European Urology

Eur Urol 2001;40:102–110

EAU Guidelines on Testicular Cancer

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Key Words

Testis cancer · Guidelines · Diagnosis · Treatment · Follow-up

Abstract

Objectives: To establish guidelines for the diagnosis, staging, treatment and follow-up of germ cell testicular cancer.

Methods: A search of published work was conducted using Medline. Highly evidence-based articles were selected and their findings analysed by the members of the Oncological Urology Working Group of the EAU.

Testis cancer is rare and affects young men in their 3rd and 4th decades of life. The majority of these tumours are derived from germ cells (seminomatous and non-seminoma germ cell testicular cancer), and more than 50% of patients are diagnosed with stage I disease. Epidemiological, pathological and clinical risk factors are well established. The tumour, node, metastasis (TNM) staging system is endorsed, and for metastatic disease a recently devised prognostic-factor-based staging system has proven to be useful. Staging assessment includes pre- and post-orchiectomy marker levels, pathology of the testis, and nodal and visceral status. Following orchiectomy, treatment depends on the tumour type, pathological risk factors for stage I disease and clinical prognostic factors for advanced disease. The cure rate is excellent for disease stages I and II, irrespective of the treatment adopted. However, the pattern of relapse (rate, timing and site) is highly influenced by therapeutic policy. For metastatic disease, survival depends on clinical prognostic factors and treatment. Follow-up schedules are tailored according to stage, tumour type and post-orchiectomy treatment schedules.

Conclusions: Excellent cure rates are achieved for early-stage germ cell testis tumours following accurate staging at diagnosis. Satisfactory survival rate can be achieved in advanced metastatic disease using a multidisciplinary therapeutic approach. Follow-up schedules vary, depending on the pathology and stage of the primary tumour and on the treatment policy adopted following orchiectomy.

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Table 1. TNM classification for testicular cancer (UICC, 1997)

Primary tumour (only pathologically defined)
pTx radical orchiectomy not performed
pT0 histological scar or no evidence of primary tumour
pTin intratubular germ cell neoplasia
pT1 tumour limited to testis, including rete testis and albuginea
pT2 tumour limited to testis with evidence of vascular (haematic or lymphatic) invasion, or tunica vaginalis involved by tumour
pT3 tumour involving spermatic cord, with or without vascular invasion
pT4 Tumour involving scrotum, with or without vascular invasion

Regional lymph nodes (retroperitoneal plus inguinal following inguinal surgery)
Clinical
Nx regional nodes cannot be assessed
N0 no regional node metastasis
N1 single or multiple metastases, all < 2 cm in greatest diameterr
N2 single or multiple metastases, 2-5 cm in greatest diameter
N3 lymph node metastasis > 5 cm
Pathological
Nx regional nodes cannot be assessed
N0 no regional node metastasis
N1 metastases to 1–5 nodes, none > 2 cm in the greatest diameter
N2 metastases 2–5 cm, or > 5 metastases < 5cm, or extranodal extension of tumour
N3 lymph node metastasis > 5 cm

Distant metastases
Mx presence of distant metastasis cannot be assessed
M0 no distant metastasis
M1 distant metastases
M1a metastases to extraregional lymph nodes and/or to the lung
M1b distant metastasis in other sites (non-pulmonary visceral metastasess)

Background

Testicular cancer is rare and accounts for 1–1.5% of all male cancers. Although rare, it is the most common cancer affecting young men in their 3rd and 4th decades of life. In the developed world, 3–6 new cases of testicular cancer per 100,000 males are diagnosed each year [1]. Today, most patients with testicular cancer are cured with standard available treatments.

Epidemiological, pathological and clinical risk factors have been identified for testicular cancer. The epidemiological risk factors include cryptorchidism, Klinefelter's syndrome, infertility, family history and the presence of a contralateral tumour and/or intratubular testicular neoplasm. The most important pathological factors for stage I disease are histological type, the presence of peri-tumoural vascular and lymphatic invasion, and tumour size [2, 3]. For metastatic disease, the primary location, elevation of tumour marker levels and the presence of a non-pulmonary visceral metastasis are the recognized risk factors [4].

Classification

The modified World Health Organization pathological classification system for testicular cancer is recommended in these guidelines. Testicular epithelial cancer is classified into three categories: (a) germ cell tumours; (b) sex cord stromal tumours, and (c) mixed germ cell/sex cord stromal tumours. Germ cell tumours account for 90–95% of cases of testicular cancer according to the WHO classification system [1].

The 1997 tumour, node, metastasis (TNM) staging system is recommended (table 1). This staging system includes: (a) the determination of the anatomical extent of the disease with clear definition of the regional nodes, and identification of sites and extent of metastases; (b) S-category or nadir post-orchiectomy values of serum tumour markers (β-human chorionic gonadotrophin β-hCG, α-fetoprotein AFP, and lactate dehydrogenase, LDH). According to the 1997 TNM classification system, stage I testicular cancer can be divided into three substages – IA, IB and IS. For practical purposes, the Peckham staging system is used throughout this text (stage I = any T, N0, M0; small volume stage II = any T, N1-2, M0; large volume stage II = any T, N3, M0).

Large population-based patient studies have shown that 75–80% of patients with testicular seminoma and 55% of those with non-seminoma germ cell testicular cancer (NSGCT) have stage I at diagnosis [5]. Recently, the International Germ Cell Collaborative Group (IGCCG) has devised a prognostic factor-based staging system for metastatic germ cell cancer that includes good- and intermediate-prognosis seminoma germ cell testicular cancer and good-, intermediate- and poor- prognosis NSGCT [4] (table 2).

Diagnosis of Testicular Cancer

Testicular cancer is usually diagnosed by physical examination and generally appears as a painless, unilateral intrascrotal mass. A physical examination will reveal the features of the mass and must always be carried out in association with a general examination to find possible (supraclavicular) distant metastases, a palpable abdominal mass or gynaecomastia [1].

Table 2. IGCCG prognostic classification for metastatic germ cell testicular cancer

Groups	Non-seminoma	Seminoma
Goog prognosis	56% of cases	90% of cases
5-year progression-free survival	89%	82%
5-year survival	92%	86%
With all of	testis/retroperitoneal primary	any primary site
	no non-pulmonary visceral metastases	no non-pulmonary visceral metastases
	AFP $<$1,000 ng/ml	normal AFP
	hCG $<$5,000 mIU/l (1,000 ng/ml) and	any hCG
	LDH $<$1.5$\times$ upper limit of normal	any LDH
Intermediate prognosis	28% of cases	10% of cases
5-year progression-free survival	75%	68%
5-year survival	80%	73%
With all of	testis/retroperitoneal primary	any primary site
	no non-pulmonary visceral metastases	non-pulmonary visceral metastases
	AFP $\geq$1,000 and $\leq$10,000 ng/ml or	normal AFP
	hCG $\geq$5,000 and $\leq$50,000 mIU/l	any hCG
	LDH $\geq$1,5 and $\leq$10$\times$ upper limit of normal	any LDH
Poor prognosis	16% of cases	no patients classified as poor prognosis
5-year progression-free survival	41%	
5-year survival	48%	
With all of	mediastal primary	
	non-pulmonary visceral metastases	
	AFP $>$10,000 ng/ml or	
	hCG $>$50,000 mIU/l (10,000 ng/ml) or	
	LDH $>$10$\times$ upper limit of normal	

Diagnostic Tools

Accurate TNM staging predetermines the treatment choice following inguinal surgery (orchiectomy). Thus, it is necessary to determine: (a) pre- and post-orchiectomy levels of the serum tumour markers β-hCG, AFP and LDH; (b) the pathology of the testis; (c) the status of the abdominal and supraclavicular nodes and the liver; (d) the presence or absence of mediastinal nodal involvement and lung metastases; and (e) the status of the brain and bone if there are any suspicious symptoms.

Serum Tumour Markers

Globally, there is an increase in the level of these markers in 51% of cases of testicular cancer [6]. Increased levels of AFP are seen in 50–70% of patients with NSGCT and a rise in β-hCG is also seen in 40–60% of the patients with NSGCT. Up to 30% of the patients with testicular seminoma present or develop elevated levels of β-hCG during the course of the disease [7]. LDH is a less specific marker, and its concentration is proportional to the tumour volume. Elevated levels of LDH occur in 80% of patients with advanced testicular cancer [7]. The measurement of AFP, β-hCG and LDH is recommended in all cases, while that of other markers, such as neuron-specific enolase and placental alkaline phosphatase, is optional in seminoma cases. The normal post-orchiectomy half-life decay is 5 days for AFP and 1 day for β-hCG.

Inguinal Exploration and Orchiectomy

Orchiectomy has to be performed using an inguinal approach. The spermatic cord is isolated at the external inguinal ring and clamped with a soft vascular clamp. The testis is then exteriorised with its tunics and the surgical field protected with surgical sponges. The tunica vaginalis is opened and the testis is carefully inspected and palpated. If the diagnosis is unclear, a testicular biopsy is taken for a frozen-section histological examination. Once the diagnosis of testicular cancer has been established, the testis is enveloped into the sponges that protect the surgical field, gloves are changed, the inguinal canal is opened and the spermatic cord is divided at the level of the internal inguinal ring. The specimen obtained is then sent for definitive histology.

Table 3. Pathology of the testis: investigations

(1) Macroscopic features: side, testis size, tumour size and macroscopic features of the epididymis, spermatic cord and tunica vaginalis
(2) Sampling: a 1-cm^2 section for every centimeter of maximal tumour diameter, including normal macroscopic parenchyma (if present), albuginea and epididymis selection of suspected areas; at least one proximal and one distal section of the spermatic cord plus any suspected area
(3) Microscopic features and diagnosis: histological type (specify individual components and estimate amount as a percentage); presence or absence of peri-tumoural venous and/or lymphatic invasion; presence or absence of albuginea, tunica vaginalis, epididymis or spermatic cord invasion, and presence or absence of intratubular germinal neoplasia in non-tumoural parenchyma
(4) pT category according to TNM 1997
(5) Immunohistochemical studies: AFP and β-hCG in seminoma and mixed germ cell tumours

Table 4. Guidelines for the diagnosis and staging of testicular cancer

(1) A physical examination may be sufficient to diagnose testicular cancer
(2) A testis ultrasound is necessary when a tumour is clinically suspected but the examination of the scrotum is normal, or if there is any doubt about the clinical findings of the scrotum
(3) A pathological examination of the testis is necessary to determine the diagnosis and local extension (pT category)
(4) Serum determination of the tumour markers AFP, β-hCG and LDH must be performed before and after surgery for staging and prognostic purposes
(5) Retroperitoneal, mediastinal and supraclavicular nodes and the visceral state have to be assessed in testicular cancer; in testicular seminoma, a chest CT scan is not necessary if the abdominal nodes are negative

Pathology of the Testis

Following orchiectomy, the pathological examination of the testis should include a number of investigations (table 3).

Abdominal, Mediastinal and Supraclavicular Nodes, and State of the Viscera

An abdominal computed tomography (CT) scan is necessary to determine the state of the retroperitoneal nodes. CT scan has a sensitivity of 70–80% and its accuracy depends on the size of the nodes. In slim young men and children who lack retroperitoneal fat, an ultrasound should be performed instead of an abdominal CT scan [8]. The landing zones are the left paraortic nodes for the left testis and preaorto-caval nodes for the right side.

In patients diagnosed with testicular seminoma and negative abdominal CT scan, an antero-posterior and lateral chest X-ray examination is enough to assess the thorax [9, 10]. Patients diagnosed with testicular seminoma who have a positive abdominal CT scan are recommended to have a chest CT scan [10]. A chest CT scan should be routinely performed in patients diagnosed with NSGCT because in 10% of cases small subpleural nodes are presented that are not visible radiologically [1].

Ultrasound of the testis is an optional test. Its main value is to screen the contralateral testis in the follow-up of patients at risk. An ultrasound of the testis must be performed in young men without a palpable testicular mass who have retroperitoneal or visceral masses or elevated serum β-hCG or AFP levels [10]. Magnetic resonance imaging is not recommended for the routine staging of testis cancer [11]. However, it can be helpful when abdominal CT scans or ultrasound are inconclusive or in cases of contrast hypersensitivity. Other examinations, such as brain or spinal CT, bone or liver ultrasound scans, should be carried out if there is a suspicion of metastases.

Supraclavicular nodes are best assessed by a physical examination [1]. Guidelines for the diagnosis and staging of testicular cancer are given in table 4.

Treatment of Testicular Cancer

The aim of post-orchiectomy treatment is to prevent metastasis in clinical stage I and to improve survival rate in metastatic disease. The choice of therapy depends on the tumour type, the presence or absence of pathological risk factors (stage I disease) and clinical prognostic factors (metastatic disease).

Stage I Seminoma

About 15–20% of patients diagnosed with stage I testicular seminoma have subclinical metastatic disease and will relapse after orchiectomy [12]. Seminoma cells are highly radiosensitive, and radiotherapy treatment at a total dose of 24–30 Gy to the dog leg field, for the right side and to a para-aortic field for the left side will reduce this relapse rate to 1–3% [13]. However, there is an increased risk of a second cancer associated with prophylactic radiotherapy [14].

Surveillance is an alternative option for seminoma stage I. Once a relapse occurs, up to 70% of cases can be cured with radiotherapy alone [14].

Adjuvant (carboplatin based) chemotherapy is a promising treatment option, but more long-term observations are required before it is introduced into routine practice [15]. This policy is recommended in the setting of clinical trials only.

Retroperitoneal lymphadenectomy (RPLND) is not recommended as a primary treatment option for stage I testicular seminoma [16].

Stage I NSGCT

Following orchiectomy, up to 30% of patients diagnosed with stage I NSGCT have subclinical metastases and will relapse if surveillance is used as the treatment option. The main predictor of relapse in patients managed with surveillance is peritumoral vascular invasion [3, 17, 18]. About 70% of patients with clinical stage 1 NSGCT do not have vascular invasion and have a 15–20% risk of relapse on surveillance compared with a 50% relapse rate in patients with vascular invasion. If nerve-sparing RPLND is properly performed, the risk of retroperitoneal relapse is very low [19].

Several studies have shown reduced relapse rates in patients with high-risk stage I NSGCT when treated with two courses of PEB (cisplatin, etoposide and bleomycin) adjuvant chemotherapy [20, 21]. However, the risk of slow-growing teratoma developing retroperitoneally and that of chemoresistant cancer relapse after PEB chemotherapy needs to be established before the routine use of such treatment for these patients can be recommended.

The primary treatment option for clinical stage IS patients is still controversial. If serum marker levels do not drop or increase after surgery, residual disease is highly suspected. Indeed, if RPLND is performed, up to 87% of these patients will have disease-positive nodes in the retroperitoneum [22]. These patients should be treated with three courses of primary PEB chemotherapy in a clinical trial setting or with RPLND (eventually followed by chemotherapy).

Metastatic Germ Cell Tumours

The histology of the primary tumour and the prognostic factor group, as defined by the IGCCG classification, determine the primary treatment option for metastatic germ cell tumours after orchiectomy. The general consensus is to use chemotherapy except in cases of low-volume stage II disease, where non-seminoma can also be treated with primary bilateral RPLND eventually followed by chemotherapy or surveillance, and pure seminoma may be treated with radiotherapy [23].

The treatment of choice for good prognosis metastatic NSGCT is three courses of chemotherapy with cisplatin, etoposide (VP-16) and bleomycin according to the British BEP or American PEB schedule [24, 25]. For intermediate- and poor-prognosis metastatic NSGCT, the primary treatment schedule is four courses of the American PEB.

In patients who have NSGCT with normal or normalized levels of serum tumour markers, surgical resection of residual masses after first-line chemotherapy is the universally recommended treatment. The key to the successful management of residual masses is complete resection. The use of adjuvant chemotherapy following complete resection of residual tumor is still being questioned.

Salvage chemotherapy is used after first-line chemotherapy in non responders, marker-positive partial responders and in case of relapse. The current schedules include four courses of VIP (VP-16, ifosfamide, cisplatin) or VeIP (Vel-

Table 5. Guidelines for the treatment of testicular cancer

Stage I Seminoma
(1) Prophylactic radiotherapy to a para-aortic or dog leg field at a total dose of 24–30 Gy
(2) Surveillance
(3) Carboplatin-based chemotherapy only in the setting of clinical trials

Stage I NSGCT
Clinical stage IA (pT1, no vascular invasion)
(1) If the patient is able and willing to comply with a surveillance policy and long-term (at least 5 years) close follow-up is feasible, surveillance is equivalent to nerve-sparing RPLND
(2) If RPLND reveals PN+ (regional lymph node disease), adjuvant chemotherapy with two courses of PEB should be considered

Clinical stage IB (pT2–pT4, vascular invasion)
Active treatment is recommended:
(1) Nerve-sparing RPLND, which must be bilateral if PN+ (regional lymph node disease) is revealed peri-operatively (nerve-sparing on the opposite side)
(2) Primary chemotherapy with two courses of PEB; this option should only be considered in a clinical trial as further long-term results regarding the risk of retroperitoneal relapse are awaited

Metastatic germ cell tumours
(1) Low-volume stage II NSGCT can be treated either by RPLND (eventually followed by surveillance or by two cycles of chemotherapy) or by primary chemotherapy
(2) Three courses of PEB chemotherapy is the primary treatment of choice for patients with good prognosis metastatic NSGCT
(3) Four courses of PEB chemotherapy is the primary treatment of choice for patients with intermediate- and poor-prognosis metastatic NSGCT
(4) Surgical resection of residual masses after chemotherapy in NSGCT is recommended when tumour marker levels are normal or normalizing
(5) Metastatic seminoma with less than N3M1 disease can be treated first with radiotherapy; when necessary, chemotherapy can be used as a salvage treatment with the same schedule as for the corresponding prognostic factor groups of NSGCT
(6) Advanced seminoma (N3 or M1) should be treated with primary chemotherapy according to the same principles used for NSGCT, but with radiotherapy to (persistent) residual masses instead of surgery

Table 6. Patterns of recurrence in early-stage testicular cancer

Type	Treatment	Relapse rate, %	Time	Site
Stage I NSGCT	surveillance	30	12 months	retroperitoneum, mediastinum, lungs
	nerve sparing-RPLND	10–12	2 years	lungs, neck, surgical margins
	chemotherapy	3	ND	ND
Stage I Seminoma	radiotherapy	1–2	18 months	supradiaphragmatic nodes, mediastinum, lungs, bones
	surveillance	15–20	12–18 months[a]	retroperitoneum, inguinal nodes, lungs
	chemotherapy	2	ND	ND
Stage II NSGCT	RPLND + chemotherapy	6	4 years	outside surgical field
	RPLND + surveillance	35[b]	4 years	outside surgical field
	chemotherapy[c]	5	8 months	ND
Stage II Seminoma	radiotherapy	5–15	2 years	supraclavicular, mediastinum

ND = Not determined.
[a] But 29% of relapses can develop later.
[b] Depending on the pathological stage II (a or b).
[c] Provided complete response (reached in 68–78% of cases).

Table 7. Recommended follow-up for stage I seminoma after radiotherapy

Procedure	Year			
	1	2	3	4–5
Physical examination	4 times	3 times	3 times	twice/year
Chest X-ray	4 times	3 times	3 times	twice/year
Tumour markers	4 times	3 times	3 times	twice/year
Abdominal CT scan	once	once	if indicated	if indicated
Abdominal ultrasound	once[a]	once[a]	once	if indicated

[a] Alternating with abdominal CT scan.

ban, ifosfamide, cisplatin) following either PVB or PEB [26]. New drugs that act synergistically with cisplatin are being studied (paclitaxel and gemcitabine). Salvage surgery should be performed for any resectable residual mass subsequent to salvage chemotherapy and for any resectable NSGCT refractory to chemotherapy.

Patients with metastatic seminoma can be treated with radiotherapy (34–40 Gy) alone and relapsing patients may be further treated with salvage chemotherapy. Advanced seminoma is unusually highly responsive to primary PEB chemotherapy and, as a general rule, residual masses that do not shrink within 6 months of completion of chemotherapy should be treated with radiotherapy instead of surgery.

Recommended guidelines for the treatment of testicular cancer are summarized in table 5.

Follow-Up of Patients with Testicular Cancer

Regular follow-up is vital for patients with testicular cancer, and they should be watched closely for several years. Follow-up schedules depend on the histology, stage and post-orchiectomy treatment option chosen. The aim is to detect early disease recurrence and contralateral testis tumours and to avoid unnecessary treatment.

Stages I and II (A and B)

The more advanced the nodal stage of the cancer, the higher the chance of disease recurrence. The different timing and pattern of relapse according to the tumour type and treatment policy adopted are presented in table 6 [5, 15, 21, 27–32]. For primary chemotherapy treatment policies, the time and site of relapse is still uncertain.

Whatever the tumour type, if RPLND has been performed the follow-up is simpler and less expensive [33]. In a surveillance policy, more intensive and longer follow-up with repeated imaging of the retroperitoneum is required. In general, a close follow-up is adopted during the first 2 years. The recommended schedules of follow-up are included in tables 7–13.

The schedule presented in table 12 can be used in stage II NSGCT treated with RPLND followed by surveillance, but all of the tests need to be performed more frequently. After primary chemotherapy in stage II disease, an abdominal and pelvic CT scan should be performed twice during the first 2 years.

Table 8. Recommended follow-up for stage I seminoma on surveillance or after chemotherapy

Procedure	Year				
	1	2	3	4–5	6–10
Physical examination	6 times	4 times	3 times	twice/year	once/year
Tumour markers	6 times	4 times	3 times	twice/year	once/year
Chest X-ray	6 times	4 times	3 times	twice/year	once/year
Abdominal CT scan	4 times	4 times	twice	once/year	if indicated
Abdominal ultrasound	NN	NN	twice[a]	once/year[a]	if indicated

NN = Not necessary.
[a] Alternating with abdominal CT scan.

Table 9. Recommended follow-up for patients with stage I NSGCT on surveillance

Procedure	Year			
	1	2	3–5	6–10
Physical examination	6 times (monthly for the first 6 months A)	4 times (6 times A)	twice/year	once/year A
Tumour markers	6 times (monthly for the first 6 months A)	4 times (6 times A)	twice/year	once/year A
Chest X-ray	6 times (monthly for the first 6 months A)	4 times (6 times A)	twice/year	once/year A
Abdominal CT scan	3 times (4 times A)	twice (3 times OP)	once/year	If indicated

A = Advisable; OP = optional.

Clinical Stage IIc and More Advanced Disease (Seminoma and NSGCT)

The overall survival rate in advanced disease (IGCCG) is 92% for the good-prognosis group, 80% for the intermediate group and 48% for the poor-prognosis group [4] (table 2). Stage IIc disease is generally considered to be a good prognostic factor. Close follow-up is recommended for those patients during the first 2 years as most relapses occur within this time. Retroperitoneal CT scanning monitors the shrinkage of retroperitoneal masses and is indicated at least annually if a teratoma is found in the retroperitoneum. As the risk of cerebral metastasis is increased in these disease stages, a brain CT scan is recommended in case of any focality. The recommended follow-up schedule is presented in table 13.

Table 10. Recommended follow-up for stage I NSGCT after RPLND or adjuvant chemotherapy

Procedure	Year			
	1	2	3–5	6–10
Physical examination	6 times	3 times	twice/ year	once/year A
Tumour markers	6 times	3 times	twice/year	once/year A
Chest X-ray	6 times	3 times	twice/year	once/year A
Abdominal CT scan	twice	once	if indicated[a]	if indicated
Abdominal ultrasound	twice A[b]	twice A[b]	twice/year	once/year

A = advisable.
[a] Due to a risk of late, slow-growing teratoma in the retroperitoneum after adjuvant chemotherapy.
[b] Alternating with abdominal CT scan.

Conclusions

Most of the testis tumors are derived from germ cells and diagnosed in early stages. Staging is the corner stone and the TNM system is recommended although the Peckham classification is still widely used for practical purposes. Following orchiectomy, excellent cure rates are achieved for those early stages irrespective of the treatment policy adopted, although pattern and relapse rate are going to depend on it. In metastasic disease a multidisciplinary therapeutic approach offers an acceptable survival. Follow-up schedules are tailored to initial diagnosis and treatment.

Table 11. Recommended follow-up for stage IIa–IIb seminoma after radiotherapy

Procedure	Year					
	1	2	3	4	5	>5
Physical examination	6 times	4 times	3 times	twice	twice	once/year
Tumour markers	6 times	4 times	3 times	twice	twice	once/year
Chest X-ray	6 times	4 times	3 times	twice	twice	once/year
CT abdomen and pelvis[a]	if indicated	if indicated	if indicated	if indicated	if indicated	if indicated
CT chest[b]	if indicated	if indicated	if indicated	if indicated	if indicated	if indicated

[a] Baseline CT of the abdomen/pelvis after treatment and repeated only if indicated.
[b] Only if there is an abnormal chest X-ray or if clinical symptoms indicate.

Table 12. Recommended follow-up for stage IIa–IIb NSCGCT[a] after RPLND and chemotherapy or primary chemotherapy

Procedure	Year					
	1	2	3	4	5	>5
Physical examination	bimonthly	4 times	twice	twice	twice	once/year
Tumour markers	bimonthly	4 times	twice	twice	twice	once/year
Chest X-ray	bimonthly	4 times	twice	twice	twice	once/year
Abdominal CT[a, b, c]	baseline, then as indicated	as indicated	if indicated	if indicated	if indicated	if indicated
Abdominal ultrasound	twice	twice	if indicated	if indicated	if indicated	if indicated

[a] Patients treated with RPLND followed by surveillance can follow this schedule, but the tests should be performed more frequently: monthly during the 1st year, bimonthly during the 2nd year, every 3 months during the 3rd year, every 4 months during the 4th year, twice in the 5th year and annually thereafter.
[b] After RPLND, a baseline CT scan of the abdomen and pelvis should be obtained and repeated if clinically indicated thereafter.
[c] After primary chemotherapy, the retroperitoneum has to be monitored by means of CT at least twice during the first 2 years.

Table 13. Recommended follow-up for advanced seminoma and NSGCT

Procedure	Year					
	1	2	3	4	5	thereafter
Physical examination	monthly	bimonthly	4 times	3 times	twice	once/year
Tumour markers	monthly	bimonthly	4 times	3 times	twice	once/year
Chest X-ray	monthly	bimonthly	4 times	3 times	twice	once/year
Abdominal CT[a]	as indicated	as indicated	as indicated	as indicated	as indicated	as indicated
Chest CT[b]	as indicated	as indicated	as indicated	as indicated	as indicated	as indicated
Brain CT[c]	as indicated	as indicated	as indicated	as indicated	as indicated	as indicated

Abdominal CT scanning has to be performed at least annually if teratoma are found in the retroperitoneum.
[a] If the post-chemotherapy evaluation shows any mass >3 cm, the appropriate CT scan should be repeated 2 and 4 months later to ensure that the mass is continuing to regress.
[b] A chest CT is indicated if abnormality is detected on chest X-ray and after pulmonary resection.
[c] In patients with headaches, focal neurological findings or any central nervous system symptom.

References

1 Richie JP: Neoplasms of the testis; in Walsh PC, et al. (eds): Campbell's Urology, ed 7. Philadelphia, Saunders, 1997, pp 2411–2452.
2 Bokemeyer C, Kuczyk MA, Serth J, Hartmann JT, Schmoll HJ, Jonas U, Kanz L: Treatment of clinical stage I testicular cancer and a possible role for new biological prognostic parameters. J Cancer Res Clin Oncol 1996;122:575–584.
3 Klepp O, Olsson AM, Henrikson H, Aass N, Dahl O, Stenwig AE, Persson BE, Cavallin-Ståhl E, Fosså SD, Wahlqvist L: Prognostic factors in clinical stage I nonseminomatous germ cell tumors of the testis: Multivariate analysis of a prospective multicenter study. J Clin Oncol 1990;8:509–518.
4 International Germ Cell Collaborative Group: International Germ Cell Consensus Classification: A prognostic factor-based staging system for metastatic germ cell cancers. J Clin Oncol 1997;15:594–603.
5 Klepp O, Flodgren P, Maartman-Moe H, Lindholm CE, Unsgaard B, Teiqum H, Fosså SD, Paus E: Early clinical stages (CS1, CS1Mk+ and CS2A) of non-seminomatous testis cancer. Ann Oncol 1990;1:281–288.
6 Hermes ER, Harstad K, Fosså SD: Changing incidence and delay of testicular cancer in southern Norway (1981–1992). Eur Urol 1996;30:349–357.
7 Klein EA: Tumor markers in testis cancer. Urol Clin North Am 1993;20:67–73.
8 Husband JE, Barrett A, Peckham MJ: Evaluation of computed tomography in the management of testicular teratoma. Br J Urol 1981; 53:179–183.
9 See WA, Hoxie L: Chest staging in testis cancer patients: Imaging modality selection based upon risk assessment as determined by abdominal computerized tomography scan results. J Urol 1993;150:874–878.
10 Doherty FJ: Ultrasound of the nonacute scrotum; in Raymond HW et al. (eds): Seminars in Ultrasound, CT and MRI. New York, Saunders, 1991, pp 131–156.
11 Ellis JH, Bies JR, Kopecky KK, Klatte EC, Rowland RG, Donohue JP: Comparison of NMR and CT imaging in the evaluation of metastatic retroperitoneal lymphadenopathy from testicular carcinoma. J Comput Assist Tomogr 1984;8:709–719.
12 Sternberg CN: The management of stage I testis cancer. Urol Clin North Am 1998;25: 435–449.
13 Fosså SD, Horwich A, Russell JM, Roberts JT, Cullen MH, Hodson NJ, Jones WG, Yosef H, Duchesne GM, Owen JR, Grosch EJ, Chetiyawardana AD, Reed NS, Widmer B, Stenning SP: Optimal planning target volume for stage I testicular seminoma: A Medical Research Council randomized trial. J Clin Oncol 1999;17:1146–1154.
14 Travis LB, Curtis RE, Storm H, Hall P, Holowaty E, Van Leeuwen FE, Kohler BA, Pukkala E, Lynch CF, Andersson M, Bergfeldt K, Clarke EA, Wiklund T, Stoter G, Gospodarowicz M, Sturgeon J, Fraumeni JF Jr, Boice JD Jr: Risk of second malignant neoplasms among long-term survivors of testicular cancer. J Natl Cancer Inst 1997;89:1429–1439.
15 Warde P, Jewett MAS: Surveillance for stage I testicular seminoma. Is it a good option? Urol Clin North Am 1998;25:425–433.
16 Warszawski N, Schmucking M: Relapses in early-stage testicular seminoma: Radiation therapy versus retroperitoneal lymphadenectomy. Scand J Urol Nephrol 1997;31:335–339.
17 Lashley DB, Lowe BA: A rational approach to managing stage I nonseminomatous germ cell cancer. Urol Clin North Am 1998;25:405–423.
18 Freedman LS, Parkinson MC, Jones WG, Oliver RT, Peckham MJ, Read G, Newlands ES, Williams CJ: Histopathology in the prediction of patients with stage I testicular teratoma treated by orchiectomy alone. Lancet 1987;2: 294–298.
19 Donohue JP, Thornhill JA, Foster RS, Rowland RG, Bihrle R: Clinical stage B nonseminomatous germ cell testis cancer: The Indiana University experience (1965–1989) using routine primary retroperitoneal lymph node dissection. Eur J Cancer 1995;31A:1599–1604.
20 Cullen MH, Stenning SP, Parkinson MC, Fossa SD, Kaye SB, Horwich AH, Harland SJ, Williams MV, Jakes R: Short-course adjuvant chemotherapy in high-risk stage I nonseminomatous germ cell tumours of the testis: A Medical Research Council report. J Clin Oncol 1996;14:1106–1113.
21 Böhlen D, Borner M, Sonntag RW, Fey MF, Studer UE: Long-term results following adjuvant chemotherapy in patients with clinical stage I testicular nonseminomatous malignant germ cell tumors with high risk factors. J Urol 1999;161:1148–1152.
22 Pont J, Albrecht W, Postner G, Sellner F, Angel K, Holtl W: Adjuvant chemotherapy for high risk clinical stage I nonseminomatous testicular germ cell cancer: Long-term results of a prospective trial. J Clin Oncol 1996;14:441–448.
23 Frohlich MW, Small EJ: Stage II nonseminomatous testis cancer: The roles of primary and adjuvant chemotherapy. Urol Clin North Am 1998;25:451–459.
24 Saxman S, Finch D, Gonin R, Einhorn LH: Long-term follow-up of a phase III study of three versus four cycles of bleomycin, etoposide and cisplatin in favorable-prognosis germ-cell tumors: The Indiana University Experience. J Clin Oncol 1998;16:702–706.
25 De Wit R, Stoter G, Kaye SB, Sleijfer DT, Jones WG, ten Bokkel Huinink WW, Rea LA, Collette L, Sylvester R: Importance of bleomycin in combination chemotherapy for good-prognosis testicular nonseminoma: A randomized study of the European Organization for Research and Treatment of Cancer Genitourinary Tract Cancer Cooperative Group. J Clin Oncol 1997;15:1837–1843.
26 Loehrer PJ Sr, Gonin R, Nichols CR, Weathers T, Einhorn LH: Vinblastine plus ifosfamide plus cisplatin as initial salvage therapy in recurrent germ cell tumor. J Clin Oncol 1998; 16:2500–2504.
27 Warde P, Gospodarowicz MK, Panzarella T, Catton CN, Sturgeon JF, Moore M, Goodman P, Jewett MA: Stage I testicular seminoma: Results of adjuvant irradiation and surveillance. J Clin Oncol 1995;13:2255–2262.
28 Fossa SD, Aass N, Kaalhus O: Radiotherapy for testicular seminoma stage I: Treatment results and long-term post-irradiation morbidity in 365 patients. Int J Radiat Oncol Biol Phys 1989;16:383–388.
29 Read G, Stenning SP, Cullen MH, Parkinson MC, Horwich A, Kaye SB, Cook PA: Medical Research Council prospective study of surveillance for stage I testicular teratoma. J Clin Oncol 1992;10:1762–1768.
30 Gels ME, Hoekstra HJ, Sleijfer DT, Marrink J, de Bruijn HW, Molenaar WM, Freling NJ, Droste JH, Schraffordt Koops H: Detection of recurrence in patients with clinical stage I nonseminomatous testicular germ cell tumors and consequences for further follow-up: A single-center 10-year experience. J Clin Oncol 1995; 13:1188–1194.
31 Bukowski RM: Management of advanced and extragonadal germ-cell tumors. Urol Clin North Am 1993;20:153–160.
32 Williams SD, Stablein DM, Einhorn LH, Muggia FM, Weiss RB, Donohue JP, Paulson DF, Brunner KW, Jacobs EM, Spaulding JT: Immediate adjuvant chemotherapy versus observation with treatment at relapse in pathological stage II testicular cancer. N Engl J Med 1987;317:1433–1438.
33 Baniel J, Donohue JP: Cost and risk benefit considerations in low stage (I and II) nonseminomatous testicular tumors. AUA Update Series 1997;26:50– 55.

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