Eplet Mismatches in Predicting de Novo Donor-Specific Antibodies (dnDSA) in Liver Transplant Patients

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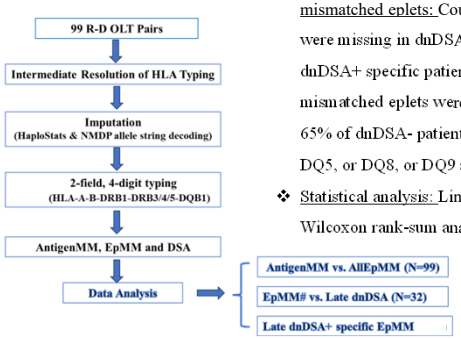
INTRODUCTION

- There is increasing interest in the potential for HLA "molecular mismatch" approaches to better stratify patients at risk of de novo DSA (dnDSA) production and rejection than traditional antigen level mismatching.
- Typical two-field HLA high resolution typing is required for accurate eplet mismatching (EpMM). However, two-field high resolution HLA typing is not often available for solid organ transplant recipients. EpMM has been reported by using imputation from existing low or intermediate resolution genotyping instead.
- It has been reported that the number of Eplet mismatch (EpMM#) of HLA-DRB1, DQB1 was associated with dnDSA post-transplant in liver transplant patients. In addition, specific EpMMs may differentially predict immunogenicity.
- The aim of this study was to assess the association of HLA EpMM# and specificities in predicting dnDSA (≥6-month post-transplant) in orthotopic liver transplant (OLT) patients.

METHODS



- Assessment of dnDSA+ DQ5, DQ8, DQ9 specific mismatched eplets: Counting the EpMMs which were missing in dnDSA- patients but common in dnDSA+ specific patients, respectively. When mismatched eplets were not found in more than 65% of dnDSA- patients, they were considered as DQ5, or DQ8, or DQ9 specific EpMMs.
- Statistical analysis: Linear regression and Wilcoxon rank-sum analysis was used.

CONCLUSIONS

1. In this study OLT patients, the majority dnDSAs were DQ (71.4%).
2. AllEpMM# positively correlated with antigenMM# in both HLA class I and II.
3. AbVEpMM# of DRB1 increased significantly in dnDSA+ patients vs. dnDSA- patients.
4. EpMMs 167R, 45G, **45GV**, **55R**, **74S** and **116I** were likely specific to dnDSA DQ5+ and **4Q**, 30G, **70R**, 70RE, 74E were specific to DQ9+.
5. In conclusion, besides the increased EpMM#, the specific EpMMs may predict dnDSA development in OLT patients. A larger cohort is needed.

• **Disclosure: There is no disclosure.**

RESULTS

Figure 1. HLA-Class I&II AntigenMM vs AllEpMM (N=99)

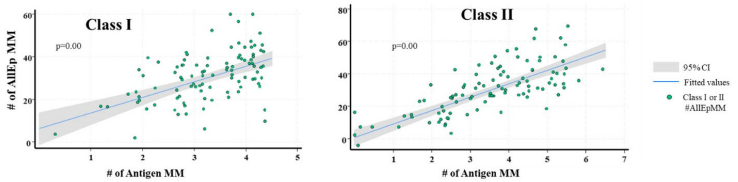


Figure 1. Correlation of the number of AllEpMM and HLA-Class I&II antigenMM, respectively. There was significant positive correlation between HLA-Class I antigenMM# and AllEpMM#, p value=0.00; and the similar trend was shown in Class II, p value=0.00.

Figure 2. Number of EpMM in Patients with dnDSA+ (N=7) vs dnDSA- (N=25)

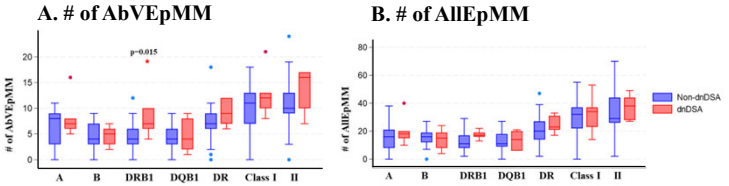


Figure 2. The number of EpMM in dnDSA+ patients vs. dnDSA- patients.
In 32 no preformed DSA patients at pre-transplant, 7 patients developed dnDSA post-transplant. **A**. This graphs is showing us the # of AbVEpMM in patients with dnDSA+ vs. dnDSA-, at each HLA locus and Class I, Class II, respectively. DRB1 AbVEpMM# significantly increased in dnDSA+ patients compared with dnDSA- patients, p=0.015. **B.** #AllEpMMs were also compared between dnDSA+ vs. dnDSA- patients, there were no significant differences between the two groups at each HLA locus and Class I/II, respectively, it might be due to the # of different AbVEpMM was diluted by other EpMMs in the two groups.

Table 1. DSA in dnDSA+ Patients (N=7)

PID#	1	2	3	4	5	6	7
dnDSA	B13	DQ5	DQ5, DP3	DQ8, DQ9	DQ9	DR51	DR53, DQ7, DQ8

There were 7/32 (21.9%) patients with late dnDSA+ post-transplant. And 5/7 (71.4%) were DQ+, 2/7 (28.6%) were DR+, 1/7 (14.3%) were B13+. (PID: patient ID)

Table 2. Specific EpMMs to DQ5+, DQ8+ or DQ9+ dnDSA

Late dnDSA	Specific EpMM to dnDSA+						Major Alleles Contributing to Specific EpMM
DQ5	45G	**45GV**	**55R**	**74S**	**116I**	167R	DQB1*05:02, DQB1*05:03, DQB1*03:03
DQ8	0						-
DQ9	**4Q**	30G	**70R**	70RE	74E		DRB1*09:01, DRB1*04:06
	AbVEpMM						

EpMMs 45G, **45GV**, **55R**, **74S**, **116I** and 167R were likely specific to dnDSA DQ5+ and **4Q**, 30G, **70R**, 70RE, 74E were specific to DQ9+. No DQ8 specific EpMM was recognized in this study met current criteria described in Methods.