

**American College of Radiology  
ACR Appropriateness Criteria®**

**Clinical Condition:** Staging of Testicular Malignancy

**Variant 1:** Staging testis tumor. Diagnosed by orchiectomy.

Radiologic Procedure	Rating	Comments	RRL*
CT abdomen and pelvis with IV contrast	9		☼ ☼ ☼
X-ray chest	8		☼
CT chest with IV contrast	7	This procedure can be used when combined with staging abdomen and pelvis CT with IV contrast. If ordered alone (ie, not with the CT abdomen and pelvis examination), without contrast is preferred.	☼ ☼ ☼
CT chest without IV contrast	7		☼ ☼ ☼
MRI abdomen and pelvis without and with IV contrast	7	This procedure can be an alternative for CT with comparable performance and the added advantage of no radiation. The disadvantage is longer exam times.	O
CT abdomen and pelvis without IV contrast	6		☼ ☼ ☼
MRI abdomen and pelvis without IV contrast	6		O
FDG-PET/CT whole body	4	This procedure is possibly indicated for follow-up of residual or recurrent seminoma. It has no clear benefit in initial staging over CT.	☼ ☼ ☼ ☼
Tc-99m bone scan whole body	3		☼ ☼ ☼
US abdomen and retroperitoneum	3	This procedure has variable and usually limited visualization of the retroperitoneum.	O
US scrotum	2	This procedure is essential for initial diagnosis but is usually not useful for staging.	O
CT abdomen and pelvis without and with IV contrast	2		☼ ☼ ☼ ☼
CT chest without and with IV contrast	2		☼ ☼ ☼
X-ray intravenous urography	1		☼ ☼ ☼
<b>Rating Scale:</b> 1,2,3 Usually not appropriate; 4,5,6 May be appropriate; 7,8,9 Usually appropriate			<b>*Relative Radiation Level</b>

## STAGING OF TESTICULAR MALIGNANCY

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### **Summary of Literature Review**

#### **Introduction/Background**

Although carcinoma of the testicle is relatively uncommon, representing only 1% of all malignancies occurring in men, it is the most frequent malignancy in men between the ages of 20 and 34, accounting for 10%–14% of cancer incidence in that age group [1]. The National Cancer Institute estimates that there will be about 8430 new cases of testicular cancer in the United States and about 380 deaths from the disease in 2015 [1].

Over 90% of testicular tumors are of germ cell origin and are malignant. Of these, 40% are seminomas. The nonseminomatous tumors are clinically more aggressive and include embryonal cell carcinoma (15%–20%), teratoma (5%–10%), and choriocarcinoma (<1%) [2,3]. Testicular cancer has an excellent prognosis, with 10-year survival rates exceeding 96% [4]. Non-germ-cell tumors are typically benign and have their origin from the Leydig and Sertoli cells or from connective tissue stroma.

Various systems have been used for staging patients with testicular cancer, but most commonly the American Joint Commission on Cancer's system for staging and end-results reporting is used [5].

Testicular tumors metastasize by either the hematogenous or lymphatic route. Most follow the testicular lymphatic drainage alongside the testicular veins to regional lymph node groups. Tumors from the left testis will typically metastasize to the left para-aortic nodal group just below the left renal vein, and right testicular tumors will typically metastasize to the paracaval, precaval, and aortocaval nodes. Crossover of lymphatic involvement may occur in either right-sided or left-sided tumors; however, it is unusual to have contralateral metastasis without involvement of the ipsilateral nodes [6]. Regional lymph node disease can further spread to nonregional lymph node groups, including common iliac, internal iliac, and external iliac nodes, or via the thoracic duct to the left supraclavicular nodes and subsequently to the lungs, constituting distant metastasis [5]. Prior scrotal/inguinal surgery can alter the lymphatic drainage and therefore external iliac and inguinal lymph nodes are considered regional in that context [7].

#### **Tumor Markers**

Tumor markers such as lactate dehydrogenase, alpha fetoprotein (AFP), and beta-human chorionic gonadotropin ( $\beta$ -hCG) are helpful not only in diagnosing patients with testicular tumors but in staging them as well. Approximately 90% of patients with advanced nonseminomatous tumors will have elevated levels of 1 or more of these markers [5].

AFP is elevated in approximately 50%–70% of those with embryonal cell carcinoma, yolk sac carcinoma, or tumors of mixed composition [3,8].  $\beta$ -hCG is elevated in 40%–60% of patients with testicular cancer, including all those with choriocarcinoma, 80% of those with embryonal cell carcinoma, and 10%–25% of those with histologically pure seminoma [9,10]. An elevated AFP is never found in pure seminomas or choriocarcinomas.

Obtaining tumor markers before and after orchiectomy is also very helpful in determining whether any residual disease is present and in planning further therapy. Additionally, tumor markers are essential in the follow-up evaluation to assess both the need for and response to therapy (eg, chemotherapy). Some patients may exhibit an elevation in serum markers at any time despite normal clinical findings and imaging studies. If causes for false-

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positive marker elevation are ruled out, these patients need to be treated for active disease [11]. Significant marker elevation at presentation often portends a worse prognosis for the patient.

A minority of patients with nonseminomatous tumors post-treatment may develop retroperitoneal masses of relatively low attenuation, which represent mature teratoma (differentiated teratoma in the British literature) rather than new or residual lymphadenopathy [12]. This process is referred to as growing teratoma syndrome. It is a benign process; however, the tumors continue to grow over time and may result in significant morbidity due to their bulk. Mature teratoma is treated by surgical resection. Differentiation between mature teratoma and residual or recurrent lymphadenopathy may be possible by measuring serum marker levels. Treatment options may differ depending on the histology of the mass(es). Neither computed tomography (CT) nor magnetic resonance imaging (MRI) can reliably separate the 2 entities, which may sometimes coexist.

### **Overview of Imaging Modalities**

Many imaging studies have been used in assessing patients with testicular tumors. In years past, intravenous urography and lymphangiography [2,13-15] were commonly used for staging purposes; however, with the development of newer techniques the use of these imaging studies is of historical interest for this purpose. Studies used today to assess the retroperitoneum include abdominal ultrasonography (US), CT, MRI, and positron emission tomography imaging with fluorine-18-2-fluoro-2-deoxy-D-glucose (FDG-PET). Studies used to assess pulmonary disease include chest radiography and chest CT. US continues to be used preferentially for assessing the primary tumors.

### **Ultrasonography Scrotum**

Scrotal US is frequently used and should always be the initial imaging modality in assessing patients with scrotal masses. This study can differentiate fluid-filled spermatoceles and hydroceles from solid intratesticular tumors [16]. Oftentimes the diagnosis of a testicular mass is apparent by clinical evaluation, and US can be used for confirmation [17].

CT, MRI, and sometimes PET/CT are used for staging testicular cancer instead of US of the abdomen and retroperitoneum. Relative to those modalities, US of the abdomen and retroperitoneum is less reproducible due to operator dependence and frequently is nondiagnostic due to bowel gas interfering with retroperitoneal node evaluation.

### **Computed Tomography Abdomen and Pelvis**

CT is the most common study used for assessing the retroperitoneum for the presence of metastatic testicular malignancy. It is reproducible and provides excellent imaging of the para-aortic and paracaval regions [18-20]. Difficulties with CT are that many young men have little retroperitoneal fat, which tends to be an impediment to the study, and that CT cannot detect metastatic disease in lymph nodes of normal size. Additionally, inflammatory lymph nodes cannot be differentiated from those that are enlarged secondary to malignant disease [21].

CT interpretation is aided by understanding the lymphatic drainage of the testicles. Node involvement is usually limited to the side of the primary tumor, and crossover is usually present only in the presence of advanced disease. Various benign conditions have also been found to mimic metastases from testicular tumors [22]. Lymph nodes >1 cm in short axis are highly suspicious for metastatic disease, particularly if they are located in the hilar regions of the kidney or in the para-aortic or caval areas. Various studies have established the accuracy of CT in detecting metastatic retroperitoneal lymph nodes, which ranges from 73%–97%. Sensitivity ranges from 65%–96% and specificity from 81%–100% [2,14,15,23-26]. Experience also indicates that accuracy declines in patients with limited disease (stage N1 and stage N2) and also if the upper limit of normal lymph node size is lowered to 4 mm [20,23,25]. Of note, most of these studies are relatively old and were done with single-slice CT. Limited new data suggest similar accuracy with multislice CT compared to single-slice CT [27]. It is important to recognize that a significant percentage of metastatic lymph nodes will be <1 cm, up to 60% in one series [28]. For this reason some authors suggest using a cutoff value of 0.7–0.8 cm in testicular cancer at the expense of reduced specificity [28,29]. These cut-off values are for the short-axis measurement when assessing the likelihood of nodal disease (N0 versus N1 disease); however, when assessing the nodal burden the lymph nodes should be measured in long axis (N1 versus N2 and N3 disease) [7,29]. For reporting purposes as regards staging, providing bidimensional measures for lymph nodes is a useful solution.

Surveillance is becoming the strategy of choice for an increasing number of patients with stage I germ cell tumor, with repeated CT imaging playing a critical role in this strategy [30]. Due to the young age of this patient

population, increasing use of CT has led to concerns regarding the increasing risk of radiation exposure. However, available data are still controversial. Studies have estimated an increased lifetime risk of cancer in patients on surveillance, based on the observed cumulative effective dose [31,32], nevertheless, in a population-based study of patients with stage I testicular cancer, secondary malignancies of the abdomen-pelvis were found to be uncommon, and the risk of secondary cancer did not vary with the amount of diagnostic radiation exposure [33]. The concern about radiation exposure has led to radiation reduction strategies in surveillance protocols, which no longer include chest CT [34], but eliminate pelvic CT except in cases where the pelvis is deemed high risk [35,36], and include the use of a low-dose multidetector CT protocol [37]. The 2014 National Comprehensive Cancer Network guidelines have reduced the maximum number of CTs to 13 scans over 6 years [38].

### **Magnetic Resonance Imaging**

MRI has also been used in the staging of testicular tumors [13,39-42]; evidence indicates that it is comparable to CT [13,40]. It can be useful in patients in whom iodinated contrast cannot be given [43,44]. Diffusion-weighted imaging is a promising technique that can improve identification of lymph nodes based on degree of restricted diffusion; however, it is still limited by significant overlap between benign and malignant lymph nodes [7]. As more attention is turned to radiation exposure in testicular cancer patients undergoing repeated cross-sectional imaging at a young age [31], MRI may represent an advantageous alternative to CT [27,42]. The disadvantages of MRI are longer examination times, high cost, and low availability.

MRI could also be useful as a second-line investigation for preoperative evaluation of the testes when US is inconclusive, with some evidence that it can distinguish germ cell tumors from benign mimics and lymphoma and therefore may have the potential to spare a small subset of patients from getting unnecessary orchiectomies [45-48]. MRI of the brain is indicated in few cases where there is clinical suspicion of brain metastases.

### **Chest Radiography and Computed Tomography Chest**

Many studies have addressed the value of chest radiography in assessing pulmonary metastases [49,50]. These studies indicate that chest radiography alone is satisfactory in the initial staging in patients with testicular malignancies. Chest CT offers little in these patients; however, it is indicated in cases with positive abdominal CT or abnormal chest radiography. Although CT is more sensitive for detecting recurrent disease in the chest [34,51], recent studies indicate that chest radiography is sufficient for follow-up for stage I seminomas [34,36,50,52] and stage I nonseminomas [34,50]. In stage II and higher nonseminomas, chest CT is the study of choice, with no additional value for routine chest radiographs [36,49,53]. There were no studies specifically addressing seminomas with retroperitoneal lymphadenopathy. Therefore, chest CT remains the study of choice for follow-up in those patients.

### **Positron Emission Tomography**

FDG-PET has been used in assessing patients with testicular cancers, but its true value in staging patients has yet to be defined. In initial staging, PET may be only slightly more sensitive than CT [54-59]. FDG-PET is superior to CT in the prediction of viable tumor in postchemotherapy seminoma residuals [60-65], and therefore it can be helpful for follow-up of patients with stage IIB, IIC, and III seminoma who have a residual mass >3 cm and normal markers. In nonseminoma, on the other hand, the value of FDG-PET is limited. It has limited predictive value for evaluation of tumor viability in the residual masses [66] and cannot differentiate mature teratoma from necrosis or fibrosis [34,43,67].

Furthermore, a recent trial by the National Cancer Research Institute's Testis Cancer Clinical Studies Group using FDG-PET in an effort to predict relapse in patients with high-risk stage I nonseminomatous germ cell tumors was terminated early due to unacceptable relapse rates among PET-negative patients [68].

### **Bone Scan**

Bone scans can be useful in assessing early bone lesions before they are detectable by CT [69], although one study suggests that FDG-PET scans are more sensitive and can substitute for conventional bone scans [70].

### **Summary of Recommendations**

- In most instances, the diagnosis of testicular tumors is established with a carefully performed physical examination and scrotal US.
- Tumor markers are useful for determining the presence of residual disease.
- Cross-sectional imaging studies (CT, MRI) are useful in determining the location of metastases.

- FDG-PET scans have a slightly higher sensitivity than CT, but their role in staging testicular cancer has not been determined in a large study. FDG-PET may play a role in follow-up of higher-stage seminoma after chemotherapy.
- Bone scans are useful in the absence of FDG-PET scans and should be used when bone metastases are suspected.

### Summary of Evidence

Of the 70 references cited in the *ACR Appropriateness Criteria® Staging of Testicular Malignancy* document, 63 are categorized as diagnostic references including 12 good quality studies and 18 quality studies that may have design limitations. Additionally, 6 references are categorized as therapeutic references including 1 good quality study and 1 quality study that may have design limitations. There are 37 references that may not be useful as primary evidence. There is 1 reference that is a meta-analysis study.

The 70 references cited in the *ACR Appropriateness Criteria® Staging of Testicular Malignancy* document were published from 1981-2015.

While there are references that report on studies with design limitations, 13 good quality studies provide good evidence.

### Relative Radiation Level Information

Potential adverse health effects associated with radiation exposure are an important factor to consider when selecting the appropriate imaging procedure. Because there is a wide range of radiation exposures associated with different diagnostic procedures, a relative radiation level (RRL) indication has been included for each imaging examination. The RRLs are based on effective dose, which is a radiation dose quantity that is used to estimate population total radiation risk associated with an imaging procedure. Patients in the pediatric age group are at inherently higher risk from exposure, both because of organ sensitivity and longer life expectancy (relevant to the long latency that appears to accompany radiation exposure). For these reasons, the RRL dose estimate ranges for pediatric examinations are lower as compared to those specified for adults (see Table below). Additional information regarding radiation dose assessment for imaging examinations can be found in the *ACR Appropriateness Criteria® Radiation Dose Assessment Introduction* document.

Relative Radiation Level Designations		
Relative Radiation Level*	Adult Effective Dose Estimate Range	Pediatric Effective Dose Estimate Range
○	0 mSv	0 mSv
⊕	<0.1 mSv	<0.03 mSv
⊕ ⊕	0.1-1 mSv	0.03-0.3 mSv
⊕ ⊕ ⊕	1-10 mSv	0.3-3 mSv
⊕ ⊕ ⊕ ⊕	10-30 mSv	3-10 mSv
⊕ ⊕ ⊕ ⊕ ⊕	30-100 mSv	10-30 mSv

\*RRL assignments for some of the examinations cannot be made, because the actual patient doses in these procedures vary as a function of a number of factors (eg, region of the body exposed to ionizing radiation, the imaging guidance that is used). The RRLs for these examinations are designated as “Varies”.

### Supporting Documents

For additional information on the Appropriateness Criteria methodology and other supporting documents go to [www.acr.org/ac](http://www.acr.org/ac).

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The ACR Committee on Appropriateness Criteria and its expert panels have developed criteria for determining appropriate imaging examinations for diagnosis and treatment of specified medical condition(s). These criteria are intended to guide radiologists, radiation oncologists and referring physicians in making decisions regarding radiologic imaging and treatment. Generally, the complexity and severity of a patient's clinical condition should dictate the selection of appropriate imaging procedures or treatments. Only those examinations generally used for evaluation of the patient's condition are ranked. Other imaging studies necessary to evaluate other co-existent diseases or other medical consequences of this condition are not considered in this document. The availability of equipment or personnel may influence the selection of appropriate imaging procedures or treatments. Imaging techniques classified as investigational by the FDA have not been considered in developing these criteria; however, study of new equipment and applications should be encouraged. The ultimate decision regarding the appropriateness of any specific radiologic examination or treatment must be made by the referring physician and radiologist in light of all the circumstances presented in an individual examination.