Cancer Day for Primary Care

Testicular Cancer Overview

Piotr Czaykowski MD MSc FRCPC

May 31, 2024

Presenter Disclosure

- **Faculty / Speaker's name: Piotr Czaykowski**

- **Relationships with commercial interests:**
  - **Grants/Research Support:** CIHR, CancerCare Manitoba Foundation, Research Manitoba, Seagen Inc
  - **Speakers Bureau/Honoraria:** Winnipeg Community Urology Group
  - **Consulting Fees:** none
  - **Other:** none

Mitigating Potential Bias

- For clinical trials sponsored by an industry partner funding goes directly to the institution; I receive no direct compensation/remuneration
- I receive no direct compensation/remuneration from research funding

Learning Objectives

1. At the end of the presentation, learners will be able to describe the epidemiology and risk factors associated with testicular cancer.
2. At the end of the presentation, learners will be able to discuss the diagnostic and staging work-up for testicular cancer.
3. At the end of the presentation, learners will understand the standard treatments and outcomes for patient with testicular cancer.

Outline

In the next 15 minutes we will cover the following:

- Epidemiology
- Risk Factors
- Diagnosis/Staging
- Management

[picture of rollercoaster - Google Search]

Epidemiology

- The most common cancer in males aged 15-44 in 62 countries worldwide[1]
- Rate seems to be increasing gradually

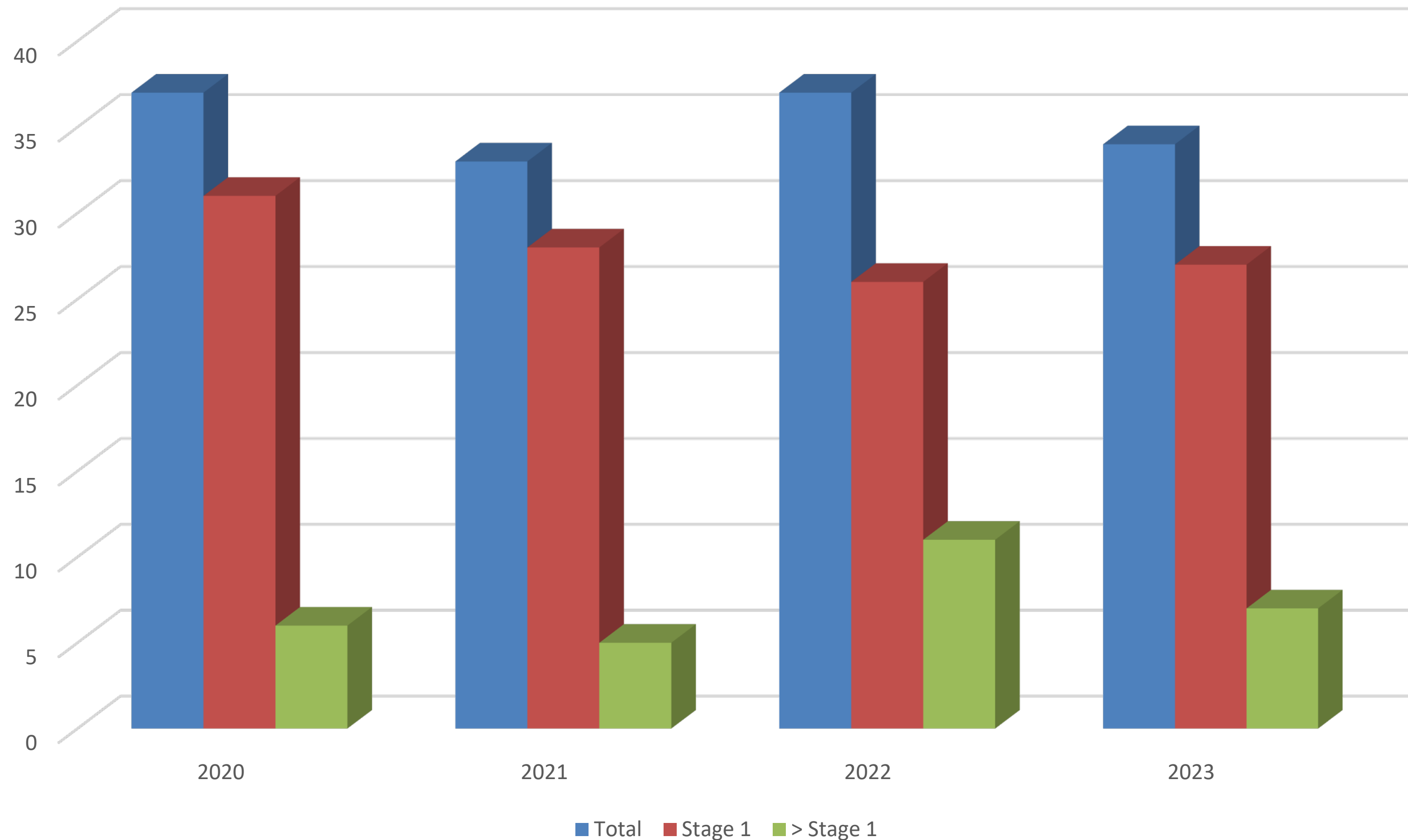
Incidence in Canada:

- – 🚹 - 1250 cases/yr
- – 30 deaths in Canada annually

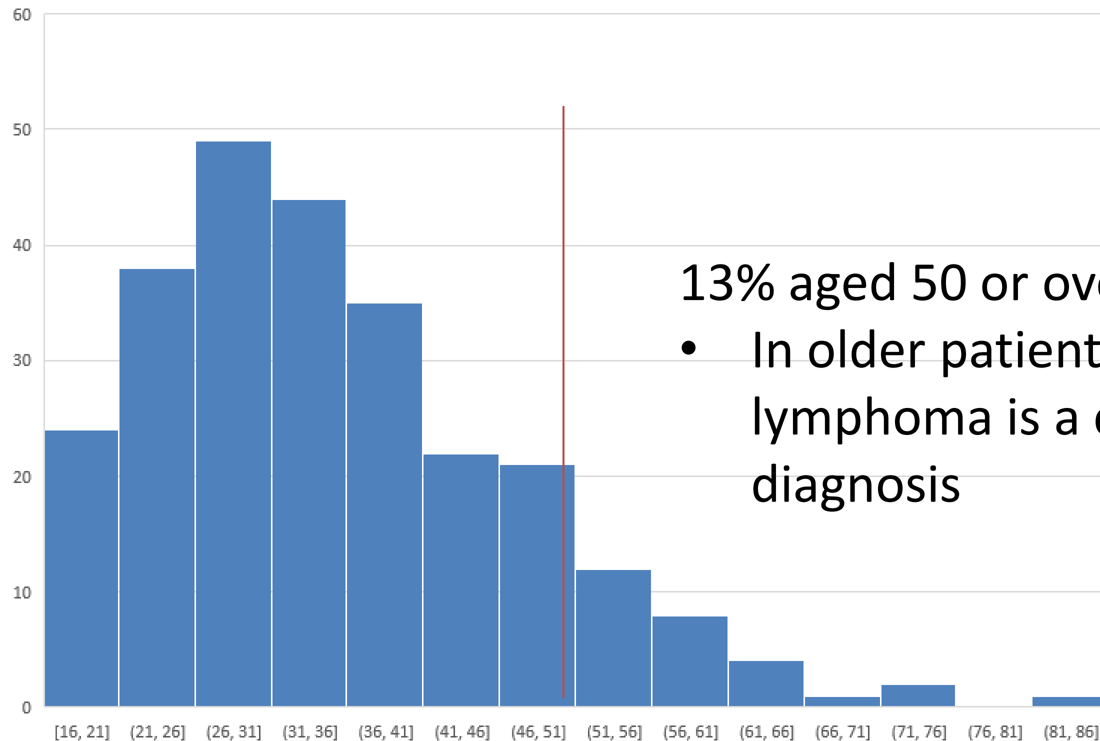
- MB numbers: 30 - 50 per year, on average 1 death per year

- 95% are germ cell tumors, 5% sex cord/stromal tumors
  - ~ 50% seminoma, 50% non-seminomatous germ cell tumors (NSGCTs); seminoma more common with increasing age
  - NSGCT elements: embryonal carcinoma, choriocarcinoma, yolk sac, teratoma
  - Not all GCTs arise in testis: mediastinal, intracranial, ?retroperitoneal

Manitoba GCT numbers



Age Distribution of GCT Patients (2002-2023) N=261



13% aged 50 or over at diagnosis

- In older patients testicular lymphoma is a competing diagnosis

Risk Factors

- Cryptorchidism – accounts for 10% of testicular cancer
  - Orchiopexy before puberty appears to decrease the risk
- Contralateral testicular cancer (2-3% lifetime risk)
- Family history: risk is 6-10x higher in a brother/son of index case
- Genetic disorders: Klinefelter syndrome (especially mediastinal GCTs), Down syndrome
- Marijuana use (two-fold increase compared to never users)

- Germ cell neoplasia in situ – 50% progress to malignancy in 5 years

Presenting symptoms

- Swollen testicle – 73%
  - Often noted by partner
  - Occasionally the larger testicle is normal, and the smaller one is atrophic and contains a tumor
- Pain – 18-46%
  - Torsion of neoplasm, infarction, intratumoral bleeding
- Gynecomastia – HCG secreting tumor
- Back or flank pain – metastatic disease
  - Often back pain alleviated by fetal position

Diagnosis

5 key elements:

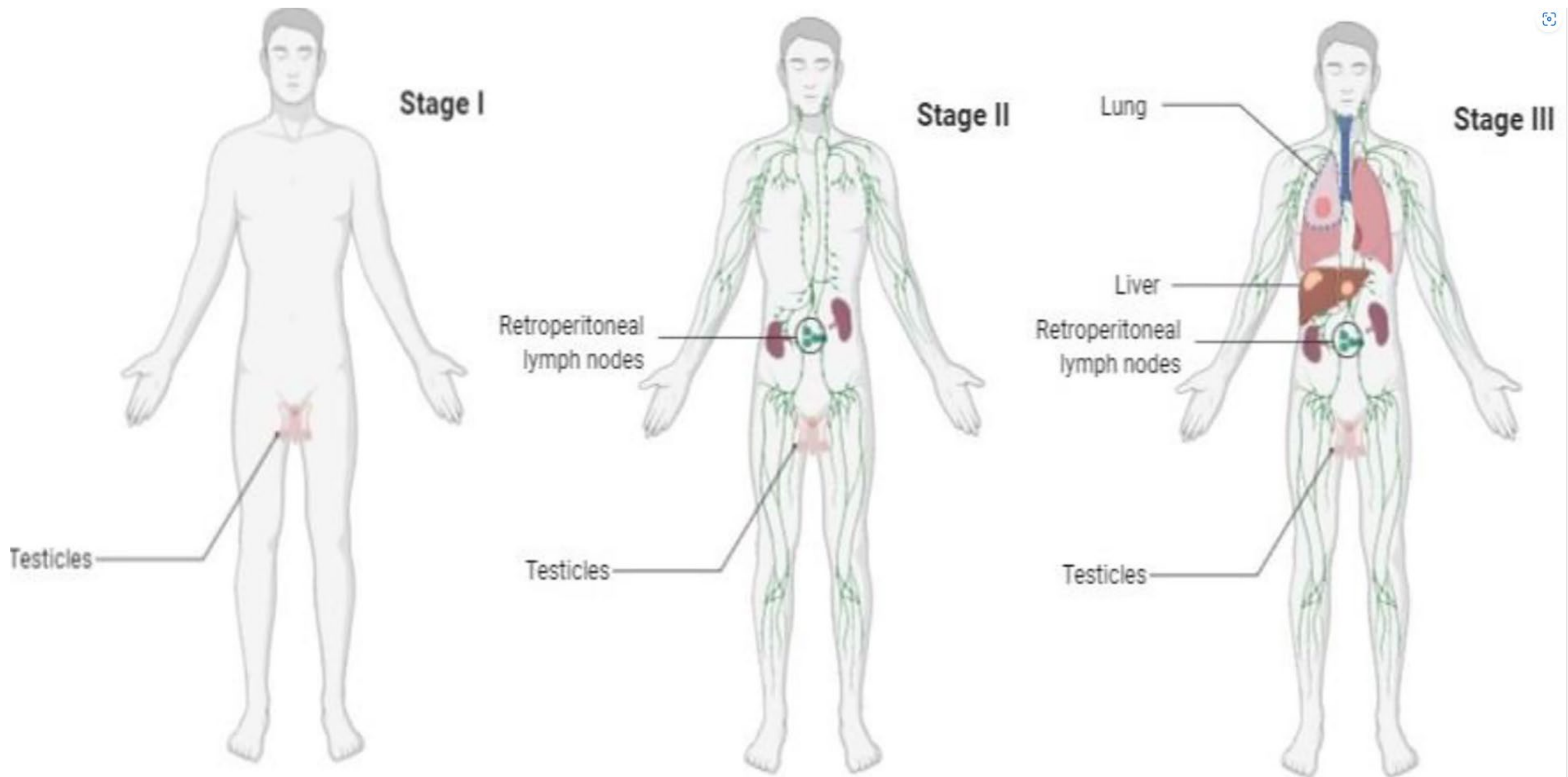
- High index of suspicion in younger men with testicular mass or unexplained midline adenopathy
- Scrotal ultrasound
- Tumor markers: Alpha-fetoprotein, beta-human chorionic gonadotropin, LDH
- Imaging: CT abdomen/pelvis, chest imaging (CT preferred)
  - If HCG > 5,000, extensive lung mets, choriocarcinoma – need to scan brain
  - Bone scan only if symptoms or very high alkaline phosphatase
- Urgent orchiectomy or biopsy (but not of testicle)

Key steps for the astute primary care provider

1. Get an urgent scrotal ultrasound – put the words "Rule out testicular cancer" and call and ask for it to be done urgently
2. Get an alpha-fetoprotein, quantitative beta-HCG and an LDH level
3. *If any of these is significantly elevated, get an urgent CT Chest, abdomen and pelvis*
   - *Normal results DO NOT exclude testicular cancer*
4. If ultrasound is abnormal, call Urologist on-call, independent of ordering additional tests
5. Do NOT stick a needle in and attempt to drain

Staging

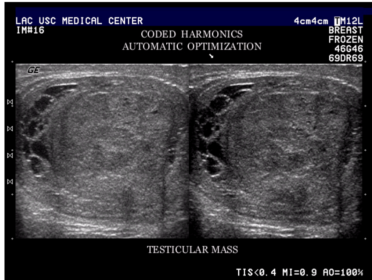
No Stage IV

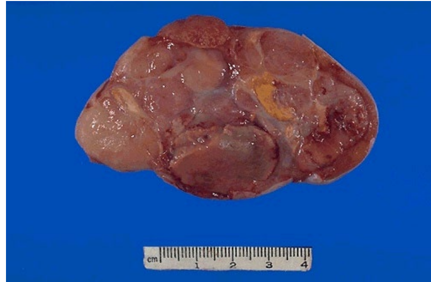


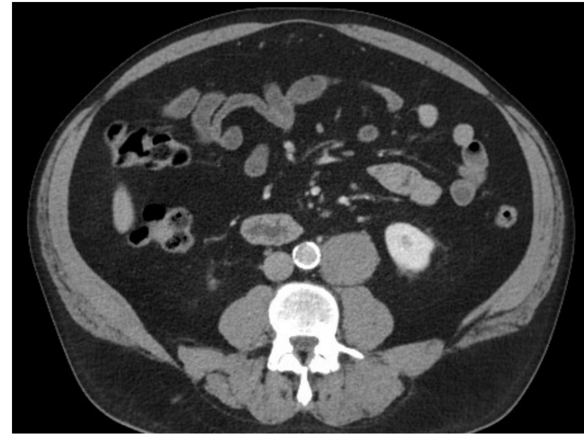
fonc-10-587523-g001.jpg (2362×1190) (frontiersin.org)

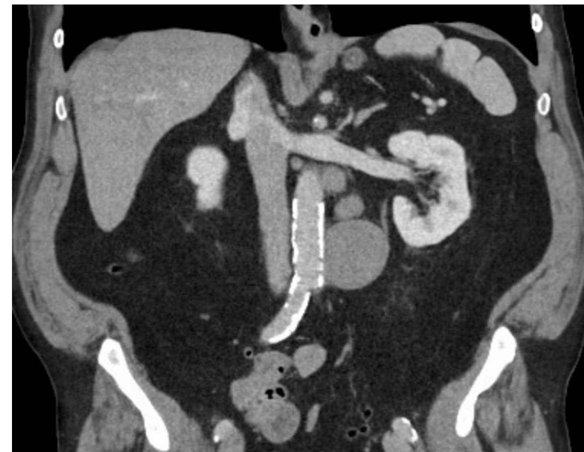
Also – non-RP nodes, brain, bone

Seminoma



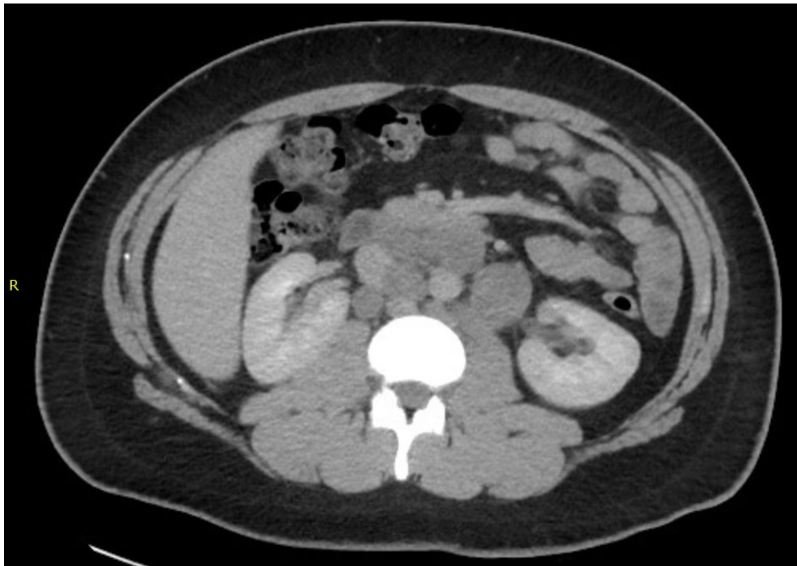


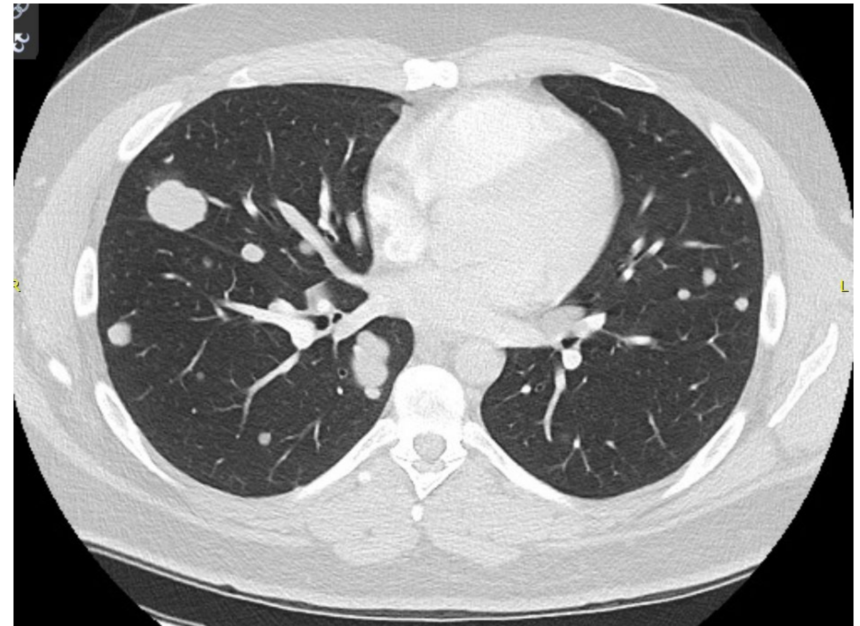


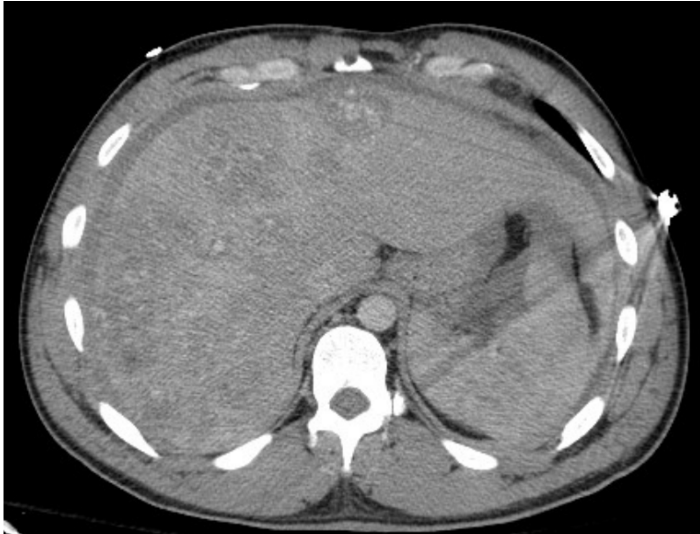


Non-seminoma

9.4 cm right testicle
pure embryonal carcinoma
AFP 234 (N < 7); HCG 3508 (N < 0.1)

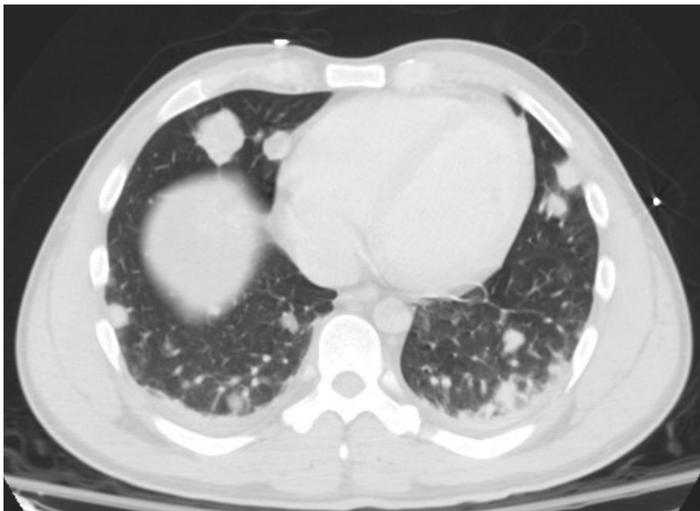


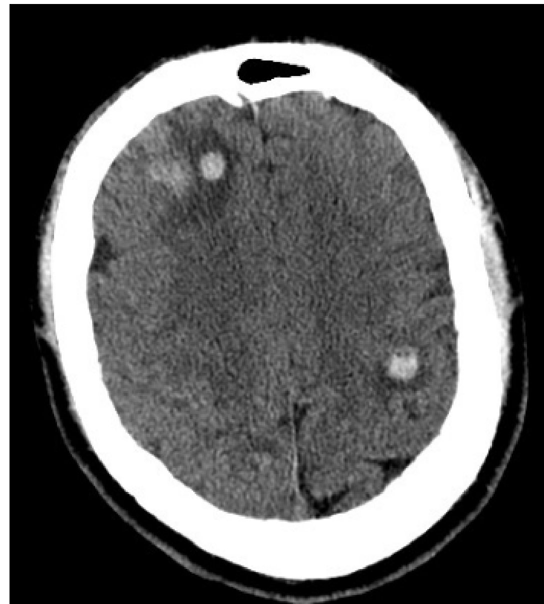




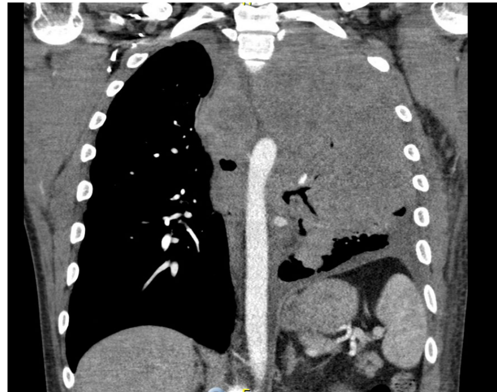
Non-seminoma

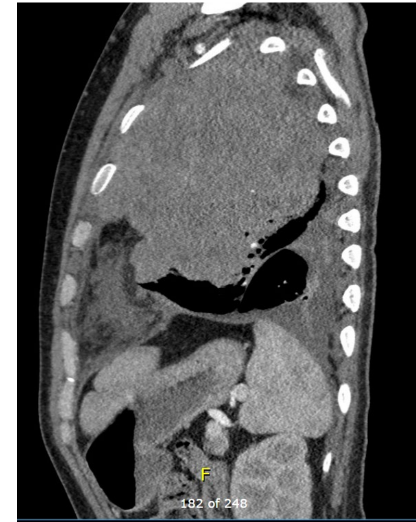
Choriocarcinoma
Beta-HCG went from 50,000 to
> 300,000 in 1 week





Rarities





- PMNSGCT
- Primary retroperitoneal
- Message: young male with big mid-line nodes (chest or abdomen) – consider GCT even in absence of testicular mass
  - Don't just think "lymphoma"
  - Do tumor markers, get urgent biopsy

MANAGEMENT

Stage I Seminoma

- Risk of recurrence post orchiectomy: ~ 15-20%
- Recommended approach: surveillance
  - Protocolized follow-up with bloodwork, imaging (CT versus MRI) for 5-10 years
- Alternatives:
  - Adjuvant radiotherapy: risk of recurrence 3%
  - Adjuvant chemotherapy: risk of recurrence 4%
    - Still need follow-up; risk of long-term toxicity
- Overall 5 year survival: 98% irrespective of approach

Stage I Non-seminoma

- Risk of recurrence: 25-50%
    - Lymphovascular invasion (LVI) increases risk of recurrence
- Recommended approach: surveillance
    - Protocolized follow-up with bloodwork, imaging (CT) for 5-10 years
- Alternatives:
    - Diagnostic and therapeutic retroperitoneal lymph node dissection -
    - Adjuvant chemotherapy – recurrence ~5%

- Overall cure rate ~99% irrespective of initial step

Chemotherapy for Advanced (Stage II and III) GCTs

- Cisplatin, bleomycin and etoposide (BEP) has been gold standard since mid-1980s
  - 3 cycles for good prognosis
  - 4 cycles for intermediate or poor prognosis
- In good prognosis disease EP x 4 can be substituted (if you want to avoid bleomycin)
- In intermediate and poor prognosis disease VIP (etoposide, ifosphamide, cisplatin) can be substituted to avoid bleomycin
- Biggest challenge – what to do in the patient with poor renal function (cisplatin-ineligible)

Exceptions to BEP in Advanced Stage GCTs

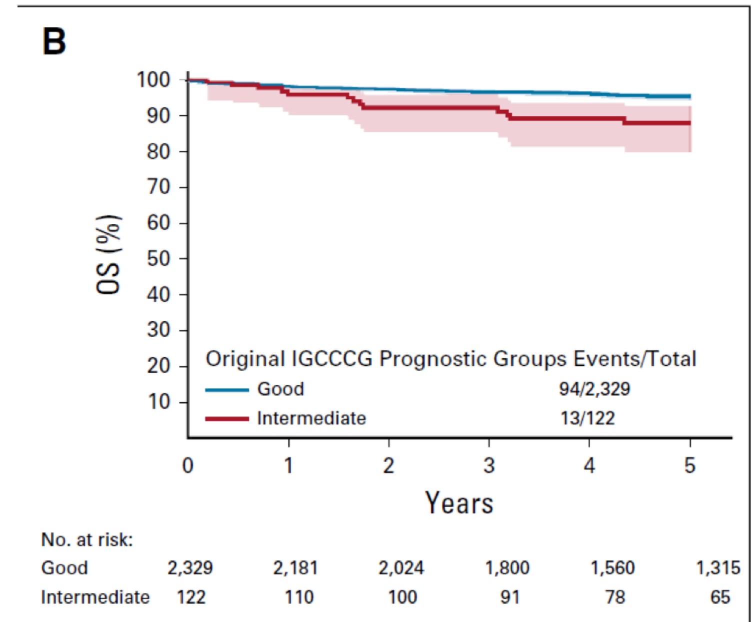
- Stage II seminoma – exquisitely sensitive to radiotherapy, so that is an alternative
- Stage II NSGCT – retroperitoneal lymph node dissection can be curative
  - Teratoma is not sensitive to chemotherapy or radiotherapy and must be resected
  - If teratoma in the testicular specimen, may be teratoma in the metastases-

Seminoma

Parameter	Good Risk	Intermediate Risk
AFP HCG, LDH Site of Primary Non-pulmonary visceral metastases	N Any Any No	N Any Any Yes
% Patients	90%	10%
5-year survival	86%	72%

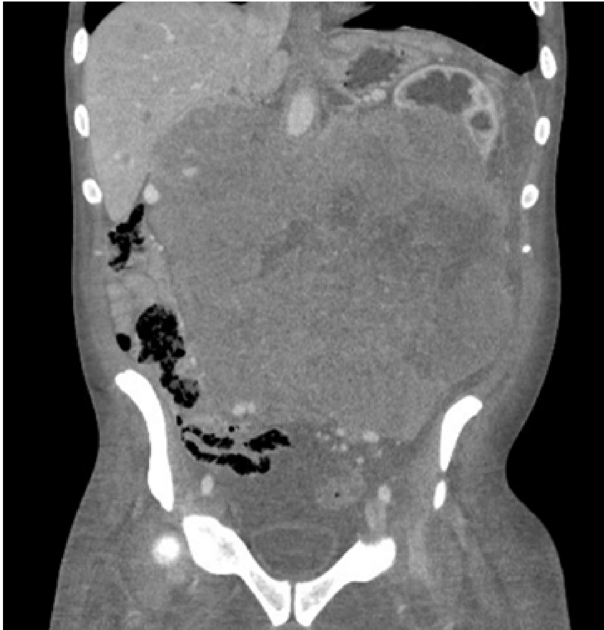
International Germ Cell Consensus Classification
J Clin Oncol 15:594-603, 1997

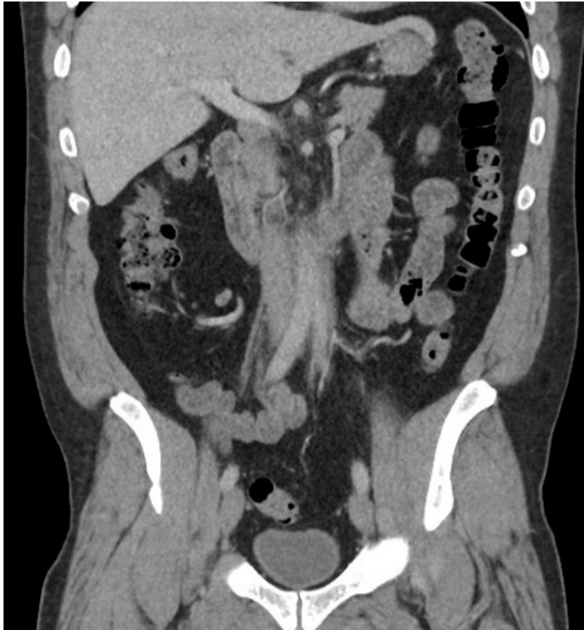
Updated IGCCC
J Clin Oncol 39: 1553-1562, 2021

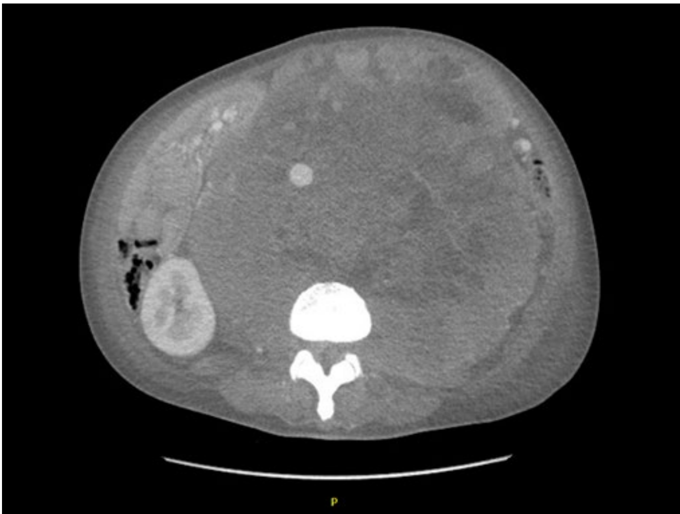


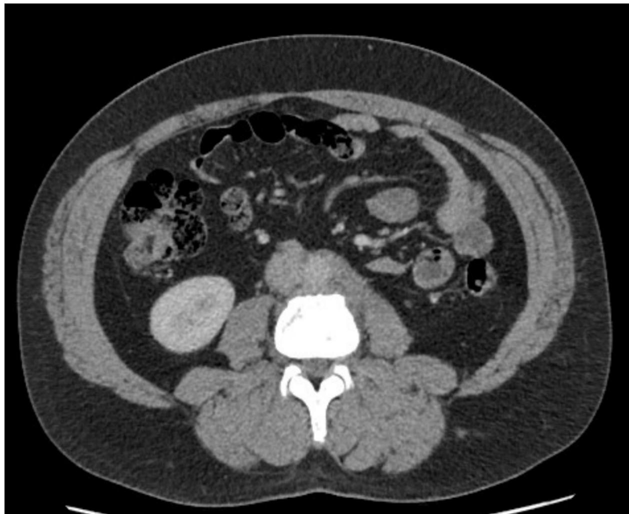
	5-yr OS Original (%)	5-yr OS Updated (%)
Good	86	95
Good with Lower LDH		97
Good with LDH ≥ 2.5 x ULN		92
Intermediate	72	88

Really bad seminoma



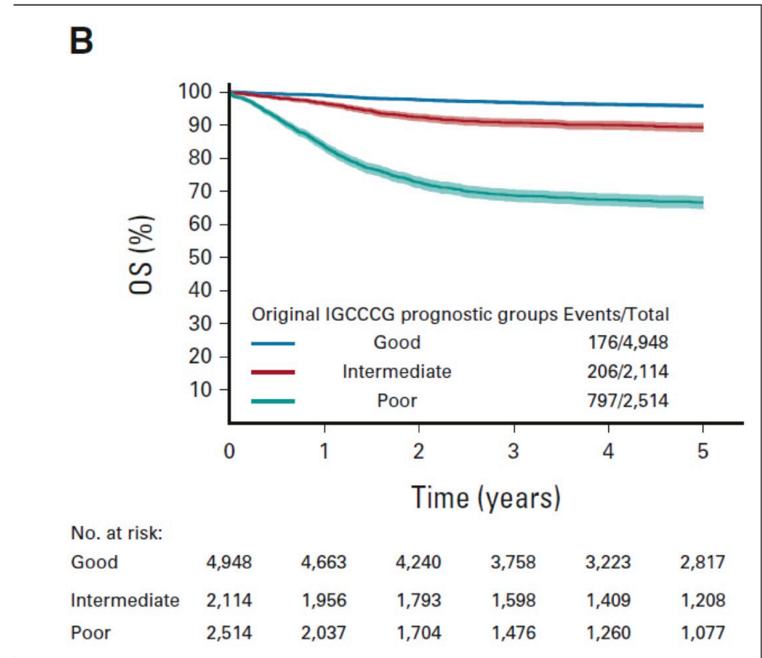






NSGCT

Parameter	Good Risk	Intermediate Risk	Poor Risk
AFP HCG LDH Site of Primary Non-pulmonary visceral metastases	<1000 <5000 <1.5xULN Testis/RP No	1000-10,000 5000-50,000 1.5-10xULN Testis/RP No	>10,000 >50,000 >10xULN Mediastinal Yes
% Patients	56%	28%	16%
5-year survival	92%	80%	48%



	5-yr OS Original (%)	5-yr OS Updated (%)
Good	92	96
Intermediate	80	89
Poor	48	67

International Germ Cell Consensus Classification
J Clin Oncol 15:594-603, 1997

J Clin Oncol 39: 1563-1574, 2021

Salvage treatment

- High Dose Chemotherapy + autologous stem cell transplant
- Long term remissions in 10-30%
- Highly dependent on selection criteria as well as regimen
- Most commonly “tandem” transplant
- We generally use high dose carboplatin and etoposide

HD Chemo and Tandem SCT – Single Centre Overall survival (N=184)

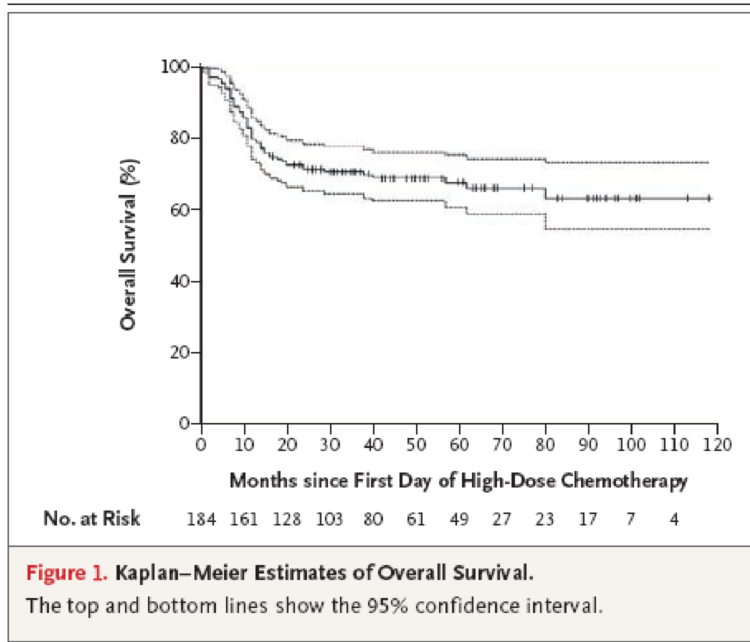


Figure 1. Kaplan–Meier Estimates of Overall Survival.
The top and bottom lines show the 95% confidence interval.

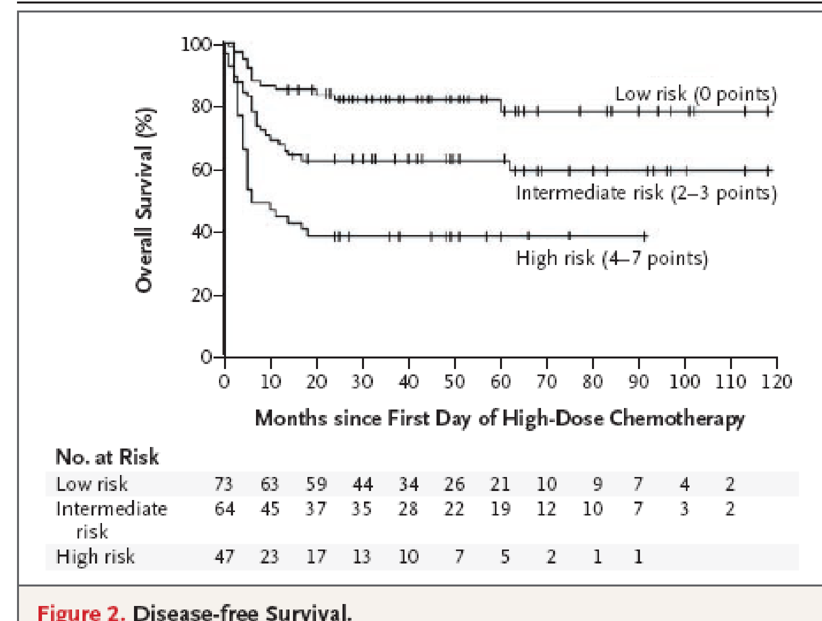


Figure 2. Disease-free Survival.

No mediastinal NSGCTs

Einhorn et al. NEJM 2007; 357: 340-348

Take home messages

- This is a highly curable cancer, generally in a young man with many life-years left
- It can behave very aggressively
- Consider this urgent, verging on emergent in a symptomatic patient

- If a young male thinks his testicle feels funny…it does
  - Until you prove otherwise
- If a young male has a testicular abnormality, it should be dealt with urgently

Role of the Primary Care Provider

- Maintain a high index of suspicion in males under 50 presenting with testicular abnormality
- Order a scrotal ultrasound
  - Pick up the phone and talk to the radiologist
  - Indicate that you are concerned about testicular cancer
  - The ultrasound should be done within 2-3 working days

Role of the Primary Care Provider

- Refer urgently to urology
  - Pick up the phone and indicate that you are concerned about testicular cancer
- Make sure that there is a clear post-op follow-up plan from the urologist
- Don't hesitate to call a GU Medical Oncologist if you have any concerns – for example in a patient with very high tumor markers – in patients with larger tumor burden, chemotherapy may be considered ahead of orchiectomy

Barriers to Change

- Lack of sufficient knowledge – rare entity
- “wellness of youth” bias

References

- Excellent (although a bit dated) review article:
  - Testicular cancer – discoveries and updates. N. Hanna, L. Einhorn *N Engl J Med* 2014; 371: 2005-2016