Corneal transplantation:
HLA and age

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Background

• Immune rejection is an important risk factor and allograft rejection is a major cause of graft failure

• The majority of keratoplasty are performed as HLA not matched, “random” transplants

• Data showed in works from Central European ophthalmologists in long-term corneal transplant survival by HLA matching lead to presume that HLA matching should have a practical value for high risk patients (Sundmacher R (ed): Adequate HLA Matching in Keratoplasty. Dev. Ophthalmol. Basel, Karger, 2003, vol. 36)
standard risk for rejection

HLA random graft

HLA matched graft

high risk for rejection

Deep stromal vascularization
standard risk for rejection

→

HLA random graft

HLA matched graft

previous organ transplantation
Aim of the study

Since 2000 we developed a program for the allocation of HLA matched corneas for high risk patients afferent to Departments of Ophthalmology in 14 Piedmont Hospitals.
Aim of the study

to establish if a set of coincidental covariates, included HLA matches, is associated with an improved corneal graft survival
Eye Bank
DATASET
CORNEAL TRANSPLANTS SINCE JAN-2000 TO JULY-2011 (MINIMUM FOLLOW-UP: 6 MONTHS)

CORNEAL TRANSPLANTS (4360)

189
HLA MATCHED CORNEAL TRANSPLANTS

33
FIRST TRANSPLANT

156
RETRANSPLANT
Methods

• All corneal graft recipient-donor pairs were tissue typed by serological and molecular (low resolution) methods for HLA-A, -B and –DR
• allowed MM: Class I ≤3, Class II ≤1 (broad)
• Comparability of donors, patients and graft characteristics (age, gender, graft cell count, pathology, HLA MM, ABO compatibility … ) was analyzed by chi-squared test for categorized variables and Mann-Whitney U test for continuous ones
• Unadjusted survival probabilities were estimated by Kaplan Meier method
• Hazards (RR) for relevant covariates were set by multivariate proportional Cox regression
• All tests were two sided and p-value less than 0,05 was taken as statistically significant
<table>
<thead>
<tr>
<th></th>
<th>FIRST TRANSPLANT</th>
<th>RETRANSPLANT</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Median donor age</td>
<td>50 yrs</td>
<td>57 yrs</td>
<td>(p = 0.031)</td>
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</table>
Kaplan Meier univariate survival analysis
First Transplants – Retransplants

p = 0.03
Kaplan Meier univariate survival analysis
Retranplants

156 tissue survival graft (2000-2011)

Cumulative Proportion Surviving

survival time (yrs)

p=0.00461

< 60 donor age (90)

>= 60 donor age (66)
Kaplan Meier univariate survival analysis
Retransplants HLA Class II MISMATCHES

- Influence of HLA class I (loci A and B) matching seems not to be relevant for graft survival.
- HLA class II MM (locus DRB1) shows a better trend for survival (0 HLA-DR MM)
Kaplan Meier univariate survival analysis
Retranplants HLA CLASS I MISMATCHES

**DONOR AGE <60 YRS**

**DONOR AGE ≥60 YRS**

Influence of HLA class I (loci A and B) suggests a better trend for survival for younger donors (0-1 HLA-A, -B MM), but not statistically significant.
Kaplan Meier univariate survival analysis
Retranplants HLA CLASS II MISMATCHES

DONOR AGE <60 YRS

DONOR AGE ≥60 YRS

HLA-DR MM seems to be important for donor age ≥60 yrs
<table>
<thead>
<tr>
<th></th>
<th>N=189</th>
<th>β</th>
<th>s.e.</th>
<th>RR (eβ)</th>
<th>Wald stat</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>First transplant</td>
<td></td>
<td>0.2778</td>
<td>0.1265</td>
<td>1.3202</td>
<td>4.8205</td>
<td>0.0281</td>
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<tr>
<td>HLA CLASS I MM</td>
<td></td>
<td>-0.1140</td>
<td>0.4753</td>
<td>-0.8922</td>
<td>0.0576</td>
<td>0.8104</td>
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<tr>
<td>HLA CLASS II MM</td>
<td></td>
<td>0.3512</td>
<td>0.4116</td>
<td>1.4207</td>
<td>0.7280</td>
<td>0.3936</td>
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<td>DONOR AGE&lt;60</td>
<td></td>
<td>0.9083</td>
<td>0.3015</td>
<td>2.4802</td>
<td>9.0773</td>
<td>0.0026</td>
</tr>
</tbody>
</table>

- underlines the outcome of the univariate analysis,
- relative risk (RR) =2.48 for donor aged ≥60yrs,
- relative risk (RR) =1.32 for failure.
Conclusions

The successful results in first HLA matched corneal transplants suggest that the fundamental idea of our transplantation program is correct.

The result of our analysis of retransplants shows that:

1. HLA class I (loci HLA-A and –B) MM is not relevant for our cohort in overall age;

2. HLA class II (locus HLA-DR) MM trend suggests a relevant role according to MM number, but we don’t reach statistically significance, for poor data set in overall age;

3. according to donor age, HLA class I MM might be relevant for graft from younger donors, and HLA class II MM for graft from older donors.

TO BE DONE: a major dataset for graft and follow-up to assess the trend of the results obtained in this preliminary study, including the role of HLA matching vs. non HLA matching in cornea transplantation.
to Be Careful with my Criticism and Liberal with my Praise; to Build up and not Destroy

Thank you