13b Transfusion-Associated Circulatory Overload (TACO) n=89

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Transfusion-associated circulatory overload (TACO) remains without an agreed definition. The International Society of Blood Transfusion (ISBT) working party continues its work to refine and agree a definition that can be used to identify cases and assign a level of likelihood.

Key SHOT message

- TACO must be suspected where there is respiratory distress that improves with treatment for circulatory overload (diuretics, morphine and nitrates). It is important to report these cases to SHOT

Definition:

Current ISBT definition (revision in progress)

Any 4 of the following within 6 hours of transfusion

- **Acute respiratory distress**
- **Tachycardia**
- **Increased blood pressure**
- **Acute or worsening pulmonary oedema**
- **Evidence of positive fluid balance**

89 cases were analysed compared to 91 in 2014.

Demographic overview of cases

Table 13b.1: Demographic overview of cases

Demographic	Number of reports
Deaths	7
Major morbidity	34
Age	6 days to 97 years (median 73 years)
Top three clinical specialties	Acute medicine (15), general medicine (13), haematology (12)
Bleeding patients	21 (indication code R1 – acute blood loss)
Non-bleeding patients	60 (other indication codes)
Unknown bleeding status	8 (no indication code given)
Single unit of red cells transfused	14

Where death was recorded, TACO was reported to be contributory in 7 cases (likely/probable n=2; possible n=5; excluded/unlikely n=6; not assessable n=1). There were 34 cases reported with either long-term morbidity (2, likely/probable n=1; possible n=1), or where there were signs and symptoms with risk to life with full resolution (n=32, certain n=2; likely/probable n=20; possible n=10).

The age range was 6 days to 97 years. Two cases involved neonates, one a month-old baby, and one

baby aged 1 year. One patient was aged 16 years, and the remaining cases were over 18 years of age. TACO can occur at any age and more commonly occurs in older adults. The young and elderly are both highly transfused populations, yet the incidence of TACO is reported disproportionately. This may reflect the more common practice of body weight dosing in the young, and the presence of comorbidities that predispose to circulatory overload in the elderly. The majority of patients were in medical specialties and received transfusion for normovolaemic anaemia. There were 14 reports that involved only a single unit of red cells. It is probable that TACO is more likely with red cell transfusion as red cells represent mass as opposed to a fluid which may be more readily removed by diuresis.

Diagnosis of TACO

It is accepted that current definitions for TACO are unsatisfactory. Some symptoms and signs are non-specific and some diagnostic procedures may not be readily available, or are more suited to a high care environment. This may result in under or over-attribution of TACO and/or the level of diagnostic certainty. Given the lack of agreement on a suitable definition for TACO, cases were assessed (as last year) against two sets of diagnostic criteria: clinical prioritisation of key features (CPKF) and the draft revised ISBT (DISBT) criteria.

CPKF

- Acute respiratory distress (in the absence of other specific causes)
- Acute or worsening pulmonary oedema on imaging
- Evidence of a positive fluid balance
- Evidence of volume intolerance (response to treatment for circulatory overload or evidence of pulmonary oedema on clinical examination)

TACO was considered to be ‘highly likely’ with three or more features, or acute respiratory distress with pulmonary oedema on imaging; ‘probable’ with acute respiratory distress and clinical improvement with diuretic therapy (volume intolerance); and ‘possible’ with acute respiratory distress with evidence of a positive fluid balance.

DISBT

Acute or worsening respiratory distress within 6 hours of transfusion (some cases may occur up to 12 hours)

Primary features

- Evidence of acute or worsening pulmonary oedema with bilateral infiltrates
- Enlarged cardiac silhouette on imaging – enlarged heart contour should always be present if looked for
- Evidence of fluid overload – could be a positive fluid balance or a response to diuretic therapy combined with clinical improvement

Supporting features

- Elevated brain-natriuretic peptide (BNP) or N-terminal (NT)-pro BNP to more than five times the pre-transfusion value (if available)
- Increased mean arterial pressure (MAP). MAP=DBP+1/3 (SBP-DBP) or, increased pulmonary wedge pressure. The MAP is typically raised, often with a widened pulse pressure. There may be hypotension in acute cardiac collapse. (DPB=diastolic blood pressure and SBP=systolic blood pressure)

‘Definite’ cases must have at least two primary features, or one primary and two supporting features. Cases with only one primary feature (e.g. without chest imaging) may be considered ‘probable’ or ‘possible’ depending on the presence of other supporting features.

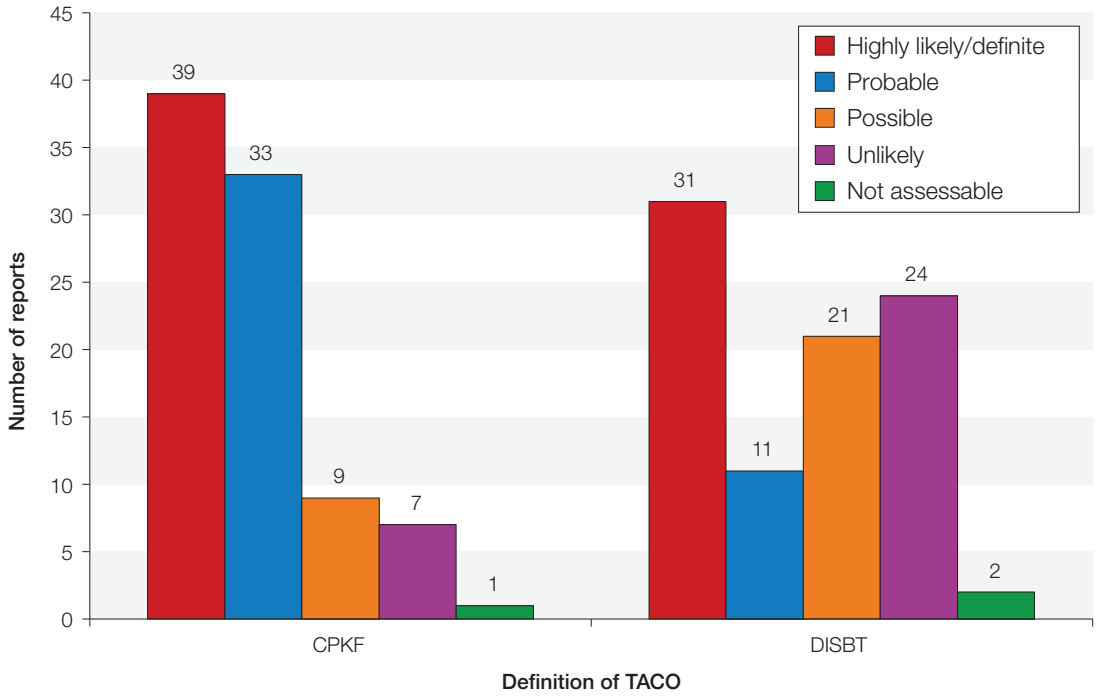
Comparison of assessments

This year 89 cases were analysed after withdrawals and transfer of some cases to other categories. Table 13b.2 and Figure 13b.1 below compare the likelihood of TACO by each definition.

Table 13b.2: Diagnostic likelihood by two definitions

Likelihood	CPKF	DISBT
Highly likely/definite	39	31
Probable	33	11
Possible	9	21
Unlikely	7	24
Not assessable	1	2
Total	**89**	**89**

Figure 13b.1: Likelihood by two definitions



Two observations can be made. More cases are identified by CPKF criteria compared to DISBT criteria. This reflects both the lack of availability of BNP testing and routine reporting of the cardiac silhouette. The numbers of 'probable' and 'possible' cases are reversed when both definitions are compared. This probably reflects the lack of demarcation between 'probable' and 'possible' in the DISBT definition.

Inter-assessor variability: a case for standardisation of assessment

This year a sample of reports was assessed by two experienced individuals using both definitions (CPKF and DISBT) to understand inter-assessor variability and to identify issues with the current criteria. Table 13b.3 shows the results of the audit.

Assessment variability	Number of reports audited
Number of assessments with complete agreement	27 (34.6%)
Number of assessments with minor discrepant assessments (within one likelihood level)	40 (51.3%)
Number of significantly discrepant assessments (more than one likelihood level)	11 (14.1%)
Total number of reports audited	**78**

Table 13b.3: Audit of inter-assessor variability

There was a high level of concordance for assessments that were in complete agreement or were discrepant to only a minor extent (within one level of likelihood). However the level of significantly discrepant assessments highlighted potential issues with interpretation and application of existing criteria, and these cases were further analysed by a panel case review. The rationale for all discrepant assessments were agreed to be justifiable and highlighted a number of issues.

- There was evidence of deviation from strict application of assessment criteria. Current criteria may not be sufficiently sensitive or flexible to account for the impact of incomplete history or investigations (or serial investigations for comparison), and for the presence of confounding medical factors in some presentation scenarios. This is especially evident with respect to the DISBT criteria concerning imaging of the cardiac silhouette and BNP/N-terminal (NT)-pro BNP which are often not performed. This limits the usable assessment criteria resulting in some cases having the likelihood of TACO reduced when there is an overall persuasive picture
- The diagnostic assessment could be finessed by weighting the strength of evidence from a particular clinical finding, and accounting for confounding factors such as the concomitant administration of diuretics and anti-allergy medications. A logic-based application may further support a standardised approach (discussed in the next section)

The findings and recommendations from this audit will be shared with the ISBT Haemovigilance Working Party to contribute to the ongoing refinement of the TACO definition and assessment criteria.

The following case was assessed as 'highly likely' by CPKF and 'unlikely' by DISBT definitions. It highlights the difficulty in diagnosing TACO when confounding clinical features are present.

Case 13b.1: Confounding clinical features leading to conflicting assessments

A patient with pre-existing congestive cardiac failure (CCF) and acute renal failure was admitted to an emergency department complaining of shortness of breath and swollen legs. The patient was prescribed a diuretic and two units of red cells (Hb 74g/L). Pre-transfusion vital sign observations were normal except for slightly low oxygen saturation. After three quarters of the unit had been transfused the patient experienced rigors, tachycardia, shortness of breath, tachypnoea, mild fever, mild periorbital oedema and bilateral wheeze. The transfusion was stopped and the patient was treated with a bronchodilator, antihistamine and steroid, and continued on oxygen. Six hours later the oxygen saturation dropped further and crackles could be heard in the chest. The chest X-ray revealed increased pulmonary oedema compared to the previous image. Treatment with an intravenous diuretic did not result in adequate diuresis and there was no change to the patient's respiratory function. The patient eventually recovered and survived.

Comment: This case was complicated by the presence of inflammatory symptoms, but TACO was considered 'highly likely' by panel review given pre-existing CCF and increasing pulmonary oedema. Lack of improvement following medication for allergy also suggests the respiratory distress was more likely to be related to TACO than to the allergic features. The lack of improvement following diuretics was due to inadequate diuresis because of renal failure. Consequently, the case had only one primary feature (increasing pulmonary oedema) by the DISBT criteria and no supporting features and therefore categorised as 'unlikely'. It also highlights that transfusion complications can co-exist.

TACO calculator: the effect of standardised assessment

A Microsoft Excel-based application was developed which calculated the likelihood of TACO based on the presence of weighted symptoms and signs across four diagnostic categories (Figure 13b.2) to produce an aggregated score. Every permutation of scenarios was evaluated as 'certain', 'probable', 'possible' or 'unlikely' depending on the score.

Figure 13b.2: TACO calculator weightings

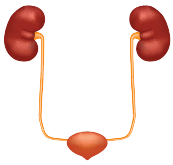
Diagnostic Category	Status	Score
 Respiratory	Acute or worsening respiratory distress with no apparent alternative cause	2
	Acute or worsening respiratory distress with possible alternative cause	1
 Imaging	Pulmonary oedema (+/- cardiomegaly) not on pre-transfusion image, OR worsening compared to pre-transfusion image	2
	Pulmonary oedema (+/- cardiomegaly) on imaging with no pre-transfusion image for comparison, OR no change from previous image	1
	Pulmonary oedema not present on image, OR no image available	0
 Fluid Balance	Clinically significantly positive fluid balance	1
	Unable to assess fluid balance	0
	Neutral or negative fluid balance	-1
 Diuretics	Improvement with diuretics and/or morphine and nitrates alone (not administered with steroid, anti-histamine or bronchodilator)	2
	Improvement with diuretics and/or morphine and nitrates (also administered with steroid, anti-histamine or bronchodilator)	1
	No improvement or worsening after diuretic	-1
	Unable to assess response to diuretic or diuretic not given	0

Table 13b.4 and Figure 13b.3 show a comparison of the results.

Table 13b.4: Comparison of CPKF and DISBT assessments against TACO calculator assessments

Assessment	CPKF	DISBT	TACO calculator
Highly likely/definite/certain	39	31	2
Probable/likely	33	11	43
Possible	9	21	36
Unlikely	7	24	7
Not assessable	1	2	1
Total	**89**	**89**	**89**

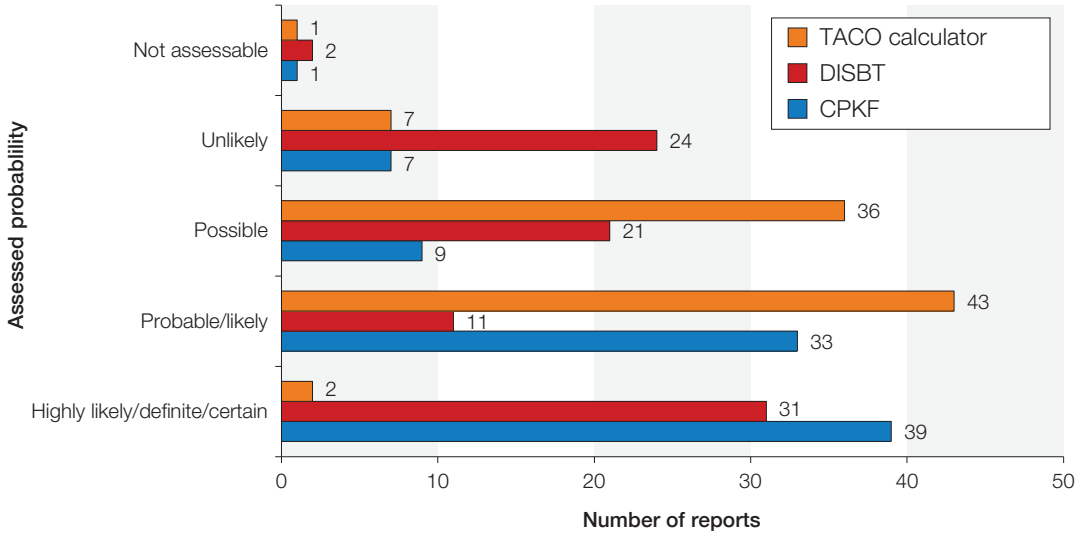


Figure 13b.3: Comparison of CPKF and DISBT assessments against TACO calculator assessments

The TACO calculator had strict high scoring criteria for 'certain' and produced fewer definite cases. The calculator is a prototype and requires further validation and possible re-calibration. It may be a useful tool in the future to facilitate reproducible and standardised diagnostic assessments, especially where there are confounding features and lack of an agreed definition for TACO.

Thematic analysis of 'definite' and 'highly likely' cases

There were 41 cases where the diagnostic likelihood was considered to be 'highly likely' by CPKF and/or 'definite' by DISBT definitions. The assessment for each case was summarised by the key factors that were judged to have contributed to TACO. These summaries were thematically analysed and results shown in Figure 13b.4.

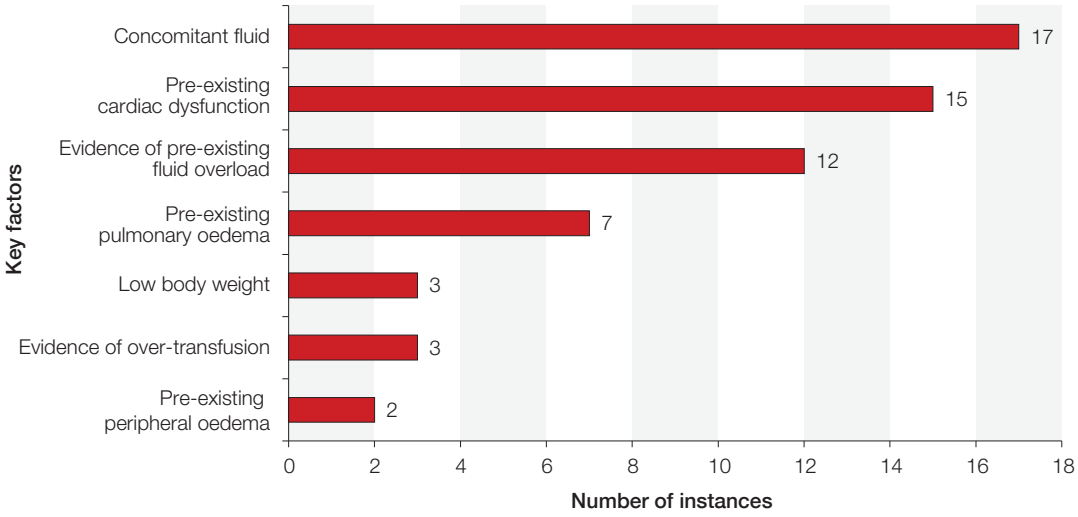
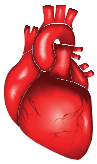


Figure 13b.4: Thematic analysis of 'definite' and 'highly likely' case summaries

Fifty nine instances of significant key factors were identified across the 41 cases. Fluid management was the most significant theme. The administration of concomitant fluid with the transfusion or in the 24 hours prior was the most frequent finding, followed by evidence of pre-existing fluid overload and pre-existing cardiac dysfunction. Other signs of potential fluid intolerance were pre-existing pulmonary oedema, low body weight and pre-existing peripheral oedema. Three patients developed TACO after being given an excessive volume of red cells to achieve their target Hb. These themes provide a useful basis for a pre-transfusion TACO risk assessment in the form of a checklist (Figure 13b.5).

An order set and checklist for TACO has been successfully piloted in Toronto demonstrating increased compliance following their introduction (Tseng et al. 2016).

Figure 13b.5: TACO risk assessment/ pre-transfusion checklist

TACO Checklist	Red Cell Transfusion for Non-Bleeding Patients
	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?
	Is the patient known to have pulmonary oedema? Does the patient have respiratory symptoms of undiagnosed cause?
	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?

If 'yes' to any of the above

1. Review the need for transfusion (do the benefits outweigh the risks)?
2. Can the transfusion be safely deferred until the issue can be investigated, treated or resolved?
3. Consider body weight dosing for red cells (especially if low body weight)
   - Transfuse one unit (red cells) and review symptoms of anaemia
   - Measure the fluid balance
   - Consider giving a prophylactic diuretic
   - Monitor the vital signs closely, including oxygen saturation

Case 13b.2: Inappropriate transfusion in a patient with CCF and poor fluid management

A patient with pre-existing CCF developed rectal bleeding following surgery. Four units of FFP were given to reverse warfarin over a total duration of one hour (two of which were given simultaneously), and a litre of crystalloid was also given. Three hours after the transfusion, the patient developed shortness of breath, reduced oxygen saturation, tachycardia, tachypnoea, hypertension and pulmonary oedema. No fluid balance had been recorded. The patient's respiratory function improved following treatment with diuretics, antihistamine and nitrates. The patient required admission to the intensive therapy unit and subsequently recovered.

Comment: Patients with cardiac dysfunction are at risk of fluid overload and require careful fluid management including the decision whether to transfuse. FFP had been given inappropriately (the patient should have received prothrombin complex concentrate which also represents a smaller infusion volume). The FFP had been given quickly with concomitant non-blood fluid, and with no fluid balance assessment in place.

Recomendation

- A formal pre-transfusion risk assessment for transfusion-associated circulatory overload (TACO) should be performed whenever possible as TACO is the most commonly reported cause of death and major morbidity. An example is shown in Figure 13b.5

Action: Trust/Health Board Chief Executive Officers and Medical Directors responsible for all clinical staff

Reference

Tseng E, Spradbrow J et al. (2016) **An order set and checklist improve physician transfusion ordering practices to mitigate the risk of transfusion-associated circulatory overload**. Transfus Med http://onlinelibrary.wiley.com/doi/10.1111/tme.12284/pdf [accessed 15 May 2016]