1580. Characteristics of Early vs. Late Onset Post-transplant Lymphoproliferative Disorder After Liver Transplant:– A Descriptive Study of the United Network of Organ Sharing (UNOS) Database

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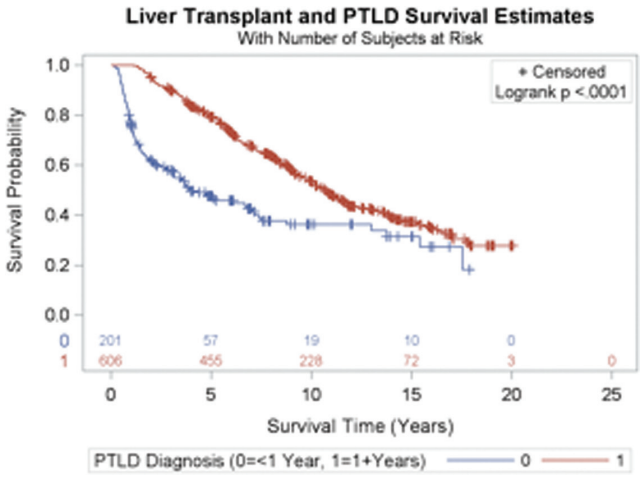
Background. Post-transplant lymphoproliferative disorder (PTLD) is a devastating complication of solid-organ transplant. In liver transplant, studies comparing the risk factors for early vs. late onset PTLD have been limited to single centers. Using a national database, we sought to compare early and late onset PTLD in adult and pediatric liver transplant patients in terms of patient characteristics, immunosuppressive regimens, and mortality.

Methods. We conducted a retrospective analysis of the UNOS database to compare early (<1 year) and late (1+ year) onset PTLD in pediatric (<18) and adult (18+) liver transplant patients. We compared patient demographics, co-morbid conditions, immunosuppressive regimens, Epstein-Barr virus (EBV) and cytomegalovirus (CMV) risk status, reason for transplant, and mortality. We categorized EBV and CMV risk status into high, intermediate, and low based on donor and recipient serostatus. Categorical variables were analyzed using Fisher's exact test. The Kaplan–Meier method, log-rank test, and multivariable Cox regression were used to examine mortality.

Results. Ninety-two pediatric patients and 807 adult patients met study criteria. Overall mortality was 35.87 and 53.78% for pediatric and adult patients, respectively. In adults, unadjusted survival was significantly different for early vs. late onset PTLD ($P < 0.001$; Figure 1); the latter was associated with a 64.33% decreased mortality risk (95% CI: 51.17–73.95%; $P < 0.001$). There was no difference in mortality in pediatric patients ($P = 0.549$). In neither population was EBV risk status associated with early vs. late onset PTLD. In adults, tacrolimus, mycophenolate mofetil (MMF), and steroid maintenance therapy were associated with late onset PTLD ($P < 0.001$; 0.006; <0.001).

Conclusion. We conclude the following: (1) Mortality is greater for early vs. late onset PTLD in adult patients; the converse has been shown previously. (2) Tacrolimus, MMF, and steroids are associated with late onset PTLD in adult patients. (3) EBV risk status did not differ between early and late onset PTLD in both the adult and pediatric populations. This contradicts established reports that EBV negative serostatus of the recipient at the time of transplant is a risk factor for early onset PTLD.

Figure 1.



Disclosures. **All authors:** No reported disclosures.

1581. Impact of Colonization with Fluoroquinolone-Resistant Enterobacteriaceae on the Risk of Gram-Negative Bacteremia in Hematopoietic Stem Cell Transplant Recipients Who Receive Prophylactic Levofloxacin

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Background. Fluoroquinolone (FQ) prophylaxis is widely used to prevent bloodstream infections (BSIs) in neutropenic patients undergoing hematopoietic stem cell transplantation (HCT). In order to assess whether increasing FQ resistance threatens the effectiveness of FQ prophylaxis, we screened HCT recipients for colonization with FQ-resistant Enterobacteriaceae (FQRE) and assessed the impact of colonization on the risk of BSI.

Methods. We collected stool samples on admission for HCT and weekly until neutrophil engraftment from patients at NewYork-Presbyterian Hospital/Weill Cornell Medical Center from November 2016 to March 2018. Patients received FQ prophylaxis during neutropenia. Perianal swabs were used when stool was unavailable. Stool and swab samples were plated onto MacConkey agar with 1 µg/mL ciprofloxacin, and colonies were identified and underwent antimicrobial susceptibility testing. We determined the prevalence of colonization with FQRE on admission for HCT, the risk of acquiring FQRE, and compared the risk of BSI during the transplant admission in colonized and noncolonized patients.

Results. We evaluated 178 HCT recipients and found that 35 (20%) had pre-transplant FQRE colonization (allogeneic: 20/89, 22%; autologous: 15/89, 17%). Thirty FQRE (86%) were *Escherichia coli*, 5 (14%) were *Klebsiella pneumoniae*, and 13 (37%) were extended-spectrum β-lactamase producers. Five (14%) of the 35 patients with pre-transplant FQRE colonization developed BSI due to an Enterobacteriaceae, and all bloodstream isolates had identical susceptibility profiles to the colonizing FQRE. In contrast, only one (1%) of 143 patients without pre-transplant FQRE colonization developed Enterobacteriaceae BSI ($P = 0.001$). Patients with pre-transplant FQRE colonization also had higher rates of any Gram-negative BSI (20% vs. 1%, $P < 0.001$), but did not have increased risk of Gram-positive BSI (6% vs. 11%, $P = 0.5$). Of 123 patients without initial FQRE colonization who had follow-up samples collected, 10 (8%) acquired FQRE during post-HCT neutropenia.

Conclusion. FQRE colonization is common on admission for HCT and is associated with decreased effectiveness of levofloxacin prophylaxis in preventing Gram-negative BSI during post-transplant neutropenia.

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1582. Is Antibiotic Prophylaxis Needed for All Acute Variceal Bleeds in Decompensated Cirrhosis? A Retrospective Pilot Study

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Background. Guidelines recommend empiric antibiotic prophylaxis for acute variceal bleeding, but no studies compare the outcomes between those treated with guideline recommended duration and those not treated (low suspicion) or treatment duration truncated (negative work up). We hypothesized that outcomes may not be different between the two groups.

Methods. Retrospective pilot study for the period 2013–2017. Cases were extracted using ICD 9(4,560) and ICD 10(I8501, I8511) codes and the following criteria were applied. Inclusion: Age >18 years and decompensated cirrhosis with acute variceal bleeding. Exclusion: Age <18 years, septic shock, receipt of antibiotics <14 days before admission, human immunodeficiency virus infection. Data gathered on demographics, APACHE II, Charlson score, modified Child-Turcotte-Pugh classification (CTP), mortality at 6 weeks, re-bleeding within 7 days, readmissions (30 and 90 days), incidence of infections at admission and follow-up. Using SPSS, we compared those who received antibiotics <3 days to ≥ 3 days.

Results. Eighty-three cases met criteria (M:F = 52:31, age = 54.5 ± 11.6 years), CTP: A = 20(24.1%), B = 34 (41.9%), C = 29(33.7%). Alcohol was etiology in 57(68.67%) [52(91.2%) alcohol only, 5(8.8%) with alcohol and viral hepatitis]; hepatitis C virus (HCV): 12/83 (14.6%)[6(50%) HCV only]; hepatitis B virus: 3(3.6%); NASH: 12(14.6%) [9(75%) NASH only, 2(16.7%) with HCV, 1 with autoimmune hepatitis)]; cryptogenic: 3(3.6%); autoimmune: 2(2.4%), others: 4(ischemic, metastases, biliary cirrhosis, transplant). Antibiotics were either not administered or truncated in 21(25.3%) patients. In comparing guideline concordant (≥3 days) and truncated (<3 days) groups, no statistically significant difference was present for APACHEII, Charlson score, mortality (10 vs. 3, P 0.928), re-bleeding (2 vs. 0, P 0.387) and readmission at 30 and 90 days (18 vs. 3, P 0.147; 11 vs. 3, P 0.715). Drug-resistant infections were seen in 4(4.8%) patients requiring readmissions within 90 days.

Conclusion. We found no differences in outcomes between guideline concordant and truncated duration of antimicrobial prophylaxis for acute variceal bleeding.

Truncating the duration of empiric prophylactic antibiotics reduces unnecessary antibiotic use.

Disclosures. **All authors:** No reported disclosures.

1583. The Utility of the Immunodeficiency Scoring Index (ISI) to Predict Outcomes of Coronavirus (HCoV) Infections in Hematopietic Cell Transplant (HCT) Recipients

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Background. Respiratory viral infections in HCT recipients are associated with high morbidity and mortality, especially after progression from upper respiratory tract infection (URI) to lower respiratory tract infections (LRI). Data on risk factors (RF) for LRI and mortality is lacking for HCoV infections after HCT. We aimed to validate our ISI in HCoV infections.

Methods. All adult HCT recipients with HCoV infection from 2015 to 2017 were evaluated. An ISI based on RF was used to classify patients as low (0–2), moderate (3–6), or high (7 or higher) risk for progression to LRI or death. We defined LRI as HCoV detected in nasal wash and/or bronchoalveolar lavage and new lung infiltrates on diagnostic imaging. Clinical parameters were collected and ISI were calculated for comparison.

Results. A total of 144 adult HCT recipients with 166 episodes of HCoV infections were analyzed. The most common HCoV serotype for LRI and URI was 229E (42.4%) and OC43 (37.6%), respectively, and most patients were infected between November and March each year (Figures 1 and 2). When compared with URI, patients with LRI were more likely in the pre-engraftment period, had multiple respiratory viruses infections, had nosocomially acquired HCoV, required hospitalization, ICU transfer, and mechanical ventilation (all, $P < 0.05$). Overall mortality rate was 4% at Day 30 from diagnosis and all patients who died had LRI with an 18% mortality. Among those who died, 33% had nosocomial infection, 67% were co-infected with another respiratory virus and 67% required mechanical ventilation. Using an ISI cut off of <4, the negative predictive value (NPV) for progression to LRI was 86% with a specificity of 76%.

Conclusion. HCT recipients with HCoV LRI were more likely to have a fatal outcome. The NPV of the ISI for progression to LRI was high and could be used as a prognostic tool for future studies and for therapeutic clinical trials.

Figure 1. The seasonal distribution of HCT recipients by month of diagnosis and human coronavirus serotypes for upper respiratory infections (URIs).

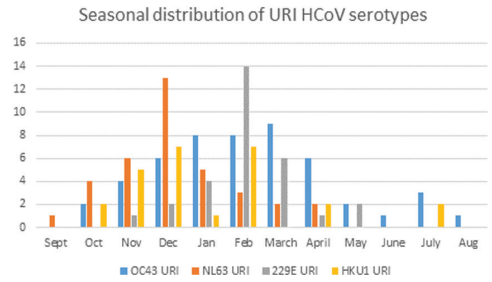
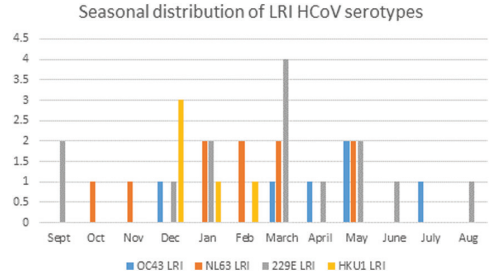


Figure 2. The seasonal distribution of HCT recipients by month of diagnosis and human coronavirus serotypes for lower respiratory infections (LRI).



Disclosures. **All authors:** No reported disclosures.

1584. Development and Dynamics of Cytomegalovirus UL97 Ganciclovir Resistance Mutations in Transplant Recipients Detected by Next-generation Sequencing

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Background. (Val)ganciclovir resistance mutations (GRMs) in CMV UL97 (UL97-GCV-R) complicate prophylaxis and therapy of solid-organ transplant (SOT) and hematopoietic (stem) cell transplant (HCT) recipients, but data on prevalence and dynamics are scarce. We investigated UL97-GCV-R using next-generation sequencing (NGS) in transplant recipients with refractory CMV DNAemia episodes and a control group.

Methods. Between January 1, 2010–July 16, 2016, 385 transplant recipients were screened for plasma CMV DNAemia. Eighty-seven patients (54 SOT, 33 HCT) with available plasma samples had refractory CMV replication at viral loads ≥910 IU/mL and were analysed by NGS. If UL97-GCV-R were detected in >10% of the NGS reads, all earlier plasma samples were also analysed by NGS. For comparison, this approach was also performed in a control group of 21 patients (14 SOT, 7 HSCT) with DNAemia episodes resolving under antiviral therapy. UL97-targeted NGS was performed using Illumina MiSeq and analysed by LoFreq for variant calling.

Results. Of the 87 recipients with refractory CMV replication, 19 (22%) had ≥1 UL97-GCV-R detected by NGS (Table 1, Figure 1), in comparison to 0/21 (0%) of the controls ($P = 0.02$). Fourteen of 19 of the resistant cases (20 induced mutations) had NGS performed <4 week from onset of infection; in this sample, the mutation was either not detected, detected as minority or dominating variant for 11, 7 and 2, respectively. In the majority of recipients one dominant mutant was induced (68%); ≥2 mutations were detected in the remaining recipients (Table 1). Most frequent UL97-GCV-R affected codon-595 (42%), -594 (32%) or -603 (32%). The % of C592G was low in in all episodes (<15%) without changing during the course (Figure 1). There was a trend toward higher frequencies of donor (D)/recipient (R) CMV high-risk mismatch, CMV disease and prior failure to valganciclovir prophylaxis (SOT) or treatment (HCT) among the cases with UL97-GCV-R (Figure 2).

Conclusion. UL97-GCV-R was seen in 22% of refractory CMV replication episodes. CMV D/R mismatch and CMV disease were more common amongst resistant cases. The C592G mutation was present in low frequency in all patients, suggesting that this mutation was part of the quasispecies, and not selected by ganciclovir resistance. Implications for clinical management will be discussed.

Table 1. Details on clinical and genotypic features of 19 transplant recipients with induced* ganciclovir resistance mutations in the CMV UL97 gene.

Patients	Tx type	CMV IgG D/R status	CMV disease	Prophylaxis or treatment failure	Codon in amino acid							Number of mutations induced/ patient
					460I or V	520Q	594V or G	595S or F	596G	603W	607Y or F	
1	MAC HCT	D-/R+	CMV GI disease	No							++ (both in same)	2
2	MAC HCT	D-/R+	CMV GI disease	No						++		1
3	MAC HCT	D-/R-	CMV Retinitis	No	++				++			2
4	MAC HCT	D-/R+	CMV GI disease	No			++	++				2
5	MAC HCT	D-/R+	No	Yes			++					1
6	NMA HCT	D-/R+	CMV GI disease	No			++					1
7	Liver	D+/R-	CMV pneumonia	Yes		++				++		2
8	Liver	D+/R-	No	Yes						++		1
9	Liver	D+/R-	No	Yes						++		1
10	Lung	D+/R-	CMV pneumonia	No				++				1
11	Lung	D+/R-	CMV GI disease	Yes				++				1
12	Kidney	D+/R-	No	Yes			++			++	++	3
13	Kidney	D+/R-	No	Yes				++				1
14	Kidney	D+/R-	No	Yes		++	++			++		3
15	Kidney	D+/R-	CMV Pneumonia	No			++ (both in same)	++				3
16	Kidney	D+/R-	No	Yes				++				1
17	Kidney	D+/R+	No	Yes				++				1
18	Kidney	D+/R-	No	Yes	++							1
19	Kidney	D+/R-	No	Yes				++				1
Number of patients with mutation					2/19	2/19	6/19	8/19	1/19	6/19	2/19	
% with mutation induced					10,5	10,5	31,6	42,1	5,3	31,6	10,5	

*Induced mutations defined as mutations with a maximum frequency ≥25%, and a minimum increase of 10% in the subsequent sample.
Abbreviations: GI; gastro-intestinal, HCT; hematopoietic stem cell transplantation, MAC; myeloablative conditioning, NMA; non-myeloablative conditioning.