Overview of testicular cancer

Great Lakes SUNA 2015 Conference

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Testicular anatomy

[Diagram of male pelvic anatomy with labeled structures]

http://www.urologyhealth.org/urology/articles/images/anatomy_MalePelvis_midsagital.jpg
Testicular lymphatic drainage and cancer spread

http://www.urologyhealth.org/urology/index.cfm?article=36
Testicular cancer incidence and survivors

SEER Stat Fact Sheets: Testis Cancer

Statistics at a Glance

At a Glance

- Estimated New Cases in 2014: 8,820
- % of All New Cancer Cases: 0.5%
- Estimated Deaths in 2014: 380
- % of All Cancer Deaths: 0.1%

Number of New Cases and Deaths per 100,000: The number of new cases of testis cancer was 5.6 per 100,000 men per year. The number of deaths was 0.2 per 100,000 men per year. These rates are age-adjusted and based on 2007–2011 cases and deaths.

Lifetime Risk of Developing Cancer: Approximately 0.4 percent of men will be diagnosed with testis cancer at some point during their lifetime, based on 2009–2011 data.

Prevalence of this cancer: In 2011, there were an estimated 227,406 men living with testis cancer in the United States.
Decreasing death from testicular cancer

New Cases, Deaths and 5-Year Relative Survival

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</thead>
<tbody>
<tr>
<td>5-Year Relative Survival</td>
<td>80.0%</td>
<td>89.6%</td>
<td>92.5%</td>
<td>96.1%</td>
<td>96.0%</td>
<td>95.8%</td>
<td>96.2%</td>
<td>98.0%</td>
</tr>
</tbody>
</table>

How common is testicular cancer relative to other cancers?

<table>
<thead>
<tr>
<th>Common Types of Cancer</th>
<th>Estimated New Cases 2014</th>
<th>Estimated Deaths 2014</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Prostate Cancer</td>
<td>233,000</td>
<td>29,480</td>
</tr>
<tr>
<td>2. Breast Cancer (Female)</td>
<td>232,670</td>
<td>40,000</td>
</tr>
<tr>
<td>3. Lung and Bronchus Cancer</td>
<td>224,210</td>
<td>159,260</td>
</tr>
<tr>
<td>4. Colon and Rectum Cancer</td>
<td>136,830</td>
<td>50,310</td>
</tr>
<tr>
<td>5. Melanoma of the Skin</td>
<td>76,100</td>
<td>9,710</td>
</tr>
<tr>
<td>6. Bladder Cancer</td>
<td>74,690</td>
<td>15,580</td>
</tr>
<tr>
<td>7. Non-Hodgkin Lymphoma</td>
<td>70,800</td>
<td>18,990</td>
</tr>
<tr>
<td>8. Kidney and Renal Pelvis Cancer</td>
<td>63,920</td>
<td>13,860</td>
</tr>
<tr>
<td>9. Thyroid Cancer</td>
<td>62,980</td>
<td>1,890</td>
</tr>
<tr>
<td>10. Endometrial Cancer</td>
<td>52,630</td>
<td>8,590</td>
</tr>
<tr>
<td>25. Testis Cancer</td>
<td>8,820</td>
<td>380</td>
</tr>
</tbody>
</table>

Testis cancer represents 0.5% of all new cancer cases in the U.S.
Testicular cancer survival

How Many People Survive 5 Years Or More after Being Diagnosed with Testis Cancer?

Relative survival statistics compare the survival of patients diagnosed with cancer with the survival of people in the general population who are the same age, race, and sex and who have not been diagnosed with cancer. Because survival statistics are based on large groups of people, they cannot be used to predict exactly what will happen to an individual patient. No two patients are entirely alike, and treatment and responses to treatment can vary greatly.

Based on data from SEER 18 2004–2010. Gray figures represent those who have died from testis cancer. Green figures represent those who have survived 5 years or more.
Testicular cancer stage and survival

Percent of Cases & 5-Year Relative Survival by Stage at Diagnosis: Testis Cancer

Percent of Cases by Stage:
- Localized (68%) Confined to Primary Site
- Regional (18%) Spread to Regional Lymph Nodes
- Distant (12%) Cancer Has Metastasized
- Unknown (1%) Unstaged

5-Year Relative Survival:
- Localized: 99.2%
- Regional: 96.0%
- Distant: 73.1%
- Unstaged: 79.1%

SEER 18 2004–2010, All Races, Males by SEER Summary Stage 2000
Testicular cancer primarily diagnosed in young men

Percent of New Cases by Age Group: Testis Cancer

Testis cancer is most frequently diagnosed among men aged 20–34.

Median Age At Diagnosis

33

SEER 18 2007–2011, All Races, Males
Testicular cancer and race

Number of New Cases per 100,000 Persons by Race/Ethnicity

- **All Races**: 5.6
- **White**: 6.6
- **Black**: 1.4
- **Asian / Pacific Islander**: 1.9
- **American Indian / Alaska Native**: 4.5
- **Hispanic**: 4.8
- **Non-Hispanic**: 5.7

SEER 18 2007–2011, Age-Adjusted
Testicular Cancer – Risk factors and screening

- An undescended testis (cryptorchidism).
- A family history of testis cancer (particularly in a father or brother).
- A personal history of testis cancer.
- Surgical correction of an undescended testis (orchiopexy) before puberty appears to lower the risk of testis cancer, but this isn't certain.

Based on fair evidence, screening for testicular cancer would not result in an appreciable decrease in mortality, in part because therapy at each stage is so effective.

http://www.cancer.gov/cancertopics/pdq/treatment/testicular/HealthProfessional
Testicular cancer evaluation and treatment

**NCCN Guidelines Version 1.2015**

**Testicular Cancer**

### WORKUP
- Suspicious testicular mass
  - H&P
  - Alpha-fetoprotein (AFP)
  - beta-hCG
  - LDH
  - Chemistry profile
  - Chest x-ray
  - Testicular ultrasound

### PRIMARY TREATMENT
- Discuss sperm banking
- Radical inguinal orchietomy
- Consider inguinal biopsy of contralateral testis if:
  - Suspicious ultrasound for intratesticular abnormalities
  - Cryptorchid testis
  - Marked atrophy

### PATHOLOGIC DIAGNOSIS
- Pure seminoma (pure seminoma histology and AFP negative; may have elevated beta-hCG)
  - Nonseminomatous germ cell tumor (NSGCT) (includes mixed seminoma/nonseminoma tumors and seminoma histology with elevated AFP)

See Postdiagnostic Workup and Clinical Stage (TEST-2)

See Postdiagnostic Workup and Clinical Stage (TEST-6)
Ultrasound

Radical orchiectomy

- High ligation of the spermatic cord
- Ilioinguinal nerve injury, resulting in hypoesthesia of the ipsilateral groin and lateral hemiscrotum

http://emedicine.medscape.com/article/449033-overview#a15
Testicular Cancer - Types

• Types of testicular germ cell tumors
  – Seminomas versus nonseminomas

• The five histopathological subtypes of testicular germ cell tumors include:
  – Seminomas
  – Embryonal carcinomas
  – Teratomas
  – Yolk sac tumors
  – Choriocarcinomas

http://www.cancer.gov/cancertopics/pdq/treatment/testicular/HealthProfessional
Clinical Staging

- **Pathological T stage (pT)**
  - **Orchiectomy specimen**

- **Clinical N stage**
  - **Imaging of abd/pelvis**

- **Clinical M stage**
  - **Imaging**

- **Serum Marker stage**

<table>
<thead>
<tr>
<th>Stage</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>SX</td>
<td>Marker studies not available or not performed.</td>
</tr>
<tr>
<td>S0</td>
<td>Marker study levels within normal limits.</td>
</tr>
<tr>
<td>S1</td>
<td>LDH &lt;1.5 × Nb and hCG (mlu/ml) &lt;5,000 and AFP (ng/ml) &lt;1,000.</td>
</tr>
<tr>
<td>S2</td>
<td>LDH 1.5–10 × N or hCG (mlu/ml) 5,000–50,000 or AFP (ng/ml) 1,000–10,000.</td>
</tr>
<tr>
<td>S3</td>
<td>LDH &gt;10 × N or hCG (mlu/ml) &gt;50,000 or AFP (ng/ml) &gt;10,000.</td>
</tr>
</tbody>
</table>

http://www.cancer.gov/cancertopics/pdq/treatment/testicular/HealthProfessional
Serum Staging

- **Beta-human chorionic gonadotropin (bHCG)**
  - 14% of the patients with stage I pure seminoma prior to orchiectomy
  - About half of patients with metastatic seminoma.
  - 40% to 60% of men with nonseminomas have an elevated serum beta-hCG
  - T1/2 24-36 hr - 1 week

- **Alpha-fetoprotein (AFP)**
  - Elevation of serum AFP is seen in 40% to 60% of men with nonseminomas
  - Seminomas do not produce AFP
  - T1/2 : 5-7 days - 5 weeks

- **LDH lactate dehydrogenase**
  - Seminomas and nonseminomas may result in elevated (LDH)
  - Less clear prognostic significance, due to conditions unrelated to cancer
  - T1/2 3 days

- **At least 5 half lives to eliminate marker after orchiectomy**
AJCC 2010 Clinical staging

<table>
<thead>
<tr>
<th>pTX</th>
<th>Primary tumor cannot be assessed.</th>
</tr>
</thead>
<tbody>
<tr>
<td>pT0</td>
<td>No evidence of primary tumor (e.g., histologic scar in testis).</td>
</tr>
<tr>
<td>pTis</td>
<td>Intratubular germ cell neoplasia (carcinoma <em>in situ</em>).</td>
</tr>
<tr>
<td>pT1</td>
<td>Tumor limited to the testis and epididymis without vascular/lymphatic invasion; tumor may invade into the tunica albuginea but not the tunica vaginalis.</td>
</tr>
<tr>
<td>pT2</td>
<td>Tumor limited to the testis and epididymis with vascular/lymphatic invasion, or tumor extending through the tunica albuginea with involvement of the tunica vaginalis.</td>
</tr>
<tr>
<td>pT3</td>
<td>Tumor invades the spermatic cord with or without vascular/lymphatic invasion.</td>
</tr>
<tr>
<td>pT4</td>
<td>Tumor invades the scrotum with or without vascular/lymphatic invasion.</td>
</tr>
</tbody>
</table>

Clinical

<table>
<thead>
<tr>
<th>NX</th>
<th>Regional lymph nodes cannot be assessed.</th>
</tr>
</thead>
<tbody>
<tr>
<td>N0</td>
<td>No regional lymph node metastasis.</td>
</tr>
<tr>
<td>N1</td>
<td>Metastasis with a lymph node mass ≤2 cm in greatest dimension; or multiple lymph nodes, none &gt;2 cm in greatest dimension.</td>
</tr>
<tr>
<td>N2</td>
<td>Metastasis with a lymph node mass &gt;2 cm but not &gt;5 cm in greatest dimension; or multiple lymph nodes, any one mass &gt;2 cm but not &gt;5 cm in greatest dimension.</td>
</tr>
<tr>
<td>N3</td>
<td>Metastasis with a lymph node mass &gt;5 cm in greatest dimension.</td>
</tr>
</tbody>
</table>

http://www.cancer.gov/cancertopics/pdq/treatment/testicular/HealthProfessional/page3
Radiographic Staging

- **Chest**
  - CXR - if abnormal or CT A/P (+) → Chest CT
  - CT – most common initial clinical staging modality

- **Abdominal & Pelvic CT**
  - 70% sensitivity for retroperitoneal metastases at 1 cm (94% specificity)

- **MRI/PET**
  - Minimal advantage for initial staging
Prognosis

- Histology (seminoma vs. nonseminoma).
- The extent to which the tumor has spread (testis only vs. retroperitoneal lymph node involvement vs. pulmonary or distant nodal metastasis vs. nonpulmonary visceral metastasis).
- For nonseminomas, the degree to which serum tumor markers are elevated.
Prognosis

• **Disseminated seminomas**
  – Presence of metastases to organs other than the lungs (e.g., bone, liver, or brain) worse.

• **Disseminated non-seminoma**
  – Metastases to organs other than the lungs.
  – Highly elevated serum tumor markers.
  – Tumor that originated in the mediastinum rather than the testis.
  – Even patients with widespread metastases at presentation, including those with brain metastases, may have curable disease and should be treated with this intent.

http://www.cancer.gov/cancertopics/pdq/treatment/testicular/HealthProfessional
Standard chemotherapy for testicular cancer - BEP

- **Bleomycin**
  - Pulmonary fibrosis

- **Etoposide**
  - Neutropenia
  - Nausea/vomiting

- **Platinum (cisplatin)**
  - Ototoxicity
  - Renal insufficiency
  - Neuropathy
Treatment combinations based on stage of disease and tumor markers

- Radical orchiectomy
- Radiation therapy
- Chemotherapy
- Retroperitoneal lymph node dissection
Primary sites of lymphatic drainage from the right testis, as defined by early lymph node metastases from right-sided testis tumors. (From Donohue JP: Metastatic pathways of nonseminomatous germ cell tumors. Semin Urol 1984;2:217.)
Donohue Left

- Para-aortic lymph nodes
- Preaortic lymph nodes
- Nerve-dissection techniques preserve antegrade ejaculation in 90% of cases

Primary sites of lymphatic drainage from the left testis, as defined by early lymph node metastases from left-sided testis tumors. (From Donohue JP: Metastatic pathways of nonseminomatous germ cell tumors. Semin Urol 1984;2:217.)
Retroperitoneal surgery for testicular cancer

- **1950s**
  - En bloc dissection from diaphragm (suprahilar) to bifurcation of common iliacs, ureter to ureter with ipsilateral gonadal excision
  - Cooper - extraperitoneal thoracoabdominal approach

- **1980s**
  - Sympathetic postganglionic nerve preservation using modified dissection – antegrade ejaculation
  - Based on low volume metastatic LN distribution
  - Preserved contralateral SANS
  - Low stage tumors I, IIA, IIB
  - Suprahilar dissection only in advanced cases s/p chemotherapy – Retrocrural space
Nerve sparing may be performed even in post-chemotherapy setting

Prospective identification:
1) Sympathetic chain
2) Post-ganglionic SANS fibers
3) Hypogastric plexus
Right Modified RPLND - Interaortocaval

- Right side ejaculation preservation greater than left
- Never compromise surgical margins

Campbell's Urology
Figure 82–6. Surgical template for modified, right-sided retroperitoneal lymph node dissection.
Left Modified RPLND – Para-aortic

- May sacrifice IMA if marginal artery of Drummond intact

Campbell’s Urology
Figure 82–5. Surgical template for modified, left-sided retroperitoneal lymph node dissection.
‘Split and Roll’
Altered Patterns of Lymph Node Metastasis

- **Direct tumor invasion**
  - Inguinal nodes with TA or scrotal invasion
  - Pelvic nodes with epididymal/SC invasion

- **Previous scrotal, groin surgery**
  - Orchiopexy, trans-scrotal orchiectomy, trans-scrotal biopsy, hernia repair

- **RP gross LN involvement**

- **Right to left lymphatic metastases spread**
Post-Chemotherapy RPLND

- Standard bilateral dissection template

- Desmoplastic reaction

- Nerve-sparing if no gross tumor involvement
  - 20% candidates with low volume residual disease

- Laparoscopic and robotic techniques
RPLND operating room considerations

• **Bleomycin induced pulmonary fibrosis**
  – Screening PFT, room air ABG
  – Conservative IVF most critical factor
  – Minimize FiO2
  – 50% mortality if develop toxicity
  – Colloid preferred

• **Renal insufficiency** - cisplatin, avoid nephrotoxins

• **Myelosuppression** – cisplatin, etoposide

• Preop IS teaching, bowel prep, IV hydration
RPLND Complications

- **Lymphatic**
  - Chylous ascites 2-3%
  - Lymphocele 1%
- **Pulmonary**
  - Bleomycin toxicity
- **Vascular**
  - Selective preservation of lumbar arterial branches
- **GI**
  - Pancreatitis, ileus, SBO
- **Postoperative tachycardia** common - SANS discharge
Survivorship - long-term effects

• Fertility
• Secondary leukemias
• Renal function
• Hearing
• Lung function
• Cardiac disease
Case Study

- 22 y/o WM
- Left testis mass x 8 months
History

- PMH – None
- PSH – Wisdom tooth extraction
- All – NKDA
- Med – None
- SH – No tobacco/EtOH/illicit drugs
- FH – No GU malignancy/calculus disease
- ROS – Neg
Physical Exam

- Afebrile, vss
- HEENT, Lungs, CVS – wnl
- Abdomen - Soft, NT, ND, no masses/hernias
- GU – Nl circumcised phallus, right testis/epididymis wnl, left testis ~6cm firm mobile mass, nt
- Back/Extremities - No edema/CVAT
Laboratory

<table>
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<tr>
<th>Test</th>
<th>Results</th>
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<tbody>
<tr>
<td>CBC</td>
<td>HCT: 45, WBC: 6.4, PLT: 210</td>
</tr>
<tr>
<td>Coag</td>
<td>PT 13.6, INR 1.00, PTT 29.2</td>
</tr>
<tr>
<td>UA</td>
<td>Neg</td>
</tr>
<tr>
<td>βHCG</td>
<td>&lt;5</td>
</tr>
<tr>
<td>AFP</td>
<td>166</td>
</tr>
<tr>
<td>LDH</td>
<td>142</td>
</tr>
</tbody>
</table>
Imaging – Scrotal Ultrasound
Right Testis
Imaging – Scrotal Ultrasound Left Testis
Imaging – Scrotal Ultrasound

- Right testis unremarkable
- Left testis
  - 7.2 x 5.3 x 7.7 cm
  - Large mass replacing testis parenchyma containing multiple solid and cystic components likely representing testicular malignancy
Pathology – Left Radical Orchiectomy
Radical Orchiectomy

pT1 Mature Teratoma

- 6.5 cm greatest dimension
- No evidence of invasion of tunica albuginea
- Spermatic cord and epididymis uninvolved
- No evidence of lymphatic/vascular invasion
- Intratubular germ cell neoplasia (IGCNU)
Imaging – CT Abdomen/Pelvis
Imaging – CT Abdomen/Pelvis
Imaging – CT Abdomen/Pelvis
Imaging – CT Abdomen/Pelvis
Imaging – CT Abdomen/Pelvis
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Imaging – CT Abdomen/Pelvis

- Precaval soft tissue attenuation lymph node measuring 1.6 cm
- Low attenuation lymph node or conglomeration of lymph nodes measuring 3.9 x 2.3 cm in the left paraaortic chain
- No other lymphadenopathy in the chest, abdomen or pelvis
Stage IIb

T1 N2 M0 S1 Non-Seminomatous Germ Cell Tumor

AFP 151
Chemotherapy

- 3 cycles of bleomycin, etoposide, cisplatin (BEP)
- AFP
  - Pre-orchiectomy: 138
  - Pre-chemotherapy: 151
  - 1st cycle: 36
  - 2nd cycle: <5
  - 3rd cycle: <5
Imaging – CT Abdomen/Pelvis
Imaging – CT Abdomen/Pelvis

• Enlarged lymph node inferior to the left renal vein measures 2.8 x 1.3 cm

• Previously measured 4 x 2.4 cm
Pathology – Laparoscopic RPLND
Pathology – Laparoscopic RPLND
Pathology – Laparoscopic RPLND
LYMPH NODES, LEFT PERIAORTIC, DISSECTION
- METASTATIC MATURE CYSTIC TERATOMA IN THREE OF SIXTEEN LYMPH NODES (3/16)

LYMPH NODES, INTERAORTOCAVAL, DISSECTION
- NO EVIDENCE OF MALIGNANCY IN ELEVEN LYMPH NODES (0/11)

SPERMATIC CORD, LEFT, RESECTION
- NO EVIDENCE OF MALIGNANCY
- SUTURE GRANULOMA
Follow up

- Discharged home POD#1
- 3, 6, 12 month CT Chest / Abdomen / Pelvis – NED
- AFP <5
- HCG <5
- LDH 123
Thank you