Testicular Cancer - Right-Sizing Management

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Objectives

- Snapshot of what are the expected outcomes and resource utilization for testicular cancer in 2014
- Snapshot of what are the current outcomes and resource utilization for testicular cancer in the US
- What accounts for the delta between expected good outcomes and actual national results?
- The way forward- classic clinical trials or cancer care delivery research
- The call for collaborative integrated care for all patients
Best outcomes in testicular cancer in 2014

- Overall cure rates in CSI seminoma and non-seminoma approach 100%.
- Cure rate for all stage seminoma should approach 100%.
- Initial cure rates for regional and IGCCCC good risk disseminated nonseminoma should exceed 97%.
- IGCCCC intermediate risk nonseminoma should have overall cure rates exceeding 90% and IGCCC poor risk cure rates should exceed 70%.
- Less than 200 deaths in the US annually.
Optimal resource utilization for testicular cancer in 2014

- Adjuvant therapies for CS I seminoma (carbo or abd radiation) or CSI nonseminoma (primary RPLND or adj chemotherapy) should be uncommon.

- Active surveillance and post treatment surveillance should include a parsimonious schedule of imaging.

- There are almost no indications for PET scans.

- All RPLNDs should be performed in high volume centers which maximizes therapeutic effect and minimizes complications.
Actual outcomes for testicular cancer in the US

- About 400 deaths/year!
- High percentage of CSI patients receiving adjuvant treatment
- Most CSI receiving active surveillance are imaged on older, aggressive and long duration schedules
- Many patients receiving surgery at low volume centers
- Lots of PET scans, significant path errors and rookie mistakes
- Inferior outcomes by race, ethnicity, and initial care at low volume centers
Why this outcome gap?
Population-Based Outcomes in Testicular Cancer

- SWENOTECA-1384 patients with seminoma (5 deaths from disease or treatment-CSS 99.6) of the 1192 (86%) with CSI seminoma there were no cancer deaths (one treatment related death)

- Oregon/BCCA- 649 patients with seminoma. No deaths from either treatment or disease in 545 CSI patients. No disease related deaths and 3 treatment related deaths in 104 patients with CSII/III disease

- Denmark- 1832 patients with CSI seminoma managed with surveillance. 10 year CSS was 99.6 %
Population-based outcomes in non-seminoma

- Multiple series of active surveillance in CSI nonseminoma show cure rates approaching 100%

- IGCCC good risk disease-Oregon/BCCA 4 deaths/233 (<2%), Intermediate risk 1/11 (<10%), poor risk 5/29 (17%)

- SWENOTECA IGCCC Good risk 10 year CSS (96%), Intermediate risk (91%), Poor risk (69%)

- Indiana University Intermediate risk disease treated with BEP X 3 or 4 (>90% DFS and OS at 2 years)
Why the gap in outcomes?

- Rookie mistakes?
  - Delay in diagnosis
  - Poorly prepared or poorly interpreted pathology
  - Mis-assignment of stage or risk category
  - Inconsistent delivery of chemotherapy
  - Non-expert, non-open RPLND
  - Misinterpreting clinical imaging and markers esp at relapse or in remission
  - PET scans
  - Blind adherence to esp guidelines (NCCN)
Why the “gap” in outcomes?

- Access/Late Presentation??
  - In men with Stage III disease non-seminoma, African-American and Hispanic race were associated with a 1.6 and 1.3-fold higher risk of death (both $p<0.01$), respectively, than their Caucasian counterparts, after adjustment for chemotherapy and surgery use, facility type, year of diagnosis and comorbidities.
Why the “gap” in outcomes?

- 10000 hours??

Within the NCDB, of 79119 patients with TGCT, 8205 (10.4%) were diagnosed with CSIII. Median age at diagnosis was 32 years (range 18-84) and median follow-up was 5.7 years (range 0.1-14.9). Therapy was delivered in community, "comprehensive" community and academic hospitals in 10.0%, 47.3% and 40.5%, respectively. PC-RPLND was performed in 1295 (15.8%) patients. Median hospital volume was 8 and ranged from 1 to 115 cases per year. Death occurred in 1225 (24.8%) patients. At 5 years, overall survival was 74.3%, 76.9%, 75.2%, 86.1% for hospital volume categories 1-5, 6-10, 11-60 and >60, respectively. The greatest disparity for risk of death was recorded between groups 1-5 and >60 (HR: 0.85, p=0.03).
Why the “gap” in outcomes?

- Multidisciplinary Care??
  - Randomized trial demonstrates higher in field failures, scrotal recurrences and higher complications in patients receiving primary RPLND in community centers (Albers et al JCO)
  - Guidelines around the world all call for complex surgery, evaluation and management of poor risk patients and all patients requiring salvage treatments to be seen within high volume centers
Classic Clinical Trials to improve outcomes in germ cell tumors?

- No US clinical trials in early stage disease or good risk disease since early 1990s. Last European trial (BEP X 3 vs EP X 4) concluded in early 2000s.

- No current int/poor risk trials in US. Last trial ended in early 2000s. Last European trial in intermediate risk disease takes 13 years and is negative (BEP vs T-BEP).

- Last completed poor risk trial in Europe recently reported (BEP X 4 vs complex dose dense treatment) likely negative but does confirm the predictive value of marker decline with first cycle of treatment.
Challenges in classic therapeutic clinical trials in testicular cancer

- Standard management is too good.
- Disease is too uncommon (8100 new patients in US annually)
- Other higher priority cancer questions in the US and around the world.
- Even in the most dire clinical settings (poor risk or recurrent disease) randomized trials will require 400-500 patients. There are only about 700 or so poor risk pts in the US annually.
Current clinical trials

- Untreated poor risk disease- Phase II TIP X 4
- Limited institutional/pharma trials for orphan clinical settings (multiple recurrent disease, growing teratoma, CD-30 + ECC)
- Some trials investigating predictive biomarkers for relapse for CSI disease or failure of standard treatment in poor risk disease.
Outstanding questions?

- Biological questions- causation, prognostic and predictive biomarkers
- Survivorship research- late effects/interim surrogates of toxicity, QOL, judicious reduction in imaging and follow up
- Other germ cell tumors and populations- children and adolescents, ovarian germ cell tumors and extragonadal germ cell tumors
The single most important remaining question!!

- How do we deliver the extremely effective and well tolerated treatments available for this disease to ALL populations who could benefit?

- Why is there a relatively unfavorable outcome for AA and hispanic patients and why is there a difference in outcomes using standard therapies in high and low volume centers?
Cancer Care Delivery Research - NCI

- Cancer care delivery research is the multidisciplinary field of scientific investigation that studies how social factors, financing systems, organizational structures and processes, health technologies, provider and individual behaviors affect cancer outcomes including:
  - access to cancer care
  - the quality and cost of cancer care
  - ultimately the health and well-being of cancer patients

- Its focus includes individuals, families, organizations, institutions, providers, communities, populations and their interactions.
Collaborative care models for testicular cancer

- Expert multidisciplinary real time decision making for all patients
- Centralized imaging and pathology review
- Ongoing oversight and clinical decision making from high volume centers
- Aggregation and analysis of all clinical and biological data to inform a rapid learning system in germ cell tumors
Collaborative care models for rare diseases

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Collaborative care models for rare diseases

- Expert multidisciplinary real time decision making for all patients *
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- *** CAN BE DONE VIRTUALLY
Conclusions

- Using standard available and cheap management strategies, superb outcomes and low resource utilization can be achieved in testicular cancer.

- Unacceptable poor outcomes are seen in low volume centers and in patients of certain races and ethnicity and in the US.

- Guidelines and experts are all calling for collaborative management strategies with robust information and experience exchange between high volume and lower volume centers.
Conclusion

- To improve outcomes and quality of life in patients with testicular cancer and to reduce resource utilization, we must extend the experience and multidisciplinary decision support available in high volume centers to our populations as a whole.