Skin Cancer in Organ Transplant Recipients: Update 2018

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Disclosures

- Investigator
  - Menlo Therapeutics
  - Leo Pharma
  - SunPharma
  - Castle Biosciences
  - Pfizer
  - Eli Lilly
  - Kiniksa
  - Regeneron
  - Sanofi/Genzyme

- Consultant
  - Genentech
  - Biossance/Amyris
  - Zebra MedTech
  - Castle Creek Pharmaceuticals
  - Pennside Partners
  - Gerson Lehrman Group

Skin Cancer in Transplant Recipients

SCC risk in Medicare patients
among patients with dermatology visits, adjusted for age, sex, UV, non-dermatology and dermatology visit frequency

Yanik et al., Cancer Epidemiol Biomarkers Prev. 2017
Should We Screen OTR for Skin Cancer?

- 2016 USPSTF statement: insufficient data to support skin cancer screening based on a goal of reducing mortality

  • Potential Benefits
    - Possible reduction of morbidity/mortality
    - Opportunity to educate patients about modifiable sun exposure/lifestyle factors
    - Opportunity to identify specific medication-associated risks
    - Opportunity to intervene on other transplant-associated dermatologic conditions

  • Potential Harms
    - Cost to the health care system
    - Potential to increase invasive procedures and complications
    - Potential anxiety arising from biopsy

  • Obstacles to Screening
    - Patient health status, travel time
    - Referring physician awareness
    - Access to dermatologic care (ex. rural areas)

Skin Cancer Mortality in US OTR 1987-2013 (N=496,951)

<table>
<thead>
<tr>
<th>Gender</th>
<th>Overall*</th>
<th>Cancer, All Sites</th>
<th>All Cancers</th>
<th>Cancers, All Sites</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male</td>
<td>821.5</td>
<td>5,308</td>
<td>168.5</td>
<td>11.52</td>
</tr>
<tr>
<td>Female</td>
<td>5,308</td>
<td>168.5</td>
<td>21.5</td>
<td>11.52</td>
</tr>
</tbody>
</table>

- Per 100,000 person/years

http://www.cdc.gov/nchs/fastats/deaths.htm
http://seer.cancer.gov/statfacts/

Should We Screen OTR for Skin Cancer?

- Our goal: Risk prediction algorithm and formal consensus on skin cancer screening based on US incidence and risk factors

- Gap in the data: population-based incidence in OTR
Transplant Skin Cancer Network

- A research network focused on multicenter studies of skin cancer in organ transplant recipients,
  - Seed funded by the AAD and Galderma
  - Membership largely drawn from researchers in the ITSCC and SCOPE networks
- Goal: to determine the population-based incidence and predictors of post-transplant skin cancer.
- Retrospective review of all OTR at 26 centers transplanted in 2003, 2008
  - 10,649 OTR contributed 59,923 years of follow-up

### Post-Transplant Skin Cancer Incidence

#### Incidence Rate in the US population (SEER Registry Data)

<table>
<thead>
<tr>
<th>Skin Cancer</th>
<th>N=408,739</th>
<th>Male</th>
<th>237,642</th>
<th>58.0%</th>
<th>Female</th>
<th>171,097</th>
<th>42.0%</th>
<th>p&lt;0.001</th>
</tr>
</thead>
<tbody>
<tr>
<td>SCC</td>
<td>812</td>
<td>536</td>
<td>66.1%</td>
<td>636</td>
<td>78.5%</td>
<td>145</td>
<td>17.9%</td>
<td>190</td>
</tr>
<tr>
<td>MM</td>
<td>75</td>
<td>44</td>
<td>58.7%</td>
<td>35</td>
<td>46.7%</td>
<td>26</td>
<td>34.7%</td>
<td>14</td>
</tr>
</tbody>
</table>

#### Incidence Rate in nontransplant population

<table>
<thead>
<tr>
<th>Skin Cancer</th>
<th>N=411,625</th>
<th>Male</th>
<th>249,434</th>
<th>60.9%</th>
<th>Female</th>
<th>162,191</th>
<th>40.1%</th>
<th>p&lt;0.001</th>
</tr>
</thead>
<tbody>
<tr>
<td>SCC</td>
<td>812</td>
<td>527</td>
<td>64.9%</td>
<td>645</td>
<td>79.4%</td>
<td>167</td>
<td>21.6%</td>
<td>195</td>
</tr>
<tr>
<td>MM</td>
<td>75</td>
<td>45</td>
<td>60.0%</td>
<td>32</td>
<td>42.7%</td>
<td>23</td>
<td>30.7%</td>
<td>12</td>
</tr>
</tbody>
</table>

### Delphi Consensus Panel: Skin Cancer Screening after Transplantation

- 84 dermatologists and transplant physicians
- 42 US institutions
- Three rounds of anonymous surveys and aggregate results to achieve 80% consensus on 3 topics:
  - Risk assessment vs. cancer screening by full body examination
  - Which OTR should be screened
  - When OTR should be risk assessed and screened
- Recommendations are endorsed by the ITSCC and ISHLT for use in the US

#### Specialty N

<table>
<thead>
<tr>
<th>Specialty</th>
<th>N</th>
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</thead>
<tbody>
<tr>
<td>Dermatology</td>
<td>47</td>
</tr>
<tr>
<td>Medical Dermatology</td>
<td>26</td>
</tr>
<tr>
<td>Mohs Micrographic Surgery</td>
<td>11</td>
</tr>
<tr>
<td>Transplant</td>
<td>0</td>
</tr>
<tr>
<td>Cardiology</td>
<td>15</td>
</tr>
<tr>
<td>Pulmonology</td>
<td>12</td>
</tr>
<tr>
<td>Nephrology</td>
<td>2</td>
</tr>
<tr>
<td>Hepatology</td>
<td>2</td>
</tr>
<tr>
<td>Surgery</td>
<td>2</td>
</tr>
<tr>
<td>Total</td>
<td>84</td>
</tr>
</tbody>
</table>

#### Years Treating SOTR

| N=1105 | Mean (Range) | 13.2 (1-42) |

#### Practice Type

<table>
<thead>
<tr>
<th>Type</th>
<th>N (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Academic</td>
<td>81</td>
</tr>
<tr>
<td>Private</td>
<td>3</td>
</tr>
</tbody>
</table>

#### Risk assessment vs. cancer screening by full body examination

- Clinical history
- Physical examination
- Laboratory tests
- Imaging studies
- Genetic testing

#### Which OTR should be screened

- Adult recipients
- Pediatric recipients
- Recipients with a history of skin cancer
- Recipients with a history of organ rejection

#### When OTR should be risk assessed and screened

- Annually
- Biannually
- Quarterly
- Monthly

#### Cancer Screening Recommendations

- Baseline skin examination
- Annual skin examination
- Monthly sun protection
- Use of sunscreens with a high SPF
- Avoidance of tanning beds
- Early detection of skin cancer

- Contact dermatologist
- Referral to dermatologist
- Referral to oncologist

Reference:

Garrett et al., JAMA Dermatol. 2017
Panel Recommendations

- The transplant team should perform risk assessment at either the time of listing or at the time of transplant.
- The panel recommends that the transplant team perform risk assessment with the aid of an evidence-based risk stratification tool.
- The panel would prefer a risk assessment tool that can be completed in less than five minutes.
- The panel would prefer a risk assessment tool that can be completed by non-physician office staff.
- Skin cancer screening by full body skin examination should be completed by a dermatologist.
- Solid organ transplant recipients who have a history of skin cancer should continue standard skin cancer surveillance as recommended by their dermatologists.

Preferred threshold:
Screen 50 patients to detect one cancer (2% incidence)

Skin Cancer Risk Evaluation after transplant (SCREEN):
5 minute, evidence-based tool to predict post-transplant skin cancer

<table>
<thead>
<tr>
<th>Variable</th>
<th>Beta [95% CI]</th>
<th>Points</th>
</tr>
</thead>
<tbody>
<tr>
<td>White race</td>
<td>8.8 [6.05 - 12.76]</td>
<td>2.17</td>
</tr>
<tr>
<td>Pretransplant skin cancer</td>
<td>4.6 [3.45 - 6.1]</td>
<td>1.52</td>
</tr>
<tr>
<td>Age &gt;50</td>
<td>2.5 [2.03 - 2.98]</td>
<td>0.9</td>
</tr>
<tr>
<td>Male</td>
<td>1.5 [1.29 - 1.82]</td>
<td>0.43</td>
</tr>
<tr>
<td>Heart or Lung Tp</td>
<td>1.3 [1.08 - 1.53]</td>
<td>0.25</td>
</tr>
</tbody>
</table>

SCREEN Risk Category (points)
1: Low Risk (0-6)
2: Medium Risk (7-13)
3: High Risk (14-17)
4: Immediate Risk (18-22)

SCREEN Decision Tree
Important Considerations for Use

• “Screening” applies only to asymptomatic patients, with no active lesions.
  – Subjects with pretransplant skin cancer should have an FBSC within the recommended time period at a minimum; or sooner as directed by their dermatologist.

• A patient with a concerning lesion should be referred immediately for evaluation.

• Other patient-specific pretransplant risk factors should be considered at the time of patient visit.
  – Pretransplant sun damage/UV exposure, pretransplant immunosuppression

• This tool does not incorporate risk for KS or genital dysplasia, both of which may be higher in OTR of color or HIV positive OTR.