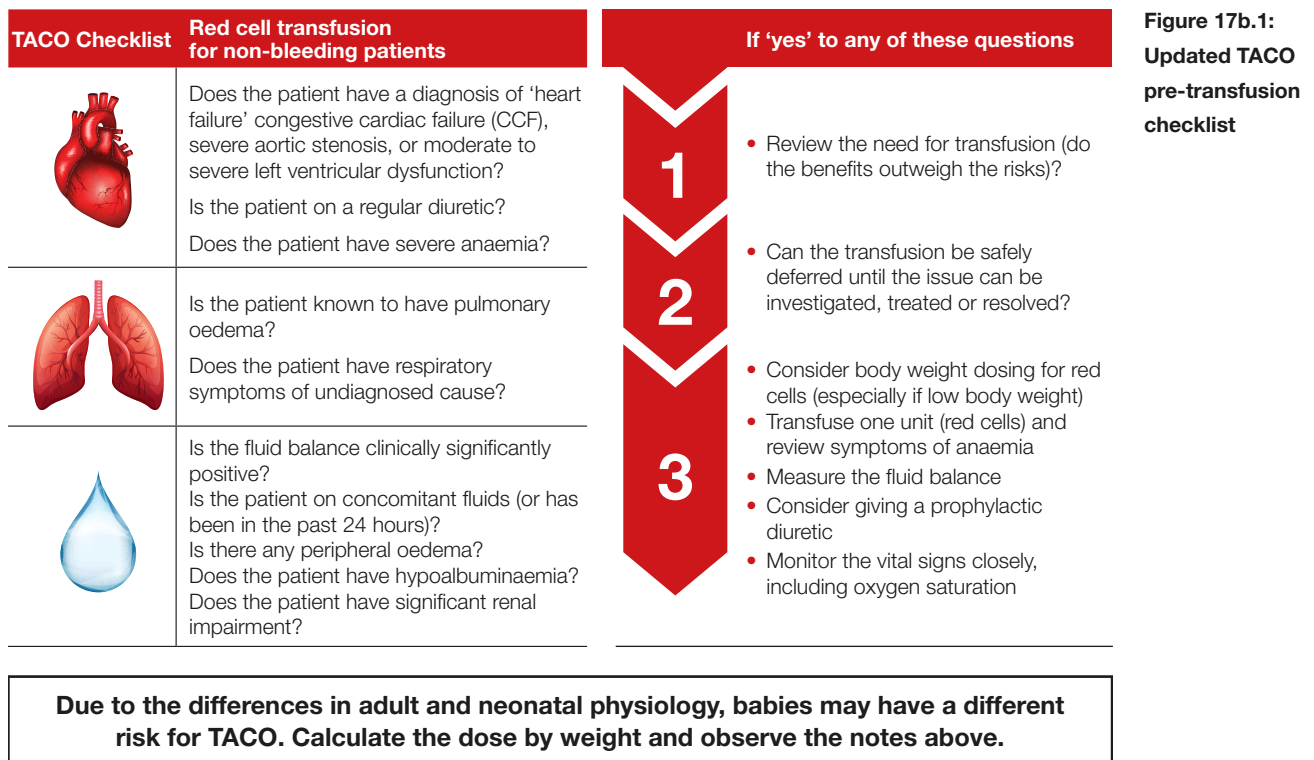
The consensus of the workshop was agreement that the validated TACO definition criteria should now be published and with the objective of improving and standardising TACO surveillance. The transfusion-related acute lung injury (TRALI) definition has also been revised (Vlaar et al. 2019). There was recognition of the problematic nature of delineating the pulmonary complications of transfusion due to probable overlap and compounded by gaps in knowledge of the pathogenesis of these conditions. It is important this does not act as a barrier in reporting to SHOT and the transfusion-associated dyspnoea (TAD) category remains essential to ensure capture of all relevant pulmonary cases. There was considerable interest in the role of the inflammatory response in pulmonary complications of transfusion and new research is emerging in this area which will no doubt inform future revision of the definitions.

2017 saw the publication of the National Comparative Audit (NCA) of TACO and for the first time provided large-scale data on related clinical practice (Morton et al. 2017, NCA 2017). It was encouraging and useful confirmation to observe the high degree of concordance between the recommendations of the audit report and the recommendations and key messages from SHOT. This year's recommendation has been aligned to the TACO NCA recommendations with respect to patient age and body weight.

Recommendation

- A formal pre-transfusion risk assessment for transfusion-associated circulatory overload (TACO) should be undertaken whenever possible (especially if older than 50 years or weighing less than 50kg), as TACO is the most commonly reported cause of transfusion-related mortality and major morbidity

Action: All staff authorising transfusion



TACO=transfusion-associated circulatory overload

TACO developing with transfusion for severe anaemia is an emerging signal from the data, and is an under-recognised independent risk-factor. This was highlighted in last year's Annual SHOT Report (Bolton-Maggs et al. 2018, Case 18b.3) and continues to feature in this year's data. TACO can develop in patients with severe anaemia even in the absence of other risk factors for TACO (see Cases 17b.1 and 17b.3). For this reason, 'severe anaemia' has been added to the pre-transfusion risk assessment infographic (Figure 17b.1).

The data continues to show TACO in non-bleeding patients where the volume of red cells was in excess of that calculated for their body weight and target haemoglobin (see Case 17b.2). Weight-adjusted red cell dosing for non-bleeding patients remains a recommendation.

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, National Comparative Audit, 2017)

Action: All staff authorising transfusion

Deaths n=5

TACO resulted in death of the patient in 5 reported cases.

Major morbidity n=36

TACO remains the leading cause of transfusion-related mortality and major morbidity.

Demographic overview of cases

Table 17b.1:
Demographics of
TACO cases

Demographic	Number of reports
Deaths (imputability 3)	0
Deaths (imputability 2)	2
Deaths (imputability 1)	3
Major morbidity outcome (serious sequelae)	4
Major morbidity outcome (minor sequelae)	6
Major morbidity (signs and symptoms with risk to life with full resolution/unknown outcome)	26
Age	Range: 1 day - 97 years Median: 76 years
Top 3 medical specialties	Acute medicine (19/110) Haematology (18/110) Anaesthesia (10/110)
Bleeding patients (indication code R1 or 'massive bleeding' indicated)	21
Non-bleeding patients (other indication codes or not stated)	89

As seen in previous years, the demographics show 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, and this should be considered when delivering TACO mitigation and education plans.

Analysis by definition criteria

This year's data have been analysed using the reporting criteria developed by the joint working group described in the introduction (Wiersum-Osselton et al. 2019). The 2018 TACO case surveillance definition criteria are summarised below:

Patients classified with TACO (surveillance diagnosis) should exhibit at least one required criterion* with onset during or up to 12 hours after transfusion (SHOT continues to accept cases up to 24 hours), and a total of 3 or more criteria i.e. *A and/or B, and total of at least 3 (A to E)

* Required criteria (A and/or B)

A. Acute or worsening respiratory compromise and/or

B. 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

Additional criteria

C. Evidence for 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

D. Evidence of fluid overload including any of the following: a positive fluid balance; clinical improvement following diuresis

E. Supportive result of a relevant biomarker, e.g. an increase of B-type natriuretic peptide levels (BNP) or N-terminal-pro brain natriuretic peptide) NT-pro BNP to greater than 1.5 times the pre-transfusion value

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 surveillance purposes and the criteria do not constitute clinical diagnosis for the purpose of real-time clinical interventions.

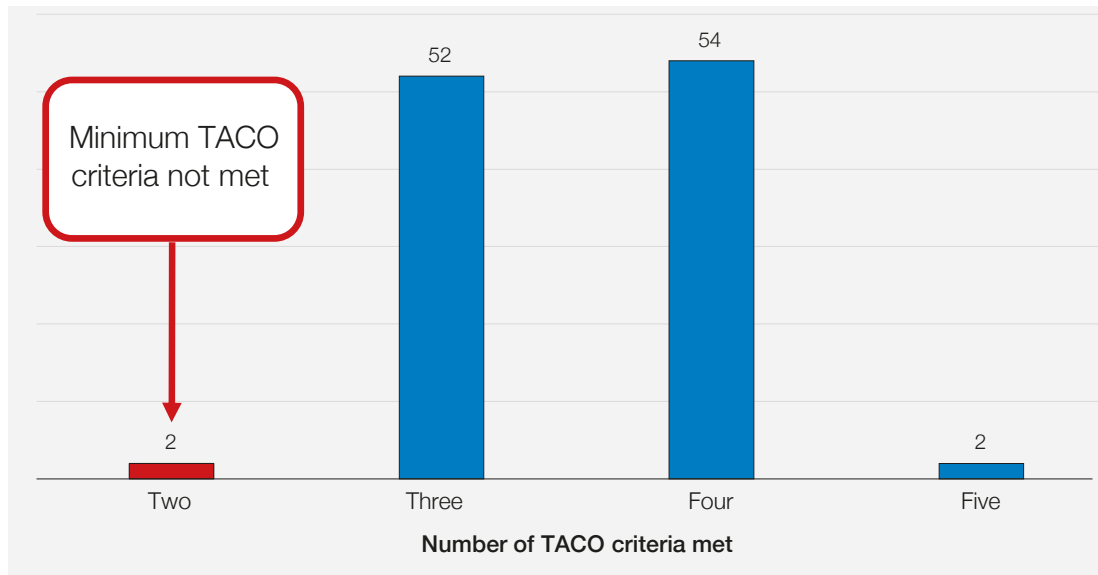


Figure 17b.2:
Analysis of reports
by the revised
surveillance
diagnosis criteria
(number of criteria
versus number of
accepted cases)

TACO=transfusion-associated circulatory overload

There were 2 cases that scored only two criteria but were nevertheless accepted into the TACO category. This first case demonstrated respiratory distress during transfusion and radiological evidence of pulmonary oedema. The patient's condition worsened following diuretics but the patient had severe renal failure. No vital sign observations or fluid balance were available for assessment. The patient had additional comorbidities and risk factors predisposing to circulatory overload (aortic stenosis and hypoalbuminaemia). The second case had a similar respiratory and radiological picture with no response to diuretics. The fluid balance and vital sign observations were also unavailable. There was also a primary cardiac cause for pulmonary oedema (acute coronary syndrome) which complicated the assessment, and the patient had received a large volume of non-blood fluid. Taking the cases in their overall context, the evidence for TACO was clinically compelling and failure to meet the requisite number of criteria was due to lack of available data.

Demonstrating left atrial hypertension (LAH): an important aspect for categorisation of pulmonary complications of transfusion

Left atrial hypertension is an important discriminator when categorising the pulmonary complications of transfusion as radiological features in TACO and TRALI can be difficult to distinguish, and other clinical signs can be similar. This year 10/110 (9.1%) cases had echocardiography performed which was useful in demonstrating LAH. However, it is accepted that while useful for haemovigilance categorisation purposes the clinician assessing the patient may not require this investigation in order to clinically manage the patient. The 2018 TACO case surveillance definition criteria includes BNP/NT-pro BNP as an 'additional' criterion to support TACO. The role of BNP is to regulate blood pressure and blood volume. Only 3/110 (2.7%) cases reported to SHOT in 2018 provided BNP/NT-pro BNP test results. This information is especially useful when data for other criteria are not available, for example when a chest X-ray has not been performed, fluid balance not recorded or uncertain response to diuretics (especially when given in combination with allergy medications). NT-pro BNP is available on most biochemistry platforms (requiring a serum or ethylenediaminetetraacetic acid (EDTA) sample). Most laboratories will offer the test as part of primary care heart failure diagnostic service, or will be able to refer tests. It is valuable for professionals with haemovigilance responsibilities to enquire about their local services and the possibility of testing suspected TACO cases, which would only comprise a small number. The test is generally performed on an EDTA sample and therefore convenient to test the pre and post-transfusion samples without the need for separate samples to be taken. Non-cardiac comorbidities and pre-existing cardiac disease can raise NT-pro BNP. It is worth noting that NT-pro BNP is affected by a number of conditions not related to LAH. Further information can be accessed here: <https://fpnotebook.com/cv/lab/BrnNtrtcPptd.htm>. Scale change is important with a >1.5x increase from pre-transfusion value supporting TACO. A post-transfusion value in the normal range is not compatible with TACO and is therefore a good negative predictor.

Illustrative cases

Case 17b.1: Rapid correction of anaemia can precipitate TACO in the absence of other comorbidities and risk factors

A male in his 50s presented to the emergency department (ED) with a 3-4-week history of weakness and dizziness, and had felt unwell for the past 6 months. He was hypotensive (blood pressure (BP) 92/47) but did not show signs of acute haemorrhage though there was some altered blood on rectal examination. On admission his haemoglobin (Hb) was 34g/L, ferritin 26micrograms/L and the electrocardiogram (ECG) showed cardiac ischaemia. He was transfused two units of red cells with a plan for endoscopy and intravenous (IV) iron the following day. A third unit was planned if the post-transfusion Hb was <60g/L. The first unit was transfused over 31 minutes and the second over 65 minutes. After the second unit his oxygen saturations began to fall despite being on supplemental oxygen and his post-transfusion Hb was 51g/L. A third unit was transfused over 125 minutes and he developed worsening hypoxia, dyspnoea and crackles on chest auscultation. The chest X-ray showed an enlarged cardiac silhouette and pulmonary congestion. He was treated with diuretics and improved. Fortunately, the attending doctor cancelled the fourth unit which had been planned.

This patient certainly required transfusion to treat the symptoms of severe anaemia and cardiac ischaemia prior to IV iron replacement. The case is a good example of the risk of rapid correction of severe anaemia in the absence of haemorrhage. This patient had no other comorbidities or risk factors predisposing circulatory overload except severe anaemia. There was no indication for rapid transfusion. The development of increasing hypoxia after the second unit was a warning of TACO developing in this patient. In the absence of bleeding, the speed of correction should be commensurate with the pre-transfusion Hb level. This patient had iron deficiency anaemia, but it is worth noting that severe megaloblastic anaemia can cause cardiomyopathy, thereby increasing the risk of circulatory overload. Red cell transfusion should be avoided or minimised in these patients.

Case 17b.2: Excessive red cell volume given to an overloaded small patient where TACO was not initially suspected

A female in her 80s was admitted with a fractured neck of femur. She weighed 40kg and had a preoperative Hb of 109g/L. She received 2L of Hartmann's in theatre and returned to the ward with a positive fluid balance (+2425mL). Her postoperative Hb was 65g/L and she was haemodynamically stable. She was prescribed three units of red cells and her pre-transfusion vital sign observations were normal. Her vital sign observations after the first unit were normal but her fluid balance was then +3454mL. The second unit was given after which she became shaky and developed hypertension (175/82), pyrexia (38°C), tachycardia (102 beats per minute), tachypnoea (22 breaths per minute) and her oxygen saturation was 96% on 5L of oxygen. This was reported to the on-call orthopaedic doctor who requested further fluid to be administered stat (250mL Hartmann's) which resulted in a further deterioration of her respiratory status. The attending doctor suspected acute lung injury or sepsis (not circulatory overload). A chest X-ray was performed on the advice of the consultant haematologist whose opinion had been sought for a possible transfusion reaction. This was consistent with pulmonary oedema.

There were two striking aspects to this case. Firstly, was the choice of volume of red cells to correct the surgical anaemia. The calculation below is based on 4mL/kg raising the Hb by 10g/L (Norfolk, 2013), with a target Hb of 80g/L (cardiovascular risk factors have been assumed in a patient in her 80s).

Target Hb (g/L) – actual Hb (g/L) x [body weight (kg) x 0.4mL] = volume of red cells to transfuse to meet target Hb (mL)

80g/L – 65g/L x [40kg x 0.4mL red cells] = 240mL

This is equivalent to a single unit of red cells for a patient of this body weight. Three units are certainly excessive underlining the importance of weight-adjusted red cell dosing for non-bleeding patients. Although Norfolk states that 4mL/kg 'should only be applied as an approximation for a 70–80kg patient', Grey et al. (2018) have shown that the above calculation achieves the post-transfusion Hb target in around 90% of patients across a range of body weights.

The second aspect is failure to suspect circulatory overload in this patient. The patient already had a significantly positive fluid balance before transfusion and this had increased after the first unit of red cells. The development of deteriorating respiratory status, with hypertension, tachycardia, and pyrexia was interpreted as acute lung injury or sepsis and was treated with fluids which clearly exacerbated the circulatory overload. This illustrates the importance of measuring (and assessing) the fluid balance, and that the presence of pyrexia does not exclude TACO. Indeed, there is an increasing recognition that TACO may have an inflammatory component (see 2017 Annual SHOT Report (Bolton-Maggs et al. 2018)).

Case 17b.3: A complex presentation with difficult decision-making

A male in his 60s with history of factor XI deficiency and chronic obstructive pulmonary disease (COPD) had been referred to the colorectal team on a two-week pathway for investigation of anaemia (Hb 82g/L, platelets 92x10⁹/L). He had felt increasingly unwell and presented to the ED. His Hb was 34g/L, platelets 27x10⁹/L, neutrophils 0.58x10⁹/L, he had renal failure (eGFR 36mL/min), hypoalbuminaemia, and prolonged clotting times (prothrombin time (PT) 23.1 seconds (s) and activated partial thromboplastin time (APTT) 90s). Per rectum examination showed melaena and endoscopy was planned for the following day. He had tachycardia and hypotension. The ED consultant suspected acute gastrointestinal bleeding and the patient was transfused a total of four units of red cells, three units of fresh frozen plasma (FFP), and one dose of platelets over 9 hours (total >2L in volume). He developed hypoxia (oxygen saturations <70%) and bradycardia (heart rate 35 beats per minute), and was pale and clammy. He was given oxygen therapy (15L) and diuretics which produced a good diuresis. He received cardiac monitoring and was transferred to the intensive therapy unit (ITU). The chest X-ray was consistent with pulmonary oedema and peripheral blood film was reported later and showed blast cells.

This was a complex presentation and although the local reviewer found rapid multi-component transfusion to be clinically justified at the time of admission, unfortunately the patient was later found not to have acute bleeding and developed TACO. The presence of blast cells in the peripheral blood was more suggestive of bone marrow failure as the cause of pancytopenia. The reviewer identified hypoalbuminaemia and renal failure as risk factors for TACO, but in common with Case 17b.2, severe anaemia is also a risk for TACO. However, if major bleeding was suspected, recognition of this may not have changed the course for this patient. The reviewer correctly stated that TACO may not be avoidable in major haemorrhage where a risk-balanced decision has to be taken for the consequences of major bleeding versus TACO. Local review identified the need for clinical reassessment after each unit which was not documented in this case, especially in the absence of signs of ongoing bleeding. It is easy to focus on the blood transfusion and clinical management aspects of TACO cases, but establishing a timely diagnosis can also have a critical role. An early blood film report has the potential to significantly change the management of a patient, and in this case may have led to more conservative blood component transfusion. This is not to say a patient with leukaemia could not also have acute gastrointestinal bleeding!

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