CHANGING TRENDS IN CORNEAL TRANSPLANTATION IN AOTEAROA / NEW ZEALAND 1991-2020

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EVOLUTION of TRANSPLANTATION over the last 250 years

1750-1900: 150 year of experimentation
1905: First successful PKP by Zirm
1905-1950: PKP more widely established
1995-2020: Renaissance of DALK & DSEK
2000's: Cell based transplantation?

Corneal endothelial transplantation:
a very brief history DSEK, DSAEK, DMEK

1965 Pollack & Barraquer – hinged flap PLK
1993 Ko et al – PLK via scleral tunnel in rabbits
1998 Gerrit Melles – first EK in humans
2000 Mark Terry – first human DLEK in USA
2005 Price reports DSEK results (N=50)
2008 Melles reports DMEK results (N=10)

TRENDS IN CORNEAL TRANSPLANTATION

- Increased number of procedures
- Changing indications
- Lamellar now > penetrating
- Eye Bank lamellar tissue preparation
- Increasing popularity of DMEK
- Reporting of longer term outcomes of lamellar procedures
- Sources: NZNEB, ACGR, EBAA
Factors influencing keratoplasty trends?

- Evolving surgical techniques
  - Descemet’s Stripping Endothelial Keratoplasty (DS(E)EK)
  - Descemet Membrane Endothelial Keratoplasty (DMEK)
- Corneal crosslinking for keratoconus (CXL)
- Significant population growth
- Rising number of cataract surgeries per 100,000 population

NZNEB a 30-year analysis: Methods
(Anita Corina Chilbeck et al Cornea 2021)

Electronic NZNEB database analysed (January 1991 to January 2020)

- Recipient demographics and pre-operative diagnoses
- Type of transplant and location surgery performed

A priority scheme was applied to identify the PRIMARY INDICATION for transplantation e.g.
- Corneal hydrops: primary indication = keratoconus
- Penetrating injury: primary indication = trauma

However, diagnosis of re-graft (repeat keratoplasty) was given priority over all others

New Zealand National Eye Bank (NZNEB):
Transplant Indications 1991-1999

Results:
- 6840 cornea transplanted
- 54.3% male
- Mean age 50.1 +/- 21.6 years
- 72.1% performed in public (range 60.8-85.4%)

By region (2010-2019):
- Auckland 54.6%
- Wellington 17.5%
- Christchurch 13.2%

Rapid increase in age 60-79 years correlates with endothelial keratoplasty
Five most common primary indications:
1. Keratoconus
2. Re-graft
3. Bullous keratopathy
4. Corneal dystrophy
5. Keratitis

Overall total each year is increasing 2.55-6.06
Re-graft and corneal dystrophy are increasing
Keratoconus and bullous keratopathy are decreasing indications

The Era of repeat keratoplasty in NZ?

Background & Participants

In New Zealand, repeat keratoplasty has become the second leading indication for corneal transplantation.


Indications for repeat keratoplasty

<table>
<thead>
<tr>
<th>Repeat keratoplasty Indication</th>
<th>N=279</th>
<th>Percent</th>
</tr>
</thead>
<tbody>
<tr>
<td>Endothelial decompensation without history of rejection</td>
<td>105</td>
<td>37.6%</td>
</tr>
<tr>
<td>Endothelial decompensation with history of rejection</td>
<td>88</td>
<td>31.5%</td>
</tr>
<tr>
<td>Recurrent ectasia or high astigmatism in keratoplasty</td>
<td>44</td>
<td>15.8%</td>
</tr>
<tr>
<td>Acute infection</td>
<td>11</td>
<td>3.9%</td>
</tr>
<tr>
<td>Acute trauma</td>
<td>10</td>
<td>3.6%</td>
</tr>
<tr>
<td>Corneal scar</td>
<td>10</td>
<td>3.6%</td>
</tr>
<tr>
<td>Primary graft failure</td>
<td>6</td>
<td>2.2%</td>
</tr>
<tr>
<td>Other</td>
<td>5</td>
<td>1.8%</td>
</tr>
</tbody>
</table>
Survival of repeat keratoplasty (PKP)

Kaplan-Meier survival plot of time to re-graft failure (in penetrating keratoplasty only): comparing 1st, 2nd and 3rd re-grafts.

Time to re-graft failure: ethnicity

Kaplan-Meier survival plot of time to re-graft failure comparing European and Non-European patients (penetrating keratoplasty only).

Re-graft survival by original indication

<table>
<thead>
<tr>
<th>Indication</th>
<th>Mean survival (years)</th>
<th>95% CI</th>
<th>Median survival (years)</th>
<th>Standard error (SE)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Keratoconus</td>
<td>13.0</td>
<td>9.4 – 16.6</td>
<td>13.2</td>
<td>0.6</td>
</tr>
<tr>
<td>Fuchs' endothelial dystrophy</td>
<td>9.2</td>
<td>7.9 – 10.4</td>
<td>NA</td>
<td></td>
</tr>
<tr>
<td>Acute trauma</td>
<td>6.6</td>
<td>4.1 – 9.1</td>
<td>NA</td>
<td></td>
</tr>
<tr>
<td>Scar</td>
<td>5.3</td>
<td>3.8 – 6.8</td>
<td>4.3</td>
<td>0.7</td>
</tr>
<tr>
<td>Acute infection</td>
<td>4.2</td>
<td>1.2 – 7.3</td>
<td>3.7</td>
<td>0.8</td>
</tr>
<tr>
<td>Other</td>
<td>3.5</td>
<td>0.8 – 6.2</td>
<td>1.9</td>
<td>0.4</td>
</tr>
<tr>
<td>Bullous keratopathy</td>
<td>3.3</td>
<td>2.5 – 4.1</td>
<td>2.8</td>
<td>0.4</td>
</tr>
</tbody>
</table>

Re-graft survival by original indication for corneal transplant (penetrating keratoplasty only)

Trend 2: Lamellar vs penetrating

Significant decrease in penetrating keratoplasty since introduction of DSEK in 2007

By 2018 the ratio of PK to Lamellar grafts approaching 50:50

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EBAA: USA Domestic trends in PK and EK 2005-2018
Transition to lamellar keratoplasty 2011

Figure 2: Domestic PK vs. EK vs. ALE Surgery Trends. The relative frequency of PK, EK, and ALE procedures performed in the US over the last 14 years can be seen above.

Trends: Lamellar versus penetrating For common indications 2010-20

<table>
<thead>
<tr>
<th></th>
<th>PK (n=1703)</th>
<th>DS(A)EK (n=888)</th>
<th>DMEK (n=98)</th>
<th>DALK (n=266)</th>
<th>Other/ blank (n=44)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Keratoconus (n=965)</td>
<td>77.5%</td>
<td>0.1%</td>
<td>0%</td>
<td>21.7%</td>
<td>0.7%</td>
</tr>
<tr>
<td>Re-graft (n=738)</td>
<td>68.8%</td>
<td>77.8%</td>
<td>2.6%</td>
<td>0.8%</td>
<td>0%</td>
</tr>
<tr>
<td>Corneal Dystrophy (n=542)</td>
<td>6.3%</td>
<td>81.0%</td>
<td>2.6%</td>
<td>0.8%</td>
<td>0%</td>
</tr>
<tr>
<td>Bullous Keratopathy (n=273)</td>
<td>32.6%</td>
<td>63.4%</td>
<td>3.7%</td>
<td>0%</td>
<td>0%</td>
</tr>
<tr>
<td>Other (n=725)</td>
<td>78.3%</td>
<td>9.5%</td>
<td>0.7%</td>
<td>6.3%</td>
<td>5.1%</td>
</tr>
</tbody>
</table>

Keratoconus – still largely penetrating though 22% DALK
Regraft – majority penetrating but DSAEK (28%) becoming more common
Endothelial corneal dystrophy and PBK mainly DSAEK or DMEK

Trend 3: Effect of Corneal Cross-Linking in respect to Keratoconus as indication

The beneficial effect of corneal crosslinking on keratoplasty for keratoconus
Approximately 10-years after diagnosis, those with progressive keratoconus typically undergo corneal transplant surgery

What is happening elsewhere:
NZ/Aotearoa versus global trends?

Similar trend in increasing number of transplants per population per year
NZ still has disproportionately high rates of penetrating keratoplasties
The introduction of DMEK to NZ didn’t significantly affect proportion of DSAEK, (unlike observations in Spain, Canada and Germany)
Bullous keratopathy continues to decrease, suggesting better overall phacoemulsification surgical technique
**Future modifications and alternatives to endothelial keratoplasty**

- Small diameter Descemet’s stripping
- Use of ROCK inhibitors
- 1 donor → split cornea, multiple DMEK
- Descemet’s membrane endothelial transfer
- Tissue engineered grafts
- Endothelial Cell therapy
- Stem cells


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**Purpose:** The purpose of this study was to identify trends in the various indicators for transplantation in New Zealand/Aotearoa (NZ) after significant population growth, increase in the number of cataract surgeries per population, widespread adoption of endothelial keratoplasty, and introduction of corneal cross-linking for keratoconus.

**Conclusion:** Keratoconus cases in Auckland/NZ have changed considerably because of the evolution of phototherapeutic and keratoplasty techniques. Unlike projections showed earlier, NZ will probably maintain keratoconus in round half of all transplants. Corneal cross-linking may be having an early effect of reducing keratoconus cases for keratoconus.

Thank you