**Update on transfusion-related acute lung injury: An overview of its diagnosis**

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**Abstract**

Transfusion-related acute lung injury (TRALI) is a serious adverse reaction, which is associated with blood transfusion. TRALI can be life-threatening and typically require prompt medical intervention. Distinguishing it from other forms of acute lung injury is crucial for effective treatment. Hence, an urgent need exists for the development of early and accurate detection methods for TRALI. This mini review summarizes the ongoing research related to the diagnosis of TRALI. The goal of this review is to address that develops better diagnostic tools for TRALI is essential.

**Keywords: Transfusion-related acute lung injury (TRALI); diagnosis; diagnostic tools;**

The main causes of transfusion-associated death are transfusion-related acute lung injury (TRALI) and transfusion-associated circulatory overload (TACO). These diseases have a similar clinical manifestation, both of which are characterized by acute respiratory distress [1]. A great challenge that differentiates between TRALI and TACO stands ahead of us due to overlapping symptomatology, as the management differ greatly [2]. Early detection is helpful to improve clinical outcomes. It is worthy to note that patients in the ICU face at higher risk of transfusion-associated respiratory complications, thus recognizing TRALI from TACO may be challenging [3]. Current clinical diagnosis still depends on the redefinition of TRALI updated in 2019 and radiological signs, due to no specific laboratory test available for diagnose TRALI. Accurate diagnosis of TRALI based on redefinitions need to recognize acute respiratory acute respiratory distress syndrome (ARDS) risk factors, distinguish the characteristics of pulmonary edema, and evaluate whether pulmonary statues are stable within 12 hours before transfusion of blood components in patients with ARDS risk factors [4]. The main diagnostic criteria of TRALI meets acute onset within 6 hours, hypoxemia (PaO2/FiO2 ≤300 mmHg\* or SpO2 <90% on room air), diffuse bilateral infiltrates without pleural fluid on chest imaging, and no evidence of left atrial hypertension [2, 5].

Although no specific laboratory tests are available to clearly distinguish TRALI from TACO, progress has been made on this issue. Roubinian et al. [6], in a case-control study, discovered that BNP levels higher than 1000 pg/mL occurred in TACO patients in age older than 70 years. Both BNP and pro-BNP in plasma were confirmed to be positively related to TACO patients [3, 7-9]. Additionally, analysis of cytokines may further assist to differentiate between TRALI and TACO. Semple et al. [7] demonstrated combining decreased IL-8 levels with increased IL-10 levels may potentially support a diagnosis of TACO, whereas elevated IL-8 levels in combination with low IL-10 levels may potentially help in the diagnosis of TRALI. Similarity, a recent clinical study showed that IL-10 levels contributed to the evaluation of outcomes in TRALI patients [10]. However, a systematic review revealed that serologic cytokine profiles still lacked a definite diagnostic capacity to distinguish TRALI from TACO [8]. Whether these cytokines profiles have diagnostic value in TRALI and TACO requires further validation in larger population-based studies.

As for antibody-mediated TRALI, confirmed diagnoses are established once antibodies are detected in donors. Several detection technologies are available for testing anti -human leukocyte antigen (HLA) and anti-human neutrophil antigen (HNA) antibodies to recognize it. The complement-dependent cytotoxicity (CDC) assay was considered as the golden standard for testing anti-HLA antibodies [11]. However, non-complement bound HLA-antibodies or low tire antibodies may be undetected. With the advance of technology, most laborites have introduced antigen-based assays instead of the CDC assay. The commercially available detecting systems based on bead assays including FlowPRA screening assay and Luminex platform, aid to classify HLA-antibodies phenotype, require less labour-intensive, and detect low tire antibodies with high sensitivity and specificity [12]. In addition to HLA antibodies, HNA-antibodies also exert detrimental role in antibody-dependent TRALI. Classical serological methods that test HNA-antibodies are the granulocyte immunofluorescence test (GIFT) and granulocyte agglutination test (GAT). The advantage of GIFT and GAT are the most sensitive tool and has a better capacity to test HNA-3a antibodies, respectively [13, 14]. Luminex platforms also have been exploited to detect HNA-antibodies [15]. However, the experimental methods detecting non-antibody- mediated TRALI still remains unknown.

In conclusion, this overview sheds light on the challenging landscape of diagnosing and distinguishing between TRALI and TACO, both of which present with acute respiratory distress. While current clinical diagnosis relies on redefined criteria and radiological signs, specific laboratory tests for TRALI remain elusive. Recent progress has shown promise in using biomarkers such as BNP, pro-BNP, and cytokine profiles to aid in differentiation, but further validation in larger population-based studies is necessary. Additionally, for antibody-mediated TRALI, detection methods for antibodies in donors have evolved, with antigen-based assays on advanced platforms offering increased sensitivity and specificity. Nevertheless, challenges still persist, particularly in detecting certain antibodies. Further research is required to unravel the complexities of TRALI, its diagnosis, and the role of various antibodies. This ongoing pursuit of improved diagnostic tools and methods is essential in our commitment to enhancing patient care and outcomes in the context of transfusion-related complications.

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