Complete Summary

GUIDELINE TITLE

Staging of testicular malignancy.

BIBLIOGRAPHIC SOURCE(S)

Papanicolaou N, Francis IR, Baumgarten DA, Bluth EI, Bush WH Jr, Casalino DD, Curry NS, Israel GM, Jafri SZ, Kawashima A, Remer EM, Sandler CM, Spring DB, Fulgham P, Expert Panel on Urologic Imaging. Staging of testicular malignancy. [online publication]. Reston (VA): American College of Radiology (ACR); 2007. 6 p. [60 references]

GUIDELINE STATUS

This is the current release of the guideline.

This guideline updates a previous version: Choyke PL, Bluth EI, Bush WH Jr, Casalino DD, Francis IR, Jafri SZ, Kawashima A, Papanicolaou N, Rosenfield AT, Sandler CM, Segal AJ, Tempany C, Resnick MI, Expert Panel on Urologic Imaging. Staging of testicular malignancy. [online publication]. Reston (VA): American College of Radiology (ACR); 2005. 6 p. [57 references]

The appropriateness criteria are reviewed annually and updated by the panels as needed, depending on introduction of new and highly significant scientific evidence.

COMPLETE SUMMARY CONTENT

SCOPE

DISEASE/CONDITION(S)

Testicular cancer

GUIDELINE CATEGORY

Evaluation

CLINICAL SPECIALTY

Nuclear Medicine
Oncology
Radiology
Urology

INTENDED USERS

Health Plans
Hospitals
Managed Care Organizations
Physicians
Utilization Management

GUIDELINE OBJECTIVE(S)

To evaluate the appropriateness of radiologic procedures for patients with testicular cancer

TARGET POPULATION

Patients with testicular cancer

INTERVENTIONS AND PRACTICES CONSIDERED

1. Computed tomography (CT)
    - Abdomen and pelvis
    - Chest
2. X-ray
    - Chest
    - Abdomen
    - Intravenous urography
3. Magnetic resonance imaging (MRI), abdomen and pelvis
4. Fluorodeoxyglucose positron emission tomography (FDG-PET)
5. Nuclear medicine (NUC), bone scan whole body
6. Invasive (INV) lymphangiography, bipedal, abdomen and pelvis
7. Ultrasound (US)
    - Scrotum (gray-scale)
    - Abdomen, retroperitoneal

MAJOR OUTCOMES CONSIDERED

Utility of radiologic procedures in staging of testicular malignancy

METHODOLOGY

METHODS USED TO COLLECT/SELECT EVIDENCE

Searches of Electronic Databases

DESCRIPTION OF METHODS USED TO COLLECT/SELECT THE EVIDENCE

The guideline developer performed literature searches of peer-reviewed medical journals, and the major applicable articles were identified and collected.

NUMBER OF SOURCE DOCUMENTS

Not stated

METHODS USED TO ASSESS THE QUALITY AND STRENGTH OF THE EVIDENCE

Weighting According to a Rating Scheme (Scheme Not Given)

RATING SCHEME FOR THE STRENGTH OF THE EVIDENCE

Not stated

METHODS USED TO ANALYZE THE EVIDENCE

Systematic Review with Evidence Tables

DESCRIPTION OF THE METHODS USED TO ANALYZE THE EVIDENCE

One or two topic leaders within a panel assume the responsibility of developing an evidence table for each clinical condition, based on analysis of the current literature. These tables serve as a basis for developing a narrative specific to each clinical condition.

METHODS USED TO FORMULATE THE RECOMMENDATIONS

Expert Consensus (Delphi)

DESCRIPTION OF METHODS USED TO FORMULATE THE RECOMMENDATIONS

Since data available from existing scientific studies are usually insufficient for meta-analysis, broad-based consensus techniques are needed for reaching agreement in the formulation of the appropriateness criteria. The American College of Radiology (ACR) Appropriateness Criteria panels use a modified Delphi technique to arrive at consensus. Serial surveys are conducted by distributing questionnaires to consolidate expert opinions within each panel. These questionnaires are distributed to the participants along with the evidence table and narrative as developed by the topic leader(s). Questionnaires are completed

by the participants in their own professional setting without influence of the other members. Voting is conducted using a scoring system from 1 to 9, indicating the least to the most appropriate imaging examination or therapeutic procedure. The survey results are collected, tabulated in anonymous fashion, and redistributed after each round. A maximum of three rounds is conducted and opinions are unified to the highest degree possible. Eighty percent agreement is considered a consensus. This modified Delphi technique enables individual, unbiased expression, is economical, easy to understand, and relatively simple to conduct.

If consensus cannot be reached by this Delphi technique, the panel is convened and group consensus techniques are utilized. The strengths and weaknesses of each test or procedure are discussed and consensus reached whenever possible. If "No consensus" appears in the rating column, reasons for this decision are added to the comment sections.

RATING SCHEME FOR THE STRENGTH OF THE RECOMMENDATIONS

Not applicable

COST ANALYSIS

A formal cost analysis was not performed and published cost analyses were not reviewed.

METHOD OF GUIDELINE VALIDATION

Internal Peer Review

DESCRIPTION OF METHOD OF GUIDELINE VALIDATION

Criteria developed by the Expert Panels are reviewed by the American College of Radiology (ACR) Committee on Appropriateness Criteria.

RECOMMENDATIONS

MAJOR RECOMMENDATIONS

ACR Appropriateness Criteria®

Clinical Condition: Staging of Testicular Malignancy

Variant: Testis tumor (diagnosed by orchiectomy)

Radiologic Procedure	Rating	Comments	RRL*
CT abdomen and pelvis	9		High
X-ray chest	8		Min

Radiologic Procedure	Rating	Comments	RRL*
CT chest	7		Med
MRI abdomen and pelvis	5	Alternative method of imaging nodes if CT is indeterminate or technically unsatisfactory. See comments regarding contrast in text under "Anticipated Expectations."	None
FDG-PET whole body	4	Most likely indicated for follow-up of residual or recurrent disease/differentiation of residual nonseminomatous tumor from mature teratoma.	High
NUC bone scan whole body	3		Med
US abdomen retroperitoneal	3	In patients with lean or average body habitus it is worth trying to visualize the retroperitoneum.	None
INV lymphangiography abdomen and pelvis bipedal	2		IP
US scrotum gray-scale only	2	Essential for initial diagnosis, usually not useful for staging. If questionable for opposite testes.	None
X-ray abdomen	1		Low
X-ray intravenous urography	1		Low
Rating Scale: 1=Least appropriate, 9=Most appropriate			***Relative Radiation Level**

Note: Abbreviations used in the table are listed at the end of the "Major Recommendations" field.

Summary of the Literature

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 35 and accounts for 11% to 14% of all deaths due to cancer in the 25 to 34 year age group. The American Cancer Society estimates that in 2005, over 8,000 men will be diagnosed with the disease and that the number of deaths secondary to testicular cancer will be 390.

Over 90% of testicular tumors are of germ cell origin and are malignant. Of these, 40% are seminoma. The nonseminomatous tumors include embryonal cell carcinoma (15%–20%), teratoma (5%–10%) and choriocarcinoma (less than 1%). Non-germ-cell tumors are typically benign and have their origin from the Leydig and Sertoli cells or from connective tissue stroma.

Various staging systems have been used for staging patients with testicular cancer, but most commonly the American Joint Commission on Cancer's staging and end-results reporting are used (see Appendix 1 in the original guideline document).

Testicular tumors spread or metastasize by either the hematogenous or lymphatic route. Most follow the regional lymphatic chain alongside the spermatic vessels. Typically, the first order of metastases is the "sentinel" lymph node, which on the left is located at the renal hilar region and on the right in the paracaval region below the renal artery and vein. Left-sided tumors typically spread to the periaortic nodes and preaortic nodes, and right-sided tumors most commonly involve interaortocaval, precaval, and preaortic nodes. Crossover is not uncommon, but typically is from the right to the left. Further drainage is through the thoracic duct, resulting in more widespread metastases.

Tumor Markers

Tumor markers such as alpha-fetoprotein (AFP) and beta-human chorionic gonadotropin (β-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 one or both of these markers.

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

The obtaining of 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 (e.g., chemotherapy).

A number 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 lymphadenopathy, new or residual. This process is benign; however, the tumors continue to grow over time and may result in significant morbidity due to its 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). CT and, often, MRI cannot reliably separate the two entities, which may sometimes coexist.

Imaging Studies

Many imaging studies have been used in assessing patients with testicular tumors. In years past, intravenous urography was commonly used for staging purposes; however, with the development of newer techniques the use of this imaging study is of historical interest for this purpose. Studies used today to assess the retroperitoneum include abdominal ultrasonography (US), CT, MRI, and pedal lymphangiography. Studies used to assess pulmonary disease include chest x-ray and chest CT. US continues to be used preferentially for assessing the primary tumors.

Ultrasonography

Scrotal ultrasonography is frequently used, and should always be the initial imaging modality, in assessing patients with scrotal masses. This study can often differentiate fluid-filled spermatoceles and hydroceles from solid intratesticular tumors. Oftentimes, the diagnosis is apparent by clinical evaluation, and ultrasound can be used for confirmation and for local staging. The finding of testicular microlithiasis should increase the suspicion of testicular malignancy, and if none is found periodic follow-up is recommended.

With the development of newer imaging studies, (e.g., CT) staging with US has found little application in the assessment of patients with some metastatic testicular tumors to the retroperitoneum. Unfortunately, US is operator-dependent, making the uniformity and the reproducibility of the study less than would be desirable. Additionally, because of the interference of overlying intestinal gas and obesity, this study is nondiagnostic in approximately 15%–17% of patients.

Computed Tomography

CT is the most common study used for assessing the retroperitoneum for the presence of metastatic testicular malignancy. This study is noninvasive and reproducible and provides excellent imaging of the periaortic and pericaval regions. 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 the presence of metastatic disease in lymph nodes of normal size. Additionally, inflammatory lymph nodes cannot be differentiated from those that are enlarged secondary to malignant disease.

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. Lymph nodes larger than 1 cm are suspicious for metastatic disease, particularly if they are located in the hilar regions of the kidney or in the periaortic or caval areas. Various studies have established the accuracy of CT in detecting metastatic retroperitoneal lymph nodes, which ranges from 73% to 97%. Sensitivity ranges from 65% to 96% and specificity from 81% to 100%. 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.

Lymphangiography

Lymphangiography is now rarely used because of its disadvantages, which include its invasiveness, its inability to opacify the sentinel lymph node, and its inability to demonstrate the upper limits of involvement in patients with extensive disease. The accuracy of bipedal lymphangiography has been shown to be comparable to that of CT and varies from 62% to 89%. Sensitivity ranges from 54% to 90% and specificity from 67% to 100%. Studies have also indicated that a combination of lymphangiography and CT improves accuracy, but evidence indicates that this approach is not cost-effective. Magnetic resonance lymphangiography may have potential in the future, but experience is still too limited and the agent, ferumoxtran, has not yet been approved by the FDA for clinical use.

Magnetic Resonance Imaging

Magnetic resonance imaging has also been used in the staging of testicular tumors; however, evidence indicates that it is comparable to CT. MRI does offer an advantage, allowing for the differentiation of blood vessels from lymph nodes, and it may also have the potential of distinguishing residual tumor from fibrosis.

Chest X-Ray

Many studies have addressed the value of chest x-ray in assessing pulmonary metastases. These studies indicate that chest x-ray alone is satisfactory in the initial staging in patients with testicular malignancies. Chest CT offers little in these patients; however, it may offer slight benefit in those with more advanced disease. More recent studies have suggested that initial and recurrent disease in the chest can be detected on chest CT and that routine chest x-rays have a very low yield for early disease and are not considered useful for initial staging for follow-up after therapy.

Radionuclide Imaging

Radionuclide studies have limited value for detecting retroperitoneal metastases. Radioimmunoassays for β-hCG and AFP the labeled antibodies to these markers, show promise, but further experience with them is needed. Gallium scintigraphy has also been used to detect metastatic disease, but clinical experience is limited. Positron-emission tomography (PET) imaging with 2-(F-18)-fluoro-2-deoxy-D-glucose (FDG) has been used in assessing patients with testicular cancers and, though its true value in staging patients has yet to be defined, initial experience has been promising. In initial staging PET has proven only slightly more sensitive than CT. Its use in follow-up for residual masses is more controversial, with some authors recommending it routinely to distinguish mature teratoma from residual disease and others seeing no benefit in assessing residual masses. The study may be most efficacious for assessing the presence of residual disease after chemotherapy.

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

Summary

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, and cross-sectional imaging studies (CT, MRI) are useful in determining the location of metastases. FDG-PET scans are have a slightly higher sensitivity than CT, but their role in staging testicular cancer has not been determined in a large study. Bone scans are useful in the absence of FDG-PET scans and should be used when bone metastases are suspected.

Anticipated Exceptions

Nephrogenic systemic fibrosis (NSF, also known as nephrogenic fibrosing dermopathy) was first identified in 1997 and has recently generated substantial concern among radiologists, referring doctors and lay people. Until the last few years, gadolinium-based MR contrast agents were widely believed to be almost universally well tolerated, extremely safe and non-nephrotoxic, even when used in patients with impaired renal function. All available experience suggests that these agents remain generally very safe, but recently some patients with renal failure who have been exposed to gadolinium contrast agents (the percentage is unclear) have developed NSF, a syndrome that can be fatal. Further studies are necessary to determine what the exact relationships are between gadolinium-containing contrast agents, their specific components and stoichiometry, patient renal function and NSF. Current theory links the development of NSF to the administration of relatively high doses (e.g., >0.2mM/kg) and to agents in which the gadolinium is least strongly chelated. The FDA has recently issued "black box" warning concerning these contrast agents (http://www.fda.gov/cder/drug/InfoSheets/HCP/gcca_200705HCP.pdf).

This warning recommends that, until further information is available, gadolinium contrast agents should not be administered to patients with either acute or significant chronic kidney disease (estimated GFR <30 mL/min/1.73m^2), recent liver or kidney transplant or hepato-renal syndrome, unless a risk-benefit assessment suggests that the benefit of administration in the particular patient clearly outweighs the potential risk(s).

Abbreviations

- CT, computed tomography
- FDG-PET, fluorodeoxyglucose positron emission tomography
- INV, invasive
- IP, in progress
- IVU, intravenous urography
- Med, medium
- Min, minimal
- MRI, magnetic resonance imaging
- NUC, nuclear medicine
- US, ultrasound

CLINICAL ALGORITHM(S)

None provided

EVIDENCE SUPPORTING THE RECOMMENDATIONS

TYPE OF EVIDENCE SUPPORTING THE RECOMMENDATIONS

The recommendations are based on analysis of the current literature and expert panel consensus.

BENEFITS/HARMS OF IMPLEMENTING THE GUIDELINE RECOMMENDATIONS

POTENTIAL BENEFITS

Selection of appropriate radiologic imaging procedures for evaluation of patients with testicular malignancy

POTENTIAL HARMS

- Computed tomography (CT) 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.
- Lymphangiography is used with decreasing frequency because of its disadvantages, which include its invasiveness, its inability to opacify the sentinel lymph node, and its inability to demonstrate the upper limits of involvement in patients with extensive disease.
- The relative radiation level is high for computed tomography (CT) of the abdomen and pelvis and fluorodeoxyglucose positron emission tomography (FDG-PET) of the whole body; medium for CT of the chest and nuclear medicine (NUC) bone scan of the whole body; and low for X-ray of the abdomen and X-ray intravenous urography.

QUALIFYING STATEMENTS

QUALIFYING STATEMENTS

An American College of Radiology (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 radiologist, radiation oncologist, 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 exams 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 U.S. Food and Drug Administration (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.

IMPLEMENTATION OF THE GUIDELINE

DESCRIPTION OF IMPLEMENTATION STRATEGY

An implementation strategy was not provided.

IMPLEMENTATION TOOLS

Personal Digital Assistant (PDA) Downloads

For information about availability, see the "Availability of Companion Documents" and "Patient Resources" fields below.

INSTITUTE OF MEDICINE (IOM) NATIONAL HEALTHCARE QUALITY REPORT CATEGORIES

IOM CARE NEED

Living with Illness

IOM DOMAIN

Effectiveness

IDENTIFYING INFORMATION AND AVAILABILITY

BIBLIOGRAPHIC SOURCE(S)

Papanicolaou N, Francis IR, Baumgarten DA, Bluth EI, Bush WH Jr, Casalino DD, Curry NS, Israel GM, Jafri SZ, Kawashima A, Remer EM, Sandler CM, Spring DB, Fulgham P, Expert Panel on Urologic Imaging. Staging of testicular malignancy. [online publication]. Reston (VA): American College of Radiology (ACR); 2007. 6 p. [60 references]

ADAPTATION

Not applicable: The guideline was not adapted from another source.

DATE RELEASED

1996 (revised 2007)

GUIDELINE DEVELOPER(S)

American College of Radiology - Medical Specialty Society

SOURCE(S) OF FUNDING

American College of Radiology (ACR) provided the funding and the resources for these ACR Appropriateness Criteria®.

GUIDELINE COMMITTEE

Committee on Appropriateness Criteria, Expert Panel on Urologic Imaging

COMPOSITION OF GROUP THAT AUTHORED THE GUIDELINE

Panel Members: Nicholas Papanicolaou, MD; Isaac R. Francis, MD; Deborah A. Baumgarten, MD, MPH; Edward I. Bluth, MD; William H. Bush, Jr., MD; David D. Casalino, MD; Nancy S. Curry, MD; Gary M. Israel, MD; S. Zafar H. Jafri, MD; Akira Kawashima, MD; Erick M. Remer, MD; Carl M. Sandler, MD; David B. Spring, MD; Pat Fulgham, MD

FINANCIAL DISCLOSURES/CONFLICTS OF INTEREST

Not stated

GUIDELINE STATUS

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The appropriateness criteria are reviewed annually and updated by the panels as needed, depending on introduction of new and highly significant scientific evidence.

GUIDELINE AVAILABILITY

Electronic copies: Available in Portable Document Format (PDF) from the American College of Radiology (ACR) Web site.

ACR Appropriateness Criteria® *Anytime*, *Anywhere*™ (PDA application). Available from the ACR Web site.

Print copies: Available from the American College of Radiology, 1891 Preston White Drive, Reston, VA 20191. Telephone: (703) 648-8900.

AVAILABILITY OF COMPANION DOCUMENTS

The following are available:

- ACR Appropriateness Criteria®. Background and development. Reston (VA): American College of Radiology; 2 p. Electronic copies: Available in Portable Document Format (PDF) from the American College of Radiology (ACR) Web site.
- ACR Appropriateness Criteria®. Relative radiation level information. Reston (VA): American College of Radiology; 2 p. Electronic copies: Available in Portable Document Format (PDF) from the American College of Radiology (ACR) Web site.

PATIENT RESOURCES

None available

NGC STATUS

This NGC summary was completed by ECRI on March 7, 2006. This NGC summary was updated by ECRI Institute on December 5, 2007.

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