

17a Transfusion-Associated Circulatory Overload (TACO) n=131

Author: Sharran Grey

Definition:

TACO is defined as acute or worsening respiratory compromise and/or acute or worsening pulmonary oedema during or up to 12 hours[†] of transfusion, with additional features including cardiovascular system changes not explained by the patient's underlying medical condition; evidence of fluid overload and a relevant biomarker[‡].

[†]SHOT accepts cases up to 24 hours

[‡]see Table 17a.2 for details of required and additional criteria for a surveillance diagnosis

Abbreviations used in this chapter

BSH	British Society for Haematology	NCA	National comparative audit
CT	Computed tomography	NT-pro BNP	N-terminal-pro B-type natriuretic peptide
Hb	Haemoglobin	TACO	Transfusion-associated circulatory overload
HDU	High dependency unit	TRALI	Transfusion-related acute lung injury
WEG	Working expert group		

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 TACO definition criteria can be used as guidance, but this should not be restrictive. SHOT pulmonary WEG can transfer cases between categories

Recommendations

- A formal pre-transfusion risk assessment for TACO should be undertaken whenever possible for all patients receiving blood transfusion (especially if older than 50 years or weighing less than 50kg) and appropriate mitigating actions taken
- 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, NCA 2017)

Action: All staff authorising transfusion

- A structured review and incident investigation should be undertaken for every case of TACO to optimise organisational and individual patient-safety measures

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

The TACO pre-transfusion risk assessment infographic (Figure 17a.1) was updated in the 2020 Annual SHOT Report to make it suitable for incorporation into clinical documents. No further update was required this year.

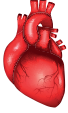


TACO Checklist	Patient Risk Assessment	TICK	If Risks Identified	YES	NO
	Does the patient have a diagnosis of 'heart failure' congestive cardiac failure (CCF), severe aortic stenosis, or moderate to severe left ventricular dysfunction?		Review the need for transfusion (do the benefits outweigh the risks)?		
	Is the patient on a regular diuretic?		Can the transfusion be safely deferred until the issue can be investigated, treated or resolved?		
	Does the patient have severe anaemia?		If Proceeding with Transfusion: Assign Actions		
	Is the patient known to have pulmonary oedema?		Body weight dosing for red cells		
	Does the patient have respiratory symptoms of undiagnosed cause?		Transfuse a single unit (red cells) and review symptoms		
	Is the fluid balance clinically significantly positive?		Measure fluid balance		
	Is the patient receiving intravenous fluids (or received them in the previous 24 hours)?		Prophylactic diuretic prescribed		
	Is there any peripheral oedema?		Monitor vital signs closely, including oxygen saturation		
	Does the patient have hypoalbuminaemia?		Name (PRINT):		
	Does the patient have significant renal impairment?		Role:		
			Date:	Time (24hr):	
			Signature:		

Figure 17a.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.

TACO=transfusion-associated circulatory overload

Introduction

The traditional hypothesis for the pathophysiology of TACO is increased hydrostatic pressure in the pulmonary capillaries which surround the alveoli which results in a transudate and increased interstitial pressure. This is forced into the alveoli causing pulmonary oedema which compromises normal lung function, leading to hypoxia. Other mechanisms have been proposed. These include a TRALI-like response where inflammatory cells disrupt the endothelial barrier resulting in the passage of transudate and exudate. The interstitium becomes widened and epithelial layer of the alveolus is disrupted allowing the passage of inflammatory cells and exudate resulting in pulmonary oedema. Mechanical destruction (barotrauma) may cause increased permeability and dysfunction of the capillary endothelial layer. The increased intra-capillary pressure disrupts the endothelial glycocalyx of the capillary allowing transudate and exudate to penetrate the epithelial barrier of the alveolus. Storage lesions such as the presence of microparticles or cell-free haemoglobin may induce vasoconstriction of the capillary resulting in transudate and exudate which disrupts the epithelial barrier of the alveolus (Bosboom et al. 2019). The emerging complexity of the mechanism of transfusion-related pulmonary oedema creates significant difficulties for definitive categorisation for haemovigilance purposes, and increasingly strengthens the hypothesis that pulmonary complications of transfusion may not be mutually exclusive.

Although the pathophysiology of TACO is not fully understood, the evolving understanding of risk factors for TACO and the development of tools to mitigate risks has been a significant advance in recent years. This chapter describes the demographics of patients reported to have TACO, haemovigilance categorisation, and the adoption of TACO risk-reduction strategies, and highlights areas requiring further focus.

Deaths related to transfusion n=11

TACO resulted in the death of a patient in 11 reported cases. With exception of 1 case the imputability level was low (possibly related to transfusion). There were fewer deaths compared to the previous reporting year (18 in 2020) which was significantly affected by COVID-19. This was likely to have been influenced by the severity of underlying illness of those with COVID-19 and as such were more likely to die.

Major morbidity n=23

There were a similar number of cases that resulted in major morbidity compared to the previous reporting year (25 in 2020). This may reflect a continued increased number of patients with severe respiratory comorbid disease due to COVID-19 but fewer that resulted in the patient's death, as COVID-19 related deaths began to fall. TACO remains the leading cause of transfusion-related combined mortality and major morbidity.

Table 17a.1:
Demographic
overview of cases

Demographic	Number of reports
Deaths (imputability 3)	0
Deaths (imputability 2)	1
Deaths (imputability 1)	10
Major morbidity outcome	23
Age	Range: 2 months-97 years (five age under 18 years) Median: 74.5 years
Gender	76 female: 55 male
Body weight (adults)	Female (n=38): average 65.2kg (38.0-118kg) Male (n=33): average 75.2kg (51.0-125.6kg)
Top four medical specialties where TACO was reported	Acute medicine 16.0% (21), haematology 14.5% (19), emergency medicine 12.2% (16), general medicine 10.7% (14)
Bleeding patients (indication code R1 or 'massive bleeding' indicated)	28
Non-bleeding patients (other indication codes or not stated)	103

Commentary

TACO is more commonly reported in the elderly, non-bleeding patients but is seen across all age groups and is consistent with the data from previous years. There were 5 cases in the under-18 age group, (age 2 months to 16 years). TACO was reported more in adult female patients compared to male. Weight was provided in 38 adult female cases, with an average of 65.2kg (38.0-118kg). Weight was provided in 33 adult male cases, with an average of 75.2kg (51.0-125.6kg). This difference may account for the apparent higher incidence of TACO in female patients and underlines the risk of TACO in lower-weight patients and the importance of weight-adjusted red cell dosing. Adult medical specialties and haematology continue to be the most common specialties where TACO is reported, and this should be considered when delivering TACO education and mitigation plans.

Analysis by definition criteria

Cases reported in 2021 were assessed using the surveillance criteria in Table 17a.2. It should be noted that the criteria are for the purposes of reporting and surveillance and do not constitute a clinical diagnosis for the purpose of real-time interventions for the medical management of a patient presenting with respiratory compromise during or following transfusion. However, the surveillance criteria should help promote recognition of TACO.

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 BNP levels or NT-pro BNP to greater than 1.5 times the pre-transfusion value

Table 17a.2:
TACO surveillance
definition (adapted
from Wiersum-Osselton
et al. 2019)

Figure 17a.2 shows the number of accepted TACO cases versus the number of TACO surveillance criteria met. The majority of cases met four criteria. Only 2 cases met all five criteria where a pre- and post-transfusion BNP sample had been taken. This is a useful biomarker to demonstrate left atrial hypertension. In previous years, cases were accepted that did not fully meet the criteria due to missing data but were otherwise clinically compelling cases. A decision has now been taken to not include these cases and instead transfer them to the non-TACO category for separate analysis.

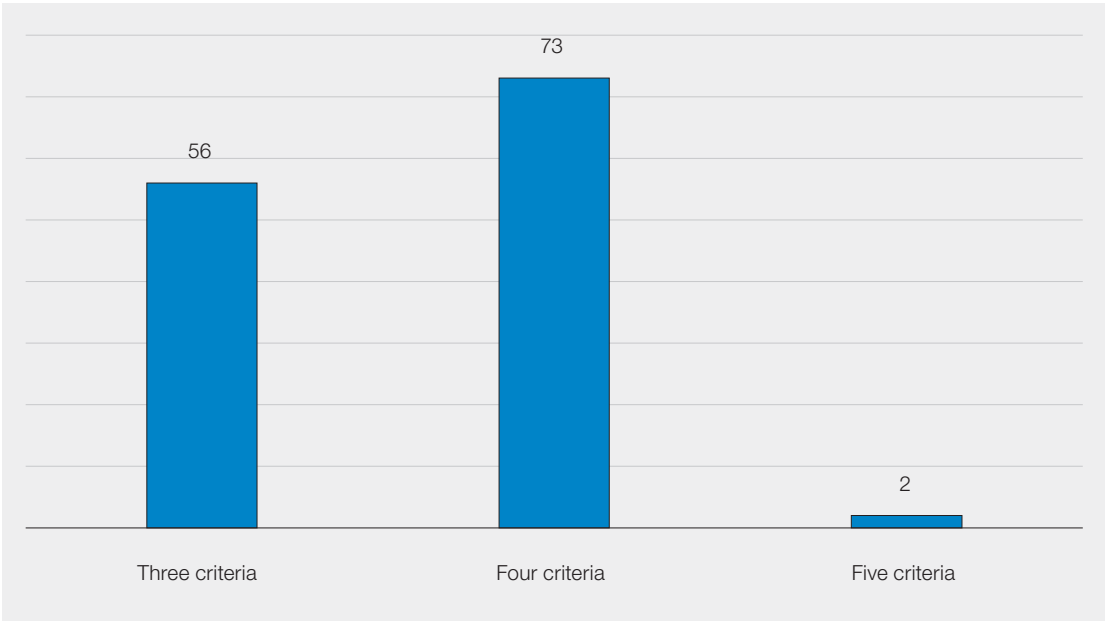
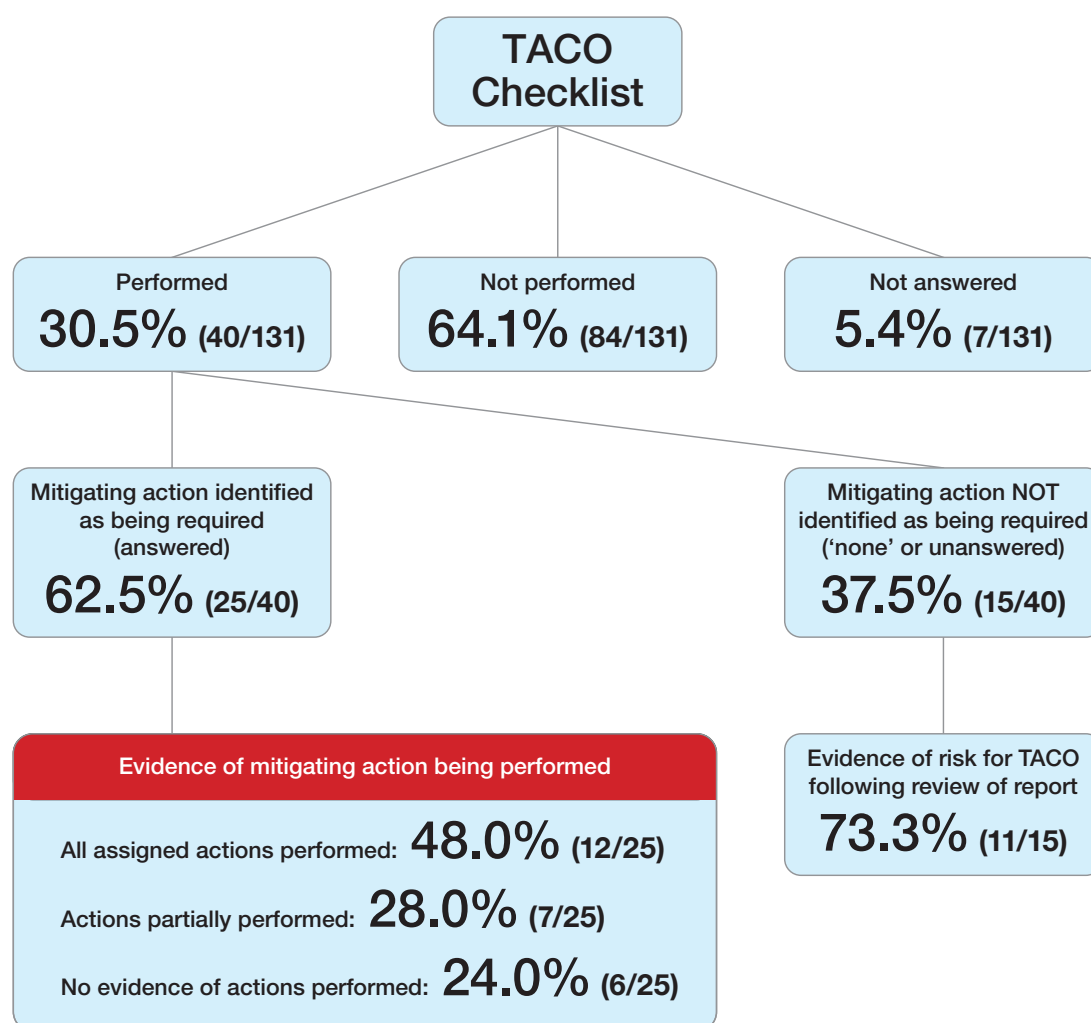


Figure 17a.2:
Number of
surveillance criteria
versus number of
accepted TACO
cases

Use of the TACO checklist

The recommendation for a formal pre-transfusion TACO risk assessment was introduced in the 2015 Annual SHOT Report (Bolton-Maggs et al. 2016). A question regarding the use of the TACO risk assessment and mitigating actions was added to the SHOT questionnaire for the 2019 reporting year. An overview is shown in Figure 17a.3.

Figure 17a.3:
Use of the checklist
to identify patients
at risk of TACO and
implementation of
mitigating actions



TACO=transfusion-associated circulatory overload

The TACO checklist was reported to have been used in only 40/131 (30.5%) cases. It is disappointing that the checklist is not universally utilised as there may have been missed opportunities to reduce the risk of TACO. This has been a SHOT recommendation since 2016 and is also highlighted in the BSH guideline on the administration of blood components (BSH Robinson et al. 2018). Where a TACO checklist was performed 25/40 (62.5%) this demonstrated the need for a mitigating action and in most cases appropriate actions were taken. There were 6 cases where assigned actions had not been performed and 7 where the actions were only partially complete. Where a TACO checklist was performed and it was determined a mitigating action was not required, a review of these reports showed that 11/15 (73.3%) did in fact have at least one risk factor for TACO. It is important to recognise that while the TACO risk assessment does not guarantee avoidance of TACO, it can provide a means of identifying patients at risk. This helps apply strategies to reduce it and help make safe transfusion decisions.

TACO cases with evidence of excessive red cell volume to meet the target Hb

The recommendation for weight-adjusted red cell dosing with tools to identify inappropriate transfusion for non-bleeding patients was introduced in the 2017 Annual SHOT Report (Bolton-Maggs et al. 2018). Analysis of the 2021 data shows that this is not sufficiently implemented in practice and is contributing to overtransfusion in some reported cases of TACO. There were 20 cases involving red cell transfusions that reported a body weight, a pre- and post-transfusion Hb level and the number of units transfused. In 3/20 (15.0%) of cases transfusion was not required because the Hb was already within the target range. There were 2/20 (10.0%) cases that received more than the calculated weight-adjusted dose, and in 3/20 (15.0%) cases, the post-transfusion Hb target was exceeded.

Case 17a.1: Omitted TACO risk assessment led to overtransfusion and TACO, with no structured investigation performed

A male patient in his 70's weighing **64kg** was admitted to a medical ward with **severe symptomatic microcytic hypochromic anaemia (Hb 47g/L)**. His pre-transfusion CT scan showed some pulmonary fibrosis and a small pleural effusion. He had **severe left ventricular systolic dysfunction, renal impairment, peripheral oedema** and was on a **regular diuretic**. He was initially transfused uneventfully with two units of red cells. A TACO risk assessment was not performed and a fluid balance chart was not in place. His post-transfusion Hb was 65g/L. He was then given a third unit of red cells. There were no signs of active bleeding. He became wheezy, hypertensive, tachycardic, pyrexial and had rigors. His oxygen saturations reduced to 75% and he had peripheral pitting oedema. His post-transfusion chest X-ray showed consolidation thought to be caused by aspiration pneumonia and new bilateral infiltrates consistent with pulmonary oedema. He received oxygen via continuous positive airway pressure, a diuretic, hydrocortisone, bronchodilator and antibiotics. He was transferred to HDU and later recovered. The local procedural review identified single unit with review and not transfusing blood for iron deficiency as preventative actions.

This patient had multiple risks for TACO (in **bold** above). A TACO risk assessment/checklist was not performed but would have identified these, and there were no reported mitigations put in place. A single unit red cell transfusion followed by intravenous iron would have sufficed to treat this patient's severe symptomatic anaemia. Three units of red cells was excessive in a relatively low weight patient with no active bleeding. TACO was almost inevitable in this scenario. Although a local review took place it did not identify all strategies to avoid TACO. The TACO structured investigation tool (see recommended resources) would have also highlighted the need for single unit transfusion and review, weight-adjusted red cell dosing, fluid balance chart, increased measurement of oxygen saturation, a prophylactic diuretic in addition to his regular medication (if not contraindicated). These measures would have helped mitigate the risk for this transfusion episode and help in planning future transfusions. It also represents an opportunity to improve practice and reduce risk for all future patients.

Learning points

- Excessive volume of red cell transfusion to meet a target Hb level remains a significant factor in cases of TACO, in non-bleeding patients. This can be minimised by weight-adjusted red cell dosing, and medical management of anaemia where possible. The calculation below helps estimate the volume of red cells required to meet the target Hb (Norfolk 2013)

$$[\text{target Hb (g/L)} - \text{pre-transfusion Hb (g/L)}] \times \text{weight (kg)} \times 0.4\text{mL red cells} \\ = \text{volume of red cells (mL) required to meet target Hb}$$

(The volume of a unit of adult-specification red cells in the UK is 220-340mL)

- A significant number of reported TACO cases do not appear to have had a TACO checklist performed, and/or TACO risk-reduction measures not implemented where risk was identified. This should be embedded into the procedure for the request and authorisation of transfusion
- Every case of TACO is an opportunity to improve practice and reduce risk for other patients. Structured incident investigation allows implementation of effective corrective and preventative actions

Conclusion

The continued adoption of the TACO checklist is encouraging though analysis of the data shows it is still under-utilised. The data suggests that there is lack of structured investigation following cases of TACO and this results in missed opportunities to mitigate the risk of TACO and to improve transfusion safety for all patients. The TACO structured investigation tool was launched last year in the 2020 Annual SHOT Report and continues to be a recommendation this year. The pulmonary reactions questionnaire in the SHOT database (Dendrite) has been updated to include a question as to whether it was performed



and what gaps and preventative actions were identified. This will inform the degree to which it is being adopted and will also provide important data regarding the implementation of risk-reduction measures.



Recommended resources

Example of weight-adjusted red cell dosing implemented in clinical practice

www.rcdcalculator.co.uk

TACO Incident Investigation Guidance Tool

TACO Checklist: in risk assessment/checklist alternative format for incorporation into clinical documents

<https://www.shotuk.org/resources/current-resources/>

SHOT Bite No. 11: Respiratory Symptoms During Transfusion

<https://www.shotuk.org/resources/current-resources/shot-bites/>

SHOT Video: TACO

<https://www.shotuk.org/resources/current-resources/videos/>

References

- Bolton-Maggs PHB (ed), Poles D, et al. On behalf of the Serious Hazards of Transfusion (SHOT) Steering Group. The 2015 Annual SHOT Report (2016). <https://www.shotuk.org/shot-reports/> [accessed 05 May 2022].
- Bolton-Maggs PHB (ed), Poles D, et al. On behalf of the Serious Hazards of Transfusion (SHOT) Steering Group. The 2017 Annual SHOT Report (2018). <https://www.shotuk.org/shot-reports/> [accessed 05 May 2022].
- Bosboom JJ, Klanderman RB, Migdady Y, et al. Transfusion-Associated Circulatory Overload: A Clinical Perspective. *Transfus Med Rev.* 2019;**33**(2):69-77. doi: 10.1016/j.tmr.2019.01.003. [accessed 05 May 2022].
- BSH Robinson S, Harris A, Atkinson S, et al. The administration of blood components: a British Society for Haematology Guideline. *Transfus Med* 2018;**28**(1):3-21. <http://onlinelibrary.wiley.com/doi/10.1111/tme.12481/full> [accessed 05 May 2022].
- Grey S, Farrar K, Kinsella P, et al. A web-App for weight-adjusted red cell dosing: post-development implementation and clinical effectiveness. *B J Haem.* 2018;**181**(1):146.
- NCA. National Comparative Audit of Blood Transfusion: 2017 Transfusion associated circulatory overload audit (2017). <https://nhsbt.dbe.blob.core.windows.net/umbraco-assets-corp/14909/2017-taco-national.pdf> [accessed 05 May 2022].
- Norfolk D, (ed) Handbook of Transfusion Medicine (5th edn) (2013). The Stationery Office, London URL <https://www.transfusionguidelines.org/transfusion-handbook> [accessed 05 May 2022].
- Wiersum-Osselton J, Whitaker BL, Grey S, et al. Revised international surveillance case definition of transfusion associated circulatory overload (TACO): a classification agreement validation study. *Lancet Haematol.* 2019;**6**(7):e350-e358. doi:10.1016/S2352-3026(19)30080-8.