

# Recognizing Transfusion-Associated Circulatory Overload

Understanding updated definitions can promote better nursing care.

## ABSTRACT

Transfusion-associated circulatory overload (TACO) is the leading cause of transfusion-related deaths in the United States, accounting for more than 30% of fatalities reported to the Food and Drug Administration between 2016 and 2020. However, TACO is widely considered to be an underdiagnosed and underreported complication of blood transfusions, and its exact incidence is unknown. One of the reasons for this is a lack of recognition of TACO and its signs and symptoms, especially as the definition of TACO has been updated twice since 2018 without full dissemination to nurses, who are responsible for bedside care of patients during and following blood transfusions. This article seeks to bridge this gap by discussing the updated definitions and signs and symptoms of TACO, as well as the management of this treatable blood transfusion reaction.

**Keywords:** blood transfusion, transfusion-associated circulatory overload, transfusion reaction

Blood transfusions are one of the most common patient procedures in the United States, with more than 17 million blood products transfused each year, including whole blood, packed red blood cells, platelets, and plasma.<sup>1</sup> People receive blood transfusions for many reasons, including to treat chronic anemias and for postsurgical bleeding and trauma. Although blood transfusions are generally considered safe,<sup>2</sup> patients may experience adverse reactions, which can range from mild to severe and can be potentially fatal. Transfusion-associated circulatory overload (TACO) is the leading cause of transfusion-related deaths in the United States, accounting for more than 30% of fatalities reported to the Food and Drug Administration (FDA) between fiscal year (FY) 2016 and FY 2020.<sup>2</sup> Yet, TACO is widely considered to be an underdiagnosed and underreported complication, with the exact incidence unknown.<sup>3, 4</sup> One reason for this is the absence of a standardized definition for TACO. There are currently two accepted definitions, stemming from revisions undertaken in 2018 and 2021, but neither is considered the gold standard.<sup>5, 6</sup> Another reason for the underreporting of

TACO is that while its definitions have been shared among medical practitioners, they have not been widely disseminated to nurses, who provide bedside care for patients undergoing blood transfusions. Since nurses see the signs of TACO when they first appear, it is imperative that nurses be familiar with the definitions, recognize the signs and symptoms, and understand how to manage this reaction and the process of reporting it to the blood bank and the FDA when it occurs. The purpose of this article is to review the most current definitions of TACO and to discuss the characteristics and management of this adverse transfusion reaction.

## DEFINITIONS OF TACO

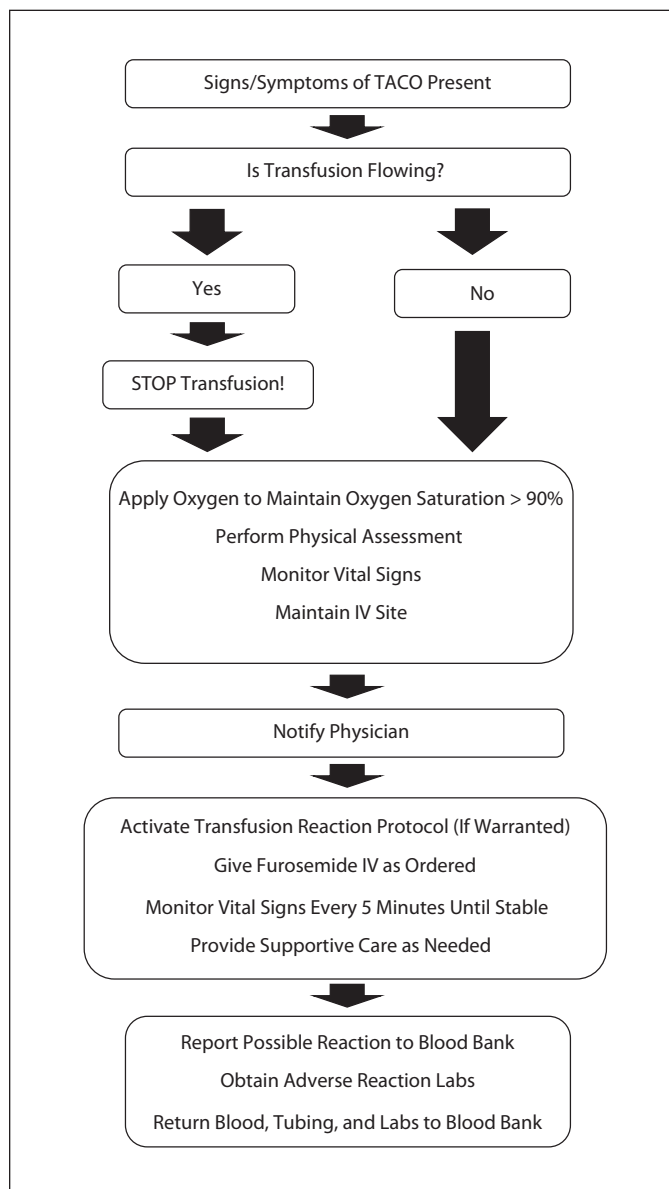
TACO can occur after transfusion of any blood product but is strongly associated with red blood cell transfusions because of the volume infused per unit of red blood cells.<sup>3, 7</sup> A typical unit of red blood cells contains about 300 to 350 mL of fluid, which is a significant amount to be transfused at one time, especially in high-risk patients.<sup>8-10</sup> By contrast, fresh frozen plasma and platelets contain about 200 to 300 mL of fluid per unit.<sup>11</sup> TACO has historically

not received much attention in the literature because it is often considered a simple case of volume overload. Yet, because it has recently been associated with prolonged hospital stays, increased costs, and lower quality of life and survival rates, researchers have paid increasing attention to TACO.<sup>12-15</sup>

In 2018, a multidisciplinary team from the International Society of Blood Transfusion (ISBT), the International Haemovigilance Network (IHN), and the Association for the Advancement of Blood and Biotherapies (AABB) published a revised definition of TACO that captures more cases than the previous 2011 definition.<sup>6, 16</sup> This definition has been validated and approved for use worldwide; however, it has not been adopted everywhere. The creation of an additional TACO definition in 2021 by the National Healthcare Safety Network and the Centers for Disease Control and Prevention (CDC) added to the confusion over which definition should take precedence. Table 1<sup>5, 6</sup> shows both definitions.

While both TACO definitions comprise the same basic features, there are some differences. Both definitions now include the development of signs up to 12 hours following the transfusion, which is an increase from six hours in the previous definition.<sup>4, 16</sup> Both definitions recognize that TACO presents with some type of respiratory distress that includes a cardiac component, with evidence of volume (fluid) overload. The definitions also include the potential use of a biomarker to help diagnose TACO. However, the signs and symptoms incorporated in the definitions vary. For example, the CDC includes pink frothy sputum in severe cases, which is not included in the ISBT/IHN/AABB definition, and the CDC does not expand on fluid overload as does the ISBT/IHN/AABB definition. Furthermore, neither definition includes fever as a potential sign, although fever is present in up to one-third of TACO cases.<sup>17</sup> These two definitions capture many more cases of TACO than the previous definition did, but there is still the need for a consensus definition. For now, however, nurses need to be aware of both definitions and should know which

**Figure 1.** Treatment Algorithm for Suspected TACO



one their facility uses for the purposes of transfusion reaction reporting.

In addition to defining relevant criteria, the CDC definition also addresses the severity and degree of imputability of TACO.<sup>5</sup> These are important considerations when reporting potential cases of TACO to the blood bank and the FDA as required.<sup>2</sup> Severity of cases ranges from nonsevere (medical intervention is required but its absence would not result in permanent damage) to death. Imputability ranges

**Table 1.** Definitions of TACO<sup>5, 6</sup>

ISBT/IHN/AABB Definition (2018)	CDC Definition (2021)
<p>TACO is defined as acute or worsening respiratory compromise and/or evidence of pulmonary edema (A and/or B below) during a transfusion or up to 12 hours following a transfusion and 3 or more of the following criteria:</p> <p>A. Acute or worsening respiratory compromise</p> <p>B. Evidence of acute or worsening pulmonary edema based on:</p> <ul style="list-style-type: none"> <li>• Clinical physical examination and/or</li> <li>• Radiographic chest imaging and/or other noninvasive assessment of cardiac function (such as echocardiogram)</li> </ul> <p>C. Evidence of cardiovascular system changes not explained by the patient's underlying medical condition, including development of tachycardia, hypertension, widened pulse pressure, jugular venous distension, enlarged cardiac silhouette, and/or peripheral edema</p> <p>D. Evidence of fluid overload including any of the following: a positive fluid balance, response to diuretic therapy, and change in the patient's weight in the peritransfusion period</p> <p>E. Supportive result of a relevant biomarker, such as an increase in BNP or NT-proBNP above the age group-specific reference range and greater than 1.5 times the pretransfusion value</p>	<p>TACO is defined as new onset or exacerbation of 3 or more of the following within 12 hours of cessation of transfusion (at least A and/or B below):</p> <p>A. Evidence of acute or worsening respiratory distress (dyspnea, tachypnea, cyanosis, and decreased oxygen saturation values in the absence of other specific causes)</p> <p>B. Radiographic or clinical evidence of acute or worsening pulmonary edema (crackles on lung auscultation, orthopnea, cough, a third heart sound, and pinkish frothy sputum in severe cases)</p> <p>C. Elevated BNP or NT-proBNP relevant biomarker</p> <p>D. Evidence of cardiovascular system changes not explained by underlying medical condition (elevated central venous pressure, evidence of left heart failure including development of tachycardia, hypertension, widened pulse pressure, jugular venous distension, enlarged cardiac silhouette, and/or peripheral edema)</p> <p>E. Evidence of fluid overload</p>

AABB = Association for the Advancement of Blood and Biotherapies; BNP = B-type natriuretic peptide; CDC = Centers for Disease Control and Prevention; IHN = International Haemovigilance Network; ISBT = International Society of Blood Transfusion; NT = N-terminal; TACO = transfusion-associated circulatory overload.

from definite (that is, the reaction is definitely related to the blood transfusion) to possible. In the latter case, the patient's history of cardiac insufficiency is more likely than a blood transfusion to explain the overload.<sup>18</sup>

### TACO INCIDENCE

The exact incidence of TACO is unknown, and published reports vary widely from 1% to 12.3%,<sup>19-23</sup> depending on the patient population studied. Table 2<sup>19-23</sup> summarizes the incidence rate by patient population. Simpson and colleagues studied ambulatory transfusion patients who were "at risk" for TACO, and found that 8% fit the definition for TACO under the 2011 definition used in their study, although they identified no actual TACO cases.<sup>24</sup> The true incidence of TACO is unknown and difficult to assess as a result of underreporting and the lack of a consensus definition, as well as not knowing when to report to the blood bank and what evidence should be reported.

In FY 2020, TACO accounted for 34% of all transfusion-related deaths reported to the FDA in the previous four years.<sup>2</sup> TACO was followed closely by

another pulmonary adverse reaction, transfusion-related acute lung injury (TRALI). There were 62 total TACO deaths reported in the United States between FY 2016 and FY 2020.<sup>2</sup> Although this may seem low given the more than 17 million units of blood transfused each year,<sup>1</sup> it represents only those deaths reported to the FDA as TACO deaths. It does not include patients who had severe TACO, resulting in the need for critical care, who eventually recovered. TACO is also associated with higher 28-day mortality and longer length of hospital stay in general and after transfusion.<sup>13, 14</sup> Li and colleagues found that patients with TACO had a longer length of stay in the ICU than patients who did not.<sup>25</sup>

### PATHOPHYSIOLOGY

Why TACO occurs is not completely understood, though it is known to result from the pulmonary edema that develops as a result of increased hydrostatic pressure following transfusion.<sup>26</sup> That is, there is respiratory distress from fluid buildup in the lungs, but it has a cardiac cause, typically some type of left ventricular dysfunction. Recent research by Bulle and colleagues indicates that TACO follows

**Table 2.** Incidence Rates of TACO

Article	Article Type	Patient Population	TACO Incidence Rate
Bosboom JJ, et al, 2018 <sup>19</sup>	Retrospective study	ICU patients	5.8%
Bulle EB, et al, 2022 <sup>20</sup>	Narrative review	Admitted patients Intraoperative patients Critically ill patients	1% 5.5% Up to 11%
Gauvin F, Robitaille N, 2019 <sup>21</sup>	Review	Critically ill adults and children	1%–8% (adults) 1.5%–76% (children)
Kim KN, et al, 2015 <sup>22</sup>	Retrospective study	All patients who received transfusions during anesthesia	1.03% <sup>a</sup>
Piccin A, et al, 2021 <sup>23</sup>	Retrospective study	Gastroenterology patients	12.3%

<sup>a</sup> Percentage was calculated by dividing number of TACO cases (20) by number of patients (1948).

a so-called two-hit model.<sup>20</sup> The first hit includes the risk factors and comorbidities that limit a patient's ability to compensate for an increased vascular volume. The second hit is the volume of the blood transfusion itself.

Additionally, since one-third of patients also present with fever, there may be an inflammatory response associated with TACO; however, this has not been adequately studied.<sup>4</sup> Moreover, absence of fever does not indicate a less serious illness in TACO patients. Why fever occurs in some TACO patients and not in others is unknown.

Patient risk factors, which contribute to the first hit in the two-hit model, are many (see Table 3<sup>13, 18, 20, 24, 27-29</sup>). Being older than 60 years of age is a risk factor for TACO, and both older and younger extremes of age increase the risk.<sup>20, 27</sup> Patients with specific comorbidities, such as a history of cardiac failure, especially of the left ventricle (that is, patients with congestive heart failure), are also at increased risk.<sup>29, 30</sup> This is because the left ventricle is overwhelmed and unable to function effectively given the increases in volume when a transfusion occurs. Heart failure is also associated with decreased renal perfusion and fluid retention, which predisposes patients to fluid overload.<sup>20</sup> Accordingly, another risk factor for TACO is a history of renal insufficiency, including kidney injuries, chronic use of loop diuretics, and treatment with dialysis.<sup>13, 18, 31</sup> Patients with a pretransfusion positive fluid balance are also at increased risk for TACO.<sup>20</sup> There is also evidence that patients who are female, White, and have a history of chronic pulmonary disease are at increased risk.<sup>27</sup>

Other risk factors for TACO include those related to infusion practices.<sup>15, 29</sup> The risk of TACO increases with the rate of infusion, though there is no established best practice for determining the appropriate rate of transfusion for at-risk patients.<sup>8, 32</sup> Other

elements that increase risk of TACO include verbal orders (which suggest the physician has not reviewed the patient's medical record or other TACO risk factors before delivering the order), transfusing more than a single unit of red blood cells, rapid rates of transfusion, and improper timing of preemptive diuretics to prevent TACO.<sup>33</sup> Historically, diuretics are given to patients either between units of blood if more than one unit is ordered or following the transfusion, which means patients receive a diuretic after a volume overload has potentially occurred. For patients at higher risk for TACO, diuretics might be more effective in preventing TACO if given prior to the transfusion, so the medication is working as volume is infused; however, this approach is still in the early stages of investigation.<sup>34, 35</sup> Importantly, as many of these risk factors can be reduced via proper nursing care, nurses need to be aware of evidence-based transfusion practices in the management and mitigation of TACO.

### ASSESSMENT

Signs of TACO can occur within the first few minutes of a transfusion and up to 12 hours after cessation of the transfusion. The nurse stays at the

**Table 3.** Risk Factors and Comorbidities Associated with TACO<sup>13, 18, 20, 24, 27-29</sup>

Risk Factors	Comorbidities
Age over 60 years History of cardiac failure History of kidney injury Chronic loop diuretic use Positive fluid balance Female sex <sup>a</sup> White race <sup>a</sup>	Congestive heart failure Chronic kidney disease Chronic obstructive pulmonary disease

<sup>a</sup> Potential risk factors.

**Table 4.** Nursing Assessment with Expected Findings in a Patient with TACO<sup>5, 6, 18, 36</sup>

Assessment	Expected Findings
Vital signs	Oxygen saturation < 90% (or decrease from baseline) Tachypnea Tachycardia Hypertension (increase in systolic blood pressure) Increased pain level from baseline Fever (increase in temperature from baseline of 2°C)
Physical assessment: cardiac	Third heart sound Increased jugular venous distention Increased central venous pressure Widened pulse pressure Peripheral edema
Physical assessment: pulmonary	Crackles on auscultation Cough Pink, frothy sputum
Physical assessment: skin	Cyanosis Cool, clammy skin Pedal edema
Fluid balance	Decreased urinary output (input > output) Peripheral edema Increase in weight from baseline

bedside for the first 15 minutes of a transfusion and is often the first person to notice a change in patient status. Thus, the nursing assessment at the bedside plays a critical role in the diagnosis of TACO. Table 4<sup>5, 6, 18, 36</sup> presents the nursing assessment, involving monitoring of vital and other signs, and expected findings in a patient with TACO.

The first sign is often a dip in oxygen saturation. A nurse may notice this drop from baseline when a patient complains of shortness of breath (dyspnea) or note an increased respiratory rate when checking vital signs, prompting a check of the oxygen saturation level. On auscultation, the nurse may hear crackles. The patient may develop a cough. If an X-ray is ordered, there will be evidence of pulmonary edema.

Upon further assessment, the nurse may note other signs consistent with a typical fluid overload. Hypertension, or an increased systolic blood pressure from baseline is often observed.<sup>5</sup> There may be an increase in central venous pressure (observed if a monitor is in place) and the nurse may note jugular venous distention. Tachycardia may also be present. The nurse should assess for peripheral edema, which is often an early sign of TACO. On X-ray, there may be signs of an enlarged heart.

The nurse must also assess for fluid balance, so a check of the patient's weight before the transfu-

sion and once signs of TACO emerge, if possible, could help to indicate fluid overload. The nurse should assess volume input and output to determine the presence of a positive fluid balance.

### DIFFERENTIAL DIAGNOSIS

In most cases, the clinical diagnosis of TACO is made based on medical history, physical evaluation, and response to a diuretic challenge.<sup>3, 18</sup> There is no set laboratory test or procedure that definitively diagnoses TACO; thus, the nursing assessment at the bedside is vital. As noted above, this assessment must include comprehensive vital signs with pain assessment, oxygen saturation, and lung auscultation.<sup>36</sup>

There is one laboratory test that can help with the diagnosis of TACO; namely, the measurement of the B-type natriuretic peptide (BNP) and N-terminal proBNP (NT-proBNP).<sup>32</sup> These neurohormones are secreted by "the atrial and ventricular myocardium in response to increased pressure and stretch of cardiac myocytes."<sup>32</sup> The release of these hormones results in decreased renal absorption, increased diuresis, and vasodilation. BNP levels are usually elevated in cases of congestive heart failure. Several studies have found that pre- and posttransfusion BNP levels are elevated in TACO cases, suggesting that checking BNP levels may be helpful in the diagnosis of TACO.<sup>28, 37, 38</sup> However, there is no conclusive evidence to support how much of an increase in posttransfusion BNP levels is indicative of TACO. A recent systematic review suggests that the cutoff limits for BNP and NT-proBNP are less than 300 pg/mL and less than 2000 pg/mL, respectively.<sup>39</sup> Both tests should be performed as soon as pulmonary signs arise and within 24 hours of onset if they are measured to assist in the definitive diagnosis of TACO.

When a patient presents with respiratory distress during or following blood transfusion, the nurse must consider possibilities other than TACO. The transfusion reaction most often confused with TACO is TRALI.<sup>7, 40, 41</sup> TRALI is an injury related to an antibody response to a component in the blood product, and administration of diuretics will not alleviate symptoms as it does with TACO. Thus, a patient whose symptoms improve with diuretic use most likely does not have TRALI.

Another adverse reaction that must be considered, especially if complications occur early in the transfusion, is an allergic reaction to a blood product with a pulmonary component.<sup>8, 18, 42</sup> In an allergic reaction, however, the nurse should expect to see evidence consistent with anaphylaxis, which includes urticaria, rash, and wheezing.<sup>3</sup> In TACO, the nurse will not observe rash or urticaria, and most often will hear crackles, not wheezing, on auscultation.

Other less common diagnoses to rule out TACO include other cardiac issues or a pulmonary embo-



lism, which require further workup for diagnosis.<sup>18</sup> Neither of these complications would resolve with the use of diuretics.

Because other diagnoses do not respond to diuretics, a key distinguishing diagnostic test for TACO is the patient's response to the diuretic challenge. The loop diuretic furosemide at a dosage of 20 to 40 mg IV is often given when TACO is suspected. Improvement in signs and symptoms is observed within 30 minutes.

## MANAGEMENT

The treatment of TACO is supportive care (see Figure 1 for a treatment algorithm).<sup>18</sup> If complications occur during the transfusion, the first step is to stop the transfusion. The nurse should assess the patient, and apply oxygen via nasal cannula at 2 L/min and titrate to maintain a saturation of greater than 90%.<sup>18</sup> The nurse should also place the patient in Fowler's position, if possible, to enhance lung expansion.<sup>3</sup> The physician and blood bank should both be notified. To rule out reactions due to the blood product itself, laboratory tests may be ordered by the blood bank medical director. The nurse should obtain specimens as directed and send them to the blood bank for evaluation. While signs and symptoms of TACO are present, the nurse should monitor vital signs frequently, most likely every five minutes, until symptoms improve and the patient is stable. In some cases, treatment with continuous positive airway pressure and mechanical ventilation is required to maintain oxygen saturation, and these may be ordered by the physician.

**Table 5.** AABB-Suggested Transfusion Rates for Patients at Risk for TACO<sup>8</sup>

Risk Category	Infusion Rates and Times
Severe risk of volume overload	All blood components issued in 0.5-unit increments so that 4-hour maximum transfusion time is not violated Time per half unit: 2.5–3.5 hours Rate per half unit: 42–60 mL/hr
Potential risk of fluid overload	Full units issued Time per unit: 2.5–3.5 hours Rate per unit: 84–120 mL/hr
Minimal to no risk of fluid overload	Full units issued Time per unit: 1.5–3.5 hours Rate per unit: 84–200 mL/hr

AABB = Association for the Advancement of Blood and Biotherapies.

Often, a patient presents with mild posttransfusion respiratory distress and the nurse notifies the physician. Furosemide is ordered and given by the nurse. Symptoms resolve, and the blood bank is never notified, resulting in undiagnosed and unreported possible cases of TACO.<sup>4, 23</sup>

## NURSING IMPLICATIONS

An ideal prevention strategy for TACO has not yet been determined. Nurses, however, should assess for risk factors prior to transfusion. Taking a patient history can identify risk factors such as left ventricular dysfunction and heart failure. Nurses should also be familiar with previous laboratory results and review fluid status using 24-hour input and output measure-

**There is no set laboratory test or procedure that definitively diagnoses TACO; thus, the nursing assessment at the bedside is vital.**

The core treatment for TACO, however, is diuresis.<sup>18, 23</sup> The most common medication used for this purpose is furosemide 20 to 40 mg.<sup>33</sup> IV is the preferred route due to its faster onset of action compared with the oral route.

When posttransfusion reactions occur, management is generally the same. The physician and blood bank should both be informed. Oxygen therapy should be initiated to maintain oxygen saturation, and furosemide should be given to alleviate symptoms. The blood bank may order additional laboratory tests to rule out other adverse reactions.

ments. It's important for nurses to communicate with patients both verbally and in writing regarding what to expect during the transfusion and what symptoms to report during and after the procedure.

If a patient is deemed to be at high risk for TACO, nurses should discuss their status with the patient's physician and advocate for pretransfusion diuretic use to prevent TACO.<sup>3, 35, 43, 44</sup> The nurse should also question orders for more than one unit of blood to be transfused in a high-risk patient,<sup>4, 45</sup> and should encourage the physician to transfuse one unit at a time and assess for improvement and the need for a second unit. For

patients at high risk for TACO, the nurse should transfuse blood products at a slower rate than usual.<sup>3, 4, 41, 46, 47</sup> An evidence-based exact rate has not been established, but Table 5<sup>8</sup> presents suggested rates given by the AABB for high-risk patients. Nurses should also educate patients, families, and others on the health care team about the incidence and seriousness of TACO.

Standardized screening criteria should be developed based on sound evidence to fully assess the risk of TACO, and patients should be screened prior to transfusion.<sup>32, 44</sup> Increased screening can reduce the incidence of TACO.<sup>30, 36</sup> Currently, the Joint Commission does not require respiratory rate, oxygen saturation, and pain level as among the transfusion vital signs to be checked, but these are often the first vital signs to change in patients with TACO.<sup>36</sup> In fact, respiratory rate and oxygen saturation are the first signs most nurses note, so monitoring these closely is important. However, patients may also complain of symptoms such as dyspnea and flank pain, so noting a change in the patient's pain level from baseline is also important. Nurses should advocate for the inclusion of these critical signs and symptoms in the standard transfusion protocol, and nurses should assess these as routinely as they do other vital signs during the transfusion. Nurses can also increase reporting to the blood bank by notifying them when there is a suspected TACO case, or when they must give a patient furosemide within 12 hours following a transfusion.

## NEXT STEPS

Future research should focus on the development of evidence-based guidelines to determine how best to mitigate the risk of TACO. This may include a pretransfusion screening tool, whether to give furosemide prior to the transfusion and the minimum effective dose to prevent TACO, and the best rate of transfusion for patients at high risk for TACO. All of these interventions have the potential to increase quality of care and decrease cost of treatment, as the incidence of TACO should decrease with the implementation of these changes. ▼

For 36 additional nursing continuing professional development activities on infusion therapy topics, go to [www.nursingcenter.com/ce](http://www.nursingcenter.com/ce).

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