TITLE: Artificial Keratoprosthesis for Corneal Transplant: Clinical Effectiveness, Cost Effectiveness, and Guidelines

DATE: 08 February 2016

RESEARCH QUESTIONS

1. What is the clinical effectiveness of artificial keratoprosthesis devices for patients requiring corneal transplant?

2. What is the cost-effectiveness of artificial keratoprosthesis devices for patients requiring corneal transplant?

3. What are the evidence-based guidelines regarding appropriate clinical indications for artificial keratoprosthesis devices?

KEY FINDINGS

Three systematic reviews, 27 non-randomized studies, one economic evaluation, and one evidence-based guideline were identified regarding artificial keratoprosthesis devices for patients requiring corneal transplant.

METHODS

A limited literature search was conducted on key resources including PubMed, The Cochrane Library, University of York Centre for Reviews and Dissemination (CRD) databases, ECRI, Canadian and major international health technology agencies, as well as a focused Internet search. No filters were applied to limit the retrieval by study type. Where possible, retrieval was limited to the human population. The search was also limited to English language documents published between January 1, 2011 and January 25, 2016. Internet links were provided, where available.

The summary of findings was prepared from the abstracts of the relevant information. Please note that data contained in abstracts may not always be an accurate reflection of the data contained within the full article.

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SELECTION CRITERIA

One reviewer screened citations and selected studies based on the inclusion criteria presented in Table 1.

<table>
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<th>Table 1: Selection Criteria</th>
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<tr>
<td><strong>Population</strong></td>
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<td><strong>Intervention</strong></td>
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<td><strong>Comparators</strong></td>
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<td><strong>Outcomes</strong></td>
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<tr>
<td><strong>Study Designs</strong></td>
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</table>

RESULTS

Rapid Response reports are organized so that the higher quality evidence is presented first. Therefore, health technology assessment reports, systematic reviews, and meta-analyses are presented first. These are followed by randomized controlled trials, non-randomized studies, economic evaluations, and evidence-based guidelines.

Three systematic reviews, 27 non-randomized studies, one economic evaluation, and one evidence-based guideline were identified regarding artificial keratoprosthesis devices for patients requiring corneal transplant. No health technology assessments or randomized controlled studies were identified.

Additional references of potential interest are provided in the appendix.

OVERALL SUMMARY OF FINDINGS

Three systematic reviews, 27 non-randomized studies, one economic evaluation, and one evidence-based guideline were identified regarding artificial keratoprosthesis devices for patients requiring corneal transplant.

Results from one systematic review demonstrated an increased likelihood of visual improvement maintenance in patients with donor corneal graft failure upon the use of the type I Boston keratoprosthesis (KPro) when compared with repeat donor penetrating keratoplasty. In addition, no higher risk of postoperative glaucoma was observed with the KPro. The second systematic review also noted successful clinical use of KPro; however, the authors highlighted accessibility issues as problematic (particularly financial issues, lack of adequately trained surgeons, and shortages of donor corneas). The third systematic review limited its inclusion criteria to randomized controlled trials. It did not identify any trials and was subsequently unable
to determine optimal treatment with regard to Artificial (keratoprosthesis) corneas in patients who had failed conventional corneal transplant.³

Twenty-seven⁴⁻³⁰ non-randomized studies were identified regarding artificial keratoprosthesis devices for patients requiring corneal transplant. While most studies identified some improvement in visual acuity, complications remain a concern. Study details and conclusions are provided in Table 2.

<p>| Table 2: Summary of Findings from Non-Randomized Studies |
|-----------------------------------------------|-------------------------------------------------|-----------------|-----------------|-----------------|</p>
<table>
<thead>
<tr>
<th>First Author, Year</th>
<th>Study Type, Size</th>
<th>Indications</th>
<th>Outcomes</th>
<th>Conclusions</th>
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<tbody>
<tr>
<td><strong>Auro Keratoprosthesis</strong></td>
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<tr>
<td>Sharma, 2015⁵</td>
<td>Prospective interventional study</td>
<td>N=10 eyes (in 10 patients)</td>
<td>End-stage corneal disease</td>
<td>BCVA, Retention, Complications, Need for second surgery</td>
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<tr>
<td><strong>Boston Type I Keratoprosthesis</strong></td>
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<tr>
<td>Wagoner, 2016⁶</td>
<td>Retrospective chart review</td>
<td>N=75 KPro-I procedures</td>
<td>NR</td>
<td>Post-operative infections</td>
</tr>
<tr>
<td>Hager, 2015⁷</td>
<td>Retrospective review</td>
<td>N=24</td>
<td>Failed keratoplasty: o Corneal edema (n=13) o Trauma (n=8) o Keratononus (n=3)</td>
<td>BCVA, Retention</td>
</tr>
<tr>
<td>Kosker, 2015⁸</td>
<td>Retrospective analysis</td>
<td>N=37 eyes (in 37 patients)</td>
<td>Failed penetrating keratoplasty (n=28) o Primary KPro (n=9)</td>
<td>BCVA, Retention, Complications</td>
</tr>
<tr>
<td>Phillips, 2015⁹</td>
<td>Retrospective review</td>
<td>N=4</td>
<td>Failed keratoplasties: o Iris atrophy (n=2) o Chandler syndrome (n=2)</td>
<td>BCVA</td>
</tr>
<tr>
<td>First Author, Year</td>
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| Rudnisky, 2015<sup>10</sup> | • Prospective parameters were collected  
• N=300 eyes (of 300 patients) | • NR | • logMAR visual outcomes | • KPro-I is an effective device for rehabilitation in advanced ocular surface disease that results in significantly improved VA. |
| Brown, 2014<sup>11</sup> | • Retrospective review  
• N=9 eyes | • Keratopathy caused by:  
   - HSV  
   - HZV | • Visual outcomes  
• Retention  
• Complications | • In eyes with HSV keratopathy, KPro-I is associated with:  
   - excellent prognosis for retention;  
   - highly satisfactory visual improvement;  
   - acceptably low prevalence of sight-threatening complications.  
• Aforementioned results were not observed in eyes with HZV keratoplasty. |
| de Oliveira, 2014<sup>12</sup> | • Prospective interventional study  
• N=30 eyes (of 30 patients) | • Failed graft (n=16)  
• Chemical injury (n=10)  
• Stevens-Johnson syndrome (n=4) | • VA  
• KPro-I stability  
• Postoperative complications | • In the developing world, KPro-I keratoprosthesis is a viable option after multiple keratoplasty failures and in conditions with a poor prognosis for keratoplasty. |
| de Rezende Couto Nascimento, 2014<sup>13</sup> | • Retrospective chart analysis  
• N=59 eyes (in 57 patients) | • Various diagnoses (most non-standard for KPro-I implantation) | • How primary diagnoses affect post-operative VA  
• Complications | • Most cases showed improvement in VA.  
• Posterior segment complications and infections resulted in persistent loss of vision. |
| Phillips, 2014<sup>14</sup> | • Retrospective review  
• N=9 eyes | • Alkali burns (n=7)  
• Acid burns (n=1)  
• Thermal burns (n=1) | • Visual outcomes  
• Retention  
• Complications | • In most cases, KPro-I is associated with:  
   - highly satisfactory visual outcomes;  
   - prosthesis retention;  
   - serious complications are common. |
| Ciolino, 2013<sup>15</sup> | • Prospective study  
• N=300 eyes (in 300 patients) | NR | • Retention | • KPro-I seems to be viable option for non-candidates of PK  
• Ocular surface disease due to autoimmune disease had lowest retention rate. |
### Table 2: Summary of Findings from Non-Randomized Studies

<table>
<thead>
<tr>
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</tr>
</thead>
</table>
| Goldman, 2013\(^{16}\) | • Retrospective chart review  
• N=98 eyes (of 94 patients) | NR | • Posterior segment completions | • These complications occur in a significant percentage of patients, resulting in persistent reduction in VA. |
| Magalhaes, 2013\(^{17}\) | • Prospective study  
• N=10 eyes (in 10 patients) | • Ocular burns | • VA  
• Retention  
• Complications | • There is support for the use of the KPro-I in managing bilateral LSCD secondary to ocular burns. |
| Munoz-Gutierrez, 2013\(^{18}\) | • Retrospective analysis  
• N=41 eyes (in 387 patients) | Most frequent diagnoses were bullous keratopathy, autoimmune diseases | • Visual function  
• Complications | • Visual function improved in most patients.  
• Increased risk for serious sight-threatening complications in patient with prior multiple ocular surgeries and alterations of systemic immunity. |
| Palioura, 2013\(^{19}\) | • Retrospective review  
• N=8 eyes (of 8 patients) | Mucous membrane pemphigoid | • VA  
• Retention  
• Complications | • Clinical outcomes associated with KPro-I implantation in these patients are guarded. |
| Chan, 2012\(^{20}\) | • Retrospective chart review  
• N=10 cases | • Chemical injuries (n=4)  
• Stevens-Johnson syndrome (n=3)  
• Ocular cicatricial pemphigoid (n=2)  
• Congenital aniridia (n=1) | • Infectious keratitis | • Infectious keratitis can occur even when patients are on prophylactic vancomycin and 4\(^{th}\)-generation fluoroquinolone.  
• Reported case of ocular *D. constricta*. |
| Patel, 2012\(^{21}\) | • Retrospective chart review  
• N=58 eyes (in 51 patients) | Various conditions | • VA  
• Retention  
• Complications | • KPro-I provides visual recovery for eyes with multiple PK failures or in those with a poor prognosis for primary PK.  
• Excellent retention rates.  
• Trend towards decline in VA with time and late complications. |
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<thead>
<tr>
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</thead>
<tbody>
<tr>
<td>Ramchandran, 2012&lt;sup&gt;22&lt;/sup&gt;</td>
<td>• Retrospective chart review • N=10 eyes</td>
<td>Infectious endophthalmitis</td>
<td>• Clinical characteristics of infectious endophthalmitis after implantation</td>
<td>Higher incidence, delayed onset, and high risk for recurrence of infectious endophthalmitis compared with postoperative endophthalmitis. Concurrent use of topical vancomycin is recommended.</td>
</tr>
<tr>
<td>Shihadeh, 2012&lt;sup&gt;23&lt;/sup&gt;</td>
<td>• Retrospective chart review • N=20 eyes (in 19 patients)</td>
<td>NR</td>
<td>• BCVA • Complications</td>
<td>Reasonable safe and effective for patients with corneal blindness (and those for whom prognosis is poor for natural corneal grafting).</td>
</tr>
<tr>
<td>Greiner, 2011&lt;sup&gt;24&lt;/sup&gt;</td>
<td>• Cohort study • N=36 eyes</td>
<td>• Failed corneal transplants (n=19) • Chemical injury (n=10) • Aniridia (n=5)</td>
<td>• VA • Complications</td>
<td>Viable option for salvaging vision; however, some patients lost vision over postoperative course. Glaucoma and complications related to glaucoma remain significant challenges.</td>
</tr>
<tr>
<td>Sejpal, 2011&lt;sup&gt;25&lt;/sup&gt;</td>
<td>• Retrospective review • N=28 procedures (in 23 eyes of 22 patients)</td>
<td>LSCD</td>
<td>• VA • Retention • Complications</td>
<td>KPro-I results in significant CDVA improvement in majority of LSCD patients and CDVA of 20/50 or better in more than two-thirds of patients 3 years post-surgery. PED was the most common complication. PED is associated with increased rate of sterile stromal necrosis and lower retention rates.</td>
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</table>

**Boston Type I and II Keratoprosthesis**

<p>| Duignan, 2015&lt;sup&gt;6&lt;/sup&gt; | • Retrospective chart review • N=31 (KPro-I implantations) • N=3 (KPro-II implantations) | NR | • BCVA • Retention • Complications | Excellent VA and retention in a long follow-up (42 months, SD 31 months). Complications remain considerable source of morbidity. |</p>
<table>
<thead>
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<th>Conclusions</th>
</tr>
</thead>
<tbody>
<tr>
<td>KeraKlear Kpro</td>
<td>Prospective study, N=15&lt;sup&gt;a&lt;/sup&gt;</td>
<td>High risk of failure with PK</td>
<td>Retention, Complications</td>
<td>Viable alternative to corneal transplantation. KeraKlear KPro is better tolerated and less prone to complications with epidescemetal implantation. Cases with poor corneal quality are better associated to lamellar fenestrated donor corneal graft.</td>
</tr>
<tr>
<td>Osteo-Odonto-Keratoprosthesis</td>
<td>Prospective study, N=18</td>
<td>OOKP (n=9), age-matched controls (n=9)</td>
<td>Optical and visual performance</td>
<td>OOKP provides patients with good level of VA, with significant reductions in glare.</td>
</tr>
<tr>
<td>Narayanan, 2012&lt;sup&gt;29&lt;/sup&gt;</td>
<td>Retrospective analysis, N=26</td>
<td>Blindness occurring due to: Stevens-Johnson syndrome (n=23), Chemical burns (n=3)</td>
<td>VA, Complications</td>
<td>Successful visual rehabilitation occurred in 19 patients. No improvement in 4 patients.</td>
</tr>
<tr>
<td>de la Paz, 2011&lt;sup&gt;30&lt;/sup&gt;</td>
<td>Retrospective cohort study, N=227</td>
<td>Various indications</td>
<td>Effect of clinical factors on long-term anatomical function and functional success</td>
<td>Surgical technique, primary diagnosis, age, and postoperative complications can affect long-term function and functional success of OOKP.</td>
</tr>
</tbody>
</table>

BCVA = best corrected visual acuity; CDVA = corrected distance visual acuity; HSV = herpes simplex virus; HZV = herpes zoster virus; KPro-I = Boston type I keratoprosthesis; logMAR = logarithm of the minimal angle of resolution; LSCD = corneal limbal stem cell deficiency; NR = not reported; OOKP = Osteo-Odonto-Keratoprosthesis; PED = persistent corneal epithelial defect; PK = penetrating keratoplasty; SD = standard deviation; VA = visual acuity.

<sup>a</sup> epidescemetic KPro was implanted intralamellar in 11 eyes and epidescemetical in four eyes.

The authors of the one identified economic analysis<sup>31</sup> reported that, from the perspective of the third party payer, the use of the type II KPro was associated with a cost utility of $63,196 per quality adjusted life year. Thus, the authors concluded that decreases in both patient and societal costs may be realized when efforts were put forth to identify patients less likely to benefit from either type I KPro or traditional corneal transplantation.<sup>31</sup>

With regard to appropriate clinical indications for artificial keratoprosthesis devices, the American Academy of Ophthalmology<sup>32</sup> noted that keratoprosthesis devices are being used for unilateral or bilateral ocular trauma, unilateral or bilateral herpetic keratitis, unilateral or bilateral aniridia, unilateral or bilateral Steven-Johnson syndrome, and unilateral or bilateral congenital corneal opacification; however, the evidence for all of these indications was determined to be
grade III, insufficient and discretionary. In addition, osteo-odonto-keratoprosthesis has provided some success for patients with severe dry eye and autoimmune ocular surface diseases; however, the evidence was graded as III, insufficient and discretionary.\textsuperscript{32}
REFERENCES SUMMARIZED

Health Technology Assessments
No literature identified.

Systematic Reviews and Meta-analyses


Randomized Controlled Trials
No literature identified.

Non-Randomized Studies

Auro Keratoprosthesis


Boston Type I or II Keratoprosthesis


Artificial Keratoprosthesis for Corneal Transplant


Artificial Keratoprosthesis for Corneal Transplant

KeraKlear Kpro


Osteo-Odonto-Keratoprosthesis


Economic Evaluations


Guidelines and Recommendations


PREPARED BY:
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APPENDIX – FURTHER INFORMATION:

Non-Randomized Studies - Alternate Comparator


Review Articles


