AJCC-Staging for Retinoblastoma: One System Predicts Both Globe Salvage and Patient Mortality
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Purpose of this Study

- To evaluate the ability of the 8th edition of the American Joint Committee on Cancer (AJCC) Cancer Staging System to estimate retinoblastoma (RB) metastasis-related mortality and globe salvage.

- Comparison with existing classification systems (CHLA and WEH).

Why AJCC?

1. Multiple RB classification systems predict local treatment outcomes after chemotherapy and not life prognosis.
2. Lack published multi-center validation.
3. Not periodically updated.
4. Different systems used by different centers complicate clinical/research/literature outcomes.
5. Limited cross-specialty penetration.

1. AJCC: Uses standard TNM (tumor, node, metastasis framework
2. Union for International Cancer Control (UICC) world-wide accepted method of multispecialty cancer staging
3. Standardized data reporting and case-to-case prognostication enabled
4. “First” heritable trait (H) biomarker
5. Approved by the AJCC Ophthalmic Oncology Task Force.
Methods - AJCC-OOTF is “World-Wide”

Internet-based, Retrospective Registry

Institutional Review Board and Ethics Approvals were obtained

Study adhered to the Declaration of Helsinki and HIPAA
Methods

- Center-specific diagnostic and treatment protocols
- Clinical details at presentation
- All Classified by AJCC, WEH and CHLA
- Treatment details noted
- Local treatment failure: need for enucleation or EBRT
- Survival outcome: Metastasis and death
Method - Statistical Analysis

- Patient survival and globe salvage data was estimated with the Kaplan-Meier method.

- Cox proportional hazards regression models: associations between treatment outcomes and tumor category.
Results

Registry

Eighteen eye cancer specialty centers from 13 countries in over 6 continents

2190 patients were enrolled between January 2001 and December 2013

105 patients excluded from analysis due to incomplete data
Life Prognosis Analysis

- Median follow-up: 48.0 months
- 109 (5.2%) children developed metastatic disease over a median time of 9.50 months from presentation.
- Cumulative Survival Proportion with respect to tumor categories showed a steep decline from cT1a (100%) to cT4 (45%) at 5-year follow-up.

<table>
<thead>
<tr>
<th>cT Category</th>
<th>Survival Risk</th>
</tr>
</thead>
<tbody>
<tr>
<td>cT3</td>
<td>8.09-fold</td>
</tr>
<tr>
<td>cT4</td>
<td>48.55-fold</td>
</tr>
</tbody>
</table>
Life Prognosis Analysis

- When compared with CHLA and WEH, AJCC TNMH classification shows a better tumor stratification in terms of risk for metastasis-related mortality.
Life Prognosis by Pathological TNM category in Enucleated Eyes

Cumulative Survival Proportion with respect to tumor categories showed a steep decline from pT1 (99%) to pT4 (48%) at the 5-year follow-up.

<table>
<thead>
<tr>
<th>Tumor Category</th>
<th>Survival Risk</th>
</tr>
</thead>
<tbody>
<tr>
<td>pT3</td>
<td>9.76-fold risk</td>
</tr>
<tr>
<td>pT4</td>
<td>77.26-fold risk</td>
</tr>
</tbody>
</table>
Local Treatment Failure

- Of the 2854 eyes, 1574 had an attempt at globe salvage.
- 434 eyes needed enucleation or EBRT.
- As the cT-categories increased from cT1a to cT3, the hazard of treatment failure increased.

<table>
<thead>
<tr>
<th>cT Level</th>
<th>Fold Risk</th>
</tr>
</thead>
<tbody>
<tr>
<td>cT1b</td>
<td>3.5-fold</td>
</tr>
<tr>
<td>cT2a</td>
<td>15.1-fold</td>
</tr>
<tr>
<td>cT2b</td>
<td>16.4-fold</td>
</tr>
<tr>
<td>cT3</td>
<td>45.0-fold</td>
</tr>
</tbody>
</table>
Local Treatment Failure

- Difference in local treatment failure rates was significant in less advanced tumors (cT1a and cT1b) compared to cT3. These results were comparable in CHLA classification.

- But they were in variance with group E in WEH classification.
Discussion

- Multicenter, International, Registry-based studies of rare cancers can be performed using internet-based data sharing. This is the first such study to assess treatment outcome measures in large, heterogeneous, real-world retinoblastoma patient population.

- AJCC-RB staging predicted metastasis related mortality.
  
  AND

- AJCC-RB staging predicted globe salvage.
  
  AND

- AJCC-UICC staging is the world’s multi-specialty cancer language.
Summary

- **AJCC RB staging:**
  - is the only comprehensive classification that predicts metastasis and globe salvage.
  - accounts for both intraocular and extraocular retinoblastoma extent.
  - has been periodically updated with the latest significant medical evidence.
  - holistically includes tumor, nodes, metastasis, and heritable trait.
  - has been adopted by the Union for International Cancer Control (UICC) making it the most common world RB cancer terminology.
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The AJCC-OOTF
Thanks You.