Testicular Tumor

Based on Campbell-Walsh-Wein's Urology12th ed. Chapters 76, Taiwan Cancer Registry, and Our Experience

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Dec. 1st, 2023

ICD10 - C62

- Germ Cell Tumor - GCT
  - Seminoma
  - Non seminoma (NSGCT)
    - Embryonal carcinoma
    - Yolk sac tumor
    - Choriocarcinoma
    - Teratoma
    - Mixed germ cell tumors
- Non-GCT
  - Leydig cell tumor
  - Sertoli cell tumor
  - Sex cord-stromal tumors

組織形態	男性			
	個案數	各形態百分比	細胞或病理證實數	細胞或病理證實百分比
精細胞瘤	145	51.24	145	100.00
卵黃囊瘤	7	2.47	7	100.00
胚胎性癌	13	4.59	13	100.00
混合性生殖細胞瘤	93	32.86	93	100.00
惡性畸胎瘤	11	3.89	11	100.00
絨毛膜癌	2	0.71	2	100.00
非特定生殖細胞瘤	4	1.41	4	100.00
性索基質腫瘤	2	0.71	2	100.00
其他惡性腫瘤	6	2.12	6	100.00
惡性淋巴瘤 [1]	18		18	100.00
總計 [2]	283	100.00	283	100.00

註：1. 自96年癌症登記報告起，惡性淋巴瘤（ICD-O-3 M-CODE請見p.496附錄五）從各部位獨立出來計算發生率，並納入排名。

2. 個案數的總計不包含惡性淋巴瘤個案數。

GCT

Germ Cell Tumor

Epidemiology

- GCT is the most common solid malignancy among males age 20 to 40 years.
- Bilateral GCT occurs in 2% of men. Metachronous lesion is the most common presentation.
- Incidence of GCT is highest in Caucasians and lowest in African-Americans.
- Cryptorchidism, personal or family history of GCT, and GCNIS are the known risk factors for GCT.
- Orchidopexy for cryptorchidism performed before puberty is associated with a decreased risk of GCT.

- Howlader N, et. al.: SEER cancer statistics review, 1975-2014. 2017. NCI.

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民國108年，睪丸惡性腫瘤發生個案數占全部惡性腫瘤發生個案數的0.23%，當年因此惡性腫瘤死亡人數占全部惡性腫瘤死亡人數的0.03%。發生率的排名於男性為第20位；死亡率的排名於男性為第33位。民國108年初次診斷為睪丸惡性腫瘤者共計283人，占男性生殖器官(ICD-O-3 C60 – C63)個案數的3.77%；當年死因為睪丸惡性腫瘤者共計16人。

項　　目	發生個案
	男性
個案數(人)	283
年齡中位數	31
粗率(每10萬人口)	2.42
年齡標準化率[2](每10萬人口)	2.37
年齡標準化率[3](每10萬人口)	2.54

項　　目	死亡個案
	男性
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粗率(每10萬人口)	0.14
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Pathogenesis

- 70%-80% of postpubertal GCTs contain extra copies of genetic material from the short arm of 12 appearing as an isochromosome (i[12p])
- Genetic material can be demonstrated with fluorescent in situ hybridization
- Used in the diagnosis of GCT (e.g., for carcinomas of unknown primary) and non-GCT somatic malignancy arising from malignant transformation of teratoma

Pathogenesis

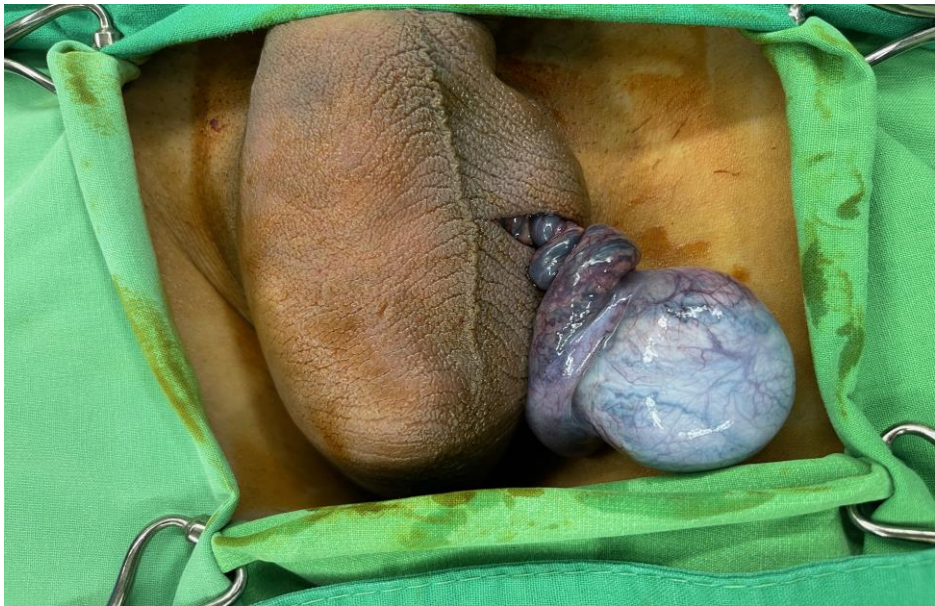
- Teratoma is histologically benign but genetically unstable.
- Thus it has unpredictable biology.
- Rare teratoma has the capacity to grow rapidly or undergo malignant transformation of its ectodermal, mesodermal, and/or endodermal elements to form a non-GCT somatic malignancy.

Symptoms & Signs

- Painless testis mass (common)
- Acute testicular pain (rare, more common with NSGCT)
- Vague scrotal discomfort or heaviness
- Gynecomastia (2%, most common with Leydig cell tumors)
- Back pain
- Neck mass

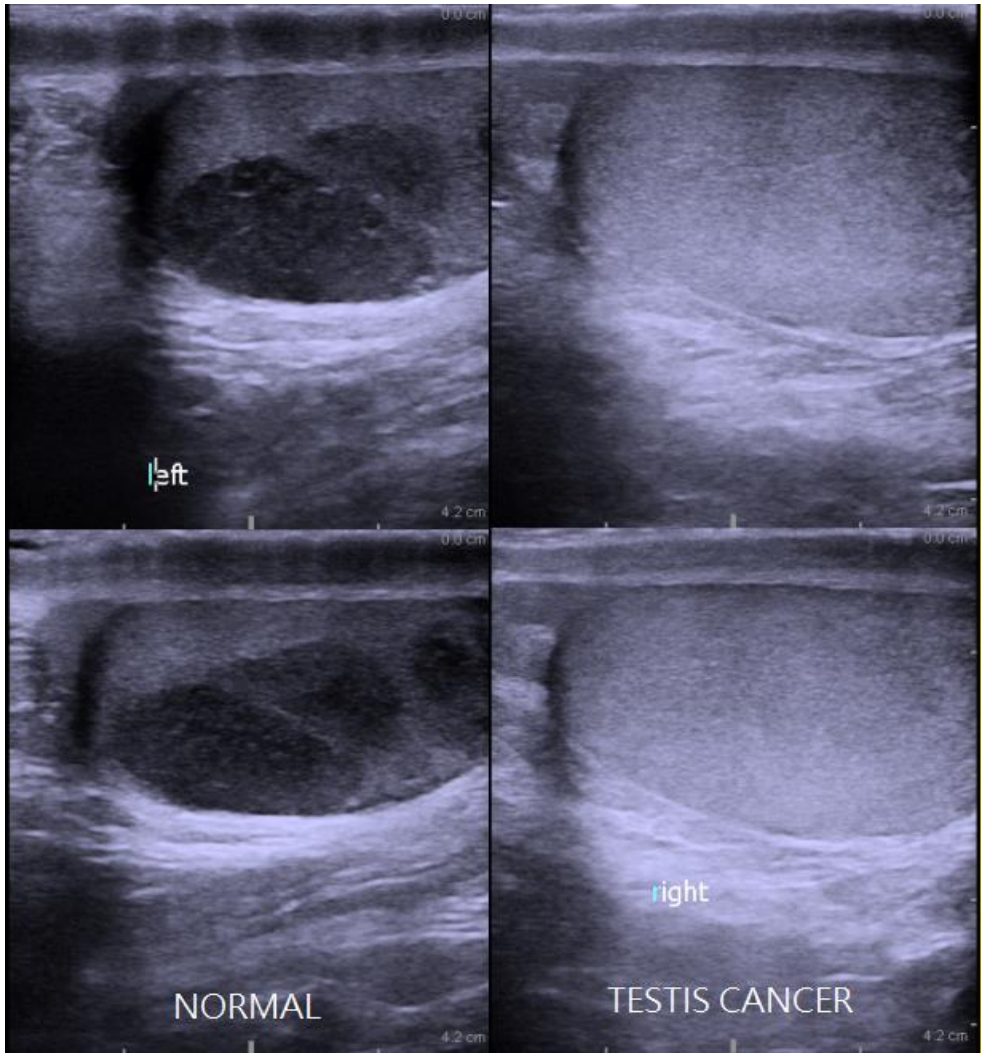
Physical Examination

- Differential Diagnosis
  - Epididymo-orchitis
  - Torsion
  - Hematoma
  - Para-testicular neoplasm (benign or malignant)
  - Hernia
  - Varicocele
  - Spermatocele



Diagnostic Testing
Ultrasound

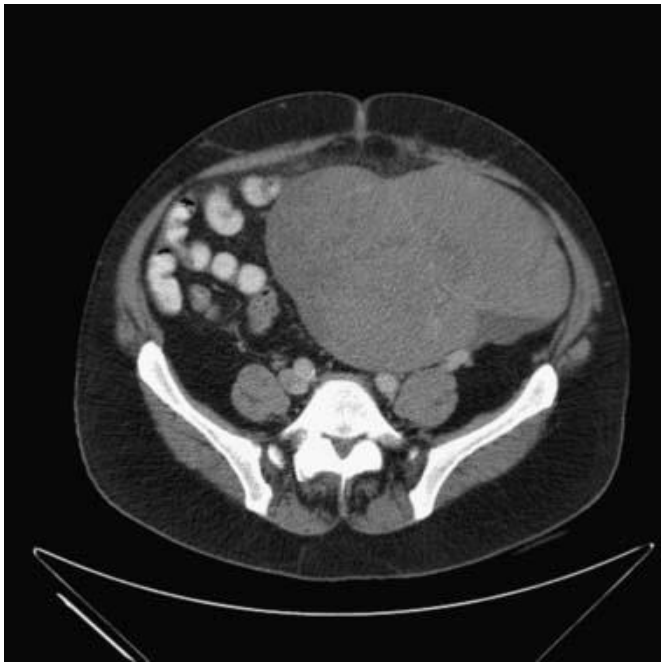
- Ultrasound:
- Typical GCT:
  - Hypoechoic and hemogeneous, two or more discrete lesions may be identified.
- NSGCT:
  - Heterogeneous echotexture within a lesion.
- Both testes should be evaluated sonographically



Fossa SD, Chen J, Schonfeld SJ, et. al.: Risk of contralateral testicular cancer: a population-based study of 29,515 U.S. men. J Natl Cancer Inst 2005; 97: pp. 1056-1066.

Diagnostic Testing
CT

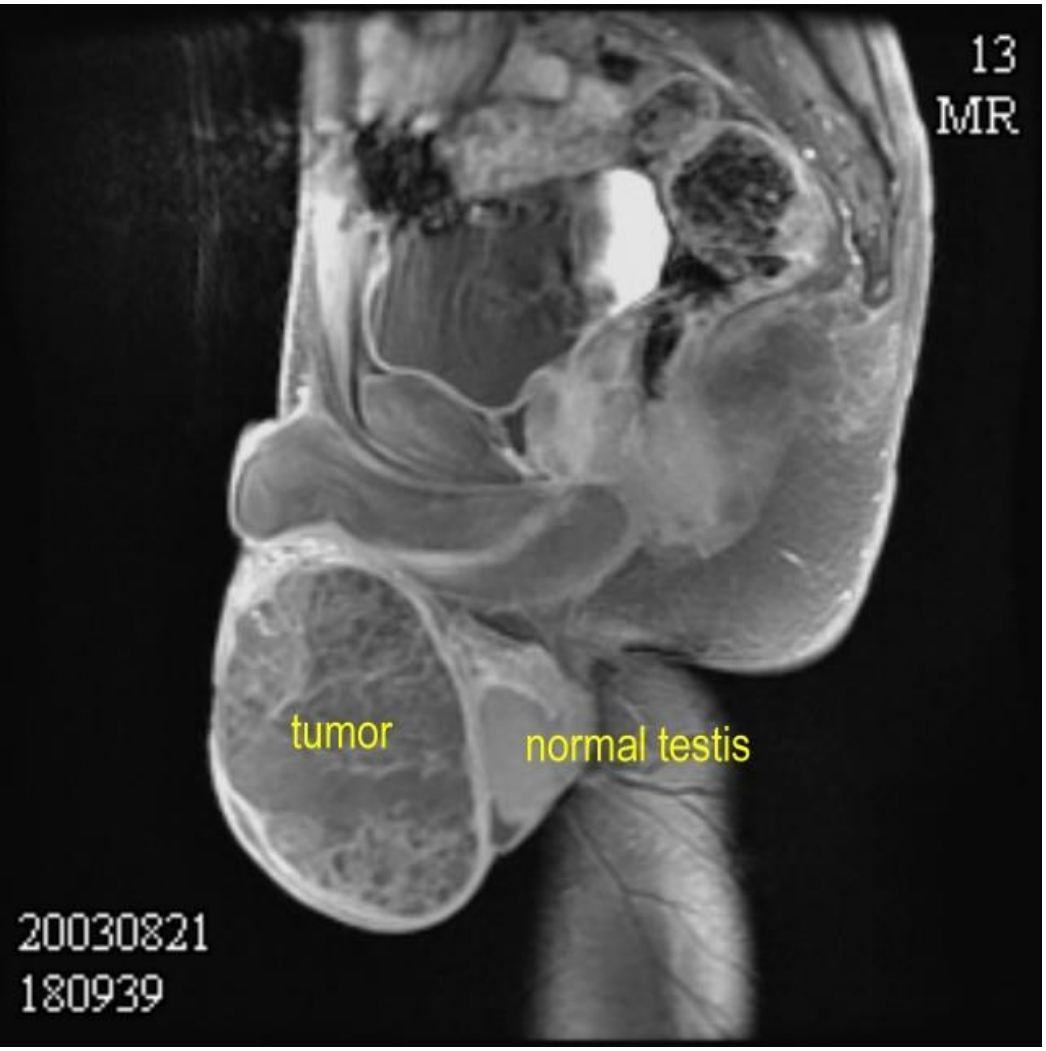
- The retroperitoneum is the initial site of metastatic spread in 70% to 80% of patients with GCT.
- Enlarged retroperitoneal lymph nodes are found on CT in approximately 10% to 20% of seminomas and 60% to 70% of NSGCT
- false-negative 25% to 35% of pathologically involved retroperitoneal lymph nodes has been a "normal" CT scan. (CS I NSGCT)
- False-negative 14-20% for seminoma

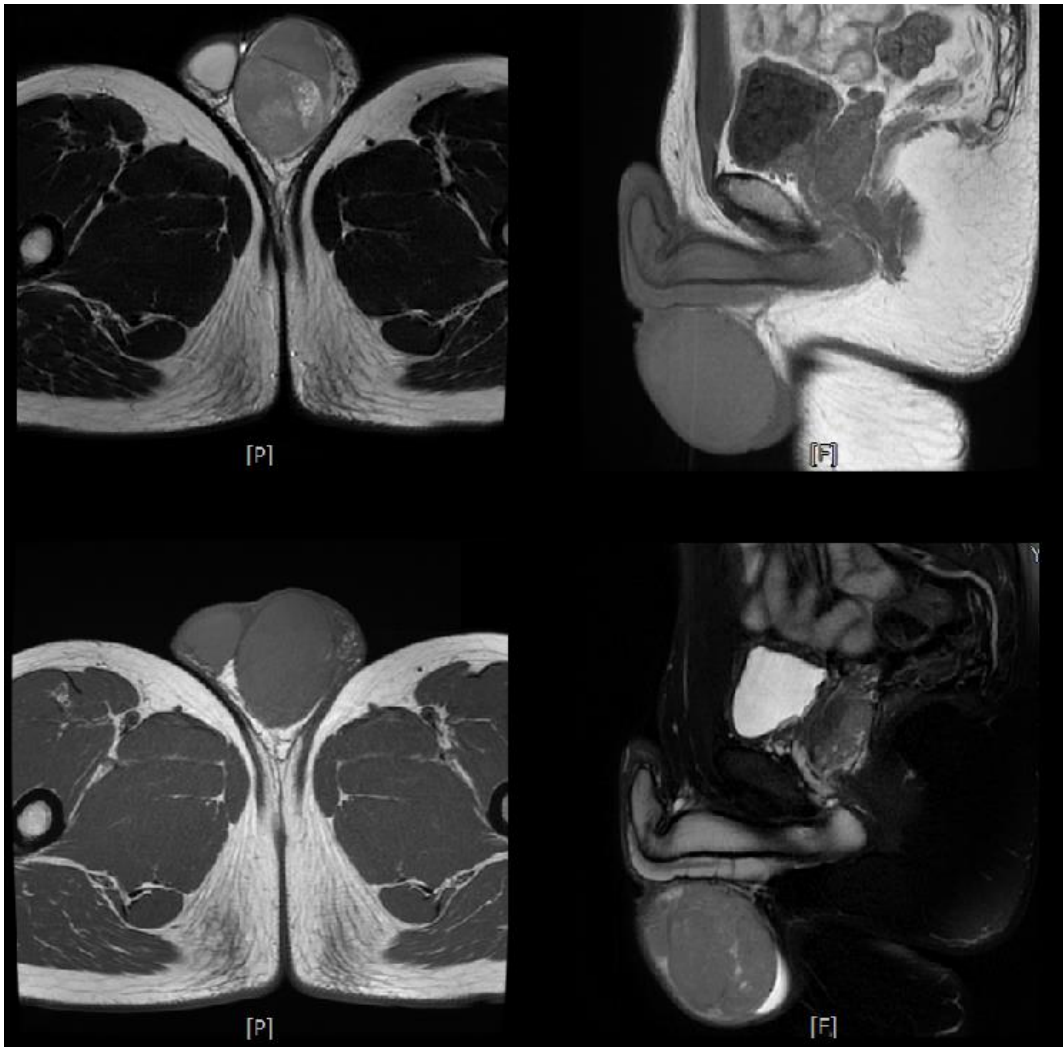


https://radiologykey.com/testicular-germ-cell-tumors/

Diagnostic Testing

Magnetic Resonance Imaging





Diagnostic Testing
FDG-PET

- **No role for FDG-PET in the routine evaluation of NSGCT and seminoma at the time of diagnosis.**

	AFP	β-hCG	LDH
Seminoma	0	+	++
Yolk sac tumor	+++	+	+
Choriocarcinoma	0	+++	+
Embryonal carcinoma	+	+	++
Teratoma	0	0	0

+++, Marker virtually always present in high amount and proportional to volume; ++, marker often seen in variable amount that is proportional to volume of disease; +, marker may be seen in variable amount, but not always; 0, never or seldom associated; AFP, alpha-fetoprotein; β-hCG, beta-human chorionic gonadotropin; LDH, lactate dehydrogenase.

https://radiologykey.com/testicular-germ-cell-tumors/

Diagnosis and work-up

- solid intratesticular mass should be considered a GCT
- inguinal orchiectomy with high ligation of the spermatic cord should be performed in men suspected of having GCT
- Trans-scrotal orchiectomy or biopsy are to be condemned
- Testis-sparing surgery for GCT is a consideration
  - small tumor
  - synchronous bilateral testis masses
  - preservation of sufficient testicular androgen production

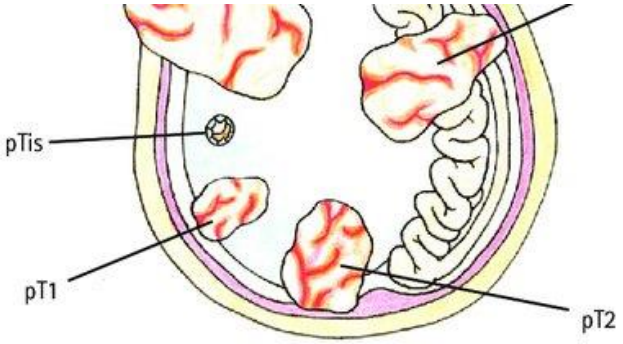
Diagnosis and work-up

- Diagnostic delay is common in GCT
- 1/3 of cases are initially misdiagnosed
- If serum tumor marker levels elevated orchiectomy, should be measured after orchiectomy to determine if levels are declining, stable, or rising
- Preorchiectomy serum tumor marker levels should not be used in management decisions.

TNM

AJCC and UICC staging systems 2002

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



pTis	Germ cell neoplasia *in situ* (GCNIS)
pT1	Testis and epididymis without lympho-vascular invasion
pT2	Testis and epididymis with lympho-vascular invasion, OR involvement of tunica vaginalis
pT3	Invades spermatic cord
pT4	Invades scrotum
pN1	Lymph node mass <2cm and <5 positive nodes
pN2	Lymph node mass 2–5cm and >5 positive nodes
pN3	Lymph node mass >5cm
M1a	Distant metastases – non-regional lymph node or lung
M1b	Distant metastases – other site
	LDH (U/L) hCG (mIU/ml) AFP (ng/ml)

Serum Tumor Marker

	LDH (U/L)	HCG (mIU/mL)	AFP (ng/mL)
SX	unavailable	unavailable	unavailable
S0	Within normal limits	Within normal limits	Within normal limits
S1	<1.5 x N and	<5000 and	<1000
S2	1.5-10 x N or	5000-50,000 or	1000-10,000
S3	>10 x N or	>50,000 or	>10,000

Stage

Stage 0	pTis	N0	M0	S0, SX
Stage I [a]	pT1–T4	N0	M0	SX
Stage IA	pT1	N0	M0	S0
Stage IB	pT2–T4	N0	M0	S0
Stage IS	Any patient/TX	N0	M0	S1–3
Stage II	Any patient/TX	N1–N3	M0	SX
Stage IIA	Any patient/TX	N1	M0	S0, S1
Stage IIB	Any patient/TX	N2	M0	S0, S1
Stage IIC	Any patient/TX	N3	M0	S0, S1
Stage III	Any patient/TX	Any N	M1a	SX
Stage IIIA	Any patient/TX	Any N	M1a	S0, S1
Stage IIIB	Any patient/TX	N1–N3	M0	S2
	Any patient/TX	Any N	M1a	S2
Stage IIIC	Any patient/TX	N1–N3	M0	S3
	Any patient/TX	Any N	M1a	S3
	Any patient/TX	Any N	M1b	Any S

[a] Stage I testicular cancer includes the following substages:

Clinical Staging

- GCT spread
  - primary tumor --> retroperitoneal lymph nodes → distant metastatic sites.
- Primary landing zone
  - Left: para-aortic, left renal hilar LNs
  - Right: inter-aortocaval, paracaval LNs
- CT imaging is the optimal modality for staging the retroperitoneum
- False-negatives occur when a 1-cm cutoff is used
  - CS I NSGCT: 25% to 35%
  - Seminoma: 14% to 20%

Clinical Staging

- **Chest x-ray and CT chest**
  - absence of retroperitoneal lymphadenopathy or
  - absence of elevated serum tumor marker levels.
- **Chest CT**
  - serum tumor marker elevated or
  - CT abdomen and pelvis shows metastatic disease
- **Rising post-orchiectomy serum tumor marker levels**
  - indicate the presence of metastatic GCT and
  - should chemotherapy

Clinical Staging

- **Predict prognosis by IGCCCG risk classification**
  - NSGCT: post-orchiectomy serum tumor marker levels, mediastinal primary tumor, presence of nonpulmonary visceral metastases
  - Seminoma: nonpulmonary visceral metastases only
- **Sperm cryopreservation should be offered to all patients before RPLND, C/T, or R/T**

Seminoma vs. NSGCT

- **Seminoma CS I/IIA/IIB compared with NSCGT**
  - lower incidence of metastatic disease
  - lower rates of occult retroperitoneal
  - lower rate of distant metastases
- **Seminoma CS I/IIA/IIB compared with NSCGT**
  - sensitivity to radiation therapy
  - sensitivity to platin-based chemotherapy
  - Only 15% HCG elevated
  - Less teratoma at metastatic sites
- **No poor-risk prognostic category in IGCCCG criteria**

GCT

- TREATMENT

GCT

Treatment for GCNIS

- **Germ Cell Neoplasia In Situ**
  - 50% risk of developing an invasive GCT
  - within 5 years
- **Radical orchiectomy or low-dose (≥ 20 Gy) radiation therapy is an effective**

GCT / Treatment for NSCGT (1/6)

CS I

- **The optimal management of CS I NSGCT is controversial.**
- **CS I NSGCT who choose to receive chemotherapy**
  - BEPx1 is the standard regimen
- **Accepted treatment options (long-term survival 100%)**
  - Surveillance,
  - primary RPLND, and
  - primary chemotherapy with BEPx2

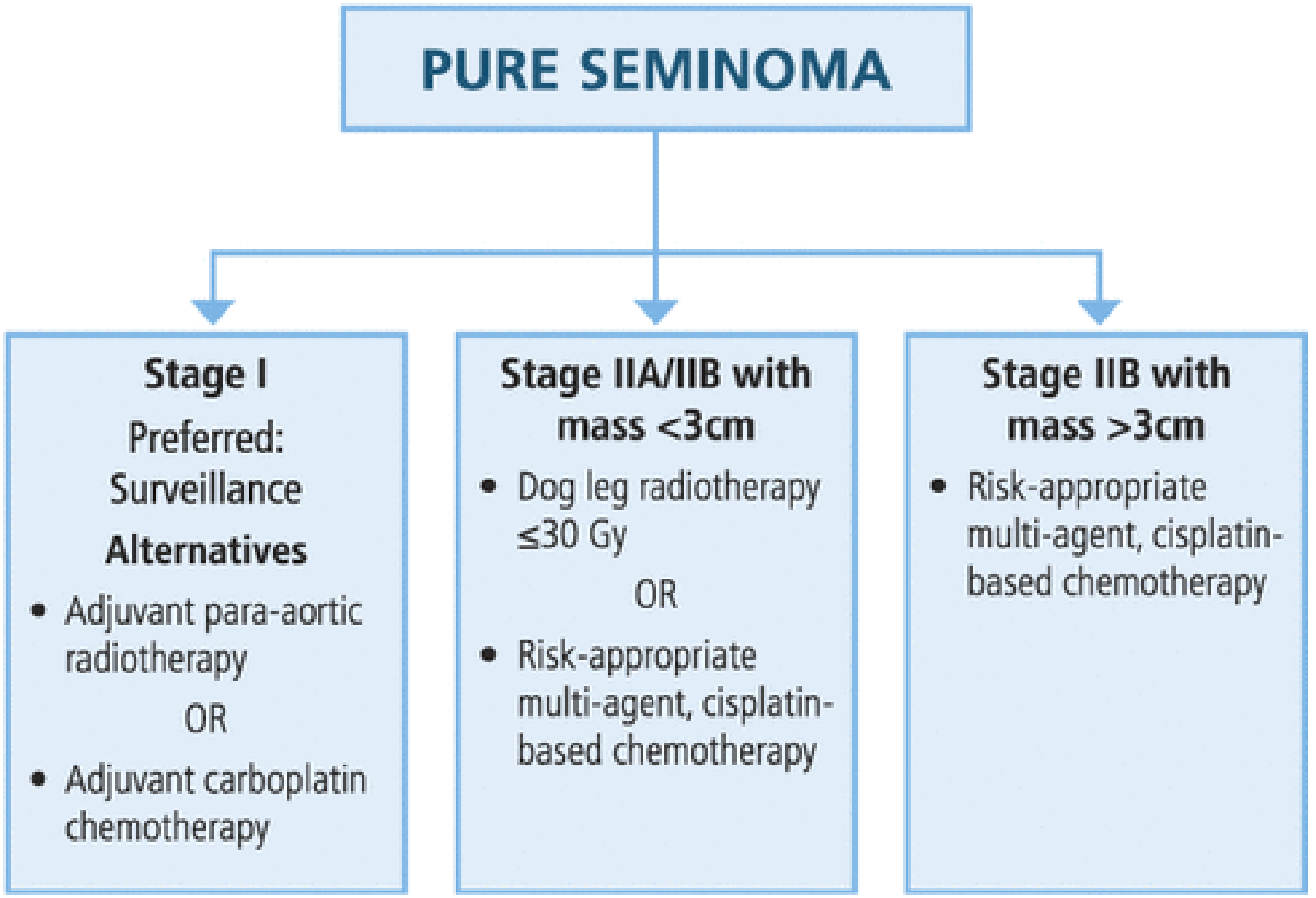
GCT / Treatment for Seminoma (1/5)

CS I

- **The optimal management of CS I seminoma is controversial**
- **Accepted treatment options (long-term survial 100%)**
  - Surveillance
  - primary radiotherapy (20–30 Gy to the para-aortic region +/− ipsilateral pelvis)
  - primary chemotherapy with carboplatin (1–2 cycles)
- **Surveillance is not recommended to poorly compliant**
- **Prognostic factors for occult metastases in CS I seminoma**

low-risk of occult metastases (15%–20%)

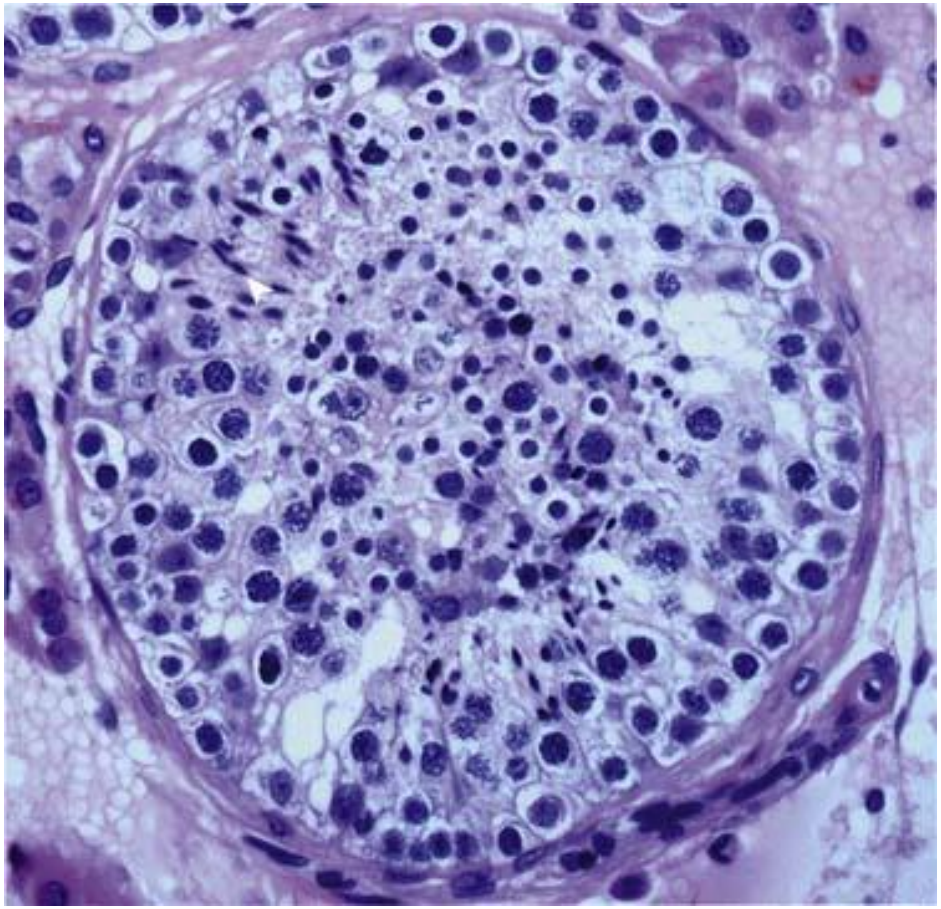
DIAGNOSIS AND TREATMENT OF EARLY STAGE TESTICULAR CANCER: AUA GUIDELINE ALGORITHM

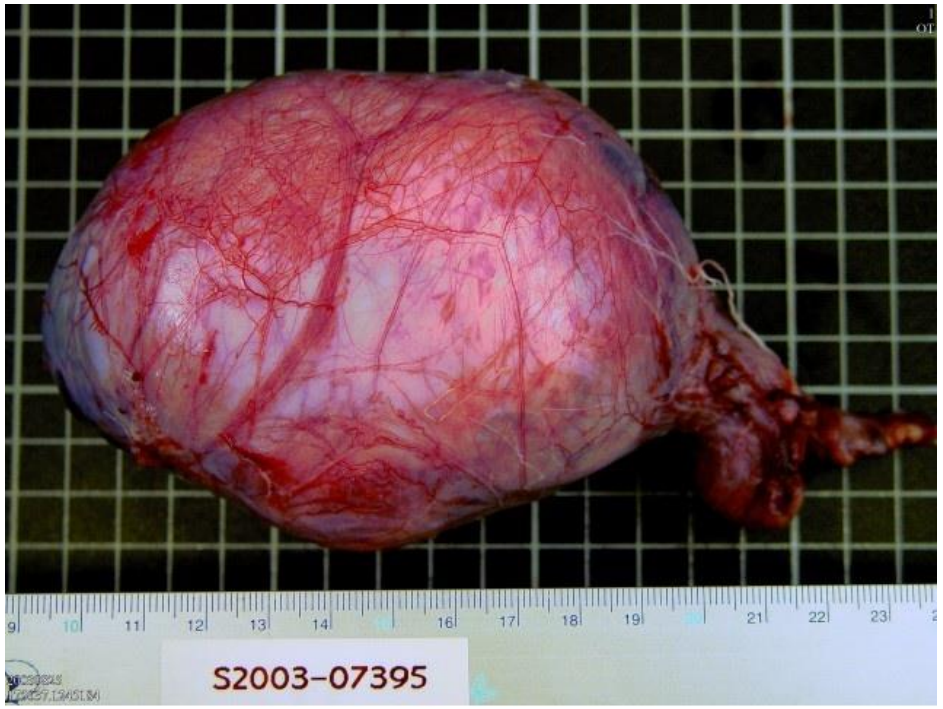


*IGCCCG good risk chemotherapy BEPx3 or EPx4.

申報治療方式*	男性	
	治療人數	百分比
手術治療	272	96.11
放射線治療	11	3.89
化學治療	95	33.57
內分泌藥物治療	1	0.35
免疫治療	1	0.35
骨髓/幹細胞移植	1	0.35
緩和照護	7	2.47
未有首次治療申報紀錄	3	1.06

申報治療方式*：每名個案所接受之治療方式均分別計數。

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NGCT

Non-Germ Cell Tumor

Treatment for NGCT

- Sex Cord-Stromal Tumors: 0.4% to 4% of testis neoplasms, 90% benign and 10% malignant.
- Leydig Cell Tumors: 75% to 80% of sex cord-stromal tumors, no association with cryptorchidism, 30 to 60-year-old, CT chest-abdomen-pelvis for staging purposes. radical inguinal orchiectomy, testis-sparing surgery can be considered for tumors smaller than 3 cm, metastatic sites are the retroperitoneum and the lung,
- Sertoli Cell Tumor: <1% of testis neoplasms, testis-sparing surgery can be considered for tumors smaller than 3 cm
- Granulosa Cell Tumors
- Gonadoblastoma
- Dermoid and Epidermoid Cyst
- Adenocarcinoma of the Rete Testis

Treatmnet for NSGCT

- Adjuvant chemotherapy after primary RPLND for pathological stage II disease is associated with a substantial reduction in the risk of relapse but no difference in long-term survival compared with an observational strategy with induction chemotherapy at the time of relapse. Adjuvant chemotherapy is usually recommended to patients with extensive retroperitoneal metastasis (pN2-3) and those anticipated to be noncompliant with postoperative cancer surveillance imaging and testing.