Research Update

Examining PCa Disparities Globally

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PGY-6
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# Prostate Cancer Epidemiology

<table>
<thead>
<tr>
<th>Common Types of Cancer</th>
<th>Estimated New Cases 2017</th>
<th>Estimated Deaths 2017</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Breast Cancer (Female)</td>
<td>252,710</td>
<td>40,610</td>
</tr>
<tr>
<td>2. Lung and Bronchus Cancer</td>
<td>222,500</td>
<td>155,870</td>
</tr>
<tr>
<td><strong>3. Prostate Cancer</strong></td>
<td><strong>161,360</strong></td>
<td><strong>26,730</strong></td>
</tr>
<tr>
<td>4. Colon and Rectum Cancer</td>
<td>135,430</td>
<td>50,260</td>
</tr>
<tr>
<td>5. Melanoma of the Skin</td>
<td>87,110</td>
<td>9,730</td>
</tr>
<tr>
<td>6. Bladder Cancer</td>
<td>79,030</td>
<td>16,870</td>
</tr>
<tr>
<td>7. Non-Hodgkin Lymphoma</td>
<td>72,240</td>
<td>20,140</td>
</tr>
<tr>
<td>8. Kidney and Renal Pelvis Cancer</td>
<td>63,990</td>
<td>14,400</td>
</tr>
<tr>
<td>9. Leukemia</td>
<td>62,130</td>
<td>24,500</td>
</tr>
<tr>
<td>10. Endometrial Cancer</td>
<td>61,380</td>
<td>10,920</td>
</tr>
</tbody>
</table>

Prostate cancer represents 9.6% of all new cancer cases in the U.S.
African Americans Have Worse PCa Outcomes

• Incidence of PCa 60% higher in African Americans (AAM)
  – Increased likelihood of presentation with metastatic disease at diagnosis (65-75%)

• Mortality rates 2-3x greater than compared to European Americans (EAM)
  – Findings consistent in pre- and post-PSA screening era
West African Men Have Similar PCa Rates

- Incidence and mortality similar to AAM
  - 1997 study in Lagos, Nigeria
    - incidence of 127/100,000 men, 64% died within 2 years of diagnosis
  - Follow up hospital based study
    - prevalence rate of 182.5 per 100,000
  - Ikuerowo et al showed:
    - 35% of patients with PCa were metastatic at diagnosis
    - 74% with aggressive PCa (Gleason score >7) at diagnosis

Badmus TA et al. 2010
Osegbe O et al.
Significance

• Nigeria is most populous West African nation and largest ancestral population of many AAM
• Unscreened population given current limitations in public health infrastructure
• Prostate cancer leading cause of cancer mortality in Nigerian men

• Possible genetic basis of outcomes seen in AAM
Objective

• Establish overall prevalence of prostate cancer and in particular, clinically undetected aggressive prostate cancer by decade of life in unscreened Nigerian population
  – Pilot of 100 Nigerian men undergoing forensic autopsy
  – Tertiary Nigerian hospitals affiliated with cancer registry

• We hypothesize that prevalence of clinically undetected PCa is higher in Nigerian men than men of European American ancestry
  – Compare prevalence of aggressive PCa by decade of age to previously published rates in established autopsy studies
Why Autopsy Studies?

• Prostate cancer has a long clinically indolent course
  – Histologically present, clinically undetected
• Incidence studies skewed by screening intensity, long lead time
• Autopsy studies are best barometer of true population prevalence
  – Especially in an unscreened population
• Lack of feasibility of widespread screening in LMIC
Autopsy Prevalence Data to date

Table 3
Autopsy prevalence of prostate cancer in the world

<table>
<thead>
<tr>
<th>Age</th>
<th>US White\textsuperscript{3}</th>
<th>US Black\textsuperscript{3}</th>
<th>Japan\textsuperscript{19}</th>
<th>Spain\textsuperscript{28}</th>
<th>Greece\textsuperscript{29}</th>
<th>Hungary\textsuperscript{30}</th>
</tr>
</thead>
<tbody>
<tr>
<td>21-30</td>
<td>8</td>
<td>8</td>
<td>0</td>
<td>4</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>31-40</td>
<td>31</td>
<td>31</td>
<td>20</td>
<td>9</td>
<td>0</td>
<td>27</td>
</tr>
<tr>
<td>41-50</td>
<td>37</td>
<td>43</td>
<td>13</td>
<td>14</td>
<td>3</td>
<td>20</td>
</tr>
<tr>
<td>51-60</td>
<td>44</td>
<td>46</td>
<td>22</td>
<td>24</td>
<td>5</td>
<td>28</td>
</tr>
<tr>
<td>61-70</td>
<td>65</td>
<td>70</td>
<td>35</td>
<td>32</td>
<td>14</td>
<td>44</td>
</tr>
<tr>
<td>71-80</td>
<td>83</td>
<td>81</td>
<td>41</td>
<td>33</td>
<td>31</td>
<td>58</td>
</tr>
<tr>
<td>81-90</td>
<td>48</td>
<td></td>
<td>40</td>
<td>73</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Global PCa Mortality

[Map of global prostate cancer mortality rates with high and low regions indicated.]

Prevalence of Latent Prostate Cancer at Autopsy in Nigerian Males

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Department of Urology
Methods

Inclusion
• Males 40-79 years of age
• <3 days post-mortem
• Undergoing forensic autopsy for any cause

Exclusion
• Men with known urological malignancy including PCa

Outcomes
• Gleason grade
• Pathological stage
• Centralized review/inter-observer variability among Nigerian GU pathologists and NU pathologist
Amputate and save the SV

Save the Bladder Neck and Apex entirely
Pathology Data Form

- Patient age
- Known family and medical history
- Cause of death
- Region of residence
- Reported tribal/ethnic identification
- PCa diagnosis:
  - Gleason score including tertiary components
  - pathological stage
  - number of lymph nodes and other suspected metastasis biopsies
  - tumor dimensions/volume
  - prostate volume/weight
- Serum PSA if available
Progress

• Traveled to Nigeria (August 2017)
  – Finalized standardized protocol across 4 sites
  – In-service instruction for all pathologists
    • Transition from ISUP 2005 Gleason grading to updates in 2014 guidelines
  – Provision for data sharing, finalized data collection instrument
  – Obtained Ethics approval at each site
  – Monthly checkpoint meeting

• Developed collaborative prostate cancer research network
  – Collecting tumor for RNA extraction to assess ancestry associated expression differences in PCa
Results To Date

Unanticipated Constraints

• Lassa Fever outbreak (Lagos)
• Administrative strike (Calabar)
• Onboarding (Ibadan)
• Subject accrual due to religious beliefs (Jos)
Results to Date

- Mean age 54.6 +/- 11.1 yrs
- Mean prostatic weight 25.8 +/- 11.1g
- Overall prostate cancer prevalence 10.3% (18.2% age > 60)

<table>
<thead>
<tr>
<th>Site</th>
<th>Cases</th>
<th>PCa</th>
<th>Histology</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lagos</td>
<td>30</td>
<td>2</td>
<td>• Gleason 3+4</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>• Gleason 5+4</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>• HGPIN</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>• BPH</td>
</tr>
<tr>
<td>Calabar</td>
<td>7</td>
<td>2</td>
<td>• Gleason 3+3</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>• Gleason 3+4</td>
</tr>
<tr>
<td>Jos</td>
<td>2</td>
<td>0</td>
<td>• BPH</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>• Normal prostatic tissue</td>
</tr>
</tbody>
</table>
Significance/Impact

• Limited biopsy capabilities and access to screening modalities hamper population wide screening in West Africa
  – Results to help shape prostate cancer screening programs
  – #1 cancer in Nigerian men

• Increased prevalence of PCa in West African population could point to less modifiable disease risk factor for AAM in the US
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  - Dr. Ima Ekanem
  - Dr. Badmos Kabir
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Methods

• Standardized protocol
  – Removal of prostate with SVs attached en-bloc within 48 hrs of death
  – Placed in buffered formalin for fixation, sectioned at 4mm intervals after weighing
  – Embedded in paraffin cassettes and H&E staining performed
  – Tru-cut biopsies to be obtained for nodes, sites of metastases
  – Sample of spleen for DNA mutational analysis