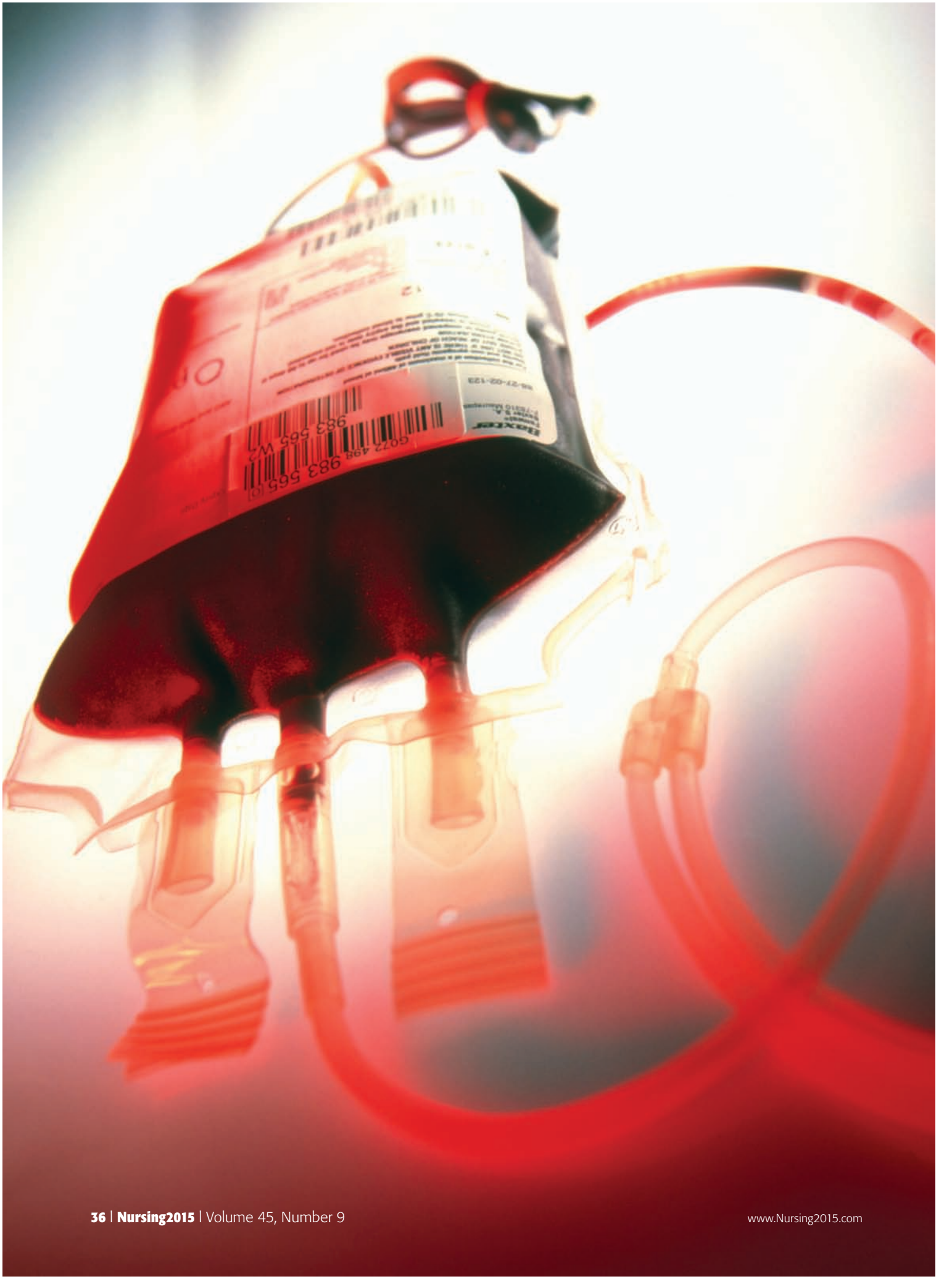

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Responding to pulmonary-related blood transfusion reactions

By Colleen Bockhold, MS, RN, CCRN, VHA-CM, and Sherron Crumpler, MSN, RN

ALTHOUGH THEY'RE CONSIDERED life-saving treatment, blood transfusions aren't without risks or potential for complications. Two distinct pulmonary-related blood transfusion reactions, transfusion-associated volume/circulatory overload (TACO) and transfusion-related acute lung injury (TRALI), are the leading causes of blood transfusion-related mortality.[1,2] These complications, which also have significant associated morbidity, are preventable.[3]

TACO and TRALI can be difficult to distinguish because they have very similar clinical presentations: respiratory distress and pulmonary edema.[4] Both present with acute onset of dyspnea, pulmonary edema, and hypoxemia. The treatment for each also differs significantly.[5]

Differentiation of TACO and TRALI can be difficult when underlying cardiopulmonary comorbidities are present, yet both can have fatal consequences if not recognized early and treated appropriately. Close monitoring for signs and symptoms of fluid overload before the patient's clinical status progresses to pulmonary edema can help prevent TACO.[3] TRALI prevention strategy is focused on donor management.[1] This article will review the similarities and differences of their presentation, recommended prevention strategies, and treatment options.

TEK IMAGE/SCIENCE SOURCE

Case study 1: TACO

Mrs. V, 79, is admitted with a history of heart failure (HF) and atrial fibrillation (AF), for which she's been taking warfarin. She was stable on her medication until this admission, when she presented with a gastrointestinal bleed. Mrs. V was given three units

of fresh frozen plasma (FFP). Although the bleeding stopped, her hemoglobin (Hgb) was reported to be 5.8 g/dL (normal in women, 12.0 to 16.0 g/dL). Four units of packed red blood cells (PRBCs) were ordered for transfusion. Pretransfusion, her oral temperature was 98° F (37° C), BP 108/78 mm Hg, heart rate (HR) 88 beats/minute (bpm), respiratory rate (RR) 16, and pulse oximetry (Spo_2) on two liters nasal cannula 95%.

One hour into her second unit of PRBCs, Mrs. V developed sudden shortness of breath and complained of a headache. Her temperature remained stable at 98° F (37° C), but her BP was elevated at 198/98 mm Hg. Mrs. V's HR was 108 bpm with an S3. An ECG showed AF with no signs of myocardial ischemia or infarction. Her RR increased to 26 and her Spo_2 dropped to 87%. Physical assessment findings included distended neck veins, a nonproductive cough, and bilateral coarse crackles throughout all lung fields. The transfusion was immediately stopped and the physician notified.

A stat portable chest X-ray (CXR) demonstrated a bilateral white-out appearance with an enlarged heart, vascular congestion, and bilateral pleural effusions. The nurse rechecked the transfusion information to verify that no procedural error had been made and returned the remaining blood and tubing to the lab along with a urine specimen. Mrs. V was placed in a semi-Fowler position and oxygen was titrated to maintain an Spo_2 greater than 90%. Her cardiac troponin T level was 0.03 mcg/L (normal, <0.02 mcg/L), ruling out myocardial infarction, but her serum brain natriuretic peptide (BNP) level was 2,340 pg/mL (normal, <100 pg/mL). Per physician orders, she received I.V. furosemide and diuresed 900 mL of clear pale yellow urine in the following hour.

Mrs. V responded well to treatment and improved quickly. The healthcare team enabled her to tolerate future transfusions by premedicating her with 20 mg of I.V. furosemide before each unit and slowing the transfusion rate to 1 mL/kg/hour. If the estimated transfusion time is more than 4 hours, the blood bank can provide smaller or "split" units.[6]

Recognizing TACO

The pulmonary edema in TACO is cardiogenic; the circulatory system is overloaded and abnormal fluid accumulation in the lungs occurs due to increased hydrostatic pressure.[7] No diagnostic study is considered the gold standard for TACO, nor does any formal universally accepted case definition exist. While evaluation of the patient's CXR, echocardiogram, and BNP can help clinicians determine if left-sided heart failure is present, the majority of evidence for a diagnosis of TACO involves transfusion-associated clinical signs and symptoms.[8]

Acute onset of hypertension and pulmonary edema are considered the hallmark signs of TACO, with dyspnea and hypoxemia being the most frequent presenting signs.[9] Other signs and symptoms include tachypnea, tachycardia, orthopnea, cough, wheezing or crackles, an S3, and jugular venous distension (JVD). These signs and symptoms most frequently present within 2 hours of the onset of transfusion and usually are fully manifested within 6 hours posttransfusion.[8]

Because signs and symptoms of TACO are similar to the exacerbation of other disorders, clinicians may treat the patient without recognizing and reporting transfusion-associated pulmonary edema. To improve recognition, the CDC outlined diagnostic criteria in 2013. Specific for a diagnosis of TACO is the new onset or exacerbation of at least three of the following criteria within 6 hours posttransfusion:

- acute respiratory distress
- hypertension
- radiographic evidence of pulmonary edema
- evidence of left-sided heart failure
- elevated central venous pressure (CVP)
- evidence of a positive fluid balance
- elevated BNP.[10]

Patients at risk for TACO include those under age 3 and over age 65. Lower body weight, chronic anemia, underlying cardiac disease such as HF, and renal insufficiency are predisposing factors. Massive transfusions due to trauma or transfusing too rapidly also increase the risk of TACO. The faster the transfusion and the more transfusions received, the higher the risk to the patient.[7]

Preventing TACO

Prevention of TACO is focused on identifying risk factors and adjusting nursing interventions accordingly. All practitioners transfusing blood on a nonemergent basis should perform a mandatory pretransfusion risk assessment to evaluate fluid balance as well as respiratory, cardiac, and renal function.[11] High-risk patients are usually given pretransfusion diuretics.

The risk of TACO can be reduced by avoiding overly rapid transfusion rates. A transfusion rate of 2.0 to 2.5 mL/kg/hour is acceptable for routine transfusions of blood components.[6] Alam et al. (2013) recommend all nonemergent inpatient blood transfusions be given at a slower rates of 85 to 120 mL/hour.[11] Rates as slow as 1 mL/kg/hour should be considered for very high-risk patients. This may require splitting the units and transfusing them over longer periods of time.

High-risk patients should be monitored every 15 minutes after transfusion has begun, followed by every-30-minute assessments for up to 6 hours posttransfusion.[11] Frequent monitoring may help the nurse recognize early signs and symptoms of fluid overload. An increase in RR, HR, and BP, and a decrease in Spo_2 will usually occur before acute pulmonary edema and respiratory distress.[8]

Managing TACO

If signs and symptoms of TACO occur, stop the transfusion immediately, assess the patient, and report the

findings to the healthcare provider and blood bank. (See *Responding to a blood transfusion reaction.*) Place the patient in a sitting position to ease the work of breathing and administer supplemental oxygen to keep the Spo_2 greater than 90%. Convert I.V. fluid lines to a saline lock or slow the rate to keep the vein open, and administer I.V. diuretics as prescribed.

For more severe cases, the patient may require noninvasive positive pressure ventilation or endotracheal intubation and mechanical ventilation. Ultrafiltration may be required for patients who don't respond adequately to aggressive diuretic therapy.[12] Although rare, therapeutic phlebotomy in 250 mL increments has been performed to reduce blood volume.[4]

Case study 2: TRALI

Mrs. G, 80, with a history of AF and warfarin therapy, required open reduction and internal fixation for a right hip fracture. She required three units of FFP to reverse anticoagulation preoperatively. Postoperatively, Mrs. G's Hgb was 6.3 g/dL (normal in women, 12.0 to 16.0 g/dL). Two units of PRBCs were ordered for transfusion. Mrs. G's pretransfusion vital signs were: temperature 98.6° F (37° C), BP 130/76 mm Hg, HR 96, RR 16, and Spo_2 96% on room air.

Two hours into her second unit, Mrs. G experienced sudden shortness of breath. Her temperature rose to 100.2° F (38° C); her BP dropped to 90/60 mm Hg. Her HR was 110 with no S3 or JVD. Her RR increased to 28 and Spo_2 decreased to 87% on room air. Mrs. G had bilateral diffuse crackles and a productive cough with frothy pink sputum. The nurse immediately stopped the transfusion and notified the physician and blood bank. Clerical checks comparing the transfusion form with the label on the PRBC bag and the patient's identification were completed and no discrepancies found. A urine specimen was sent to the lab and the transfusion bag and tubing were returned to the blood bank for analysis.

Responding to a blood transfusion reaction

Nurses must be alert to any respiratory distress occurring during or within 6 hours following blood or blood component transfusion and understand it could be TACO or TRALI. If a blood transfusion reaction is suspected:

- **Immediately stop the transfusion.**
- **Maintain venous access.**
- **Monitor vital signs.**
- **Auscultate lung and heart sounds.**
- **Intervene based on signs and symptoms, such as providing supplemental oxygen for hypoxemia.**
- **Notify the healthcare provider and blood bank.**
- **Document assessment findings, interventions, and the patient's response.**

Familiarity with facility policy is imperative to ensure the proper labs are obtained and procedures for blood transfusion reactions are followed; for example, conducting clerical checks and returning the remaining blood and tubing to the blood bank.[18]

A stat CXR revealed a normal-sized heart and bilateral pulmonary infiltrates. Supplemental oxygen was titrated to maintain Spo_2 greater than 90%.

Although Mrs. G diuresed 500 mL of urine in the first hour after receiving I.V. furosemide, she failed to improve clinically. Even with a 100% non-rebreather mask, her Spo_2 again dropped to 87% and her hypotension worsened (82/58 mm Hg). The rapid response team was called. Mrs. G required endotracheal intubation, mechanical ventilation, fluid resuscitation, and transfer to the ICU. At this point, her BNP was 100 pg/mL (normal, <100 pg/mL) and a complete blood cell count revealed neutropenia and leukopenia. A pulmonary artery catheter was placed and her pulmonary capillary wedge pressure (PCWP) after fluid resuscitation was measured at 12 mm Hg (normal, 4 to 12 mm Hg).

Mrs. G responded well to fluid resuscitation and correction of her hypoxemia. She was extubated 24 hours later, and the bilateral pulmonary infiltrates resolved over the next 2 days. She continued physical therapy and was discharged home after an additional hospital stay of 4 days.

Recognizing TRALI

In TRALI (also called pulmonary leukoagglutinin reaction), the underlying etiology is pulmonary, not cardiac. It's a noncardiogenic form of transfusion-related pulmonary edema resulting from increased pulmonary capillary permeability.[13,14] One theory is that TRALI occurs in response to infused donor leukocyte antibodies. These donor antibodies target the recipient's human leukocyte antigens (HLAs) or human neutrophil antigens (HNAs), resulting in neutrophilic influx into the lungs and injury to the pulmonary microvasculature.[5]

Another theory, called the two-hit model, suggests TRALI requires at least two clinical events. The first event (surgery, sepsis, or another stressor prior to the transfusion) leads to an initial acute inflammatory response. This event primes polymorphonuclear neutrophils (PMNs), causing them to adhere to the pulmonary endothelium. The second event is the infusion of donor antibodies that activate the PMNs, causing a release of cytotoxic agents.[14]

Both theories describe a pathway leading to pulmonary vascular endothelial damage, vascular leakage of fluid into the alveolar space, and pulmonary edema. These are central to TRALI pathogenesis.[15]

TRALI is a clinical constellation of signs and symptoms that may include:

- hypoxemia
- pulmonary infiltrates
- hypotension

- pink frothy airway secretions in endotracheally intubated patients
- cyanosis
- fever
- tachypnea
- tachycardia.[16]

The radiologic picture is of bilateral pulmonary infiltrates without cardiac enlargement or prominent pulmonary vasculature. Like TACO, signs and symptoms usually begin 1 to 2 hours after transfusion but can take up to 6 hours to manifest. Other signs and symptoms include chills and cough. Unlike TACO, TRALI usually causes no signs of fluid overload or left-sided heart failure, such as JVD or S3. A pulmonary artery catheter would reveal a normal or low PCWP.[1]

Preventing TRALI

Prevention of TRALI is aimed at hemovigilance related to donor management strategies, such as screening donors for the presence of anti-HLA and possibly anti-HNA and excluding them as future blood donors. Using leukocyte-depleted red blood cells and platelets is a standard approach to reduce the risk. Because female donors are more likely to have HLA antibodies, some facilities use only male donors. This deliberate decision has resulted in the incidence of TRALI falling from 2.57 to 0.81 per 10,000 transfusions.[17,18]

Treating TRALI

Treatment of TRALI involves correction of hypoxemia and hypotension. Up to 70% of patients with TRALI require endotracheal intubation and mechanical ventilation. As with other forms of acute lung injury, the use of low tidal volumes (6 to 8 mL/kg of the patient's ideal body weight) should be used to reduce further lung injury.[14] Some experts recommend even lower tidal volumes of less than 6 mL/kg of ideal body weight while maintaining inspiratory plateau pressures at less than or equal to 30 cmH_2O.[5]

Patients with TRALI are often hypovolemic and hypotensive, so the primary goal of hemodynamic management is to support adequate end-organ perfusion. Hypotension usually can be corrected by conservative fluid resuscitation with crystalloids or colloids. Vasopressor therapy may be required in refractory hypotension.

Although patients with TACO respond well to diuretic therapy, diuretic therapy may result in hypotension in patients with TRALI and should be used with caution. If the patient presents with hypotension, diuretics are typically avoided.[5] A restrictive transfusion strategy should be used in patients with existing acute lung injury, as subsequent transfusions may worsen the outcomes.[1]

Is it TACO or TRALI?

Because both TACO and TRALI present with acute onset of dyspnea, pulmonary edema, and hypoxemia, evaluate the patient for a hypervolemic or hypovolemic state. (See *Comparing TACO and TRALI.*) To identify the hypervolemic state of TACO, assess for a positive fluid balance, elevated CVP or PCWP, hypertension, and JVD. Auscultate for pulmonary crackles and an S3. Evidence of cardiac enlargement, left-sided heart failure, and a very high BNP (greater than 1,200 pg/mL) also support the TACO diagnosis.[16]

In TRALI, which is a hypovolemic state, BP, CVP, and PCWP are more likely to be low to normal. Fever is commonly present in TRALI. Auscultation may reveal pulmonary crackles but not an S3. Left-sided heart failure or cardiac enlargement isn't common in TRALI. If the patient's

Comparing TACO and TRALI[5]

	TACO	TRALI
Dyspnea	yes	yes
Arterial blood gas	hypoxemia	hypoxemia
Positive fluid balance	most likely	not likely
BP	normal to high	low to normal
Temperature	normal	normal to elevated
CXR	bilateral infiltrates; normal to increased heart size; vascular congestion; pleural effusions	bilateral infiltrates; normal heart size; no vascular congestion
Lung and heart sounds	pulmonary crackles and S3	pulmonary crackles, no S3
BNP	>1,200 pg/mL	<250 pg/mL
PCWP	high	low to normal
Echocardiogram	abnormal	normal
Response to diuretics	improves	no improvement; may worsen
Response to fluids	worsens	improves
White blood cell count	unchanged	transient leukopenia

BNP is less than 250 pg/mL, the diagnosis is less likely to be TACO and more likely to be TRALI.[5]

The most important clinical characteristic of TACO is the rapid resolution of pulmonary edema after diuresis.[1] In contrast, management of TRALI includes correction of the hypovolemic state with I.V. fluids.

To further complicate matters, TACO and TRALI can coexist. More treatment-focused studies are needed to determine optimum treatment strategies. If, after clinical evaluation, it appears that a blood transfusion reaction may have components of both TRALI and TACO, close monitoring and management of the patient's hemodynamic status are imperative.

Early intervention is key

Nurses play a key role in prevention, early recognition, and prompt management of TACO and TRALI. Recognition of risk factors and close patient monitoring can help prevent pulmonary-related blood transfusion reactions. ■

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