EAU GUIDELINES ON TESTICULAR CANCER

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Epidemiology, aetiology and pathology

Testicular cancer (TC) is relatively rare accounting for approximately 1-1.5% of all cancers in men. At diagnosis 1-2% are bilateral and the predominant histology is germ cell tumour (GCT).

Most malignant post-pubertal testicular GCTs or type II GCT, originate from the germ cell neoplasia *"in situ"* (GCNIS). They are clinically and histologically sub-divided into seminomas and non-seminomas. Non-seminomas include elements of embryonal carcinoma, yolk sac, choriocarcinoma and teratoma. Most of the non-related GCNIS tumours present at paediatric age with the exception of spermatocytic tumours (Type III GCT) which are diagnosed in the elderly. Type II TGCT have a low mutational burden and few somatic changes, but i12p is over-represented in most of the invasive GCNIS-related TGCT.

Peak incidence is in the third decade of life for non-seminoma testis (NST) and mixed GCT patients, and fourth decade for

pure seminoma testis (ST) patients. Epidemiological risk factors for the development of TC are components of testicular dysgenesis syndrome, which encompasses cryptorchidism, hypospadias, decreased spermatogenesis evidenced by sub- or infertility, or disorders/differences of sex development. Additional risk factors include family history TC among first-grade relatives, and the presence of a contralateral tumour, or GCNIS.

Histological classification

The recommended pathological classification is the 2016 update of the World Health Organization (WHO).

Staging and classification systems Staging systems

The 2016 Tumour, Node, Metastasis (TNM) classification of the International Union Against Cancer (UICC) is recommended to assess the anatomical extent of the disease (Table 1).

Table 1: TNM classification for testicular cancer (adapted from UICC, 2016, 8th edn.)

T - Pri	T - Primary Tumour ¹		
рТХ	Primary tumour cannot be assessed ¹		
pT0	No evidence of primary tumour (e.g., histological scar in testis)		
pTIS	Intratubular germ cell neoplasia (carcinoma <i>in situ</i>) ²		
pT1	Tumour limited to testis and epididymis without vascular/lymphatic invasion; tumour may invade tunica albuginea but not tunica vaginalis*		
pT2	Tumour limited to testis and epididymis with vascular/lymphatic invasion, or tumour extending through tunica albuginea with involvement of tunica vaginalis**		

 pT3 Tumour invades spermatic cord with or without vascular/lymphatic invasion** pT4 Tumour invades scrotum with or without vascular/ lymphatic invasion N - Regional Lymph Nodes - Clinical NX Regional lymph nodes cannot be assessed N0 No regional lymph node metastasis N1 Metastasis with a lymph node mass 2 cm or less in greatest dimension or multiple lymph nodes, none more than 2 cm in greatest dimension N2 Metastasis with a lymph node mass more than 2 cm but not more than 5 cm in greatest dimension; or more than 5 nodes positive, none more than 5 cm; or evidence of extranodal extension of tumour N3 Metastasis with a lymph node mass more than 5 cm in greatest dimension Pn - Regional Lymph Nodes - Pathological pNX Regional lymph nodes cannot be assessed
Iymphatic invasion N - Regional Lymph Nodes - Clinical NX Regional lymph nodes cannot be assessed N0 No regional lymph node metastasis N1 Metastasis with a lymph node mass 2 cm or less in greatest dimension or multiple lymph nodes, none more than 2 cm in greatest dimension N2 Metastasis with a lymph node mass more than 2 cm in greatest dimension; or more than 5 cm in greatest dimension; or evidence of extranodal extension of tumour N3 Metastasis with a lymph node mass more than 5 cm in greatest dimension Pn - Regional Lymph Nodes - Pathological
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in greatest dimension Pn - Regional Lymph Nodes - Pathological
nNX Regional lymph nodes cannot be assessed
plax Regionallymphhodes cannot be assessed
pN0 No regional lymph node metastasis
pN1 Metastasis with a lymph node mass 2 cm or less in greatest dimension and 5 or fewer positive nodes, none more than 2 cm in greatest dimension
pN2 Metastasis with a lymph node mass more than 2 cm but not more than 5 cm in greatest dimension; or more than 5 nodes positive, none more than 5 cm; or evidence of extranodal extension of tumour
pN3 Metastasis with a lymph node mass more than 5 cm in greatest dimension
M - Distant Metastasis
MX Distant metastasis cannot be assessed
M0 No distant metastasis

M1 Distant metastasis**			
Distant metastasis**			
M1a Non-regional lymph node(s) or lung metastasis			
M1b Distant metastasis other than non-regional			
lymph nodes and lung			
S - Serum tumour markers (Pre-chemotherapy)			
SX Serum marker studies not available or not performed			
S0 Serum marker study levels within normal limits			
LDH (U/I)	hCG (mIU/mL)	AFP (ng/mL)	
< 1.5 x N and	< 5,000 and	< 1,000	
1.5-10 x N or	5,000-50,000 or	1,000-10,000	
> 10 x N or	or > 50,000 or	> 10,000	
	M1a Non-regior M1b Distant me lymph nod um tumour mark Serum marker s Serum marker s LDH (U/I) < 1.5 x N and 1.5-10 x N or	M1b Distant metastasis other than lymph nodes and lung um tumour markers (Pre-chemother Serum marker studies not available Serum marker study levels within not LDH (U/I) hCG (mIU/mL) < 1.5 x N and	

N indicates the upper limit of normal.

LDH = lactate dehydrogenase; hCG = human chorionic gonadotrophin; AFP = alpha-fetoprotein.

- * AJCC eighth edition subdivides T1 Pure Seminoma by T1a and T1b depending on size no greater than 3 cm or greater than 3 cm in greatest dimension.
- ** AJCC eight edition considers the hilar soft tissue invasion as pT2, while the discontinuous involvement of the spermatic cord is considered as pM1.
- ¹ Except for pTis and pT4, where radical orchidectomy is not always necessary for classification purposes, the extent of the primary tumour is classified after radical orchidectomy; see pT. In other circumstances, Tx is used if no radical orchidectomy has been performed.
- ² The current "carcinoma in situ" nomenclature is replaced by GCNIS

The International Germ Cell Cancer Collaborative Group (IGCCCG) defined a prognostic factor-based staging system for metastatic germ cell cancer that includes 'good' and 'intermediate' prognosis seminoma and 'good', 'intermediate', and 'poor' prognosis non-seminomatous germ cell tumour (NSGCT) (Table 2).

The IGCCCG for metastatic testicular cancer

A prognostic risk factor-based staging system is widely used for metastatic TC based on identification of clinically independent adverse factors.

Table 2: Prognostic-based staging system for metastatic germ cell cancer (IGCCCG)*

Good-prognosis group		
Non-seminoma	All of the following criteria:	
5-year PFS 90%	• Testis/retro-peritoneal primary	
5-year survival 96%	 No non-pulmonary visceral 	
	metastases	
	• AFP < 1,000 ng/mL	
	• hCG < 5,000 IU/L (1,000 ng/mL)	
	• LDH < 1.5 x ULN	
Seminoma	All of the following criteria:	
5-year PFS 89%	 Any primary site 	
5-year survival 95%	No non-pulmonary visceral	
	metastases	
	Normal AFP	
	Any hCG	
	Any LDH	
Intermediate-prognosis group		
Non-seminoma	Any of the following criteria:	
5-year PFS 78%	Testis/retro-peritoneal primary	
5-year survival 89%	 No non-pulmonary visceral 	
	metastases	
	• AFP 1,000 - 10,000 ng/mL or	
	• hCG 5,000 - 50,000 IU/L or	
	• LDH 1.5 - 10 x ULN	

Seminoma 5-year PFS 79% 5-year survival 88%	All of the following criteria: • Any primary site • Non-pulmonary visceral metastases • Normal AFP • Any hCG • Any LDH
Poor-prognosis group	
Non-seminoma 5-year PFS 54% 5-year survival 67%	Any of the following criteria: • Mediastinal primary • Non-pulmonary visceral metastases • AFP > 10,000 ng/mL or • hCG > 50,000 IU/L (10,000 ng/mL) or • LDH > 10 x ULN
Seminoma	No patients classified as "poor prognosis"

AFP = alpha-fetoprotein; hCG = human chorionic gonadotrophin; LDH = lactate dehydrogenase;

PFS = progression-free survival.

* Pre-chemotherapy serum tumour markers should be assessed immediately prior to the administration of chemotherapy (same day).

Diagnostic evaluation

The diagnosis of TC is based on:

1. Physical examination

Testicular cancer usually presents as a unilateral testicular scrotal mass detected by the patient, or as an incidental ultrasound (US) finding. Around 1% of patients presenting with gynecomastia have a germ cell or sex cord/gonadal tumour of the testes and 11% present with back and flank pain. When there is suspicion of TC, physical exploration must include abdominal and supraclavicular exploration.

2. Imaging

a. Ultrasound

High frequency (> 10 MHz) testicular US should be used to confirm a testicular tumour even in the presence of clinically evident testicular lesion. Testicular US is also recommended for all men with retroperitoneal or visceral masses and/or without elevated serum human chorionic gonadotropin (hCG) or alpha-fetoprotein (AFP) in the absence of a palpable testicular mass.

b. Computerised tomography

Contrast enhanced computerised tomography (CECT) is the most sensitive means to evaluate the thorax, abdomen, and pelvis for TC staging. Contrast enhanced computerised tomography is recommended in all patients for staging before orchidectomy but may be postponed until histopathological confirmation of malignancy. Cerebral imaging by CECT is recommended in patients with NSGCT, multiple lung metastases and poor-prognosis IGCCCG risk group (for patients with hCG values > 5,000 UI/L), or if clinical symptoms are present.

c. Magnetic resonance imaging

Magnetic resonance imaging (MRI) has similar accuracy to CECT in the detection of retroperitoneal nodal enlargement and may be used for staging in case of allergy to iodine-based contrast. However, it may be useful when US is inconclusive, as local staging for TSS planning, to differentiate between paratesticular and intratesticular lesions and to characterise intratesticular masses (e.g., distinctive features of Leydig tumours).

- d. Fluorodeoxyglucose-positron emission tomography There is no evidence to support the use of fluorodeoxyglucose-positron emission tomography (FDG-PET) for initial staging and routine follow-up of TC
- e. Bone scan

There is no evidence to support the use of bone scan for staging of TC.

3. Serum tumour markers

Serum tumour markers (AFP, β -hCG and LDH,) should be determined before, and after orchidectomy until normalisation. Normal serum marker levels do not exclude the presence of TC, whilst persistence or increase of elevated serum tumour markers following orchidectomy indicates the likely presence of metastatic disease. Tumour markers should be routinely used for follow-up.

4. Inguinal exploration and initial management

- Orchidectomy including division of the spermatic cord at the internal inguinal ring represents the standard of care in patients with TC.
- Testis-sparing surgery (TSS) may be offered in cases with synchronous bilateral tumours, or metachronous contralateral tumours with previous contralateral orchidectomy, to patients with a solitary testis to attempt to preserve fertility or in cases of small or indeterminate (non-palpable) testicular masses with negative markers, to preserve fertility and hormonal function*.
- Testis-sparing surgery should always only be offered accompanied with frozen section examination.

- Testicular prosthesis should be offered to all patients receiving unilateral or bilateral orchidectomy.
- Routine contralateral biopsy for diagnosis of GCNIS should be discussed with the patient and is recommended in 'high-risk' patients (testicular volume < 12 mL. a history of cryptorchidism and age < 40 years).
- * Limited data exists on oncological safety of TSS. Local recurrence rates (0-27% when TC in specimen) necessitate close surveillance of the testis, possible use of adjuvant radiotherapy when GCNIS is present, as well as potential infertility and need for hormonal supplementation.

5. Pathological examination of the testis

Following orchidectomy, the pathological examination of the testis should include a number of investigations:

- macroscopic features: side, testis size, maximum tumour size, and macroscopic features of the epididymis, spermatic cord, and tunica vaginalis;
- sampling: a 1 cm² section for every cm² of maximum tumour diameter, including normal macroscopic parenchyma (if present), albuginea and epididymis, with selection of suspicious areas;
- 3. at least one proximal and one distal section of spermatic cord plus any suspicious areas;
- microscopic features and diagnosis: histological types (specify individual components and estimate amount as percentage) according to WHO 2016;
 - presence or absence of peri-tumoural venous and/ or lymphatic invasion;
 - presence or absence of GCNIS in non-tumour parenchyma;
 - in cases of rete testis invasion, attention should be paid to distinguishing between pagetoid involvement and stromal invasion;

- 5. pT category according to TNM 2016;
- 6. immunohistochemical studies: in seminoma and mixed GCT, AFP and $\beta\text{-hCG}.$

6. Screening

There are no high-level evidence studies supporting screening programs. In the presence of clinical risk factors, and a family history of TC, family members and the patient should be informed about the importance of physical self-examination.

7. Impact on fertility and fertility-associated issues

Sperm abnormalities and Leydig cell dysfunction are frequently found in patients with TCs prior to orchidectomy. Furthermore, treatment for TC, including orchidectomy, may have a negative impact on reproductive function. As such, all patients should be offered semen preservation.

Recommendations for diagnosis and staging of testicular cancer	Strength rating
Discuss sperm banking with all men prior to starting treatment for testicular cancer (TC).	Strong
Perform bilateral testicular ultrasound in all patients with suspicion of TC.	Strong
Perform physical examination including supraclavicular, cervical, axillary, and inguinal lymph nodes, breasts, and testicles.	Strong
Measure serum tumour markers both before and after orchidectomy taking into account half-life kinetics.	Strong

Perform orchidectomy and pathological examination of the testis to confirm the diagnosis and to define the local extension (pT category). In a life-threatening situation due to extensive metastasis, commence chemotherapy prior to orchidectomy.	Strong
Perform contrast enhanced computerised tomography (CECT) scan (chest, abdomen, and pelvis) in patients with diagnosis of TC. If iodine allergy or other limiting factors occur, perform abdominal and pelvic magnetic resonance imaging (MRI).	Strong
Perform MRI of the brain (or brain CECT if not available) in patients with multiple lung metastases, or high beta subunit of human Chorionic Gonadotropin (β -hCG) values, or those in the poor-prognosis International Germ Cell Cancer Collaborative Group (IGCCCG) risk group.	Strong
Do not use positron-emission tomography computed tomography or bone scan for staging.	Strong
Encourage patients with TC to perform self- examination and to inform first degree male relatives of the need for self-examination.	Weak
Discuss testis-sparing surgery with frozen section examination in patients with a high likelihood of having a benign testicular tumour which are suitable for enucleation.	Strong
Discuss biopsy of the contralateral testis to patients with TC and high-risk for contralateral germ cell neoplasia <i>"in situ"</i> .	Weak

Prognosis

Table 3: Pathological risk factors for occult metastatic disease in Stage I TC

Histological type	Seminoma	Non seminoma
Pathological risk factors	 Tumour size Invasion of the rete testis 	• Lympho-vascular invasion in peri-tumoural tissue

Disease management

1. Stage | Germ Cell Tumours

Germ cell neoplasia *"in situ"*, when diagnosed, can be treated by local radiotherapy (18-20 Gy in fractions of 2 Gy) or orchidectomy when the contralateral testis is normal.

Recommendations for the treatment of stage I seminoma	Strength rating
Fully inform the patient about all available management options, including surveillance or adjuvant chemotherapy after orchidectomy, as well as treatment- specific recurrence rates and acute and long-term side effects.	Strong
Offer surveillance as the preferred management option if facilities are available and the patient is compliant.	Strong
Offer one dose of carboplatin at area under curve (AUC) 7 if adjuvant chemotherapy is considered.	Strong
Do not perform adjuvant treatment in patients at very low risk of recurrence (no risk factors).	Strong

Do not routinely perform adjuvant radiotherapy.	Strong
Adjuvant radiotherapy should be reserved only for highly selected patients not suitable for surveillance and with contraindication for chemotherapy.	Strong

Recommendations for the treatment of stage I non-seminomatous germ cell tumour	Strength rating
Inform patients about all management options after orchidectomy: surveillance, adjuvant chemotherapy, and retroperitoneal lymph node dissection, including treatment- specific recurrence rates as well as acute and long-term side effects.	Strong
Offer surveillance or risk-adapted treatment based on lymphovascular invasion.	Strong
Discuss one course of cisplatin, etoposide, bleomycin as an adjuvant treatment alternative in patients with stage I non- seminomatous germ cell tumour if patients are not willing to undergo or comply with surveillance.	Strong

Recommendations for risk-adapted treatment for clinical stage I based on vascular invasion	Strength rating	
Stage IA (pT1, no vascular invasion): low risk		
Offer surveillance if the patient is willing and able to comply.	Strong	

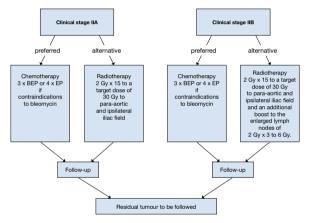
Offer adjuvant chemotherapy with one course of cisplatin, etoposide, bleomycin (BEP) in low-risk patients not willing (or unsuitable) to undergo surveillance.	Strong
Stage IB (pT2-pT4): high risk	
Offer adjuvant chemotherapy with one course of BEP, or surveillance and discuss the advantages and disadvantages.	Strong
Offer surveillance to patients not willing to undergo adjuvant chemotherapy.	Strong
Offer nerve-sparing retroperitoneal lymph node dissection (RPLND) to highly selected patients only; those with contraindication to adjuvant chemotherapy and unwilling to accept surveillance.	Strong
Primary RPLND should be advised in men with post-pubertal teratoma with somatic malignant component.	Weak

2. Metastatic Germ cell Tumours

- Clinical Stage I (CS I) patients with persistently elevated serum tumours markers require repeated imaging including US examination of contralateral testis and abdominal and extra-abdominal sites. They should be treated according to IGCCCG prognostic groups.
- Overall patients with metastatic disease should be treated with upfront chemotherapy (BEP 3 or 4 cycles) according to the IGCCCG prognostic groups ± surgery of residual masses.
- An exception to this rule is Stage II low-volume seminoma that may be treated with radiotherapy (30 Gy) in case of contraindication for chemotherapy.

 In CS IIA NSGCT without elevated tumor markers nervesparing RPLND, when performed by an experienced surgeon in a specialised centre, is the recommended initial treatment. Initial surveillance may be considered, in NSGCT patients with normal markers and lymph nodes < 2 cm of greatest axial diameter, or non-nodular shape with early re-evaluation at six weeks.

Figure 1: Treatment options in patients with seminoma clinical stage IIA and IIB*



* When enlarged retroperitoneal lymph nodes are < 2 cm and with normal markers, treatment should not be initiated unless metastatic disease is unequivocal based on biopsy, increasing nodal size/number, or subsequent marker rise. BEP = cisplatin, etoposide, bleomycin; EP = etopside and cisplatin.

Recommendations for the treatment of	Strength rating
metastatic germ cell tumours	
Treat low-volume non-seminomatous germ cell tumour (NSGCT) stage IIA/B with elevated markers like good- or intermediate- prognosis risk group IGCCCG, with three or four cycles of cisplatin, etoposide, bleomycin (BEP).	Strong
Nerve-sparing retroperitoneal lymph node dissection when performed by an experienced surgeon in a specialised centre is the recommended initial treatment in clinical stage (CS) IIA NSGCT disease without elevated tumour markers.	Weak
Repeat staging after six weeks, before making a final decision on further management in patients with small volume (CS IIA < 2 cm) marker-negative NSGCT.	Weak
Treat metastatic NSGCT (stage ≥ IIC) with an intermediate prognosis with four cycles of standard BEP.	Strong
In metastatic NSGCT with a poor-prognosis, treat with one cycle of BEP, (or cisplatin, etoposide and ifosfamide [PEI] in case of poor lung function), followed by tumour marker assessment after three weeks. Continue the same schedule up to a total of four cycles with favourable marker decline. With unfavourable decline, initiate chemotherapy intensification.	Weak
Perform surgical resection of visible (> 1 cm) residual masses after chemotherapy for NSGCT when serum levels of tumour markers are normal or normalising.	Strong

Initially offer cisplatin-based chemotherapy according to IGCCCG prognosis groups, or alternatively radiotherapy to seminoma patients with stage II A/B and, inform the patient of potential long-term side effects of both treatment options.	Weak
Treat seminoma stage IIC and higher, with primary chemotherapy according to IGCCCG classification (BEP x 3 in good prognosis and BEP x 4 in intermediate prognosis).	Strong

Relapse after chemotherapy

The treatment of relapsed GCT after chemotherapy is typically salvage chemotherapy. For patients at first relapse with good prognostic features (initial achievement of complete response/partial remission negative markers [CR/PRm-] and gonadal primary tumour) four cycles of standard-dose salvage chemotherapy is proposed. For patients with poor prognostic factors (extra-gonadal primary and/or incomplete response to first-line chemotherapy) and for all patients with subsequent (second or more) relapse, high-dose chemotherapy with autologous stem cell support is recommended.

Follow-up

The primary aim of follow-up in the first five years is the timely diagnosis of recurrent disease in order to be able to treat the patient with curative intent with the least aggressive therapy.

The following factors should be considered:

 Follow-up must be tailored to the individual patient with a schedule acceptable to the patient, the clinician, and the health care system.

- b) The interval of follow-up visits and the clinical investigations to be performed at each visit should depend on the risk of relapse, in general, as well as the likely sites of relapse in an individual patient.
- c) When possible, an effort should be made to minimise any risks associated with ionising radiation exposure.
- d) The increased risk of second malignancy (in the primary site and in other tissues that may have been exposed to the same carcinogens, or in which there is epidemiological evidence of increased risk) should also guide the selection of tests.

Table 4: Recommended minimal follow-up for seminoma stage I on active surveillance or after adjuvant treatment (carboplatin or radiotherapy)¹

Modality	Year 1	Year 2	Year 3	Years	After 5
				4&5	years
Tumour markers	2 times	2 times	2 times	Once	Further
± doctor visit					management
Chest X-ray	-	-	-	-	according to
Abdominopelvic	2 times	2 times	Once	Once	survivorship care plan
computed			at 36	at 60	cure plan
tomography (CT)/			months	months	
magnetic resonance					
imaging					

¹ Recommendations based upon ESMO (European Society for Medical Oncology) Testicular seminoma and non-seminoma consensus meeting outcomes.

Table 5: Recommended minimal follow-up for non-seminoma clinical stage I on active surveillance¹

Modality	Year 1	Year 2	Year 3	Years 4 & 5	After 5 years
Tumour markers ± doctor visit	4 times*	4 times	2 times	1-2 times	Further management according to survivorship care plan
Chest X-ray	2 times	2 times	Once, in case of LVI+	At 60 months if LVI+	
Abdominopelvic computed tomography (CT)/ magnetic resonance imaging	2 times	At 24 months**	Once at 36 months***	Once at 60 months***	

LVI+ = lymphovascular invasion.

- ¹ Recommendations based upon ESMO Testicular seminoma and non-seminoma consensus meeting outcomes.
- * In case of high risk (LVI+) a minority of the consensus group members recommended six times.
- ** In case of high risk (LVI+) a majority of the consensus group members recommended an additional CT at eighteen months.
- *** Recommended by 50% of the consensus group members.

Table 6: Recommended minimal follow-up after adjuvant treatment or complete remission for advanced disease (excluded: poor prognosis and no remission)¹

Modality	Year 1	Year 2	Year 3	Years 4 & 5	After 5 years
Tumour markers ± doctor visit	4 times	4 times	2 times	2 times	Further management
Chest X-ray	1-2 times	Once	Once	Once	according to survivorship care plan**
Abdominopelvic computed tomography (CT)/ magnetic resonance imaging	1-2 times	At 24 months	Once at 36 months	Once at 60 months	
Thorax CT	1-2 times*	At 24 months*	Once at 36 months*	Once at 60 months*	

- ¹ Recommendations based upon ESMO Testicular seminoma and non-seminoma consensus meeting outcomes.
- * In conjunction with abdominopelvic CT/MRI in case of pulmonary metastases at diagnosis.
- ** In case of teratoma in resected residual disease: the patient should remain with the uro-oncologist.

Quality of life and long-term toxicities after cure

Patients diagnosed with TC are usually between 18 and 40 years of age at diagnosis, and life expectancy after cure extends over several decades. Patients should be informed before treatment of common long-term toxicities before any treatment is planned.

During follow-up, patients should be screened and treated for known risk factors such as hypertension, hyperlipidaemia, and testosterone deficiency. When follow-up by the clinical expert is discontinued, a written cancer survivorship plan addressing late toxic effects, lifestyle recommendations, recurrence risk, and cancer-specific follow-up might be helpful.

Included among the long-term toxicity and secondary effects of TC treatment are: second malignant neoplasms, leukaemia, infections, pulmonary and cardiovascular complications, Raynaud-like phenomena, neuro- nephro- and ototoxiciy, impaired cognitive function, hypogonadism, and fatigue as well as quality of life issues.

Rare adult testicular tumours

Rare testicular tumours have similar clinical presentation as GCTs and are identified by histopathological examination. Available literature is based on case reports and retrospective series. Classification is according to the 2016 WHO Classification of Tumours of the Urinary System and Male Genital Organs.

1. Spermatocytic Tumours

Spermatocytic tumours are GCTs unrelated to GCNIS and extremely rare. Normally they do not show elevated markers and cannot be differentiated from seminomatous GCT by frozen section analysis. Radical orchiectomy is the standard treatment option. Metastatic disease is very rare and typically presents early after initial diagnosis with limited survival.

2. Sex cord-stromal tumours

Sex cord–stromal tumours are the second largest group of primary testicular tumours. They are relatively uncommon and only a small minority are malignant. Morphological features associated with malignant potential in both types include two or more of the following features:

- size > 5 cm
- infiltrative borders
- cytological atypia

- 3 or more mitotic figures per 10 high-power fields
- vascular invasion
- necrosis

Leydig cell tumours

Leydig cell tumours comprise about 4% of adult testicular tumours. They may present with hormonal manifestations, including gynecomastia and rarely accompanied by Cushing's Syndrome. Local recurrence of 7% has been reported after TSS. Survival of men with metastatic disease is poor but response to surgical and systemic treatment have been reported.

Sertoli cell tumours

Sertoli cell tumours account for approximately 1% of all testicular neoplasms. The risk of metastatic potential remains unclear. After TSS a local recurrence rate of < 1% has been reported. Survival of men with metastatic disease is poor although response to surgery has occasionally been reported.

Granulosa cell tumour

Granulosa cell tumours include adult and juvenile variants and are very rare. After TSS a local recurrence rate of 5% has been reported. Metastatic disease has only been described, albeit extremely rare, in men with adult type. Survival of men with metastatic disease is poor although rare instances of response to surgical or systemic treatment have been reported.

Thecoma/fibroma group of tumours

These tumours derive from the testicular parenchymal stroma or from the tunica albuginea. They seem to be uniformly benign.

Paratesticular tumours of the epididymis or spermatic cord

The majority of epididymal masses are benign cystic or inflammatory conditions. Solid epididymal tumours are rare and comprise numerous benign and neoplastic lesions. No clear recommendation can be provided regarding surgical approach, extent of resection and neo- or adjuvant treatment can be given.

3. Mesothelioma of the tunica vaginalis testis

Mesothelioma of the tunica vaginalis testis is a rare but aggressive disease. Aggressive local treatment with hemiscrotectomy is recommended. No clear recommendation can be given regarding adjuvant treatment. In case of metastatic disease, the median overall survival is a few months.

Conclusions

Most TCs are diagnosed at an early stage. Staging is the cornerstone of treatment. Following orchidectomy, excellent cure rates are achieved for those early stages irrespective of the treatment policy adopted, although pattern and relapse rates are closely linked to the treatment modality chosen. In metastatic disease a multidisciplinary therapeutic approach offers an acceptable survival. Follow-up schedules should be tailored to initial staging and treatment.

This short booklet text is based on the more comprehensive EAU Guidelines (ISBN 978-94-92671-16-5), available to all members of the European Association of Urology at their website, <u>http://www.uroweb.org/guidelines/</u>.