Transfusion-Associated Circulatory Overload (TACO) n=86

18b

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Last year's analysis of SHOT data made a significant contribution to progress toward internationally agreed surveillance reporting criteria for TACO. The revision group representing the International Society of Blood Transfusion (ISBT) working party on haemovigilance in collaboration with the International Haemovigilance Network (IHN) produced new draft haemovigilance reporting criteria in 2016. The reports that have contributed to the 2016 data for this year's Annual SHOT Report played a key role in validating the new draft reporting criteria for TACO.

While there is still no single agreed reporting definition, SHOT continues to emphasise the importance of reporting all suspected cases of TACO.

Key SHOT message

- TACO must be suspected when there is respiratory distress with other signs, including pulmonary oedema, unanticipated cardiovascular system changes, and evidence of fluid overload (including improvement after diuretic, morphine or nitrate treatment), during or up to 24 hours after transfusion

Recommendation

- 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 transfusion-related death and major morbidity. An example is shown in Figure 18b.1

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

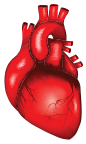
TACO Checklist	Red cell transfusion for non-bleeding patients	If 'yes' to any of these questions
	Does the patient have a diagnosis of 'heart failure' congestive cardiac failure (CCF), severe aortic stenosis, or moderate to severe left ventricular dysfunction? Is the patient on a regular diuretic?	1 • Review the need for transfusion (do the benefits outweigh the risks)?
	Is the patient known to have pulmonary oedema? Does the patient have respiratory symptoms of undiagnosed cause?	2 • Can the transfusion be safely deferred until the issue can be investigated, treated or resolved?
	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?	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

Figure 18b.1: Revised 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.

Draft ISBT reporting criteria 2016

1. Acute onset or worsening respiratory distress during or up to 12 hours after transfusion

2. Two or more of the following:

- **Evidence of acute or worsening pulmonary oedema (by physical examination or chest imaging)**
- **Evidence of unanticipated cardiovascular system changes (tachycardia, hypertension, jugular venous distension, peripheral oedema)**
- **Evidence of fluid overload (positive fluid balance, response to diuretic therapy with clinical improvement, change in the patient's weight in the peri-transfusion period)**
- **Elevation in natriuretic peptide (NP) levels (e.g. brain-natriuretic peptide (BNP), N-terminal (NT)-pro BNP) to greater than 1.5 times the pre-transfusion value**

In 2016, 86 cases were accepted as TACO which is similar to the previous year.

Deaths n=14

There were 14 deaths where the transfusion was considered to be contributory, 1 definitely related, 5 probably related and 8 possibly related.

Major morbidity n=18

There were 18 cases of major morbidity where transfusion was judged to be contributory. Ten cases of major morbidity (e.g. requirement for high level of care) resulted in major (e.g. invasive interventions to treat the TACO) or minor sequelae (non-invasive interventions) for the patient.

Demographic overview of cases

Table18b.1: Demographic overview of cases

Demographic	Number of reports	
Deaths (imputability 3)	1	
Deaths (imputability 2)	5	
Deaths (imputability 1)	8	
Major morbidity (serious sequelae)	5	
Major morbidity (minor sequelae)	5	
Major morbidity (signs and symptoms with risk to life with full resolution/unknown outcome)	8	
Age	0 days to 94 years Median 74 years	
Medical specialties (where data were provided)	Haematology Other medical specialties Surgical specialties/ anaesthetics Paediatrics/neonatal/other	29.1% (25/86) 44.2% (38/86) 16.3% (14/86) 5.8% (5/86)
Bleeding patients (indication code R1 or 'massive bleeding' indicated)	6	
Non-bleeding patients (other indication codes or not stated)	80	
Cases receiving red cells only (no other blood components)	90.7% (78/86)	
Red cells alone (without other intravenous (IV) fluids)	66.7% (52/78)	

Age analysis continues to show that TACO affects all age groups and is especially prevalent amongst the elderly because of the frequency of co-morbidities that predispose the patient to volume intolerance. This underlines the need to perform a pre-transfusion risk assessment on patients to identify those at risk, and take mitigating actions where appropriate. Haematology was the single medical specialty with the greatest number of patients developing TACO. This is because haematology patients are among the

most intensively transfused patients, many of whom are also elderly. The majority of cases occurred in non-bleeding patients requiring red cell transfusion indicating that there was probably opportunity to risk-assess the patient prior to transfusion and take mitigating actions. Concomitant IV fluids can complicate the assessment of the degree to which blood contributed to circulatory overload. The analysis shows that around a third of patients receiving red cell transfusion were also receiving non-blood fluids. If a patient develops signs of circulatory overload during or after transfusion and was also receiving fluids at the same time, or in the preceding 24 hours, it is important to report these cases to SHOT. This does not affect a diagnosis of TACO but may reduce the imputability assessment.

Surveillance diagnosis of TACO: towards internationally-agreed criteria

In order to support the advance of this collaborative work, the 2016 TACO data were analysed by three sets of criteria, two of which were used last year: clinical prioritisation of key features (CPKF); the draft ISBT 2014 criteria (DISBT 2014); and the additional new 2016 draft ISBT criteria (DISBT 2016). Multiple analyses were performed for cases reported in last year's report which highlighted several important issues that led to potential over or under-attribution of TACO. Those issues were used to revise the DISBT (2014) criteria. The purpose of this year's multiple analyses was to validate the revised DISBT (2016) criteria to ensure that valid cases were identified, providing confidence in an agreed set of reporting criteria for future use, or identifying further areas for revision.

CPKF reporting criteria

Cases accepted with symptoms and signs occurring within 24 hours of transfusion:

- Acute/worsening respiratory distress (in the absence of other specific causes)
- Acute/worsening of 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 (2014) reporting criteria

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

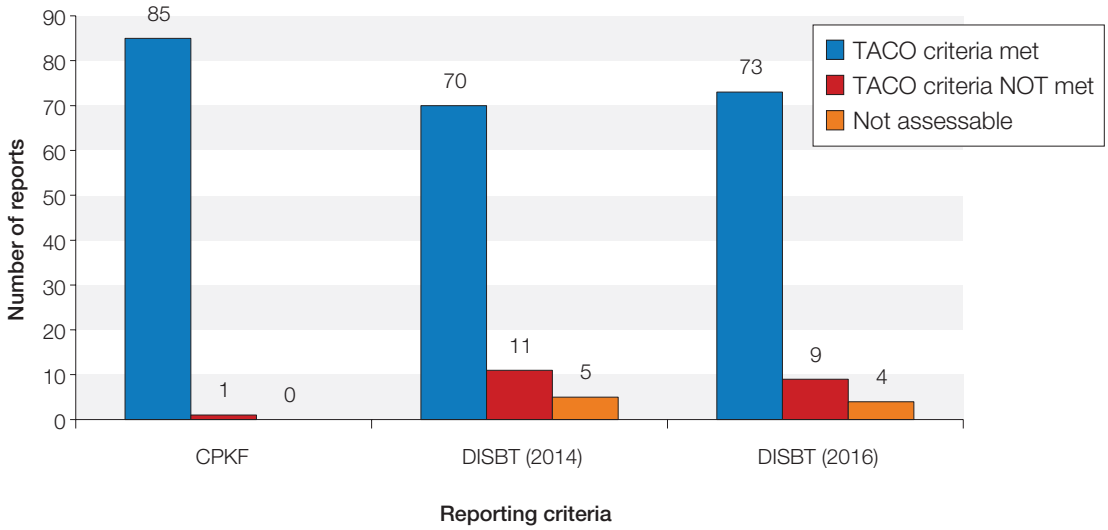
- Elevated BNP or NT-pro BNP to more than five times the pre-transfusion value (if available)
- Increased mean arterial pressure (MAP). MAP=DBP+1/3 (SBP-DBP) or, increased pulmonary wedge pressure. The MAP is typically raised, often with a widened pulse pressure. There may be hypotension in acute cardiac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

This year 86 cases were analysed after withdrawals and transfer of some cases to other categories. Figure 18b.2 below compares each set of reporting criteria for cases which met the standards for TACO. CPKF and DISBT (2014) both employ a graded likelihood assessment (highly likely/definite, probable or possible), but the DISBT (2016) criteria only require the case to meet the minimum criteria without reference to likelihood. In order to standardise the comparison any cases with a positive degree of likelihood for CPKF or DISBT (2014) were considered to meet the criteria for TACO.

Figure 18b.2: TACO assessment by three sets of reporting criteria



There were 81.4% (70/86) of cases that met the criteria for TACO across all three reporting criteria. The 18.6% of cases (16/86) which did not agree provided useful data to further evaluate reasons for discrepancy, as detailed below.

TACO reporting criteria met for CPKF but not for DISBT (2014) and DISBT (2016) n=7

This related to timing of symptoms and signs occurring after 12 hours (n=2), and when there was only one other feature in addition to acute/worsening respiratory distress (n=5). Of the latter, this related to clinical improvement after diuretic only (n=3), and acute/worsening pulmonary oedema only (n=2). The significance of this could be argued two ways. Either the CPKF set of reporting criteria is over-sensitive, or that the DISBT (2014 and 2016) sets of reporting criteria may be too exclusive. This is compounded by BNP not being performed or available in the UK, meaning that there are fewer additional criteria usually available for assessment (only one case had a BNP performed in this reporting year). However five of the cases were assessed as 'probable' or 'possible' (i.e. lower likelihood descriptors) by the CPKF set of reporting criteria suggesting some lack of confidence in certainty. The remaining two cases were assessed as 'highly likely' but this was only based on acute/worsening respiratory distress and acute/worsening pulmonary oedema alone which may be insufficient for a confident surveillance diagnosis.

TACO reporting criteria met for CPKF and DISBT (2014) but not for DISBT (2016) n=1

This related to enlarged cardiac silhouette not being represented separately in the DISBT (2016) set of criteria and therefore not meeting the required minimum of two additional features. This was a neonate in whom there was pulmonary oedema but no other features. The baby had normal mean arterial pressure and heart rate for age. Enlarged cardiac silhouette is described in the pulmonary oedema criterion of the DISBT (2016) reporting criteria. If enlarged cardiac silhouette counted as a positive feature for unanticipated cardiovascular system changes, then this case would have met the DISBT 2016 set of criteria for TACO.

TACO reporting criteria met for CPKF and DISBT (2016) but not for DISBT (2014) n=4

Tachycardia was added to the DISBT (2016) set of criteria for unanticipated cardiovascular system changes. Cases where there was only one additional feature (pulmonary oedema or evidence of fluid overload) without changes to the blood pressure and where BNP was not performed, meant that the presence of tachycardia provided further positive evidence for TACO where previously the case would have been assessed as 'unlikely'.

TACO reporting criteria met for CPKF but not assessable by DISBT (2014) and DISBT (2016) n=4

Cases where there was only acute/worsening respiratory distress and acute/worsening pulmonary oedema are assessed as 'highly likely' by the CPKF set of reporting criteria, as no other diagnostic features are required. However, if the reporter has been unable to provide details of vital sign observations, response to diuretics, fluid balance etc., these cases are un-assessable by DISBT (2014) and DISBT (2016) sets of reporting criteria. Comprehensive case data provided by the reporter are important in ensuring robustness of the assessment.

Observations to inform further revision of the DISBT (2016) reporting criteria

- It may be useful to include cases where symptoms and signs occur up to 24 hours after transfusion. SHOT data show that there were 26 cases of TACO reported as occurring within 12-24 hours of transfusion 2010-2016 inclusive
- Enlarged cardiac silhouette should be included in the criteria for unanticipated cardiovascular system changes (not in the pulmonary oedema criteria regarding radiographic imaging)
- The introduction of tachycardia into the DISBT (2016) reporting criteria regarding unanticipated cardiovascular system changes has increased inclusivity of cases
- The CPKF reporting criteria may perhaps over-attribute TACO, especially where there is only pulmonary oedema as an additional feature and/or when there may be important data missing for a comprehensive and robust assessment

Validation of the TACO checklist

A TACO risk assessment in the form of a checklist was a recommendation in last year's report. This year's data were audited against the checklist and showed that 79.1% (68/86) of cases showed at least one positive feature on the checklist. Although this does not imply that TACO could have been prevented, it does endorse the sensitivity of the checklist for identifying risk factors and co-morbidities in patients who are at risk of TACO, allowing opportunity for intervention. Some transfusions will need to proceed despite risks for TACO being present but this should be conducted as a risk-balanced decision with mitigations put in place as far as possible, such as ensuring the appropriate dose of red cells to achieve the target haemoglobin level, prophylactic diuretics and close monitoring.

Case 18b.1: Urgent transfusion in the presence of risk factors for TACO

A patient with renal failure weighing 37kg with pre-existing fluid overload required red cell transfusion for severe symptomatic anaemia, haemoglobin (Hb) 50g/L). The patient had clinical signs of pulmonary oedema (raised jugular venous pressure, dyspnoea and frothy sputum). The patient also had a pericardial effusion and had required multiple resuscitations. One unit of red cells was prescribed and within an hour of starting the transfusion the patient began to complain of chest pain with increased work breathing, pyrexia, hypertension and tachycardia. The chest X-ray showed features of pulmonary oedema. The transfusion was stopped and the patient was given oxygen and underwent urgent haemodialysis with improvement in the symptoms.

Although the reporter did not explain why the transfusion could not be given at the same time as haemodialysis for optimum fluid management in this renal patient, it was clear that the patient required urgent transfusion. The patient had multiple risk factors for circulatory overload in addition to being overloaded prior to transfusion. Urgent transfusions are required even in the presence of risk factors for circulatory overload and this must be undertaken as a risk-balanced decision.

Mitigations and control measures are sometimes difficult to perform in time-limited situations, and especially challenging in renal failure where prophylactic diuretics may be contraindicated. There were many other examples in the reports where risks were present and where transfusion could have been deferred, treated or investigated prior to transfusion, highlighting cases of TACO that could potentially have been prevented.

Case 18b.2: Multiple positive features on the TACO checklist where TACO could probably have been prevented

An elderly patient weighing 51kg with pre-existing congestive cardiac failure (CCF) (ejection fraction 30%) and aortic stenosis received regular transfusions due to non-Hodgkin lymphoma. She was admitted with worsening dyspnoea and epigastric/chest pain. Two hours into the transfusion of a red cell unit she developed tachypnoea. The chest X-ray was suggestive of some infective consolidation but also pulmonary oedema/progressive heart failure compared to the previous image. She improved after diuretic treatment. The post-transfusion Hb was 98g/L.

Interestingly, this case was submitted as transfusion-associated dyspnoea (TAD) on the basis that there was no change in blood pressure or heart rate in this patient. The presence of pulmonary oedema and clinical response to diuretic treatment is good evidence of TACO by all reporting criteria discussed in this chapter. This patient had multiple risks as defined by the TACO checklist: CCF, aortic stenosis, and dyspnoea of undiagnosed cause (which may have been developing pulmonary oedema secondary to her pre-existing CCF). The reporter did not include the pre-transfusion Hb, but the post-transfusion Hb was 98g/L suggesting that the patient did not have severe anaemia requiring transfusion at the time of admission. She had low body weight so a dose-calculated partial unit may have been appropriate if she required transfusion at all.

The 20.9% (18/86) of cases that did not register positive features on the TACO checklist were evaluated for factors that could otherwise have potentially indicated that the patient was at risk of circulatory overload. These were grouped into those that could, or could not be prospectively identified.

Could not be prospectively identified n=12

- No obvious pre-disposing risk factors (but the patient's full past medical history was not available to SHOT to fully assess) (n=6)
- A condition that pre-disposed the patient to circulatory overload that was subsequently diagnosed as a result of the patient developing TACO (acute renal failure, cardiac dysfunction, cardiac compression) (n=3)
- Possible alternative cause for pulmonary oedema (acute coronary syndrome) but TACO equally likely with no other pre-disposing risk factors for circulatory overload (n=2)
- Pulmonary oedema possibly developing before transfusion but respiratory symptoms attributed to the patient's underlying condition (e.g. asthma) (n=1)

Potentially could be prospectively identified n=6

- Neonate with severe anaemia (n=1)
- Low serum albumin in the absence of other risk factors (n=1)
- Renal failure in the absence of other risk factors (n=4)

This provides further evidence for updating the TACO pre-transfusion checklist as shown in the revised infographic (Figure 18b.1), and SHOT makes this recommendation again for this reporting year.

Persistent poor practice in common clinical scenarios

Disappointingly, there were a number of cases where inappropriate transfusion led to TACO, and this has been repeated year-on-year. The inappropriate use of fresh frozen plasma (FFP) to reverse warfarin and overtransfusion of patients with haematinic deficiency is still occurring.

Case 18b.3: FFP used instead of prothrombin complex concentrate (PCC) due to incorrect anticoagulant management rationale

A 75-year-old patient was admitted with suspected lower limb ischaemia. He was already anticoagulated with warfarin for a metallic mitral heart valve. He had a 'poor chest' making him unsuitable for general anaesthetic and therefore required regional anaesthesia. The consultant haematologist was asked to give advice regarding his perioperative anticoagulant management. The consultant advised that the patient was not suitable for PCC because he/she believed there was greater risk of valve-related thrombosis and so suggested FFP and vitamin K instead. Two units of FFP were given on the ward and a further two were to be given in theatre. On arrival in theatre his respiratory status had deteriorated with tachypnoea, reduced oxygen saturation and increased oxygen requirement. Pulmonary oedema was diagnosed. He was treated with nitrates and diuretics and recovered.

Patients with mechanical heart valves require careful perioperative anticoagulant management to prevent valve thrombosis, and also to prevent bleeding caused by the surgical procedure itself. Warfarin should be fully reversed preoperatively with PCC and vitamin K. Anticoagulation is then alternatively managed with unfractionated heparin to allow maximum control by keeping the un-anticoagulated period during surgery to a minimum. Warfarin can be resumed postoperatively. There is no advantage to using FFP over PCC to minimise the risk of thrombosis. Both provide vitamin K dependent clotting factors but PCC has the advantage of having complete and rapid reversal due to the much greater concentration of factors and is both more reliable than FFP, and gives a smaller IV volume. This was critical in this case where the larger volume of FFP caused circulatory overload and pulmonary oedema in this patient who required emergency surgery.

Case 18b.4: Bleeding on direct oral anticoagulants

A 69-year-old patient with a history of CCF had persistent bleeding while anticoagulated with a direct oral anticoagulant (anti-Xa inhibitor) for atrial fibrillation. His prothrombin time (PT) and activated partial thromboplastin time (APTT) were slightly prolonged. He was given four units of FFP to treat the bleeding. He became hypertensive and developed tachypnoea and hypoxia. Pulmonary oedema was diagnosed. The patient was treated with diuretics and recovered.

The anti-Xa inhibitor the patient was taking is known to cause prolongation of the PT and APTT. These agents are not reversible with FFP. This patient was particularly vulnerable to circulatory overload posed by the relatively large volume of the FFP dose due to his pre-existing CCF. These drugs have a relatively short half-life and therefore omission of the drug is often sufficient to restore normal haemostasis if the patient does not have renal impairment. In the presence of major bleeding, specific reversal agents should be administered where licensed and available (e.g. for dabigatran, an anti-IIa agent, see literature review in Chapter 11d, Incidents Related to Prothrombin Complex Concentrates). Omission of the drug may have been appropriate for this patient and the presence of the drug can be evaluated by drug-calibrated anti-Xa assays (where available) if there is doubt about its clearance. There are few data for the use of PCC but it may be considered if the bleeding cannot be controlled with other measures such as tranexamic acid, and if the specific reversal agent is not available.

Case 18b.5: Red cell overtransfusion in chronic megaloblastic anaemia leading to TACO

A 90-year-old patient was admitted with severe megaloblastic anaemia (Hb 41g/L) and worsening peripheral oedema due to CCF. The consultant haematologist recommended six units of red cells but the ward staff decided to administer three. The patient developed dyspnoea, hypoxia and fever during the transfusion. The duty doctor diagnosed pneumonia and then eventually fluid overload. The chest X-ray showed worsening pulmonary oedema compared to the previous image performed on admission. The patient was treated with diuretics and recovered. The reporter stated that they felt that it was difficult to attribute fluid overload to transfusion because the X-ray suggested some patchy consolidation and the patient had peripheral oedema on admission.

This elderly patient was clearly overloaded prior to transfusion due to CCF and severe anaemia, putting her at greater risk of developing TACO. Three units of red cells are excessive in this situation given the chronicity of the anaemia and the risk factors for overload, and it is fortunate the original recommendation for six units was not actioned. Severe megaloblastic anaemia causes impaired cardiac muscle function thus red cell transfusion should be avoided wherever possible because of the risk of causing potentially fatal circulatory overload. The diagnosis of TACO was complicated by the presence of fever and possible pneumonia. It is of course possible that circulatory overload and a septic condition can co-exist which may confound the diagnosis of fluid overload. It is important to recognise that a patient who has pre-transfusion fluid overload (evidenced by worsening CCF and peripheral oedema in this case) may experience exacerbation of overload by transfusion. This was a clear case of TACO caused by excessive transfusion of red cells where there were obvious risk factors for circulatory overload. A single unit or weight-based dose of red cells with a prophylactic diuretic and close monitoring, preceded by vitamin B12 therapy would have been appropriate.

References

International Society of Blood Transfusion Working Party on Haemovigilance in collaboration with the International Haemovigilance Network (2016) **Transfusion-associated circulatory overload (TACO) draft revised reporting criteria.**
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