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Revealing the Real Risks of Perioperative Transfusion: Rise of the Machines!

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Approximately 30,000,000 blood components were transfused last year in the United States. Almost half of those were transfused in the operating room or perioperatively according to the 2011 National Blood Collection and Utilization Survey Report.¹ Consequently, the anesthesiologist assumes a substantial role in mitigating adverse transfusion reactions. In fact, one adverse reaction per 414 units transfused was reported in the above survey, accounting for 50,570 total.¹ Many transfusion reactions can be identified with predictable laboratory diagnostic tests. However, when no specific test exists or concrete definitions are not established, the diagnosis is often missed or under appreciated. As a result, the transfusion reaction remains in obscurity; if proper safeguards are not implemented, the possibility of occurring again is not deterred. This is the case in Transfusion Related Acute Lung Injury (TRALI) and Transfusion Associated Circulatory Overload (TACO). In this month's edition of *Anesthesiology*, Kor, et al., have taken an enormous step in providing better detection of these common adverse reactions.^{2,3}

Why is reporting a seemingly obvious reaction that is temporally related to a visible intervention so difficult? On paper, a patient without lung injury developing acute respiratory distress within hours of receiving a blood transfusion would seem likely to raise red flags. Unfortunately, the clinical picture is often blurred with multiple confounders. Dyspnea is expected in patients presenting with preexisting cardiac conditions or underlying pulmonary disease. Isolating one culprit among multiple interventions occurring in surgical patients is often not possible or may not have clinical relevance when choosing the next therapy. Indeed, the treatment for acute respiratory failure from adult respiratory distress syndrome and circulatory overload are similar regardless of etiology. In addition, reporting depends on the specialty of the physicians and how they diagnose TRALI and TACO.⁴ Personal reasons may also factor into reporting. Fear of reprisal, apathy, or unawareness of the reporting mechanisms must be taken into account. Finally, to steal a sports phrase, the concept of “no harm, no foul” may be a reason for underreporting. To address these

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problems, Kor, et al., minimized the human element and utilized the robust databases of Mayo Clinic to examine noncardiac surgical patients over two different years. In this retrospective analysis, 83,204 patients were electronically screened for signs and symptoms consistent with TRALI or TACO. The precision of this study was augmented by natural language processing (NLP) software developed at the Mayo Clinic. This electronic “data-miner” evaluates radiographic reports looking for explicit or descriptive terms used to identify TRALI and TACO. The importance of this initial screening tool cannot be underestimated. Thousands of hours would be required for detailing such records making a study of this size implausible for many institutions. Additionally, the fidelity of the NLP software is high, producing a specificity and sensitivity of 92.5% and 93.6% respectively.² Once limited to manageable numbers, the positively screened patients were evaluated by independent physicians for actual cases of TRALI or TACO.

The Mayo Clinic studies focused on patients transfused in the perioperative period in an effort to categorize this unique population. As such, postoperative incident rates of 1.4% for TRALI and 4.3% for TACO may not be generalizable to the entire transfused population. The incidence rate of TRALI in the critically ill population, as might be common at the Mayo Clinic, has been estimated to be between 5.1-15%.^{5,6} Also, by combining highly-probable cases with actual cases, the incident rates that were calculated have the potential to be artificially high. However, requiring imputability, or identification of transfusion as the sole causal factor in acute respiratory failure from adult respiratory distress syndrome and circulatory overload results in under appreciation of the disease. Coinciding with under recognition, the Mayo Clinic researchers limited their results to 6 hours post transfusion. This was intentionally done, however, expanding their definition of the perioperative period may have identified an even greater incidence. The postoperative period can range from 6 hours to 24 hours depending on the disease studied. In an effort to generalize these results, multi-center efforts utilizing the Mayo Clinic NLP software could be used, and the definition of the postoperative period standardized. Highlighted in this study is the use of computer automation to examine thousands of records in an electronic database. In this study, language-processing software retrospectively identified low incident, high morbidity processes with astounding fidelity. Will it be possible for this same software to perform concurrent searches during a patient's hospital stay to detect disease patterns and assist in decision-making? The potential for this type of technology is extraordinary.

TRALI and TACO are the number one and two causes of transfusion related deaths in the United States. In 2013, the Federal Drug Administration reported that 38% and 24% of the deaths after transfusion were attributable to TRALI and TACO. Transfusion could not be ruled out as the cause in an additional 32% of deaths (approximately 21 of 71 cases in FY2013).⁷ Thus, recognition of the adverse reaction and accurate reporting are crucial in mitigating risk to patients. Through identification of patients with TRALI and TACO, risk stratification regimens can be better constructed. Epidemiological studies such as these studies pave the way for tailored transfusion practices to patients at high risk for TRALI or TACO. Importantly, recognition of blood components that have caused TRALI will allow for future exclusion of those donors. As well, blood component traits can be identified that put patients at higher risk for these disease processes.

Whether transfusion related adverse reactions are not reported due to human error or under recognition, the risk to patients remains high. Through use of intelligent automation, Kor, et al., have identified the overall risk of TRALI at 1.4% and TACO at 4.3% in the perioperative patient. For TRALI, dramatic under recognition of the disease was identified. Additionally, increasing volume transfused and increasing age was clinically predictive of developing TRALI. The Mayo Clinic study identified increased risk of TACO with certain surgical procedures, increased transfusion volume, and total operative fluid balance. This coincides with known risk factors published by the TRALI Study Group.⁸ When transfusion-related adverse reactions occurred, hospital stay was prolonged and mortality was augmented (OR 15.6 for TRALI).

The landscape of hemotherapy is ever-changing. Clinicians should seek to better recognize adverse transfusion reactions. The goal of minimizing transfusions to limit patient exposure to adverse reactions is reasonable and practical. To accomplish this, patient blood management strategies are being widely implemented and have been successful in reducing blood transfusions in tertiary care centers.⁹ The principles of patient blood management are based on the three pillars concept: optimizing preoperative erythropoiesis, reducing operative blood loss, and harnessing the patient's physiological tolerance of anemia.¹⁰ Anesthesiologists should recognize this changing landscape as we are often on the front lines of blood transfusion.

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