



Transfusion-Associated Circulatory Overload (TACO): Underreported and Underappreciated

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Clinical Presentation: Transfusion-associated circulatory overload (TACO) is the post-transfusion development of cardiogenic pulmonary edema that leads to acute respiratory distress. Its onset, which typically is characterized by dyspnea, orthopnea, and cough, is seen within 6-12 hours of the transfusion's completion and may be accompanied by: (1) hypoxemia, (2) distended neck veins, (3) rales/crackles, (4) an S3 heart sound, (5) orthopnea/dyspnea, (6) hypertension, (7) tachycardia, (8) increased pulse pressure, (9) elevated central venous pressure (CVP), and (10) radiographic evidence of new or worsening pulmonary edema.¹⁻³

Definitions & Diagnostic Criteria: Two main definitions for TACO are used for diagnostic and surveillance purposes:

- 1) The Centers for Disease Control and Prevention's National Healthcare Safety Network (NHSN) has defined TACO as the new onset or exacerbation of three or more of the following within six hours of the end of a transfusion: (a) acute respiratory distress (dyspnea, orthopnea, cough), (b) elevated brain natriuretic peptide (BNP), (c) elevated central venous pressure, (d) evidence of left heart failure, (e) evidence of positive fluid balance, and/or (f) radiographic evidence of pulmonary edema.¹
- 2) The International Society of Blood Transfusion recently published a revised surveillance definition for TACO designed and validated to maximize agreement across hemovigilance systems. To satisfy their new definition, clear evidence must exist of "acute or worsening respiratory compromise and/or evidence of pulmonary edema" manifesting within 12 hours after the transfusion along with the identification of at least three criteria including: (a) either/both of the two mentioned immediately above, (b) "evidence of cardiovascular system changes not explained by the patient's underlying medical condition" (e.g., jugular venous distention and/or peripheral edema), (c) "evidence of fluid overload," and/or (d) the "supportive results of a relevant biomarker" (e.g., BNP or N-terminal propeptide [NT-proBNP]).^{2,3}

The diagnostic biomarkers for TACO include BNP and NT-proBNP. The latter analyte has a longer half-life than BNP; however, its clinically relevant cutoff values are currently unknown. A recent systematic review of TACO biomarkers concluded that the combination of a BNP <300 pg/mL and an NT-proBNP <2000 pg/mL could be used to rule out TACO, whereas, for an NT-proBNP >2000 pg/mL, a post-to-pre-transfusion NT-proBNP ratio of >1.5 supported a diagnosis of TACO.⁵ Further, a post-to-pre-transfusion BNP ratio of >1.5 with a posttransfusion level of at least 100 pg/mL yielded a sensitivity and specificity for TACO of greater than 80-percent.^{4,5} Unfortunately, the overall quality of the studies included was low⁴ and there is inconsistency

Key Points

- Transfusion-associated circulatory overload (TACO) is characterized by the post-transfusion development of cardiogenic pulmonary edema with attendant acute respiratory distress.
- Well-defined clinical and laboratory diagnostic indicators for TACO exist as do standardized hemovigilance definitions.
- Laboratory biomarkers, such as BNP and NT-proBNP (defined in full below), can contribute to the diagnosis of TACO but have suboptimal sensitivity and specificity.
- The assessment of patient risk factors prior to transfusion reduces the risk of TACO and facilitates therapy.

in the performance of these tests that further reduces the diagnostic usefulness of these biomarkers.

While evidence of pulmonary edema by chest radiography does not by itself establish the diagnosis of TACO, accompanying findings, such as engorged pulmonary arteries, a widened vascular pedicle, and an enlarged heart, can lend credence to the diagnosis. Echocardiography also is useful in assessing the ventricular systolic, diastolic, and valvular function. Normal values, however, do not exclude a diagnosis of hydrostatic pulmonary edema.⁶

Pathophysiology: TACO is a form of cardiogenic pulmonary edema that results from transfusion-induced volume overload. Accumulation of fluids in the pulmonary capillaries leads to increased hydrostatic pressure, thereby driving fluids out of the vessels and into the pulmonary interstitial space. A pulmonary venous pressure (measured as the pulmonary wedge pressure) ≥ 18 mm Hg can cause interstitial edema. A further rise in the pulmonary venous pressure to ≥ 25 mm Hg may result in fluid crossing the lung epithelium into the alveolar space.⁶

Incidence: The per-patient incidence of TACO has been estimated to range between 1-percent and 12-percent following transfusion.⁶ This variation is due to multiple factors including differences in clinical definitions, a lack (until recently) of objective diagnostic criteria, and dissimilarities in the use of blood products. Furthermore, active-versus-passive surveillance and reporting of TACO are known to be important factors in incidence studies, with passive surveillance mechanisms generally being associated with underreporting.⁶ A complementary reason for underreporting of TACO is that many healthcare providers do not recognize the critical evidence that is readily available to them. A nationwide survey in the Netherlands demonstrated how changes in vital signs – which are at the core of the diagnostic criteria and clinical presentation – were found not to influence TACO recognition/reporting by bedside physicians or hemovigilance workers.⁷

Platelet and plasma transfusions are associated with a TACO incidence of approximately 1-percent while red blood cell (RBC) transfusions are associated with an incidence of up to 2.7-

percent.⁸⁻¹¹ TACO was the leading cause of FDA-reported transfusion-associated deaths for FY2016 and FY2017 as well as over the most recent five-year reporting period (FY2013-2017), the latter interval being associated with a total of 59 cases (or 32 percent of all fatalities).¹² More restrictive transfusion practices may reduce the incidence of TACO as well as its mortality rate.

Risk factors for the development of TACO: These include:

- (1) age (very young and elderly patients are at greatest risk),
 - (2) positive fluid balance in the 24 hours preceding transfusion,
 - (3) preexisting left heart failure, (4) the prior use of diuretics,
 - (5) the transfusion of plasma products, and (6) emergent surgery.
- Patients with comorbid conditions, such as chronic kidney disease, chronic pulmonary disease, and chronic severe anemia, are at particular risk for TACO.^{13,14} The TACO risk score described below corresponds to a patient's risk for developing TACO in association with transfusion.¹⁵

TACO Risk Score
1. Age ≥ 70 years.
2. Congestive heart failure (CHF) defined as a documented history of: (1) CHF, and/or (2) daily diuretic use, and/or (3) ejection fraction <60-percent.
3. Renal dysfunction defined as creatinine or glomerular filtration rate outside hospital range and/or history of dialysis.
Note: Each risk factor is one point (range: 0-to-3 points); higher score = higher risk.

Treatment: This consists of: (1) the use of intravenous (IV) diuretics (e.g., furosemide), (2) positioning the patient with head elevated, (3) providing oxygen support by non-invasive or invasive means (e.g., CPAP/BiPAP/mechanical ventilation), and (4) transferring the patient to a higher level of care.¹⁶

Preventive strategies: It is important to assess the patient for risk factors and to optimize these prior to transfusion. Other strategies include: (1) using suitable alternatives to transfusion (where appropriate), (2) applying restrictive transfusion thresholds, (3) determining if peri-transfusion IV diuretics are warranted, (4) transfusing slowly (e.g., up to four hours per RBC unit given to an adult), and (5) considering dividing the blood product (especially RBCs) into aliquots and transfusing each over up to four hours.¹⁵⁻¹⁸

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