



## Leukocyte Depleted Blood Transfusions and Post-Operative Morbidity: The Role of Leukodepletion Modality

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Allogenic blood transfusions represent one of the risk factors that has proved to enhance the incidence of post-operative morbidity and in particular the incidence of infective complications [1,2]. As a matter of fact, allogenic blood transfusions may create conditions leading to an immune down-regulation, clinical evidence known in the literature as allogenic blood transfusion-associated immunomodulation (TRIM) [3-6]. Its impact on post-operative course is not negligible considering that peri-operative transfusion rate in large cohorts of patients submitted to colorectal surgery ranges from 25,7% to 54,9% [5,7,8].

Leukocyte-depleted blood transfusions (LDBT) have been introduced in many countries over the last years to reduce negative side effects of blood transfusions [7,9,10]. On the other hand, several studies founded contrasting results regarding the real effects of LDBT on post-operative morbidity.

Anyway, when the clinical impact of LDBT is analysed, great attention should be paid to the modality of leukocyte-depletion that can be performed in a pre-storage or bedside filtration setting. Filtration of (buffy coat depleted) blood can be performed as pre-storage leukocyte depletion using pre-storage filters within 2 hours from the donation obtaining pre-storage LDBT, or performed after storage at time of transfusion (usually within 42 days from donation) using bedside filters and obtaining bedside filtered LDBT. Previous in vitro studies proved that white blood cell reduction by bedside filtration appears inadequate if compared to pre-storage filtration [11,12]. Furthermore, as it is performed few hours after blood donation, pre-storage leukocyte depletion has proved to be effective in removing leukocytes before cytokines production and before releasing of bioactive substances (histamine, 2-eosinophil cationic protein, eosinophil protein X, myeloperoxidase, and plasminogen activator inhibitor-12) contained in intracellular white cells granules; on the contrary, bedside leukocyte filtration is performed just before the transfusion and can occur even several days after the donation, therefore after production and release of cytokines and bioactive substances normally contained in WBC and supposed to be related to TRIM [13-15].

Compared to bedside-filtered, pre-storage LDBT are supposed to be associated with lower TRIM [13-15], but the clinical influence of leukodepletion modality (pre-storage vs bedside filtration) on post-operative morbidity in surgical patients was seldom investigated.

In trauma patients some retrospective studies demonstrated that the use of pre-storage leukoreduction is associated with a reduction of infective complications [16,17]. Several studies demonstrated that in open heart surgery leukoreduction reduced post-operative multiple organ dysfunction syndrome, infections and consequent short-term mortality [18,19]. A randomized controlled trial (RCT) investigating the effect of different types of leukoreduction modality in surgical patients regards open heart surgery showed that infective complication rates did not differ in patients transfused with pre or post-storage LDBT; this represent the only RCT comparing pre and post-storage LDBT in terms of post-operative complications [18]. Colorectal surgery represents one of the field in which the effects of LDBT has been more frequently studied.

In literature there are 6 randomized controlled trials (RCT)

evaluating post-operative morbidity after colorectal surgery in patients transfused with LDBT vs patients transfused with buffy coat depleted transfusions. Four of the studies demonstrated significantly reduced morbidity in patients transfused with LDBT [4,7,20,21]; two of them showed similar morbidity between groups, but both of them obtained a trend towards a lower rate of complications after LDBT [10,22]. There are no RCT investigating the effect of different types of leukoreduction modality in patients regards submitted to colorectal surgery. Nevertheless, a recent retrospective study found that post-operative morbidity and in particular post-operative infective morbidity was significantly increased in patients transfused with bedside filtered LDBT compared to patient's administered with pre-storage LDBT [23]. As a consequence, the potential role of pre-storage filtration in reducing post-operative morbidity (in particular infective complications) has already to be clarified.

In literature there are several studies investigating the effect of LDBT in different setting of patients; lots of these studies found that LDBT have a negative effect in terms of post-operative complications or on long-term survival (in oncologic patients) [24-26]. On the other hand, these surveys are mostly based on the comparison between patients transfused and patients not transfused; moreover the leukoreduction modality is sometimes not clearly specified. Basing on these results, transfusions should be restricted even when LDBT are available; nevertheless, it should be considered opportune to investigate which type of blood unit should be administered in patients who strictly necessitate to be transfused.

Since the reduction of post-operative complication is considered a main goal for surgeons of every surgical field, further RCTs comparing different leukodepletion modality in different surgical field should be considered of paramount interest.

Pre-storage leukodepletion is surely an expansive modality, but its real benefit should be clarified even in order to reduce costs related to prolonged hospital stay and for increased post-operative interventional procedures in patients with post-operative complications.

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