NIH Public Access
Author Manuscript
Liver Transpl. Author manuscript; available in PMC 2012 July 18.

Published in final edited form as:
Liver Transpl. 2011 February ; 17(2): 149–158. doi:10.1002/lt.22212.

Differential effect of plasma and red blood cell transfusion on acute lung injury and infection risk following liver transplantation

Alexander B. Benson, MD[1], **James R. Burton Jr., MD**[2], **Gregory L. Austin, MD**[2], **Scott W. Biggins, MD, MAS**[2], **Michael A. Zimmerman, MD**[3], **Igal Kam, MD**[3], **Susan Mandell, MD**[4], **Christopher C. Silliman, MD, PhD**[5], **Hugo Rosen, MD**[2], and **Marc Moss, MD**[1]

[1]Division of Pulmonary Sciences and Critical Care, University of Colorado, Aurora, CO

[2]Division of Gastroenterology and Hepatology, University of Colorado, Aurora, CO

[3]Department of Transplant Surgery, University of Colorado, Aurora, CO

[4]Department of Anesthesia, University of Colorado, Aurora, CO

[5]Senior Independent Researcher, Bonfils Blood Center; Denver, Colorado

Abstract

Rationale—Patients with chronic liver disease are at an increased risk of developing transfusion-associated acute lung injury (TRALI) from plasma containing blood products. Similarly, red blood cell transfusions have been associated with post-operative and nosocomial infections in surgical and critical care populations. Patients undergoing liver transplantation receive a large amount of cellular and plasma containing blood products, but it is presently unclear which blood components are associated with these post-operative complications.

Results—A retrospective cohort study of 525 consecutive liver transplant patients revealed a peri-operative TRALI incidence of 1.3% (7/525), 95%CI [0.6%–2.7%], associated with an increased hospital mortality (28.6% (2/7) vs. 2.9% (15/518), p=0.02) and intensive care unit (ICU) length of stay (2 days, [1–11] vs. 0 days [0–2], 0.03). Only high plasma containing blood products (plasma and platelets) were associated with the development of TRALI. A total of 14.3% (74/525) of patients developed a post-operative infection which was also associated with an increased in-hospital mortality (10.8% (8/74) vs. 2.0% (9/451), $p < 0.01$) and prolonged length of stay. Multivariate logistic regression identified the number of red blood cell units transfused (adj OR 1.08 95%CI [1.02–1.14], $p<0.01$), the presence of peri-operative renal dysfunction and re-operation to be significantly associated with post-operative infection.

Conclusions—Patients undergoing liver transplantation are at high risk of developing post-operative complications from blood transfusion. Plasma containing blood products were associated with the development of TRALI while red blood cells were associated with the development of post-operative infection in a dose dependent manner.

Keywords

transfusion-related acute lung injury; nosocomial infection; Pulmonary Edema; Blood Component Transfusion; Liver Cirrhosis

Corresponding Author: Alexander B Benson MD University of Colorado Denver Anschutz Medical Campus Research 2, Box C272, 9th floor 12770 East 19th Ave. Aurora, CO, USA 80045 Phone: (303)-724-6083 Fax: (303)-724-6042 Alexander.benson@ucdenver.edu.

Research performed at University of Colorado, Denver; Anschutz Medical Campus

NIH-PA Author Manuscript
NIH-PA Author Manuscript
NIH-PA Author Manuscript

NIH-PA Author Manuscript

NIH-PA Author Manuscript

NIH-PA Author Manuscript

Introduction

Infectious complications are among the most common causes of early death after liver transplantation (1–5). Postoperative pneumonia and surgical site infections have both been linked to intra-operative red blood cell (RBC) and plasma transfusion in liver transplant patients and other post-operative patient populations (4,6–12). However, the incidence and distribution of all postoperative infections as well as the type and pre-storage characteristics of the blood products associated with these infections in the liver transplant population is not clearly defined.

Postoperative respiratory complications following liver transplantation also carry a poor prognosis and have been previously reported to be associated with intra-operative transfusions (9,13–16). One of the most serious post-operative respiratory complications is the development of acute lung injury (ALI). Transfusion-Related Acute Lung Injury (TRALI) is diagnosed when ALI develops within six hours of receipt of blood products and is considered to be mechanistically related to transfusion (17). Epidemiologic studies in critically ill medical patients suggest that patients with chronic liver disease have the greatest individual risk of TRALI when compared to other populations (18–20). Though the incidence of acute lung injury has been reported in smaller series, the incidence of TRALI and the type of blood products associated with peri-operative TRALI in patients undergoing orthotopic liver transplant has not been described (13,16,21).

Currently, there is no consensus on what laboratory values should be used as trigger points for the transfusion of blood products during liver transplantation and as a result, transfusion strategies vary dramatically within and between transplant centers (22–25). Recently, the difference in overall mortality between transplant centers has been attributed to center-specific approaches to transfusion (26). The aim of this study was to describe both the incidence of post-operative infection and transfusion-related acute lung injury and the association between specific blood products and these complications in patient undergoing liver transplantation.

Materials and Methods

This protocol was approved by the Colorado Multiple Institutional Review Board prior to our secondary analyses of existing databases. We used a patient database from the Division of Hepatology and Liver Transplantation at the University of Colorado to identify a cohort of 525 consecutive patients who underwent liver transplantation between 2002 and 2009. We did not collect data prior to 2002 to minimize differences in practices that may have resulted from the introduction of organ allocation using the Model for End Stage Liver Disease (MELD) in 2002. Data on perioperative blood transfusion was extracted from both hepatology and anesthesia databases and the medical record. There were two main categories of primary outcome measures: the development of post-operative infectious and respiratory complications. These are defined below. Secondary outcome measures included in-hospital mortality, length of primary hospitalization and the length of stay in the intensive care unit (ICU).

Intra-operative Management

Our liver transplantation program has a team of four anesthesiologists who provide care for all recipients. This anesthesia team has established distinct criteria for the use of perioperative blood products. Therefore, transfusion practices at our institution are relatively uniform between physicians. Further all patients receive methylprednisolone (500 mg) and prophylactic antibiotics at the start of surgery.

NIH-PA Author Manuscript

NIH-PA Author Manuscript

NIH-PA Author Manuscript

In the immediate preoperative period patients are transfused with platelets if the count is less than 30/uL and given RBCs if the hemoglobin is less than 9 g/dL. No plasma is given prior to surgery. During surgery, RBCs are given to maintain a hemoglobin value of 10 g/dL. Intra-operative plasma and platelet transfusion is only considered if there is evidence of decreased clot formation. This is determined by evaluation of the thromboelastogram (TEG). When there is continued blood loss, evidence of decreased clot formation, a platelet count of less than 50/uL and the MA (clot strength) of the TEG is less than 50 mm, apheresed platelets are transfused. Fresh frozen plasma is given when the R (clotting time) value of the TEG is greater than 20 seconds. Cryoprecipitate is given when the alpha angle (rapidity of cross linking fibrin) is less than 40 degrees and the fibrinogen level is less than 100 mg/dL. Pro-hemostatic agents are only used as rescue drugs for bleeding that if it has not responded to transfusion. Aminocaproic acid (10 g) is given when there is fibrinolysis present on the TEG. Recombinant factor VII (40 ug/kg) is given when the TEG fails to deflect (straight line) or if two consecutive TEG readings show a prolongation of the R and K values with suboptimal clot formation despite adequate transfusion therapy according to the criteria described above.

Patients are managed to maintain a low CVP (6–10 mm Hg) by aggressive diuresis during surgery. Patients with renal failure have intraoperative hemodialysis with volume removal. All patients who meet standard criteria are extubated in the operating room at the conclusion of surgery using a protocol previously described by our institution (27). Perioperative management aims to maintain a low CVP by fluid restriction and diuresis and the majority of patients leave the operating room in negative fluid balance. In general, patients undergo a preoperative chest x-ray (CXR) to confirm central line placement and a post-operative CXR to assess for intra-operative changes in pulmonary status.

There were no pre-specified criteria regarding prestorage leukoreduction or male-donor plasma, but all units of red blood cells are required to be ≤ 10 days old and all platelets are allogenic and isolated via apheresis. At present all RBCs from our main blood supplier are leukoreduced and plasma is prepared from male or never pregnant donors in conjunction with the American Association of Blood Bank recommendations.

A post-operative operation was defined as a return to the operating room after transplantation and before the development of a nosocomial infection during the hospitalization that included the initial transplant. Kidney dysfunction was determined by the need for peri-operative dialysis defined as the need for dialysis within 48 hours prior to or after liver transplantation. Patients who only received 1 cycle of intra-operative dialysis, but no pre or post transplant dialysis are not included in this total as dialysis is frequently used for volume control intra-operatively and is less reflective of ongoing kidney dysfunction. Dialysis data and pre-transplant location (ie ICU, floor or home) was obtained from was gathered from our transplant database.

Definitions

The Model for End-Stage Liver Disease (MELD) score was retrospectively and prospectively shown to be highly predictive of short-term (<90 days) mortality in patients with all causes of end-stage liver disease including those on the liver transplant waiting list (28–29). This scoring system is currently used to rank patients on the liver transplant waiting list. The donor risk index (DRI) is a quantitative risk score for graft failure based on nine variables related to the characteristics of the donor and graft (30). Our calculation of the DRI is based on eight of nine variables as height of donor was not available from our database.

NIH-PA Author Manuscript

NIH-PA Author Manuscript

NIH-PA Author Manuscript

Outcome variable definitions

Post-operative Infection—Initial screening for the diagnosis of post-operative infectious diagnoses was performed using our hospital diagnostic coding database. Subsequently, the medical record of all patients identified as having any in-hospital infection was reviewed. Infections that developed prior to or within 48 hours of transplantation, after discharge from initial hospitalization, or >60 days after transplantation were not considered. Using the Centers for Disease Control (CDC) definitions for postoperative and nosocomial infections, patients were re-classified or excluded based on the results of a formal chart review (31–32). Infections that were considered to be viral in origin were not included in the analysis.

TRALI—Patients were defined as having TRALI based on the 2004 consensus conference definition requiring the development of acute lung injury (ALI) within 6 hours of the initiation of an infusion of transfused blood product (17). TRALI was defined by the development of hypoxemia and new bilateral infiltrates (see definition of ALI below) on the postoperative chest x-ray (CXR) that was temporally associated (within 6 hours) with intra-operative transfusion. We used the American-European Consensus Conference definition to define Acute Lung Injury (ALI): bilateral infiltrates on chest radiograph, a PaO_2/FiO_2 ratio < 248 (adjusting for the altitude in Denver, Colorado), and no clinical evidence of left atrial hypertension (33).

Circulatory Overload—Patients were defined as having circulatory overload and not TRALI if they had new evidence on the post-operative CXR of intravascular volume overload (large vascular pedicle, large azygos vein, cephalization of vessels or vascular indistinctness), or if the patient met TRALI criteria, but had rapid CXR resolution of their diffuse infiltrates over the subsequent 48 hours in association with a negative fluid balance. CXR abnormalities were determined by reviewing the formal dictated report on the immediate postoperative CXR.

Transfusion data

We used an internal diagnostic coding database and nurse completed transfusion slips in the medical record to identify the type, date, and time of each unit of blood product transfused during hospitalization. We were able to extract transfusion totals for each type of blood product for intra-operative, 24 and 48 hour intervals from the initiation of the transplant operation. Only intra-operative transfusion totals were analyzed for association with peri-operative TRALI while both 24 and 48 hour totals were analyzed for association with post-operative infection. We categorized whether each unit of red blood cells (RBCs) were leukoreduced or non-leukoreduced. As per protocol, none of the transfused units of RBCs were older than 10 days. All platelet preparations were either apheresed or autologous. The thawing time, sex or parity of donors with regard to plasma was unable to be obtained, but our main blood supplier began TRALI mitigation for plasma using both male-only and never-pregnant females in December, 2007. In addition, our main blood supplier adopted universal leukoreduction for RBCs in 2005.

Statistical Analysis

Chi Square test of independence was used to examine categorical variables at baseline and independent sample t-tests were used to compare continuous characteristics of the two groups. Univariate and multivariate logistic regression was used to evaluate associations between transfusion variables and other potential predictors of both primary and secondary outcome measures. A p value of < 0.1 on univariate analysis was required for inclusion in the multivariate analysis. A p value of < 0.05 was used elsewhere as the threshold for

NIH-PA Author Manuscript

NIH-PA Author Manuscript

NIH-PA Author Manuscript

statistical significance. Continuous variables are reported as medians and 25–75% quantiles denoted [ ].

Results

Data on 525 consecutive liver transplant patients were analyzed. Only, 2% (11/525) of the surgeries were re-transplants. The most common reason for transplant was cirrhosis due to hepatitis C virus [49% (259/525)]. Additionally, 42% of the hepatitis C positive patients had a coexistent history of previous alcohol abuse. The median patient age was 52 years old [46–57 years] and 67% were male. The majority of patients were of Caucasian 71% (375/525) or of Latino descent 21% (108/525). The median pre-operative MELD score was 25 [21–29]. Kidney dysfunction was present (ie. dialysis performed perioperatively) in 10% (55/525) of patients before and/or after transplantation. Pre-operative dialysis was performed in 8% (44/525) and post-operative dialysis in 9% (49/525) of all patients. A post-transplant re-operation was performed in 16% (83/525) of patients for a variety of reasons the most common of which were clot evacuation and cleanout (n=56) and anastomatic leaks (n=12). Diabetes was present in 16% (85/525) of patients. The pre-operative location of these patients included 44% (232/525) from home, 44% (231/525) were non-ICU inpatients and 12% (62/525) were in the intensive care unit immediately prior to transplantation.

Intra-operative transfusion characteristics

Eighty-six percent of all patients received an intra-operative red blood cell transfusion. Non-leukoreduced RBCs accounted for 45% of all transfused RBCs. The median number of red blood cells transfused was 8 units [3–15]. A total of 82% of patients received at least one intra-operative unit of plasma. In those patients who received a transfusion of plasma, the median amount received was 7 units [2–12]. In addition, 64% of patients received at least one unit of intra-operative platelet transfusion. In those patients who received a transfusion of platelets, the median amount received was 1 unit [0–2]. Only 14% of patients received cryoprecipitate. When transfusion trends were analyzed over time there was a significant trend toward an increase in use of both plasma ($p<0.01$) and RBCs ($p=0.03$), but statistically less albumin ($p<0.01$) was used when analyzed for differences at each two year interval from 2002 to 2009. There was no statistical difference in the laboratory MELD of the patients transplanted at each corresponding two year interval. The proportion of patients receiving non-leukoreduced RBCs also decreased significantly in the final 3 years of the study.

Characteristics of patients developing postoperative nosocomial infection— The incidence of post-operative infection in our cohort was 14% (74/525) 95%CI [11.4%–17.3%]. Surgical site infection was the most common 39% (29/74), followed by nosocomial pneumonia 30% (22/74), blood stream infection 27% (20/74), urinary tract infection 5% (5/74) and other sources 14% (10/74). In addition, 14% (10/74) of patients developed two or more post-operative infections. A total of 84% (62/74) of these infected patients had positive culture results. The most common infecting organism was enterococcus (26%) followed by staphylococcus (coagulase negative species (12%), methicillin resistant staphylococcus aureus (11%), methicillin sensitive staphylococcus aureus (7%)). Fungal infection made up 7% of infections. Pseudomonas aeruginosa accounted for 8% of infections (all pneumonia).

Risk factors for the development of nosocomial infection—A comparison of the demographics, transfusion characteristics and outcomes between the patients who did and did not develop post-operative infection is detailed in Table 1. Patients who eventually developed a post-operative infection more commonly had evidence of circulatory overload on their immediate post-operative CXR (47% vs. 27%; RR 2.08 [1.37–3.16], $p < 0.01$).

NIH-PA Author Manuscript

NIH-PA Author Manuscript

NIH-PA Author Manuscript

Multiple variables were evaluated in univariate analysis for association with post-operative infection including age, gender, etiology of liver disease, re-transplantation, re-operation, presence of kidney dysfunction, dialysis, pre-operative serum albumin, MELD and DRI scores as well as operation time and transfusion factors. DRI score was available on grafts for 86% (453/525) of patients and was not associated with post-operative infection (p=0.42). The only statistically significant non-transfusion related risk factors associated with the development of post-operative infection on univariate analysis were median length of operation in minutes (342 [283–428] vs. 305 [263–358], $p < 0.01$), re-operation rate (31% (23/74) vs. 11%(50/451), $p<0.01$) and presence of kidney dysfunction 23%(17/74) vs. 8%(34/451), $p<0.01$). All types of transfused blood products (RBCs, plasma, and platelets) showed a significant association with the development of a post-operative infection when analyzed on a per unit basis for intra-operative, 24 and 48 hour totals from the initiation of the transplant operation (Table 2). We chose to use transfusion totals for the 24 hour interval from the start of the transplant operation for all blood products in our multivariable analysis, but a similar analyses using intra-operative and 48 hour totals resulted in similar odds ratios and p values. A multivariable logistic regression model including operation time (minutes), re-operation (y/n), presence of kidney dysfunction in need of dialysis (y/n), 24 hour totals of plasma, platelets, red blood cells all analyzed as continuous variables on a per/unit basis, revealed red blood cells (adj OR 1.07 per unit 95%CI [1.02–1.14], p=.01) to be the only statistically significant transfusion-specific risk factors for the development of post-operative infection (Table 3). The presence or absence of leukoreduction did not significantly alter the presence or strength of the association. The presence of kidney dysfunction (adj OR 2,74 [1.34–5.46], $p<0.01$) and the need for a reoperation post-transplant (adj OR 2.28 [1.23–4.14], $p<0.01$) were also significantly associated with post-operative infection.

Incidence and transfusion-specific risk factors for TRALI—Overall, 2.1% (11/525) of patients had evidence of new post-operative bilateral infiltrate on CXR, but 4 of these patients were judged to have hydrostatic edema due to 48 hour resolution of hypoxemia and CXR abnormalities associated with fluid removal. Therefore, the incidence of TRALI was 1.3% (7/525) 95%CI [0.6%–2.7%]. In univariate analysis, only transfusion of plasma (OR 1.06 per unit of plasma 95% CI [1.00–1.11], $p =0.05$) and platelets (OR 1.44 per unit of platelets 95% CI [1.12–1.87], $p < 0.01$) were significant risk factors for TRALI on a per unit analysis. DRI score was not associated with the risk of TRALI (p=0.59). Other variable variables showing no statistical association with post-operative TRALI include: age, gender, etiology of liver disease, re-transplantation, serum albumin, MELD and DRI scores, operation time, pre or peri-operative dialysis, and intra-operative tidal volume. Neither volume of intra-operative albumin nor number of red blood cell transfusions received (leukoreduced or nonleukoreduced) were associated with the development of TRALI.

CXR characteristics and circulatory overload

Postoperative CXR abnormalities were common. Atelectasis or consolidation were present in 55% (287/525) of patients and 23% (122/525) had evidence of a pleural effusion or chest tube placed to drain a pleural effusion. Thirty percent (158/525) had evidence of intravascular volume overload (large vascular pedicle, enlarged azygos vein, cephalization of vessels or vascular indistinctness). In multivariable logistic regression analysis, the amount of intra-operative albumin was associated with CXR evidence of intravascular volume overload (adj OR 1.23 95% CI [1.08–1.39], $p < 0.01$).

TRALI and Post-operative infection increase both length of stay and in-hospital mortality—The development of TRALI was associated with a worse in-hospital

NIH-PA Author Manuscript

NIH-PA Author Manuscript

NIH-PA Author Manuscript

mortality with a relative risk (RR) of 9.9 [2.8–35.2], (29% (2/7) vs. 3% (15/518), p=0.01, and was associated with an increased ICU length of stay (2 days [1–11] vs. 0 days [0–2], p=0.03), but not post-operative hospital length of stay. CXR evidence of circulatory overload was associated with an increase in postoperative length of stay (10 day [8–16] vs. 9 days [7–14]), and ICU length of stay (1 day [0–2] vs. 0 days [0–2], both $p < 0.01$). Post-operative infection was also a significant risk factor for in-hospital mortality (RR 5.4 [2.2–13.6], 11% (8/74) vs. 2% (9/451), $p < 0.01$), hospital length of stay (18 [14–29] vs. 9 days [7–13], $p < 0.01$) and ICU length of stay (1.5 [0–3] vs. 0 [0–1], $p < 0.01$) (table 1).

Discussion

Multiple cohort studies in patients undergoing liver transplantation have found an association between the amount of intra-operative transfusion and worse outcomes (16,22–23,34–36). Postoperative infections are well known complications of transfusion in patients undergoing orthotopic liver transplantation, but the incidence of Transfusion Related Acute Lung Injury (TRALI) has been poorly defined (4,6,8,12,14–15,39–42). The results of this study demonstrate that patients undergoing liver transplantation have less risk of TRALI than that of bleeding critically ill patients with chronic liver disease not undergoing liver transplantation (18,20). Despite a low incidence, TRALI resulted in a 10 fold increase in hospital mortality and therefore is of clinical importance. In our cohort, only plasma containing blood products (platelets and plasma) were associated with TRALI, consistent with other reports in liver transplant and critically ill patients with chronic liver disease (16,18–19,21). In addition, transfused RBCs were associated in a dose-dependent fashion with post-operative infection which resulted in a five-fold increase in mortality. Prestorage leukoreduction did not influence this risk.

The risk of TRALI in this liver transplant cohort is much lower (1.3%) than the incidence (29.3%) seen at the same center over a similar time period (2002–2008) in patients with a similar severity of liver disease receiving similar amounts of all blood products who were admitted to the ICU for a variceal bleed (20). The two-event model of TRALI may explain this epidemiologic difference. In this model an underlying pro-inflammatory state activates pulmonary endothelial cells, resulting in the adherence and sequestration of neutrophils in the lung (43). These primed, hyperactive neutrophils are vulnerable to activation from antibodies, lipids and other biologic mediators found in blood products. These mediators cause release of the microbicidal arsenal from these adherent neutrophils leading to endothelial cell damage, capillary leak and ALI (44–45). Active sepsis is a pro-inflammatory condition that generally precludes patients from undergoing liver transplantation, but is very common in patients admitted with a variceal bleed (46–48). Also, patients undergoing transplantation generally receive high dose intra-operative glucocorticoids with potent immunosuppressive effects that may modulate the systemic inflammatory effect of the surgery. Lastly, transplant patients receive a new liver which may somehow change TRALI risk due to immunomodulatory effects of this unique event.

One third of patients had evidence of intravascular volume overload on postoperative CXR. When this circulatory overload progresses to pulmonary edema and is related to transfused blood products, the term transfusion-associated circulatory overload or TACO is utilized. The one third of patients with circulatory overload had significantly prolonged ICU and hospital length of stay as well as an increased post-operative infection risk. It is unknown whether this association is causal, but circulatory overload increases time on the mechanical ventilator, thereby leading to increased ICU length of stay and increasing the risk for post-operative infection. The amount of intra-operative albumin administration and not blood product transfusion was an independent risk factor for circulatory overload. Albumin has previously been shown to be associated with cardiopulmonary complications and increased

NIH-PA Author Manuscript

NIH-PA Author Manuscript

NIH-PA Author Manuscript

length of stay in patients undergoing liver transplantation and its use requires re-examination (49). It should be noted that only 4 patients had frank pulmonary edema attributed to a hydrostatic mechanism. The other patients in this subset had evidence of circulatory overload, but because this syndrome exists on a spectrum so it is unclear of how many of these patients would actually be given the diagnosis of TACO. Nevertheless, a low intra-operative central venous pressure strategy achieved by using diuretics and avoiding intravascular volume expansion with colloid and plasma has been shown to be safe and effective and thus should be considered (50–52).

The overall post-operative infection risk of 14% in our cohort and the incidence of pneumonia, surgical site infection and line sepsis are much lower than reported in previous clinical cohort studies (2,4,9,12,53). The reasons for this observation may be related to the fact that our transplant team has a very aggressive early extubation strategy (27). This strategy allows for rapid transfer out of the ICU or direct admission to the floor from the post-anesthesia care unit, resulting in early withdrawal of indwelling vascular and urinary catheters, and mobilization of patients. In addition, only relatively fresh RBCs (≤10 days old) are transfused into this patient population and age of blood has been shown to be a risk factor for infection (54).

As shown in other surgical populations, RBCs were an independent risk factor in a dose dependent fashion for post-operative infection in this cohort of patients undergoing liver transplantation (55–62). Each unit of RBCs transfused increases the risk of post-operative infection by 7%. Transfusion-related immunomodulation (TRIM) and its association with post-transfusion infection is a well known phenomenon, but the mechanisms are still uncertain. The are many immunomodulatory constituents some of which accumulate during storage including, but not limited to human leukocyte antigen peptides, bioactive lipids and soluble biologic response modifiers (63). Prestorage leukoreduction did not reduce this infectious risk which is consistent with studies in other surgical and critically ill patient populations; thus prestorage leukoreduction does not appear to protect against the known risks of transfused red blood cells (57,60,64–65). Because leukocytes contaminating stored red blood cells theoretically potentiate TRIM and subsequent infectious risk by increasing the amount of lipids and inflammatory cytokines (IL-6. IL-8, TNF-α) that accumulate during storage, we must consider the possibility that because our patients received only relatively fresh blood, the effect of leukoreduction may have been mitigated (66–67). Moving forward, the issue of leukoreduction is of less clinical importance as most blood centers in industrialized nations have developed a policy of universal leukoreduction.

Strategies to decrease total use of RBCs during liver transplantation should be studied clinically in a bundled approach. Some of these strategies include avoiding intravascular volume expansion (maintain low central venous pressure). Elevated hydrostatic pressures in the vascular beds have been associated with increased blood loss (50–52). Selective use of pharmacologic therapies may offer hemostatic benefit in certain patient populations though timing and validated clotting studies that accurately predict which agents will clinically benefit particular subgroups of patients are lacking (68–74). Use of cell savers and improved surgical techniques may also decrease transfusion needs (75). Though these techniques, some transplant centers have been able to eliminate transfusion of any blood products in >80% of patients undergoing transplantation (76).

The main limitation of our study is an inability to accurately differentiate TRALI from hydrostatic pulmonary edema and circulatory overload. We were stringent in our TRALI criteria in that we did not include any patients who improved with fluid removal even if they met TRALI consensus criteria which could have underestimated the incidence of TRALI. This would likely bias any transfusion effect toward the null hypothesis strengthening the

NIH-PA Author Manuscript

NIH-PA Author Manuscript

NIH-PA Author Manuscript

association found between plasma transfusion and TRALI, but falsely lowering the reported incidence. In addition, using CXR reports to diagnose circulatory overload has poor sensitivity though specificity when using a pre-operative to post-operative approach is likely quite high. For this reason, our definition of circulatory overload may have also resulted in a falsely low reported incidence. Another limitation was our inability to adequately control for the amount of tissue damage, technical difficulties and complications during the surgical procedure. These factors likely result in a greater number of transfusions and may increase infection risk unrelated to transfusion. We did include total operative time as a surrogate for these factors in our logistic regression model with transfusion variables and found that it was not an independent risk factor. To attempt to control for severity of illness post-transfusion we adjusted for the incidence of re-operation. Though re-operation was associated with infection it may not be causal, but may instead identify patients who stay longer in the hospital and therefore are at higher risk to develop infection. Due to the observational study design we can only prove association and temporal relationship between blood transfusion and post-operative complications, but we cannot be sure the association is causal. There are also potentially unmeasured confounding variables that we were unable to adjust for or identify. In addition, we were unfortunately not able to report on the sex or parity of the plasma donors which may be transfusion specific risk factors for TRALI and post-operative infection (77–78). Lastly, we were unable to evaluate the effects of qualitative parameters of liver dysfunction such as ascites and encephalopathy on our outcome measures.

Post-operative infection is common in patients undergoing orthotopic liver transplantation and is associated with the number of red blood cell units transfused. In contrast, plasma containing blood products (plasma and platelets), but not red cells are associated with the development of TRALI in this patient population. Future clinical trials in liver transplant patients should now focus on mitigating the use or preparation of a specific blood product while analyzing the effect on the appropriate clinical complication.

Acknowledgments

Funding sources: NHLBI K24 HLO89223; CCS: grant GM49222 from NIGMS, NIH; American Gastroenterological Association Research Scholar Award; National Institute of Diabetes and Digestive and Kidney Diseases (DK076565, SWB).

References

1. Torbenson M, Wang J, Nichols L, Jain A, Fung J, Nalesnik MA. Causes of death in autopsied liver transplantation patients. Mod Pathol. Jan; 1998 11(1):37–46. [PubMed: 9556421]
2. Kibbler CC. Infections in liver transplantation: risk factors and strategies for prevention. The Journal of hospital infection. Jun; 1995 30(Suppl):209–17. [PubMed: 7560952]
3. del Pozo JL. Update and actual trends on bacterial infections following liver transplantation. World J Gastroenterol. Aug 28; 2008 14(32):4977–83. [PubMed: 18763277]
4. Nemes B, Sarvary E, Sotonyi P, Gerlei Z, Doros A, Galffy Z, Fehervari I, et al. Factors in association with sepsis after liver transplantation: the Hungarian experience. Transplantation proceedings. Jun; 2005 37(5):2227–8. [PubMed: 15964385]
5. Sun HY, Cacciarelli TV, Singh N. Identifying a targeted population at high risk for infections after liver transplantation in the MELD era. Clinical transplantation. May 10.2010 epub.
6. Shen YH, Fan J, Zhou J, Wu ZQ, Qiu SJ, Huang XW, Sun J, et al. Pulmonary infection and its risk factors after orthotopic liver transplantation. Chinese journal of hepatology. Nov; 2007 15(11):833–6. [PubMed: 18073066]
7. Patel R, Portela D, Badley AD, Harmsen WS, Larson-Keller JJ, Ilstrup DM, Keating MR, et al. Risk factors of invasive Candida and non-Candida fungal infections after liver transplantation. Transplantation. Oct 15; 1996 62(7):926–34. [PubMed: 8878386]

NIH-PA Author Manuscript

NIH-PA Author Manuscript

NIH-PA Author Manuscript

8. Paya CV, Wiesner RH, Hermans PE, Larson-Keller JJ, Ilstrup DM, Krom RA, et al. Risk factors for cytomegalovirus and severe bacterial infections following liver transplantation: a prospective multivariate time-dependent analysis. Journal of hepatology. Jun; 1993 18(2):185–95. [PubMed: 8409334]
9. Xia D, Yan LN, Xu L, Li B, Zeng Y, Wen TF, Zhao JC, et al. Postoperative severe pneumonia in adult liver transplant recipients. Transplantation proceedings. Nov; 2006 38(9):2974–8. [PubMed: 17112878]
10. Motschman TL, Taswell HF, Brecher ME, Rakela J, Grambsch PM, Larson-Keller JJ, Rettke SR, et al. Intraoperative blood loss and patient and graft survival in orthotopic liver transplantation: their relationship to clinical and laboratory data. Mayo Clinic proceedings. Mar; 1989 64(3):346–55. [PubMed: 2539541]
11. Manez R, Kusne S, Martin M, Linden P, Irish W, Torre-Cisneros J, Kramer D, et al. The impact of blood transfusion on the occurrence of pneumonitis in primary cytomegalovirus infection after liver transplantation. Transfusion. Jul; 1993 33(7):594–7. [PubMed: 8392759]
12. George DL, Arnow PM, Fox AS, Baker AL, Thistlethwaite JR, Emond JC, Whitington PF, et al. Bacterial infection as a complication of liver transplantation: epidemiology and risk factors. Reviews of infectious diseases. May–Jun; 1991 13(3):387–96. [PubMed: 1866541]
13. Li GS, Ye QF, Xia SS, Chen ZS, Zeng FJ, Lin ZB, Gong NQ, et al. Acute respiratory distress syndrome after liver transplantation: etiology, prevention and management. Hepatobiliary Pancreat Dis Int. Aug; 2002 1(3):330–4. [PubMed: 14607702]
14. Pirat A, Ozgur S, Torgay A, Candan S, Zeyneloglu P, Arslan G. Risk factors for postoperative respiratory complications in adult liver transplant recipients. Transplantation proceedings. Jan–Feb; 2004 36(1):218–20. [PubMed: 15013351]
15. Snowden CP, Hughes T, Rose J, Roberts DR. Pulmonary edema in patients after liver transplantation. Liver Transpl. Jul; 2000 6(4):466–70. [PubMed: 10915170]
16. Pereboom IT, de Boer MT, Haagsma EB, Hendriks HG, Lisman T, Porte RJ. Platelet transfusion during liver transplantation is associated with increased postoperative mortality due to acute lung injury. Anesthesia and analgesia. Apr; 2009 108(4):1083–91. [PubMed: 19299765]
17. Toy P, Popovsky MA, Abraham E, Ambruso DR, Holness LG, Kopko PM, McFarland JG, Nathens AB, et al. Transfusion-related acute lung injury: definition and review. Critical care medicine. Apr; 2005 33(4):721–6. [PubMed: 15818095]
18. Gajic O, Rana R, Winters JL, Yilmaz M, Mendez JL, Rickman OB, O'Byrne MM, et al. Transfusion-related acute lung injury in the critically ill: prospective nested case-control study. American journal of respiratory and critical care medicine. Nov 1; 2007 176(9):886–91. [PubMed: 17626910]
19. Nakazawa H, Ohnishi H, Okazaki H, Hashimoto S, Hotta H, Watanabe T, Ohkawa R, et al. Impact of fresh-frozen plasma from male-only donors versus mixed-sex donors on postoperative respiratory function in surgical patients: a prospective case-controlled study. Transfusion. Nov; 2009 49(11):2434–41. [PubMed: 19624605]
20. Benson AG, Silliman C, Moss M. Transfusion-related acute lung injury in ICU patients admitted with gastrointestinal bleeding. Intensive Care Medicine. 2010; 36(10):1710–17. [PubMed: 20658125]
21. Yost CS, Matthay MA, Gropper MA. Etiology of acute pulmonary edema during liver transplantation: a series of cases with analysis of the edema fluid. Chest. Jan; 2001 119(1):219–23. [PubMed: 11157607]
22. Boin IF, Leonardi MI, Luzo AC, Cardoso AR, Caruy CA, Leonardi LS. Intraoperative massive transfusion decreases survival after liver transplantation. Transplantation proceedings. Apr; 2008 40(3):789–91. [PubMed: 18455018]
23. Massicotte L, Sassine MP, Lenis S, Seal RF, Roy A. Survival rate changes with transfusion of blood products during liver transplantation. Canadian journal of anaesthesia. Feb; 2005 52(2):148–55. [PubMed: 15684254]
24. Massicotte L, Sassine MP, Lenis S, Roy A. Transfusion predictors in liver transplant. Anesthesia and analgesia. May; 2004 98(5):1245–51. [PubMed: 15105195]

NIH-PA Author Manuscript

NIH-PA Author Manuscript

NIH-PA Author Manuscript

25. Massicotte L, Lenis S, Thibeault L, Sassine MP, Seal RF, Roy A. Reduction of blood product transfusions during liver transplantation. Canadian journal of anaesthesia. May; 2005 52(5):545–6. [PubMed: 15872137]
26. Nemes B, Polak W, Ther G, Hendriks H, Kobori L, Porte RJ, Sarvary E, et al. Analysis of differences in outcome of two European liver transplant centers. Transpl Int. May; 2006 19(5): 372–80. [PubMed: 16623872]
27. Mandell MS, Stoner TJ, Barnett R, Shaked A, Bellamy M, Biancofiore G, Niemann C, et al. A multicenter evaluation of safety of early extubation in liver transplant recipients. Liver Transpl. Nov; 2007 13(11):1557–63. [PubMed: 17969193]
28. Freeman RB Jr. Wiesner RH, Harper A, McDiarmid SV, Lake J, Edwards E, Merion R, et al. The new liver allocation system: moving toward evidence-based transplantation policy. Liver Transpl. Sep; 2002 8(9):851–8. [PubMed: 12200791]
29. Malinchoc M, Kamath PS, Gordon FD, Peine CJ, Rank J, ter Borg PC. A model to predict poor survival in patients undergoing transjugular intrahepatic portosystemic shunts. Hepatology. Apr; 2000 31(4):864–71. [PubMed: 10733541]
30. Feng S, Goodrich NP, Bragg-Gresham JL, Dykstra DM, Punch JD, Debroy MA, Greenstein SM, et al. Characteristics associated with liver graft failure: the concept of a donor risk index. Am J Transplant. 2006; 6:783–90. [PubMed: 16539636]
31. Garner JS, Jarvis WR, Emori TG, Horan TC, Hughes JM. CDC definitions for nosocomial infections, 1988. Am J Infect Control. Jun; 1988 16(3):128–40. [PubMed: 2841893]
32. Horan TC, Gaynes RP, Martone WJ, Jarvis WR, Emori TG. CDC definitions of nosocomial surgical site infections, 1992: a modification of CDC definitions of surgical wound infections. Am J Infect Control. Oct; 1992 20(5):271–4. [PubMed: 1332552]
33. Bernard GR, Artigas A, Brigham KL, Carlet J, Falke K, Hudson L, Lamy M, et al. The American-European Consensus Conference on ARDS. Definitions, mechanisms, relevant outcomes, and clinical trial coordination. American journal of respiratory and critical care medicine. Mar; 1994 149(3 Pt 1):818–24. [PubMed: 7509706]
34. Schroeder RA, Johnson LB, Plotkin JS, Kuo PC, Klein AS. Total blood transfusion and mortality after orthotopic liver transplantation. Anesthesiology. Jul; 1999 91(1):329–30. [PubMed: 10422972]
35. Palomo Sanchez JC, Jimenez C, Moreno Gonzalez E, Garcia I, Palma F, Loinaz C, Gonzalez Ghamorro A. Effects of intraoperative blood transfusion on postoperative complications and survival after orthotopic liver transplantation. Hepato-gastroenterology. Jul–Aug; 1998 45(22): 1026–33. [PubMed: 9756002]
36. Nemes B, Kobori L, Galffy Z, Lengyel G, Doros A, Sarvary E, Perner F, et al. Clinical factors influencing the complications and survival of liver transplantation in Hungary. Orvosi hetilap. Jul 24; 2005 146(30):1567–74. [PubMed: 16136733]
37. de Boer MT, Christensen MC, Asmussen M, van der Hilst CS, Hendriks HG, Slooff MJ, Porte RJ. The impact of intraoperative transfusion of platelets and red blood cells on survival after liver transplantation. Anesthesia and analgesia. Jan; 2008 106(1):32–44. [PubMed: 18165548]
38. Roffey P, Thangathurai D, Mikhail M, Riad M, Mogos M. TRALI and massive transfusion. Resuscitation. 2003; 58:121. [PubMed: 12867319]
39. Kusne S, Dummer JS, Singh N, Iwatsuki S, Makowka L, Esquivel C, Tzakis AG, et al. Infections after liver transplantation. An analysis of 101 consecutive cases. Medicine. Mar; 1988 67(2):132–43. [PubMed: 3280944]
40. Rouch DA, Thistlethwaite JR, Lichtor L, Emond JC, Broelsch CE. Effect of massive transfusion during liver transplantation on rejection and infection. Transplantation proceedings. Dec; 1988 20(6):1135–7. [PubMed: 3059596]
41. Hong SK, Hwang S, Lee SG, Lee LS, Ahn CS, Kim KH, Moon DB, et al. Pulmonary complications following adult liver transplantation. Transplantation proceedings. Nov; 2006 38(9): 2979–81. [PubMed: 17112879]
42. Koch C, Li L, Figueroa P, Mihaljevic T, Svensson L, Blackstone EH. Transfusion and pulmonary morbidity after cardiac surgery. The Annals of thoracic surgery. Nov; 2009 88(5):1410–8. [PubMed: 19853083]

NIH-PA Author Manuscript

NIH-PA Author Manuscript

NIH-PA Author Manuscript

43. Silliman CC, McLaughlin NJ. Transfusion-related acute lung injury. Blood reviews. May; 2006 20(3):139–59. [PubMed: 16360246]
44. Silliman CC. The two-event model of transfusion-related acute lung injury. Critical care medicine. May; 2006 34(5 Suppl):S124–31. [PubMed: 16617256]
45. Bux J, Sachs UJ. The pathogenesis of transfusion-related acute lung injury (TRALI). British journal of haematology. Mar; 2007 136(6):788–99. [PubMed: 17341264]
46. Soares-Weiser K, Paul M, Brezis M, Leibovici L. Evidence based case report. Antibiotic treatment for spontaneous bacterial peritonitis. BMJ (Clinical research ed). Jan 12; 2002 324(7329):100–2.
47. Deschenes M, Villeneuve JP. Risk factors for the development of bacterial infections in hospitalized patients with cirrhosis. The American journal of gastroenterology. Aug; 1999 94(8): 2193–7. [PubMed: 10445549]
48. Bernard B, Grange JD, Khac EN, Amiot X, Opolon P, Poynard T. Antibiotic prophylaxis for the prevention of bacterial infections in cirrhotic patients with gastrointestinal bleeding: a meta-analysis. Hepatology. Jun; 1999 29(6):1655–61. [PubMed: 10347104]
49. Johnson PN, Romanelli F, Smith KM, Ranjan D, Butler JS, Clifford TM. Analysis of morbidity in liver transplant recipients following human albumin supplementation: a retrospective pilot study. Progress in transplantation. Sep; 2006 16(3):197–205. [PubMed: 17007153]
50. Massicotte L, Lenis S, Thibeault L, Sassine MP, Seal RF, Roy A. Effect of low central venous pressure and phlebotomy on blood product transfusion requirements during liver transplantations. Liver Transpl. Jan; 2006 12(1):117–23. [PubMed: 16382461]
51. Massicotte L, Beaulieu D, Thibeault L, Roy JD, Marleau D, Lapointe R, Roy A. Coagulation defects do not predict blood product requirements during liver transplantation. Transplantation. Apr 15; 2008 85(7):956–62. [PubMed: 18408574]
52. Feng ZY, Xu X, Zhu SM, Bein B, Zheng SS. Effects of Low Central Venous Pressure During Preanhepatic Phase on Blood Loss and Liver and Renal Function in Liver Transplantation. World J Surg. Apr 7.2010 epub.
53. Asensio A, Ramos A, Cuervas-Mons V, Cordero E, Sanchez-Turrion V, Blanes M, Cervera C, et al. Effect of antibiotic prophylaxis on the risk of surgical site infection in orthotopic liver transplant. Liver Transpl. Jun; 2008 14(6):799–805. [PubMed: 18508358]
54. Koch CG, Li L, Sessler DI, et al. Duration of red-cell storage complications after cardiac surgery. New England Journal of Medicine. 2008; 358:1229–1239. [PubMed: 18354101]
55. Mohri Y, Tonouchi H, Miki C, Kobayashi M, Kusunoki M. Incidence and risk factors for hospital-acquired pneumonia after surgery for gastric cancer: results of prospective surveillance. World journal of surgery. Jun; 2008 32(6):1045–50. [PubMed: 18324344]
56. Izuel Rami M, Garcia Erce JA, Gomez-Barrera M, Cuenca Espierrez J, Abad Sazatornil R, Rabanaque Hernandez MJ. Relationship between allogeneic blood transfusion, iron deficiency and nosocomial infection in patients with hip fracture. Medicina clinica. Nov 15; 2008 131(17):647–52. [PubMed: 19087790]
57. Friese RS, Sperry JL, Phelan HA, Gentilello LM. The use of leukoreduced red blood cell products is associated with fewer infectious complications in trauma patients. American journal of surgery. Jul; 2008 196(1):56–61. [PubMed: 18513694]
58. Michalopoulos A, Geroulanos S, Rosmarakis ES, Falagas ME. Frequency, characteristics, and predictors of microbiologically documented nosocomial infections after cardiac surgery. Eur J Cardiothorac Surg. Apr; 2006 29(4):456–60. [PubMed: 16481186]
59. El Solh AA, Bhora M, Pineda L, Dhillon R. Nosocomial pneumonia in elderly patients following cardiac surgery. Respiratory medicine. Apr; 2006 100(4):729–36. [PubMed: 16126381]
60. Sharma AD, Slaughter TF, Clements FM, Sreeram G, Newman MF, Phillips-Bute B, Bredehoeft SJ, et al. Association of leukocyte-depleted blood transfusions with infectious complications after cardiac surgery. Surgical infections. 2002; 3(2):127–33. [PubMed: 12519479]
61. Leal-Noval SR, Rincon-Ferrari MD, Garcia-Curiel A, Herruzo-Aviles A, Camacho-Larana P, Garnacho-Montero J, Amaya-Villar R. Transfusion of blood components and postoperative infection in patients undergoing cardiac surgery. Chest. May; 2001 119(5):1461–8. [PubMed: 11348954]

NIH-PA Author Manuscript

NIH-PA Author Manuscript

NIH-PA Author Manuscript

62. Rebollo MH, Bernal JM, Llorca J, Rabasa JM, Revuelta JM. Nosocomial infections in patients having cardiovascular operations: a multivariate analysis of risk factors. The Journal of thoracic and cardiovascular surgery. Oct; 1996 112(4):908–13. [PubMed: 8873716]
63. Buddeberg F, Schimmer BB, Spahn DR. Transfusion-transmissable infections and transfusion-related immunomodulation. Best Pract Res Clin Anaesthesiol. Sep; 2008 22(3):503–17. [PubMed: 18831300]
64. Taylor RW, O'Brien J, Trottier SJ, Manganaro L, Cytron M, Lesko MF, Arnzen K, et al. Red blood cell transfusions and nosocomial infections in critically ill patients. Critical care medicine. Sep; 2006 34(9):2302–8. [PubMed: 16849995]
65. Hebert PC, Fergusson D, Blajchman MA, Wells GA, Kmetic A, Coyle D, Heddle N, et al. Clinical outcomes following institution of the Canadian universal leukoreduction program for red blood cell transfusions. Jama. Apr 16; 2003 289(15):1941–9. [PubMed: 12697796]
66. Silliman CC, Paterson AJ, Dickey WO, Stroneck DF, Popovsky MA, Caldwell SA, Ambruso DR. The association of biologically active lipids with the development of transfusion-related acute lung injury: a retrospective study. Transfusion. Jul; 1997 37(7):719–26. [PubMed: 9225936]
67. Kristiansson M, Soop M, Saraste L, Sundqvist KG. Cytokines in stored red blood cell concentrates: promoters of systemic inflammation and simulators of acute transfusion reactions? Acta anaesthesiologica Scandinavica. Apr; 1996 40(4):496–501. [PubMed: 8738697]
68. Xia VW, Steadman RH. Antifibrinolytics in orthotopic liver transplantation: current status and controversies. Liver Transpl. Jan; 2005 11(1):10–8. [PubMed: 15690531]
69. Triulzi DJ. Transfusion support in liver transplantation. Current hematology reports. Nov; 2004 3(6):444–9. [PubMed: 15496279]
70. Lodge JP, Jonas S, Jones RM, Olausson M, Mir-Pallardo J, Soefelt S, Garcia-Valdecasas JC, et al. Efficacy and safety of repeated perioperative doses of recombinant factor VIIa in liver transplantation. Liver Transpl. Aug; 2005 11(8):973–9. [PubMed: 16035095]
71. Planinsic RM, van der Meer J, Testa G, Grande L, Candela A, Porte RJ, Ghobrial RM, et al. Safety and efficacy of a single bolus administration of recombinant factor VIIa in liver transplantation due to chronic liver disease. Liver Transpl. Aug; 2005 11(8):895–900. [PubMed: 16035081]
72. Tripodi A, Mannucci PM. Abnormalities of hemostasis in chronic liver disease: reappraisal of their clinical significance and need for clinical and laboratory research. Journal of hepatology. Apr; 2007 46(4):727–33. [PubMed: 17316874]
73. Shah NL, Caldwell SH, Berg CL. The role of anti-fibrinolytics, rFVIIa and other pro-coagulants: prophylactic versus rescue? Clin Liver Dis. Feb; 2009 13(1):87–93. [PubMed: 19150313]
74. Roullet S, Pillot J, Freyburger G, Biais M, Quinart A, Rault A, Revel P, et al. Rotation thromboelastometry detects thrombocytopenia and hypofibrinogenaemia during orthotopic liver transplantation. Br J Anaesth. Apr; 2010 104(4):422–8. [PubMed: 20185519]
75. Massicotte L, Thibeault L, Beaulieu D, Roy JD, Roy A. Evaluation of cell salvage autotransfusion utility during liver transplantation. HPB (Oxford). 2007; 9(1):52–7. [PubMed: 18333113]
76. Massicotte L, Beaulieu D, Roy JD, Marleau D, Vandenbroucke F, Dagenais M, Lapointe R, et al. MELD score and blood product requirements during liver transplantation: no link. Transplantation. Jun 15; 2009 87(11):1689–94. [PubMed: 19502961]
77. Chapman CE, Stainsby D, Jones H, Love E, Massey E, Win N, Navarrete C, et al. Ten years of hemovigilance reports of transfusion-related acute lung injury in the United Kingdom and the impact of preferential use of male donor plasma. Transfusion. Mar; 2009 49(3):440–52. [PubMed: 18980623]
78. Eder AF, Herron R, Strupp A, Dy B, Notari EP, Chambers LA, Dodd RY, et al. Transfusion-related acute lung injury surveillance (2003–2005) and the potential impact of the selective use of plasma from male donors in the American Red Cross. Transfusion. Apr; 2007 47(4):599–607. [PubMed: 17381617]

NIH-PA Author Manuscript
NIH-PA Author Manuscript
NIH-PA Author Manuscript

Table 1

Characteristics and outcomes of liver transplant patients stratified by post-operative nosocomial infection

Characteristics (n=525)	No post-operative infection(n=451)	Post-operative infection (n=74)	P value
Age (years)	52 [46–57]	52 [47–57]	0.66
Gender (% male)	66% (300/451)	72% (53/74)	0.80
Race			0.11
Caucasian	72% (326/451)	64% (47/74)	
African American	4% (17/451)	5% (4/74)	
Hispanic	20% (88/451)	27% (20/74)	
Other	4% (20/451)	4% (3/74)	
Etiology			0.24
Hepatitis C Virus (HCV)	28% (128/451)	31% (23/74)	
HCV and alcohol	21% (93/451)	20% (15/74)	
Alcohol	10% (44/451)	8% (6/74)	
Hepatitis B virus	4% (19/451)	7% (5/74)	
Non alcoholic steatohepatitis	2% (10/451)	7% (5/74)	
Primary biliary sclerosis	4% (19/451)	0% (0/74)	
Primary sclerosing cholangitis	10% (46/451)	11% (8/74)	
Acute Liver Failure	3% (13/451)	3% (2/74)	
Cryptogenic Cirrhosis	4% (16/451)	4% (3/74)	
Other	14% (63/451)	9% (7/74)	
MELD	25 [21–29]	27 [22–31]	0.17
DRI score (n=453)	1.47 [1.34–1.61]	1.49 [1.36–1.65]	0.42
Albumin g/dl (n=457)	3.1 [2.6–3.5]	3.2 [2.6–3.6]	0.53
Operation time (min)	305 [263–358]	342 [283–428]	< 0.01
Re-transplant	2.2% (10/451)	1.4% (1/74)	0.61
Re-operation (y/n)	11% (50/451)	31% (23/74)	< 0.01
Kidney dysfunction-pre or post-op dialysis (y/n)	8% (38/451)	23% (17/74)	< 0.01
Pre-op dialysis (y/n)	8% (34/451)	14% (10/74)	0.10
Post-op dialysis (y/n)	7% (33/451)	22% (16/74)	< 0.01
Diabetes (y/n)	17% (75/451)	14% (10/74)	0.50
Pre-transplant location			0.42
ICU	11% (49/451)	18% (13/74)	
Hospital floor	44% (200/451)	42% (31/74)	
Home	45% (202/451)	41% (30/74)	
Outcome measures			
CXR findings			
Circulatory Overload	27% (123/451)	47% (35/74)	< 0.01
Pleural effusion	20% (91/451)	42% (31/74)	< 0.01
Atelectasis	52% (236/451)	69% (51/74)	< 0.01

NIH-PA Author Manuscript

NIH-PA Author Manuscript

NIH-PA Author Manuscript

Characteristics (n=525)	No post-operative infection(n=451)	Post-operative infection (n=74)	P value
TRALI	1% (5/451)	3% (2/74)	0.31
Mortality	2% (9/461)	11% (8/74)	< 0.01
ICU length of stay (days)	0 [0–2]	2 [1–5]	< 0.01
Postoperative length of stay (days)	9 [7–13]	18 [14–30]	< 0.01

NIH-PA Author Manuscript

NIH-PA Author Manuscript

NIH-PA Author Manuscript

Table 2

Difference in frequency and amount of transfused blood products between patients with and without post-operative infections

Transfused product and interval	No post-op infection	Post-op infection	P value
Any plasma (24h) (y/n)	80%	97%	< 0.01
plasma first (24h) (units)	6 [2–11]	10 [6–17.5]	< 0.01
plasma first (48h) (units)	6 [2–12]	12 [8–21]	< 0.01
Platelets (24h) (y/n)	61%	85%	< 0.01
Platelets (24h) (units)	1 [0–2]	2 [1–3]	< 0.01
Platelets (48h) (units)	1 [0–3]	3 [1–5]	< 0.01
Any RBCs (24h) (y/n)	84%	100%	< 0.01
Non-leukoreduced RBCs (24h)	0 [0–6]	3.5 [0–12]	< 0.01
Non-leukoreduced RBCs (48h)	0 [0–8]	4 [0–16]	< 0.01
Leukoreduced RBCs (24h)	1 [0–8]	6.5 [0–16]	< 0.01
Leukoreduced RBCs (48h)	2 [0–10]	9.5 [0–19]	< 0.01
Total albumin volume (L)	1.5 [1.0–2.5]	1.5 [0.5–2.5]	0.24

NIH-PA Author Manuscript

NIH-PA Author Manuscript

NIH-PA Author Manuscript

Table 3

Multivariate analysis of risk factors for post-operative nosocomial infection

Transfusion and patient-specific risk factors	Adj. OR	95% Confidence Interval	P value
Operation time (min)	1.00	0.99–1.00	0.33
Plasma (per unit) (24h)	0.95	0.89–1.02	0.18
Platelets (per 10 pack) (24h)	1.11	0.92–1.34	0.28
Red blood cells (per unit) (24h)	1.08	1.02–1.14	<0.01*
Pre and/or post-operative dialysis (y/n)	2.74	1.34–5.46	<0.01*
Re-operation between transplant and infection (y/n)	2.28	1.23–4.14	<0.01*