

17a Transfusion-Associated Circulatory Overload (TACO) n=160

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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.1 for details of required and additional criteria for a surveillance diagnosis

Key SHOT messages

- The number of TACO cases reported in 2022 is the highest to date. Although cases continue to increase, there is likely to be a level of under-reporting
- The continued adoption of the TACO checklist is encouraging although analysis of the data shows it is still under-used or used ineffectively
- TACO continues to be a major cause of transfusion-related mortality and morbidity

Recommendations (new)

- 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 experts can transfer cases between categories

Action: All staff involved in transfusion

Recommendations (ongoing)

- 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 mitigating actions taken, as TACO is the most commonly reported cause of transfusion-related mortality and major morbidity

Action: All staff authorising transfusion

- A structured incident review should be undertaken for every case of TACO to ensure optimum organisational and individual patient safety measures are in place to protect patients from TACO as far as possible (see 'Recommended resources')

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

- 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

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.

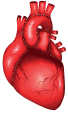


TACO Checklist	Patient Risk Assessment	TICK	If Risks Identified	YES	NO
	Does the patient have a diagnosis of 'heart failure' congestive cardiac failure (CCF), severe aortic stenosis, or moderate to severe left ventricular dysfunction?		Review the need for transfusion (do the benefits outweigh the risks)?		
	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

TACO Surveillance Definition

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.1: TACO surveillance definition (adapted from Wiersum-Osselton et al. 2019)

Introduction

The number of cases reported in 2022 is the highest to date and is an increase of 29 cases from 2021 (n=131). Although the pathophysiology of the pulmonary complications of transfusion is not fully understood, the evolving understanding of risk factors for TACO and the development of tools to mitigate

risks has advanced significantly in recent years. This chapter describes the demographics of patients reported to have TACO, the adoption of risk-reduction strategies, and highlights areas for further focus based on signals from the data and ongoing trends.

Deaths related to transfusion n=8

There were 8 deaths related to the transfusion, of which 1 was definitely related (imputability 3), 1 was probably related (imputability 2) and 6 were possibly related (imputability 1) (Table 17a.2).

Major morbidity n=25

There were 25 cases of major morbidity cases in 2022, this is similar to 2021 when there were 23 cases reported.

Table 17a.2:
Demographic
overview of
cases

Demographic	Number of reports
Deaths (imputability 3, definite)	1
Deaths (imputability 2, likely)	1
Deaths (imputability 1, possible)	6
Major morbidity outcome	25
Age	Range: newborn – 97 years (3 aged under 18 years) Median: 72 years
Gender	91 female: 69 male
Body weight (adults)	Female (n=56): average 66.6kg (range: 33.1-105kg) Male (n=33): average 77.9kg (range: 63-125kg)
Top 4 medical specialties	Haematology=32, general medicine=19, acute medicine=18, gastroenterology=10
Bleeding patients (indication code R1 or 'massive bleeding' indicated)	19
Non-bleeding patients (other indication codes or not stated)	141

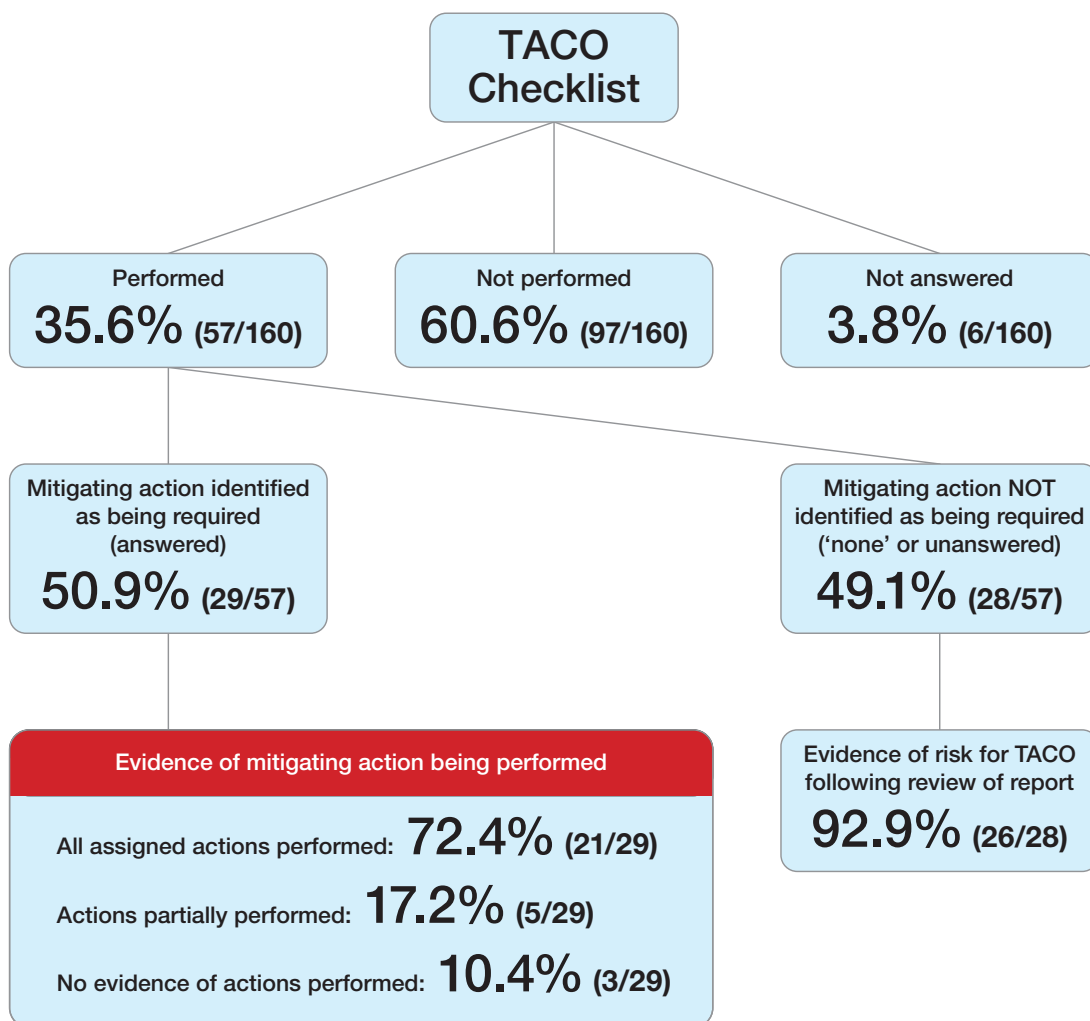
Commentary

TACO is more commonly reported in elderly, non-bleeding patients but is seen across all age groups and is consistent with the data from previous years. There were 3 cases in the under-18 age group, (newborn to age 17 years). TACO was reported more in adult female patients compared to male. Weight was provided in 33 adult female cases, with an average of 66.6kg (33.1-105kg). Weight was provided in 34 adult male cases, with an average of 77.9kg (63-125kg). 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 targeting TACO education and mitigation plans.

Use of the TACO risk assessment

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.2. The TACO risk assessment was not used in 60.6% (97/160) cases. This is a similar level compared to 2021.

Figure 17a.2:
Use of the checklist to identify patients at risk of TACO and implementation of mitigating actions



The TACO checklist was reported to have been used in only 57/160 (35.6%) 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 29/57 (50.9%), it demonstrated the need for a mitigating action and in most cases, these were taken. In some cases, additional measures could also have been instigated. There were 3 cases where assigned actions had not been carried out and 5 where the actions were only partially completed. Where a TACO checklist was performed and it was determined a mitigating action was not required, a review of these reports showed that 26/28 (92.9%) 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 risk and help make safe transfusion decisions. It is not clear from the data whether this is due to improper use of the TACO checklist or whether this reflects lack of clinical knowledge to perform the risk assessment.

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

There were 68 cases where a pre-and post-transfusion Hb was provided. In 18/68 (26.5%) cases there was evidence of excessive red cell transfusion to meet the Hb target. Of these 17/18 (94.4%) had a Hb above 100g/L. In 2 cases these were inappropriate transfusions based on the pre-transfusion Hb level.

The number of units transfused, and body weight were provided in 10/68 (14.7%) of these cases. Excluding the two inappropriate transfusions the number of units transfused was excessive based on the patient’s weight and pre-transfusion Hb level in 6/10 cases. In 2/10 cases patients with severe chronic

anaemia only required minimal transfusion to alleviate the symptoms of anaemia. Three and six units of red cells were transfused in these cases. This underlines the importance of weight-adjusted red cell dosing to avoid the risks of overtransfusion.

Cases involving severe chronic anaemia

Severe anaemia was added to the TACO checklist following a signal previously observed in the data (Narayan et al. 2019). Non-bleeding adult patients with severe chronic anaemia are particularly vulnerable to TACO even in the absence of additional risk and comorbidities that are known to predispose TACO.

In 39/160 cases there was a Hb <60g/L. Of these, 7/39 cases were severe anaemia due to haemorrhage or erroneous Hb measurement. The remaining 32/39 cases were severe chronic anaemia and 7 had clear evidence of iron deficiency. There is still evidence that iron replacement (including intravenous iron) is not being administered to patients with iron deficiency anaemia. Transfusion of excessive volumes of red cells, lack of consideration of patients with low body weight, and evidence of aiming for a Hb target that is intended for the correction of acute anaemia increase the risk of TACO in these patients. Patients with severe chronic anaemia should receive only minimal red cell transfusion with the aim of alleviating symptoms as opposed to aiming for Hb correction to meet a target Hb level.

Case 17a.1: Severe chronic iron deficiency anaemia in a patient with low body weight

A female patient in her 80s with a low body weight (49kg) was asymptomatic and haemodynamically stable with severe microcytic hypochromic anaemia (Hb44g/L) with no clinical signs of pulmonary oedema on the chest X-ray or clinical examination. Three units of red cells were transfused over a period of 15 hours because the attending doctor was aiming for a post-transfusion Hb of 70-90g/L. The patient developed respiratory compromise (desaturation from 100% on room air to 71%, with dyspnoea, wheeze, and tachypnoea). There were new cardiovascular changes: tachycardia (heart rate 131bpm) and hypertension (blood pressure 204/96mmHg). Fluid balance was not clearly documented. Additional fluid was not involved. A diuretic was given but the patient deteriorated and died, therefore a diuretic response could not be evaluated. There was clear evidence of overtransfusion as the post-transfusion Hb was 111g/L. The patient did not otherwise have comorbidities predisposing circulatory overload. The post-transfusion chest X-ray showed pulmonary oedema.

This was a complex case which was referred to the coroner. The post-mortem examination report described pulmonary oedema and congestion of the lungs. The histopathology findings on the lung tissue were interpreted as TRALI by the histopathologist due to the presence of fibrinous exudate and neutrophil polymorphs in the alveoli which is indicative of an inflammatory process. The symptoms, signs and the clinical context met the haemovigilance criteria for TACO and was reported as such by the hospital to SHOT and per legal obligations to the MHRA. As TRALI had been cited in the post-mortem report there was an obligation to report this to the Blood Service. A clinical assessment for TRALI was performed and it was agreed the case met the TACO criteria, not TRALI. Blinded opinion was sought from the two other members of the SHOT Pulmonary Complications of Transfusion WEG who also agreed this was TACO. All agreed that a TRALI investigation (involving the testing of recipient and donors) was not indicated based on the clinical assessment criteria for pulmonary complications of transfusion. A TRALI assessment had only been initiated based on the interpretive comments in the histopathology and the post-mortem reports.

The purpose of considering a TRALI investigation was not to differentiate TACO and TRALI for the purpose of determining the cause of death, rather a potential public health concern should any of the donors have a clinically significant HLA or HNA antibody that could potentially cause a similar reaction in another recipient. A TRALI investigation would normally require testing of the recipient to demonstrate a match between donor antibody and recipient tissue-type. The only biological specimen available were paraffin blocks of lung tissue. As testing procedures are validated on blood samples (not tissue in paraffin histology blocks), any results would be unvalidated and reliability unknown. The absence of HLA/HNA antibodies in the donors would exclude antibody-mediated TRALI, however if present it could not be excluded if recipient typing was not possible.

The conclusions regarding the type of pulmonary complication of transfusion differed as haemovigilance criteria and histopathology are each based upon different evidence however it was agreed the patient had a pulmonary complication of transfusion. The understanding of the pathogenesis of TACO is incomplete and it is widely agreed that there may be an inflammatory aspect, and therefore the presence of fibrinous exudate and neutrophil polymorphs in the alveoli of the lung does not exclude TACO. A negative TRALI investigation would not exclude 'antibody-negative' TRALI, and indeed TACO and TRALI may co-exist (Bosboom et al. 2019).

The patient was at risk of TACO due to her low body weight and severe anaemia. A TACO risk assessment would have identified this and should have prompted single unit/weight-adjusted red cell dosing, prophylactic diuretic etc. Despite this, the attending doctor was aiming for a significantly higher target Hb as would have been appropriate if the patient had stable acute anaemia. The patient had asymptomatic severe chronic iron deficiency and therefore a small volume red cell transfusion (to improve any symptoms of anaemia and minimise risk of cardiac ischaemia), followed by intravenous iron replacement was indicated.

Cases with evidence of a structured investigation

Previous data suggested there was a lack of structured investigation following cases of TACO, resulting in missed opportunities to mitigate the risk of TACO and to improve transfusion safety for all patients. The TACO structured investigation tool was first launched 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. The template was used by only 37/160 (23.1%) of reporters in 2022. A structured review and incident investigation should be undertaken for every case of TACO to optimise organisational and individual patient-safety measures.

Learning points

- Severe chronic anaemia (asymptomatic or minimally symptomatic) requires only minimal transfusion (usually a single unit) followed by pharmacological treatment where appropriate
- Non-bleeding adult patients with severe chronic anaemia are particularly vulnerable to TACO even in the absence of other risk factors and comorbidities that predispose to TACO



Conclusion

The continued adoption of the TACO checklist is encouraging though analysis of the data shows it is still under-used or used ineffectively. There has been some uptake of the TACO structured assessment tool, but the data suggest that there is significant 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. Overtransfusion of red cells also remains an issue which could be minimised by weight-adjusted or single unit transfusion in non-bleeding patients. The transfusion management of patients with severe chronic anaemia is concerning and resulted in a patient death this year due to excessive transfusion. There are several strategies now available to mitigate the risk of TACO based on many years of haemovigilance data. Everyone involved in the transfusion process has a professional duty to protect patients from TACO wherever possible.

With an increasing number of TACO cases reported to SHOT year-on-year, including instances of preventable deaths, a TACO safety alert is being planned to be released UK-wide by SHOT through the MHRA. This will help promote implementation of measures to enhance safety and facilitate appropriate transfusion decisions. The NBTC indication codes are also being reviewed currently and an updated version is expected to be released soon. Identifying risk-factors for TACO in vulnerable patients prior to transfusion helps initiate appropriate mitigating measures. Some TACO deaths are preventable.



Recommended resources

Example of weight-adjusted red cell dosing implemented in clinical practice
www.rcdcalculator.co.uk

TACO Incident Investigation Guidance Tool
<https://www.shotuk.org/resources/current-resources/>

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/>

Patient Blood Management - Blood assist app
 Apple (<https://apps.apple.com/gb/app/blood-assist/id1550911130>)
 Google play (<https://play.google.com/store/apps/details?id=uk.nhsbt.bloodassist>)
 Web based (<https://www.bloodassist.co.uk/>)

References

- Bolton-Maggs PHB (Ed), D Poles 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 27 April 2023].
- 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.tmv.2019.01.003. Epub 2019 Feb 7. PMID: 30853167.
- 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 28 April 2023].
- 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.
- Narayan S, Grey S, Bolton-Maggs P, et al. Is severe anaemia an independent risk factor for TACO? Case based discussions based on TACO reports to SHOT, the United Kingdom haemovigilance scheme. *Vox Sang.* 2019;**114(1)**:5-240.P-533.
- Narayan S (Ed), Poles D, et al. on behalf of the Serious Hazards of Transfusion (SHOT) Steering Group. The 2020 Annual SHOT Report (2021). <https://www.shotuk.org/shot-reports/> [accessed 27 April 2023].
- 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].
- 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.