



Saint Luke's Regional Laboratories Clinical Laboratory Letter

February 2013

Saint Luke's Hospital Excels at Blood Management

Historically, the widely accepted clinical standard was to transfuse patients when the hemoglobin level dropped below 10.0 g/dL or the hematocrit fell below 30%. This '10/30 rule' was first proposed in 1942 and served as the RBC transfusion trigger for decades. In 1988 an NIH Consensus Conference concluded that existing medical evidence did not support a single hemoglobin threshold for transfusion.

Eleven years later, the seminal Transfusion Requirements in Critical Care (TRICC) trial was published, which compared clinical outcomes in intensive care patients randomized to a restrictive versus a liberal transfusion strategy (NEJM 1999;340:409). Patients in the restrictive cohort were transfused when their hemoglobin fell below 7 g/dL and their hemoglobin was maintained between 7–9 g/dL, while patients in the liberal transfusion group were transfused when their hemoglobin concentration fell below 10 g/dL and their hemoglobin was maintained between 10–12 g/dL. The TRICC trial demonstrated that a more restrictive transfusion strategy was safe in the ICU patient population and that the liberal use of transfusions increased the risk of death.

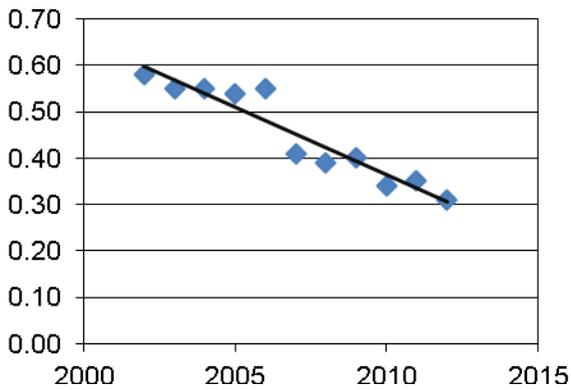
Since that time, numerous random controlled trials comparing restrictive versus liberal transfusion strategies in divergent patient populations have been published. Recently, a meta-analysis of 19 random controlled trials including 6242 patients was undertaken (Cochrane Database Syst Rev 2012;4: CD002042). Trials included surgical, medical and critical care patients in several different clinical settings including cardiac surgery, orthopedic surgery, vascular surgery, acute blood loss/trauma, cancer and critical care. There was considerable variation with regard to the restrictive and liberal transfusion strategies used in these studies. In general, restrictive strategies maintained hemoglobin between 7.0 and 9.0 g/dL, while liberal strategies maintained hemoglobin levels at or above 9.5, 10.0 or 12.0 g/dL.

As expected, a restrictive transfusion trigger reduced the risk of exposure to RBC transfusion and the total number of units transfused. Restrictive transfusion strategies reduced the absolute risk of a patient being transfused by 34% and the number of RBC units transfused per patient by an average by 1.19 (95% CI 0.53 to 1.85 units). The average hemoglobin level of patients in the restrictive cohort was 1.5 g/dL lower than patients in the liberal cohort.

This meta-analysis confirmed the most important outcomes of the TRICC trial. Restrictive transfusion strategies were associated with a statistically significant reduction in hospital mortality (RR 0.77, 95% CI 0.62 to 0.95) but not 30-day mortality (RR 0.85, 95% CI 0.70 to 1.03). Restrictive transfusion strategies did not adversely affect mortality, cardiac morbidity, stroke, wound healing, mental confusion, functional recovery, length of hospital or ICU stay. In contrast, the evidence suggested that liberal transfusion strategies increase in-hospital mortality by 23% and infection by 19%.

This meta-analysis supports the move to restrictive transfusion practice in most patients, including those with pre-existing cardiovascular disease. Trials in adult and pediatric intensive care unit patients confirm the safety of a 7.0 g/dL threshold in patients with severe acute illness. It is important to realize that no trials have studied the effects of restrictive transfusion triggers in patients with acute coronary syndrome.

Saint Luke's Hospital started a Blood Management Program in January of 2000 to improve patient outcomes by decreasing unnecessary transfusions and their attendant risk. As part of its comprehensive multidisciplinary approach, the program has promoted a restrictive transfusion policy. Recently, we reviewed our progress over the previous 11 years by calculating the number of RBC units transfused per inpatient discharge at Saint Luke's Hospital.



As illustrated in the graph, the transfusion rate has steadily decreased from 0.60 RBC per discharge in 2002 to 0.30 RBC in 2012. Over the last couple of years, inpatient mortality has decreased in parallel with the decrease in RBC transfusion. This decrease has resulted in cumulative blood procurement savings of more than \$6 million and total transfusion costs of more than \$30 million. An additional benefit has been the reduction in transfusion reactions associated with fewer transfusion exposures.

The SLH Blood Utilization Committee includes physicians from 15 specialty areas, pharmacists, perfusionists, nurses, and quality experts. The goal is to improve patient outcomes by promoting safe and effective use of blood products and standardizing transfusion practice throughout the health system. The Blood Conservation program is available to assist in anemia management for inpatients and outpatients. They can be reached at 816-932-6183.

Quantiferon Now Performed In-House

Blood assays for tuberculosis, commonly referred to as interferon gamma release assays (IGRAs), are based on the principle of interferon-gamma being critical to regulation of the cell-mediated immune response to *Mycobacterium tuberculosis* (MTB) infection. Currently available FDA-approved IGRA assays for MTB include Quantiferon and T-spot TB. Both assays measure the interferon-gamma response to MTB proteins, including early secretory antigenic target-6 (ESAT-6) and culture filtrate protein-10 (CFP-10). Because these assays quantitate a biologic response, testing of a fresh blood specimen having adequate viable white blood cells is crucial to obtaining accurate results.

The CDC has published guidelines for use of blood assays for the diagnosis of latent and active TB (MMWR 2010;59, No. RR-5).

- In general, an IGRA may be used in all situations for which TST is indicated. An IGRA is the test of choice in two instances; for people who have received BCG, either as a vaccine or as chemotherapy and under circumstances where the tested person is unlikely to return to have the TST read.
- Either TST or IGRA may be used to test contacts of people with active TB infection, and in screening for occupational exposures.
- Routine testing with both TST and an IGRA is not generally recommended. Exceptions include suspected active TB in immune compromised patients, or indeterminate results from either test.
- TST testing is preferred for children aged <5 years.

Neither IGRA nor TST can distinguish active from latent tuberculosis. CDC recommends that persons with a positive TST or IGRA be evaluated for the likelihood of TB infection. A diagnosis of latent TB requires that active TB be excluded by history & physical examination, chest X-ray, and cultures when indicated. Although both sensitivity and specificity of the IGRA tests is high, negative results are not sufficient to exclude infection in suspect cases. Positive results may occur due to infection with other mycobacterial organisms, including *M. kansasii*, *M. szulgai*, and *M. marinum*, due to their production of ESAT-6 and CFP-10.

Effective March 4, Saint Luke's Microbiology will perform Quantiferon testing in-house, replacing the T-spot TB that is currently sent to a reference laboratory. A special collection kit with specific handling requirements is required for these specimens, due to the presence of antigens and controls within the collection tubes. Specimens must be received by the laboratory as soon as possible after collection to decrease the likelihood of indeterminate results. Specimens received greater than 16 hours after collection cannot be processed. Results are reported as positive, indeterminate, or negative.