# Staging of Testicular Malignancy

## EVIDENCE TABLE

<table>
<thead>
<tr>
<th>Reference</th>
<th>Study Type</th>
<th>Patients/Events</th>
<th>Study Objective (Purpose of Study)</th>
<th>Study Results</th>
<th>Study Quality</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Siegel RL, Miller KD, Jemal A. Cancer statistics, 2015. CA Cancer J Clin. 2015;65(1):5-29.</td>
<td>Review/Other-Tx</td>
<td>N/A</td>
<td>To provide the expected numbers of new cancer cases and deaths in 2015 nationally and for each state, as well as a comprehensive overview of cancer incidence, mortality, and survival rates and trends using the most current population-based data. The article also estimates the total number of deaths averted nationally during the past 2 decades and by state in 2011 as a result of the continual decline in cancer death rates and present actual number of deaths reported in 2011 by age for the 10 leading causes of death and for the 5 leading causes of cancer death.</td>
<td>Cancer death rates have been continuously declining for the past 2 decades. Overall, the risk of dying from cancer decreased by 22% between 1991 and 2011. Regionally, progress has been most rapid for residents of the Northeast, among whom death rates have declined by 25% to 30%, and slowest in the South, where rates declined by about 15%. Further reductions in cancer death rates can be accelerated by applying existing cancer control knowledge across all segments of the population, with an emphasis on those in the lowest socioeconomic bracket and other disadvantaged populations.</td>
<td>4</td>
</tr>
<tr>
<td>2. Epstein BE, Order SE, Zinreich ES. Staging, treatment, and results in testicular seminoma. A 12-year report. Cancer 1990; 65(3):405-411.</td>
<td>Observational-Tx</td>
<td>61 patients</td>
<td>A 12-year report on staging, treatment, and results in testicular seminoma.</td>
<td>Median follow-up for these patients is 5.5 years. Overall actuarial survival (Kaplan-Meier method) was 97% at 5 years and 92% at 10 years. 5-year survival corrected for intercurrent disease was 100% for stage I, 100% for stage IIA, and 2 of 3 in stage IIB patients. There were 2 distant treatment failures among the entire cohort. 1 patient who had stage I disease was salvaged with local-field radiation and chemotherapy and is now without evidence of disease for 6 years. The second patient with stage IIB seminoma receiving the same treatments disseminated and died. There were no significant acute toxicities or serious complications. In summary, proper staging with information gained from lymphangiogram and adequate radiation dose led to a 92% 10-year disease-free survival.</td>
<td>3</td>
</tr>
</tbody>
</table>

* See Last Page for Key

Yacoub/Oto

Page 1
### EVIDENCE TABLE

<table>
<thead>
<tr>
<th>Reference</th>
<th>Study Type</th>
<th>Patients/Events</th>
<th>Study Objective (Purpose of Study)</th>
<th>Study Results</th>
<th>Study Quality</th>
</tr>
</thead>
<tbody>
<tr>
<td>4. Brenner H, Gondos A, Arndt V. Recent major progress in long-term cancer patient survival disclosed by modeled period analysis. <em>J Clin Oncol</em> 2007; 25(22):3274-3280.</td>
<td>Review/Other-Dx</td>
<td>N/A</td>
<td>To disclose most recent trends in long-term cancer patient survival.</td>
<td>Statistically significant and partly very substantial improvement in 5- and 10-year relative survival in the 1998 to 2003 period was seen for 14 of 24 of the assessed common forms of cancer, including breast and colorectal cancer. Improvement was most pronounced for patients with regional tumor spread and somewhat less so for patients with localized tumors, whereas hardly any improvement was achieved for patients with distant tumor spread. Study analysis discloses further major improvement in prognosis for most, but not all forms of cancer in recent years. The largest contribution to this improvement comes from improved prognosis of patients with regional tumor spread.</td>
<td>4</td>
</tr>
<tr>
<td>6. Pano B, Sebastia C, Bunesch L, et al. Pathways of lymphatic spread in male urogenital pelvic malignancies. <em>Radiographics</em> 2011; 31(1):135-160.</td>
<td>Review/Other-Dx</td>
<td>N/A</td>
<td>To describe the anatomy and nomenclature of the iliopelvic and para-aortic lymph nodes and outline common pathways of metastasis from tumors of the male urogenital system to these regional nodes. The advantages and limitations of anatomic and functional imaging techniques for the detection and classification of nodal disease are discussed in detail.</td>
<td>Functional imaging techniques, such as diffusion-weighted MRI performed with or without a lymphotropic contrast agent and PET, may allow a more accurate nodal assessment based on molecular or physiologic activity.</td>
<td>4</td>
</tr>
</tbody>
</table>
### Reference Table

<table>
<thead>
<tr>
<th>Reference</th>
<th>Study Type</th>
<th>Patients/Events</th>
<th>Study Objective (Purpose of Study)</th>
<th>Study Results</th>
<th>Study Quality</th>
</tr>
</thead>
<tbody>
<tr>
<td>9. Mumperow E, Hartmann M. Spermatic cord beta-human chorionic gonadotropin levels in seminoma and their clinical implications. <em>J Urol</em> 1992; 147(4):1041-1043.</td>
<td>Review/Other-Dx</td>
<td>147 patients</td>
<td>To determine the biological significance and treatment of pure seminoma associated with the serological establishment of beta-human chorionic gonadotropin.</td>
<td>Most seminomas produce beta-human chorionic gonadotropin even if it is not detectable in the cubital vein. The presence of this marker in patients with pure seminoma is not an indication of greater tumor aggressiveness but of tumor mass.</td>
<td>4</td>
</tr>
<tr>
<td>10. Vugrin D, Friedman A, Whitmore WF, Jr. Correlation of serum tumor markers in advanced germ cell tumors with responses to chemotherapy and surgery. <em>Cancer</em> 1984; 53(6):1440-1445.</td>
<td>Observational-Tx</td>
<td>103 patients</td>
<td>To examine remission rates induced by chemotherapy alone or by combined chemotherapy and surgery.</td>
<td>Patients with very high (&gt;1000 ng/mL) serum alpha-fetoprotein or HCG responded poorly to chemotherapy (complete response, 17%). Patients with both minimal and advanced metastatic disease had higher complete response rates if they had serum tumor marker levels below rather than above 1000 ng/mL.</td>
<td>2</td>
</tr>
<tr>
<td>11. Bosl GJ, Motzer RJ. Testicular germ-cell cancer. <em>N Engl J Med</em> 1997; 337(4):242-253.</td>
<td>Review/Other-Dx</td>
<td>N/A</td>
<td>Review of the classification of disease stages and staging of testicular germ-cell cancer.</td>
<td>CT of the chest is required if mediastinal, hilar, or lung parenchymal disease is suspected. CT or MRI of the brain is performed in patients with neurologic signs or symptoms.</td>
<td>4</td>
</tr>
<tr>
<td>12. Andre F, Fizazi K, Culine S, et al. The growing teratoma syndrome: results of therapy and long-term follow-up of 33 patients. <em>Eur J Cancer</em> 2000; 36(11):1389-1394.</td>
<td>Review/Other-Tx</td>
<td>33 patients</td>
<td>A report on the authors’ experience of patients with growing teratoma syndrome defined according to the Logothetis’ criteria.</td>
<td>A mature teratoma component was found in 86% of the primary GCT. 3 male patients (10%) had a complication at diagnosis of growing teratoma syndrome. 1 male patient (4%) having undergone complete resection (n=24) had a recurrent growing teratoma syndrome, compared with all but 1 patient (83%) in whom resection was partial (n=6) (P&lt;0.001). 2 (8%) and 3 (50%) male patients treated with complete and partial resection subsequently developed a malignant NSGCT respectively (P=0.01). 2 female patients treated with partial resection presented a recurrent growing teratoma syndrome. 1 of them died of this recurrent growing teratoma syndrome. Growing teratoma syndrome is an entity in its own right with respect to complications and the natural history of the disease. Complete surgical resection is the treatment of choice for growing teratoma syndrome.</td>
<td>4</td>
</tr>
</tbody>
</table>
## Staging of Testicular Malignancy

### EVIDENCE TABLE

<table>
<thead>
<tr>
<th>Reference</th>
<th>Study Type</th>
<th>Patients/Events</th>
<th>Study Objective (Purpose of Study)</th>
<th>Study Results</th>
<th>Study Quality</th>
</tr>
</thead>
<tbody>
<tr>
<td>13. 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. <em>J Comput Assist Tomogr</em> 1984; 8(4):709-719.</td>
<td>Observational-Dx</td>
<td>25 patients</td>
<td>To compare CT and nuclear MR in the evaluation of metastatic retroperitoneal lymphadenopathy from testicular carcinoma.</td>
<td>CT correctly predicted the presence or absence of adenopathy in 88% and assigned the correct stage in 84%. Nuclear MR had comparable figures of 84% and 80%.</td>
<td>3</td>
</tr>
<tr>
<td>14. Husband JE, Barrett A, Peckham MJ. Evaluation of computed tomography in the management of testicular teratoma. <em>Br J Urol</em> 1981; 53(2):179-183.</td>
<td>Review/Other-Dx</td>
<td>100 patients</td>
<td>To define the role of CT in staging patients with testicular teratoma and comparing these findings with other staging modalities.</td>
<td>CT led to a change in stage in 12% of patients compared to conventional techniques (US, lymphangiography, CXR, whole lung tomography, intravenous urography, liver-spleen scanning. Although these tumors are rare, their pattern of metastasis to the retroperitoneum, mediastinum, lungs and liver is consistent. Thus the value of CT scanning can be tested in all of these sites in each patient and the indications for scanning clearly defined.</td>
<td>4</td>
</tr>
<tr>
<td>15. Richie JP, Garnick MB, Finberg H. Computerized tomography: how accurate for abdominal staging of testis tumors? <em>J Urol</em> 1982; 127(4):715-717.</td>
<td>Observational-Dx</td>
<td>30 patients</td>
<td>A prospective study to determine the ability of CT to predict correctly the presence of retroperitoneal lymphadenopathy.</td>
<td>Sensitivity 90%, for an over-all accuracy of 73%. 7/16 CT scans interpreted as normal were false negative. False negative rate limits the reliability of a negative CT to exclude metastases. The CT scan, when positive, is highly likely to detect metastatic nodal involvement. However, the false negative rate, even in patients with tumor-filled lymph nodes 2 to 3 cm in diameter, limits the reliability of a negative CT scan to exclude metastases. Technological improvements are needed to refine the technique and, thus, to reduce the false negative rate.</td>
<td>3</td>
</tr>
<tr>
<td>17. Horstman WG, Melson GL, Middleton WD, Andriole GL. Testicular tumors: findings with color Doppler US. <em>Radiology</em> 1992; 185(3):733-737.</td>
<td>Review/Other-Dx</td>
<td>28 patients</td>
<td>To determine the appearance of testicular tumors with color Doppler US.</td>
<td>Color Doppler US scanning has only a limited role in the evaluation of testicular tumors.</td>
<td>4</td>
</tr>
</tbody>
</table>
### Staging of Testicular Malignancy

**EVIDENCE TABLE**

<table>
<thead>
<tr>
<th>Reference</th>
<th>Study Type</th>
<th>Patients/Events</th>
<th>Study Objective (Purpose of Study)</th>
<th>Study Results</th>
<th>Study Quality</th>
</tr>
</thead>
<tbody>
<tr>
<td>18. Dixon AK, Ellis M, Sikora K. Computed tomography of testicular tumours: distribution of abdominal lymphadenopathy. <em>Clin Radiol</em> 1986; 37(6):519-523.</td>
<td>Review/Other-Dx</td>
<td>145 total patients; 55 patients with definite evidence of nodal enlargement on CT</td>
<td>To assess testicular tumors referred for staging by CT.</td>
<td>Findings which correlate well with data from anatomical, surgical and direct lymphographic studies should assist in the CT interpretation of equivocal nodal enlargement and aid decisions on the optimal interval for CT follow-up during surveillance.</td>
<td>4</td>
</tr>
<tr>
<td>19. MacVicar D. Staging of testicular germ cell tumours. <em>Clin Radiol</em> 1993; 47(3):149-158.</td>
<td>Review/Other-Dx</td>
<td>Referred to 1,000+ patients from 1976-present</td>
<td>To review radiological staging methods for testicular GCTs.</td>
<td>Whole body CT and CXR are the central and essential investigations, and subsidiary techniques such as MRI, US and lymphography may be of benefit in individual patients.</td>
<td>4</td>
</tr>
<tr>
<td>20. Rowland RG, Weisman D, Williams SD, Einhorn LH, Klatte EC, Donohue JP. Accuracy of preoperative staging in stages A and B nonseminomatous germ cell testis tumors. <em>J Urol</em> 1982; 127(4):718-720.</td>
<td>Observational-Dx</td>
<td>64 patients</td>
<td>To assess the value of US and CT when combined with tumor marker determination in patients with nonseminomatous testes tumors.</td>
<td>Correct staging in 24/32 patients with stage A 21/32 with stage B. Overall, the correct results were obtained in 61% of the patients with alpha-fetoprotein, 64% with beta-human chorionic gonadotropin, 53% with US and 67% with CT. US is not of additional benefit.</td>
<td>3</td>
</tr>
<tr>
<td>21. McMahon CJ, Rofsky NM, Pedrosa I. Lymphatic metastases from pelvic tumors: anatomic classification, characterization, and staging. <em>Radiology</em> 2010; 254(1):31-46.</td>
<td>Review/Other-Dx</td>
<td>N/A</td>
<td>To illustrate the anatomic location and the nomenclature of pelvic lymph node groups and to review the patterns of nodal spread from individual pelvic tumors with a description of the effect of the location and number of nodal metastases on staging and management.</td>
<td>The spread of pelvic tumors to lymph nodes is an important means of tumor dissemination and substantially affects prognosis and management.</td>
<td>4</td>
</tr>
<tr>
<td>22. Dunnick NR, Javadpour N. Value of CT and lymphography: distinguishing retroperitoneal metastases from nonseminomatous testicular tumors. <em>AJR</em> 1981; 136(6):1093-1099.</td>
<td>Observational-Dx</td>
<td>63 consecutive patients</td>
<td>To prospectively examine patients for para-aortic metastases before undergoing a staging laparotomy with lymphadenectomies or biopsies to assess the value of CT and lymphography.</td>
<td>Accuracies were 74% for CT, 82% for lymphography, and 69% for inferior vena cava cavography. A combination of lymphography followed by CT provided the most accurate assessment of para-aortic metastases.</td>
<td>2</td>
</tr>
</tbody>
</table>
### Staging of Testicular Malignancy

**EVIDENCE TABLE**

<table>
<thead>
<tr>
<th>Reference</th>
<th>Study Type</th>
<th>Patients/Events</th>
<th>Study Objective (Purpose of Study)</th>
<th>Study Results</th>
<th>Study Quality</th>
</tr>
</thead>
<tbody>
<tr>
<td>23. Hilton S, Herr HW, Teitcher JB, Begg CB, Castellino RA. CT detection of retroperitoneal lymph node metastases in patients with clinical stage I testicular nonseminomatous germ cell cancer: assessment of size and distribution criteria. <em>AJR</em> 1997; 169(2):521-525.</td>
<td>Observational-Dx</td>
<td>70 patients; 3 observers</td>
<td>To retrospectively determine the accuracy of CT for revealing retroperitoneal lymph node metastases in patients with clinical stage I testicular nonseminomatous germ cell cancer: assessment of size and distribution criteria.</td>
<td>Using a criterion of 10 mm or larger for metastases, sensitivity was 37% and specificity 100%; with a 4 mm criterion, the sensitivity was 93% and the specificity 58%. False-negative rates were decreased from 63% using a size criterion of 10 mm to as low as 7% using a size criterion of 4 mm, with a corresponding decrease in specificity. Lymph nodes measuring larger than or equal to 4 mm, especially those located anterior to the mid portion of the aorta, should raise a suspicion of metastases.</td>
<td>2</td>
</tr>
<tr>
<td>24. Jing B, Wallace S, Zornoza J. Metastases to retroperitoneal and pelvic lymph nodes: computed tomography and lymphangiography. <em>Radiol Clin North Am</em> 1982; 20(3):511-530.</td>
<td>Review/Other-Dx</td>
<td>N/A</td>
<td>To review roles of CT and lymphangiography in the evaluation of retroperitoneal and pelvic lymph node metastases.</td>
<td>CT and lymphangiography are complementary. Lymphangiography is recommended for the evaluation of the internal architecture of the lymph node while CT is indicated to visualize large nonopacified masses. CT can be a substitute when lymphangiography is contraindicated.</td>
<td>4</td>
</tr>
<tr>
<td>25. Strohmeyer T, Geiser M, Ackermann R, Mumperow E, Hartmann M. Value of computed tomography in the staging of testicular tumors. <em>Urol Int</em> 1988; 43(4):198-200.</td>
<td>Observational-Dx</td>
<td>56 patients; 2 groups of 28 patients</td>
<td>To determine the value of CT for the exact staging of testicular tumors.</td>
<td>Stage found by CT was correct but 3 (5%) false-positive and 13 false-negative results were obtained. CT should be restricted to certain centers with guaranteed long-term standardized patient observation and extremely high patient compliance.</td>
<td>4</td>
</tr>
</tbody>
</table>
### Staging of Testicular Malignancy

**EVIDENCE TABLE**

<table>
<thead>
<tr>
<th>Reference</th>
<th>Study Type</th>
<th>Patients/Events</th>
<th>Study Objective (Purpose of Study)</th>
<th>Study Results</th>
<th>Study Quality</th>
</tr>
</thead>
<tbody>
<tr>
<td>27. Hansen J, Jurik AG. Diagnostic value of multislice computed tomography and magnetic resonance imaging in the diagnosis of retroperitoneal spread of testicular cancer: a literature review. <em>Acta Radiol</em> 2009; 50(9):1064-1070.</td>
<td>Review/Other-Dx</td>
<td>44 publications</td>
<td>To analyze whether there is evidence to recommend a substitution of multislice CT with MRI in the diagnosis of retroperitoneal spread of testicular cancer.</td>
<td>None of the publications reviewed encompassed diagnostic specificity and sensitivity of multislice CT, and they lacked systematic comparison of multislice CT and MRI. Only 1 study included sensitivity and specificity of MRI compared to single-slice CT. Both methods had sensitivity and specificity of approximately 70%. The literature review did not reveal valid data regarding diagnostic accuracy of MRI compared with multislice CT for diagnosing retroperitoneal spread of testicular cancer. A prospective blinded comparative study is needed to provide valid evidence.</td>
<td>4</td>
</tr>
<tr>
<td>28. Hudolin T, Kastelan Z, Knezevic N, Goluza E, Tomas D, Coric M. Correlation between retroperitoneal lymph node size and presence of metastases in nonseminomatous germ cell tumors. <em>Int J Surg Pathol.</em> 2012;20(1):15-18.</td>
<td>Observational-Dx</td>
<td>85 patients</td>
<td>To investigate/correlate the lymph node size and presence of metastases in them in order to find out how sure one can be when deciding on treatment options based on the lymph node size.</td>
<td>A total of 1139 lymph nodes have been removed and in 27 (31.8%) patients, metastases in 1 or more lymph nodes were detected. There were 338 (29.7%) hilar, 259 (22.7%) para-aortic, 221 (19.4%) interaortocaval, 171 (15%) paracaval, 133 (11.7%) preaortic and 17 (1.5%) precaval lymph nodes. The total number of lymph nodes with metastases was 74 (6.5%), and 1065 (93.5%) nodes did not have any metastases. The average size of a lymph node with metastases was 1.05 (0.3–3), and without metastases it was 0.55 (0.1–2.5) cm, ($P&lt;0.001$). If we use $&gt;1$ cm size of a lymph node as a “cut-off” value for enlargement and presence of metastases, 60% of metastatic lymph nodes would be missed since they were all $\leq 1$ cm.</td>
<td>3</td>
</tr>
<tr>
<td>29. Coursey Moreno C, Small WC, Camacho JC, et al. Testicular tumors: what radiologists need to know--differential diagnosis, staging, and management. <em>Radiographics.</em> 2015;35(2):400-415.</td>
<td>Review/Other-Dx</td>
<td>N/A</td>
<td>To describe the anatomy of the testes and review the risk factors for testicular cancer. An approach to the differential diagnosis of a testicular mass is presented, with a review of the staging and management of testicular malignancies.</td>
<td>No results stated in abstract.</td>
<td>4</td>
</tr>
<tr>
<td>30. Nichols CR, Roth B, Albers P, et al. Active surveillance is the preferred approach to clinical stage I testicular cancer. <em>J Clin Oncol.</em> 2013;31(28):3490-3493.</td>
<td>Review/Other-Tx</td>
<td>N/A</td>
<td>To highlight and endorse the marked shift in approach in clinical stage I testicular cancer away from the era of active intervention with major surgery, RT, or truncated but full-dose chemotherapy.</td>
<td>No results stated in abstract.</td>
<td>4</td>
</tr>
</tbody>
</table>

* See Last Page for Key
### Staging of Testicular Malignancy

#### EVIDENCE TABLE

<table>
<thead>
<tr>
<th>Reference</th>
<th>Study Type</th>
<th>Patients/Events</th>
<th>Study Objective (Purpose of Study)</th>
<th>Study Results</th>
<th>Study Quality</th>
</tr>
</thead>
<tbody>
<tr>
<td>31. Tarin TV, Somm G, Shinghal R. Estimating the risk of cancer associated with imaging related radiation during surveillance for stage I testicular cancer using computerized tomography. <em>J Urol</em> 2009; 181(2):627-632; discussion 632-623.</td>
<td>Review/Other-Dx</td>
<td>N/A</td>
<td>To estimate the lifetime risk of cancer incidence and cancer death from imaging related radiation received during surveillance of stage I NSGCT using CT.</td>
<td>With a 5-year surveillance protocol as suggested by the National Comprehensive Cancer Network (NCCN), lifetime cancer risk ranged from 1 in 52 (1.9%) for an 18-year-old to 1 in 63 for a 40-year-old patient (1.2%). If chest CT is also performed the risk increases to 1 in 39 (2.6%) and 1 in 85 (1.6%), respectively. Lung and colon cancer accounted for most of the risk. The relative risk of a secondary malignancy with surveillance compared to a single scan after retroperitoneal lymph node dissection is approximately 15.2. CT used in testicular cancer surveillance protocols imparts large radiation doses and is associated with a significant risk of cancer. This risk should be factored into counseling patients with stage I NSGCT.</td>
<td>4</td>
</tr>
<tr>
<td>32. Silva MV, Motamednia P, Badalato GM, Hruby G, McKiernan JM. Diagnostic radiation exposure risk in a contemporary cohort of male patients with germ cell tumor. <em>J Urol</em>. 2012;187(2):482-486.</td>
<td>Review/Other-Dx</td>
<td>55 patients</td>
<td>To determine the total amount of diagnostic radiation that a patient with testicular cancer receives during the course of treatment and the associated risk of secondary malignancy.</td>
<td>The cohorts included 55 patients with seminomatous and 64 with nonseminomatous germ cell tumor. Between the groups no difference was found in the lifetime (215.5 and 214.1 mSV, ( P=0.96 )) or the annual (104.6 and 104.6 mSV, respectively, ( P=1.0 )) radiation dose. Of the 41 patients with more than 5-year follow-up 32 (78%) were in violation of guidelines by exceeding 20 mSV per year of radiation. Also, 74 patients (61.7%) received 50 mSV or greater of radiation during a 1-year period. Using the previously calculated excess relative risk for solid cancer and leukemia, excluding chronic lymphocytic leukemia, the RR was 1.06 and 1.33, [corrected] respectively, with a 2.1% lifetime risk of fatal cancer over the baseline risk.</td>
<td>4</td>
</tr>
</tbody>
</table>
### Staging of Testicular Malignancy

**EVIDENCE TABLE**

<table>
<thead>
<tr>
<th>Reference</th>
<th>Study Type</th>
<th>Patients/Events</th>
<th>Study Objective (Purpose of Study)</th>
<th>Study Results</th>
<th>Study Quality</th>
</tr>
</thead>
<tbody>
<tr>
<td>33. van Walraven C, Fergusson D, Earle C, et al. Association of diagnostic radiation exposure and second abdominal-pelvic malignancies after testicular cancer. <em>J Clin Oncol</em> 2011; 29(21):2883-2888.</td>
<td>Review/Other-Dx</td>
<td>2,569 men</td>
<td>To determine evidence associating cancer risk with diagnostic radiation exposure. Population-based administrative data set was used to identify every incident case of testicular cancer between 1991 and 2004 in Ontario, Canada.</td>
<td>During the first 5 years after diagnosis, men underwent a median of 10 CT scans (interquartile range, 4 to 18) of the abdominal-pelvic area, and they were exposed to a median of 110 mSv of radiation from radiologic investigations (interquartile range, 44 to 190). After this, 14 men were diagnosed with a second abdominal-pelvic malignancy (rate, 5 per 10,000 patient-years observation, 95% CI, 3–8); the most common diagnoses were colorectal and kidney malignancies. Radiation exposure was not associated with an excess risk of second cancers (hazard ratio per 10 mSv increase, 0.99; 95% CI, 0.95 to 1.04). This association did not change if men observed for fewer than 5 years were included in the analysis (hazard ratio, 1.00; 95% CI, 0.96 to 1.04). Second malignancies of the abdomen-pelvis are uncommon in men with low-grade testicular cancer. In this study, the risk of second cancer was not associated with the amount of diagnostic radiation exposure.</td>
<td>4</td>
</tr>
<tr>
<td>34. Harvey ML, Geldart TR, Duell R, Mead GM, Tung K. Routine computerised tomographic scans of the thorax in surveillance of stage I testicular non-seminomatous germ-cell cancer—a necessary risk? <em>Ann Oncol</em> 2002; 13(2):237-242.</td>
<td>Review/Other-Dx</td>
<td>168 patients; 42 had relapse during follow-up</td>
<td>Retrospective review to evaluate the contribution of routine thoracic CT imaging in the management of stage I testicular NSGCT.</td>
<td>19% of relapsed lesions were in the chest and were detected by chest CT. In retrospect many of these could be found on CXR but CT was capable of detecting them at a smaller size. The elimination of chest CT did not compromise outcome but significantly reduced radiation exposure thereby minimizing the risk of radiation-induced secondary malignancy. Continued review of surveillance programs is essential if we are to optimize management of this disease.</td>
<td>4</td>
</tr>
<tr>
<td>35. Sohaib SA, Koh DM, Husband JE. The role of imaging in the diagnosis, staging, and management of testicular cancer. <em>AJR</em> 2008; 191(2):387-395.</td>
<td>Review/Other-Dx</td>
<td>N/A</td>
<td>To describe recent developments in imaging patients with testicular GCTs.</td>
<td>Most patients with testicular GCTs can now be expected to be cured, so the focus on management moves toward identifying patients who need more aggressive treatment and avoiding long-term complications. CT remains central in the selection of a management strategy, although the roles of MRI and PET continue to evolve.</td>
<td>4</td>
</tr>
</tbody>
</table>
### Staging of Testicular Malignancy

#### EVIDENCE TABLE

<table>
<thead>
<tr>
<th>Reference</th>
<th>Study Type</th>
<th>Patients/Events</th>
<th>Study Objective (Purpose of Study)</th>
<th>Study Results</th>
<th>Study Quality</th>
</tr>
</thead>
<tbody>
<tr>
<td>36. White PM, Adamson DJ, Howard GC, Wright AR. Imaging of the thorax in the management of germ cell testicular tumours. Clin Radiol 1999; 54(4):207-211.</td>
<td>Observational-Dx</td>
<td>623 chest CT examinations on 207 patients</td>
<td>To evaluate role of chest CT and CXR in management of patients with testicular GCT.</td>
<td>Intrathoracic metastases were identified in 1% of seminoma patients compared with 20% of nonseminoma GCT patients. Chest CT was more accurate than CXR in the detection of intrathoracic metastases at 0.97, 0.96-0.98 (95% CI) compared with 0.91, 0.89-0.93. The agreement between imaging techniques and the standard of reference (determined by Kappa statistic) was respectively 0.96 for chest CT and 0.65 for CXR. In GCT patients undergoing re-assessment with both CXR and chest CT, CXR never detected unknown intrathoracic metastatic disease. Abdominopelvic lymphadenopathy was associated with intrathoracic metastases ($P&lt;0.001$), however re-assessment chest CT did identify intrathoracic metastases in 27 cases without concurrent abdominopelvic disease. CXR was negative in 19 of these. Routine interval CXRs are unnecessary in NSGCT patients undergoing regular re-assessment chest CT due to the low additional yield and limited effect on management. Re-assessment should still include chest CT. In low risk, pure seminoma patients (abdominal CT and marker negative) re-assessment chest CT can be safely avoided. Baseline chest CT is advocated with CXR alone for re-assessment.</td>
<td>3</td>
</tr>
<tr>
<td>Reference</td>
<td>Study Type</td>
<td>Patients/Events</td>
<td>Study Objective (Purpose of Study)</td>
<td>Study Results</td>
<td>Study Quality</td>
</tr>
<tr>
<td>-----------</td>
<td>------------</td>
<td>----------------</td>
<td>-----------------------------------</td>
<td>---------------</td>
<td>---------------</td>
</tr>
<tr>
<td>37. O’Malley ME, Chung P, Haider M, et al. Comparison of low dose with standard dose abdominal/pelvic multidetector CT in patients with stage 1 testicular cancer under surveillance. <em>Eur Radiol</em> 2010; 20(7):1624-1630.</td>
<td>Observational-Dx</td>
<td>100 patients (79 with seminoma and 21 with nonseminoma); 3 independent reviewers</td>
<td>To compare the image quality and acceptability of a low dose with those of standard dose abdominal/pelvic multidetector CT in patients with stage 1 testicular cancer managed by surveillance.</td>
<td>On average, each reader scored noise and diagnostic quality of standard dose images significantly better than corresponding low dose images (P&lt;0.0001). 1 reader found all CT examinations acceptable; 2 readers each found 1/100 (1%) low dose examinations unacceptable. Median and mean dose-length product for low and standard dose protocols were 416.0 and 452.2 (range 122.9–913.4) and 931.9 and 999.8 (range 283.8–1,987.7) mGy cm, respectively. The low dose protocol provided diagnostically acceptable images for at least 99% of patients and achieved mean dose reduction of 55% compared with the standard dose protocol.</td>
<td>2</td>
</tr>
<tr>
<td>38. Su D, Faicen I, Tokarz R, Bramwit M, Weiss RE. Comparative analysis of the risk of radiation exposure and cost of reduced imaging intensity for surveillance of early-stage nonseminomatous germ cell tumors. <em>Urology</em>. 2015;85(1):141-146.</td>
<td>Review/Other-Dx</td>
<td>N/A</td>
<td>To evaluate the surveillance recommendations for early-stage testis cancer and the risk of secondary malignancies due to increased radiation exposure.</td>
<td>The 2012 NCCN protocol uses a maximum of 17 abdominal and pelvic CTs over 6 years, whereas 2014 guidelines suggest a maximum of 13 abdominal and pelvic CTs. The radiation dosage in 2014 guidelines is decreased by 25% compared to the 2012 NCCN guidelines. The minimum number of abdominal and pelvic CTs under the 2014 NCCN protocol reduced radiation dose by 38% compared to the maximum number, this compared to about 50% decrease from the 2012 NCCN guidelines. The median cost for a single abdominal and pelvic CT with contrast is $369.30; median cost for a single MRI with contrast is $772.18. As compared to the 2012 protocol, the 2014 guidelines reduced CTAP cost by approximately 24%–54% for minimum and maximum abdominal and pelvic CTs allowed.</td>
<td>4</td>
</tr>
<tr>
<td>39. Glazer HS, Lee JK, Levitt RG, et al. Radiation fibrosis: differentiation from recurrent tumor by MR imaging. <em>Radiology</em> 1985; 156(3):721-726.</td>
<td>Review/Other-Dx</td>
<td>36 total patients: 21 had RT; 15 no RT</td>
<td>To analyze the MRI of patients who had RT and compare with those who had no RT to determine differentiation of radiation fibrosis from recurrent tumor by MRI.</td>
<td>T2-weighted images (TR = 1,500 msec, TE = 90 msec) were most helpful in distinguishing recurrent tumor from radiation fibrosis. Relatively high signal intensity on T2-weighted images is not specific for tumor recurrence.</td>
<td>4</td>
</tr>
</tbody>
</table>
### EVIDENCE TABLE

<table>
<thead>
<tr>
<th>Reference</th>
<th>Study Type</th>
<th>Patients/Events</th>
<th>Study Objective (Purpose of Study)</th>
<th>Study Results</th>
<th>Study Quality</th>
</tr>
</thead>
<tbody>
<tr>
<td>40. Hogeboom WR, Hoekstra HJ, Mooyaart EL, et al.</td>
<td>Review/Other-Dx</td>
<td>10 consecutive patients</td>
<td>To prospectively compare MRI with CT in staging retroperitoneal metastases.</td>
<td>MRI and CT were equivalent in detecting and determining the anatomical localization and size of the retroperitoneal lymph node metastases. Unlike CT, MRI revealed unmistakable changes in the structure of the retroperitoneal lymph-node metastases during chemotherapy, for which no histological cause was found except in mature teratoma. On the basis of tumor consistency and signal intensity in the T1- and T2-weighted images, MRI cannot yet warrant any conclusion about the ultimate effect of chemotherapy.</td>
<td>4</td>
</tr>
<tr>
<td>41. Harisinghani MG, Saksena M, Ross RW, et al.</td>
<td>Observational-Dx</td>
<td>18 patients (42 nodes sampled; 25 benign and 17 malignant)</td>
<td>To prospectively evaluate whether lymphotrophic nanoparticle-enhanced MRI can be used as a method for detecting metastatic disease within retroperitoneal nodes in patients with testicular cancer.</td>
<td>Sensitivity of lymphotrophic nanoparticle-enhanced MRI for malignant lymph node involvement was 88.2%, specificity was 92%, and the accuracy was 90.4%. On the other hand, the sensitivity of size criteria for detecting malignant nodes was 70.5%, the specificity was 68%, and the accuracy was 69%. Lymphotrophic nanoparticle-enhanced MRI is safe and accurate for detecting nodal metastases in patients with testicular cancer. Lymphotrophic nanoparticle-enhanced MRI yields higher sensitivity and specificity when compared with unenhanced MRI or conventional CT scanning. Although the results are encouraging, the precise role of this tool in early stage testicular cancer remains to be determined.</td>
<td>2</td>
</tr>
</tbody>
</table>
### Staging of Testicular Malignancy

**EVIDENCE TABLE**

<table>
<thead>
<tr>
<th>Reference</th>
<th>Study Type</th>
<th>Patients/ Events</th>
<th>Study Objective (Purpose of Study)</th>
<th>Study Results</th>
<th>Quality</th>
</tr>
</thead>
<tbody>
<tr>
<td>42. Sohaib SA, Koh DM, Barbachano Y, et al. Prospective assessment of MRI for imaging retroperitoneal metastases from testicular germ cell tumours. <em>Clin Radiol</em> 2009; 64(4):362-367.</td>
<td>Observational-Dx</td>
<td>52 patients; 3 independent observers</td>
<td>Prospective study to determine the sensitivity of MRI in the detection of retroperitoneal lymph nodes in patients with testicular GCT.</td>
<td>22 (42%) of the 52 patients had no retroperitoneal disease; in remaining 30 patients 51 enlarged nodes were identified. On a per patient basis, readers 1, 2, and 3 identified nodal disease in 28/29, 29/30, and 24/30 patients, respectively, using MRI compared to CT. Thus for experienced radiologists (readers 1 and 2) MRI is comparable to CT for nodal detection (ie, this study excludes MRI being inferior to CT with 80% power and 5% type 1 error). MRI offers an alternative method for staging the retroperitoneum in young patients being followed for testicular GCT and has the major advantage of avoiding exposure to ionizing radiation.</td>
<td>2</td>
</tr>
<tr>
<td>43. Krege S, Beyer J, Souchon R, et al. European consensus conference on diagnosis and treatment of germ cell cancer: a report of the second meeting of the European Germ Cell Cancer Consensus group (EGCCCG): part I. <em>Eur Urol</em> 2008; 53(3):478-496.</td>
<td>Review/Other-Dx</td>
<td>N/A</td>
<td>In 2004 the first consensus paper on diagnostics and treatment in testicular cancer was prepared by the European Germ Cell Cancer Consensus Group (EGCCCG). This paper is an update with the new data emerged since 2002 integrated and prepared again on the basis of evidence-based medicine.</td>
<td>The first part of the consensus paper describes the clinical presentation of the primary tumor, its treatment, the importance and treatment of testicular intraepithelial neoplasia, histological classification, staging and prognostic factors, and treatment of stage I seminoma and nonseminoma. Whereas, the vast majority of the recommendations made in 2004 remain valid 3 years later, refinements in the treatment of early- and advanced-stage testicular cancer have emerged from clinical trials. Despite technical improvements, expert clinical skills will continue to be 1 of the major determinants for the prognosis of patients with germ cell cancer. In addition, the particular needs of testicular cancer survivors have been acknowledged.</td>
<td>4</td>
</tr>
<tr>
<td>Reference</td>
<td>Study Type</td>
<td>Patients/Events</td>
<td>Study Objective (Purpose of Study)</td>
<td>Study Results</td>
<td>Study Quality</td>
</tr>
<tr>
<td>-----------</td>
<td>------------</td>
<td>----------------</td>
<td>-----------------------------------</td>
<td>---------------</td>
<td>---------------</td>
</tr>
<tr>
<td>[44]. Pfannenberg AC, Oechsle K, Bokemeyer C, et al. The role of [(18)F] FDG-PET, CT/MRI and tumor marker kinetics in the evaluation of post chemotherapy residual masses in metastatic germ cell tumors--prospects for management. <em>World J Urol</em> 2004; 22(2):132-139.</td>
<td>Observational-Dx</td>
<td>60 residual tumors in 28 GCT patients</td>
<td>Prospective study to assess the ability of FDG-PET, CT/MRI and serum tumor marker to predict the viability of residual masses after high-dose chemotherapy in patients with metastatic GCT.</td>
<td>There were no significant differences among the sensitivities observed with PET, CT/MRI and TM, but PET was significantly more specific than CT/MRI in predicting residual mass viability. TM showed the highest specificity. The highest accuracy in classification of residual tumors was achieved by a combination of PET, CT/MRI and TM (area under the receiver-operator characteristic curve =0.91). All mature teratomas showed false-negative PET results with standardized uptake values in the same range as necrosis. For classification of residual masses after high-dose chemotherapy of metastatic GCT, FDG-PET is a valuable diagnostic method to complement the established procedures CT and TM. Positive PET results are highly correlated with the presence of viable tumor, but residual masses with negative PET findings still require resection. In cases of tumor progression diagnosed by CT and elevated TM, additional PET examinations are without benefit. PET seems useful in patients with stable disease or partial remission in CT/MRI and normalized TM as well as in marker-negative disease.</td>
<td>2</td>
</tr>
<tr>
<td>[45]. Muglia V, Tucci S, Jr., Elias J, Jr., Trad CS, Bilbey J, Cooperberg PL. Magnetic resonance imaging of scrotal diseases: when it makes the difference. <em>Urology</em> 2002; 59(3):419-423.</td>
<td>Observational-Dx</td>
<td>622 patients had US; 26 were selected for MRI</td>
<td>To investigate the utility of MRI after inconclusive US in the evaluation of scrotal disease.</td>
<td>MRI yielded additional and correct information (compared with US), coincident with the final diagnosis in 23 cases (82.1%). In regard to lesions suspected of malignancy at US (17 cases), MRI had a great concordance with the final diagnosis and was statistically significant (P&lt;0.002, kappa test). Results indicate that MRI could help elucidate scrotal dilemmas found at US, although the small percentage of inconclusive sonograms confirms this technique as the first choice when imaging is required in scrotal diseases.</td>
<td>3</td>
</tr>
</tbody>
</table>
### Staging of Testicular Malignancy

**EVIDENCE TABLE**

<table>
<thead>
<tr>
<th>Reference</th>
<th>Study Type</th>
<th>Patients/ Events</th>
<th>Study Objective (Purpose of Study)</th>
<th>Study Results</th>
<th>Study Quality</th>
</tr>
</thead>
<tbody>
<tr>
<td>46. Parenti GC, Feletti F, Brandini F, et al. Imaging of the scrotum: role of MRI. <em>Radiol Med</em> 2009; 114(3):414-424.</td>
<td>Observational-Dx</td>
<td>801 patients; color Doppler US study followed by MRI in 46 patients</td>
<td>To evaluate the usefulness of imaging for correct clinical and therapeutic management of patients with scrotal disease. Patients with suspected scrotal disease underwent color Doppler US.</td>
<td>Color Doppler US revealed an inflammatory process in 277 patients (34.58%), testicular trauma in 112 (13.9%), funicular torsion or torsion of the vestigial remnant in 44 (5.4%), findings suggestive of testicular neoplasm in 35 (4.3%) and no abnormality in 41.5%. MRI, used to further investigate the color Doppler US findings in 46 cases, showed 3 cases of intraparenchymal hematoma, 1 of intrascrotal cavernous body rupture, 1 of testicular abscess with intrascrotal fistula, 2 of testicular infarction and 15 of neoplasm. MRI allowed the exclusion of focal abnormalities in 10 patients with TM, in 3 with chronic orchitis and in 4 with atrophic involution. MRI confirmed the finding of inguinal hernia in 3 cases. Color Doppler US is irreplaceable as an initial approach to patients affected by scrotal disease, whereas MRI is an ideal second-line investigation. MRI offers useful, and in some cases decisive, information, as it is capable of revealing unexpected findings and elucidating complex aspects. MRI helps improve patient management, with an overall reduction in costs.</td>
<td>4</td>
</tr>
<tr>
<td>47. Tsili AC, Argyropoulou MI, Giannakis D, Sofikitis N, Tsampoulas K. MRI in the characterization and local staging of testicular neoplasms. <em>AJR</em> 2010; 194(3):682-689.</td>
<td>Observational-Dx</td>
<td>33 patients</td>
<td>Prospective study to assess the role of MRI in the preoperative characterization and local staging of testicular neoplasms.</td>
<td>Histologic examination revealed 36 intratesticular lesions, 28 (78%) of which were malignant and 8 benign. 13 malignant testicular tumors (46%) were confined within the testis, 12 (43%) had invaded the testicular tunicae or epididymis, and 3 (11%) had invaded the spermatic cord. The sensitivity and specificity of MRI in differentiating benign from malignant intratesticular lesions were 100% (95% CI, 87.9%–100%) and 87.5% (95% CI, 52.9%–97.7%). The rate of correspondence between MRI and histologic diagnosis in the local staging of testicular tumors was 92.8% (26/28). MRI is a good diagnostic tool for the evaluation of testicular disease. It is highly accurate in the preoperative characterization and local staging of testicular neoplasms.</td>
<td>2</td>
</tr>
</tbody>
</table>

* See Last Page for Key

2016 Review

Yacoub/Oto

Page 15
<table>
<thead>
<tr>
<th>Reference</th>
<th>Study Type</th>
<th>Patients/Events</th>
<th>Study Objective (Purpose of Study)</th>
<th>Study Results</th>
<th>Study Quality</th>
</tr>
</thead>
<tbody>
<tr>
<td>48. Woldrich JM, Im RD, Hughes-Cassidy FM, Aganovic L, Sakamoto K. Magnetic resonance imaging for intratesticular and extratesticular scrotal lesions. <em>Can J Urol.</em> 2013;20(4):6855-6859.</td>
<td>Observational-Dx</td>
<td>69 patients</td>
<td>To evaluate MRI utility in intratesticular and extratesticular scrotal diseases.</td>
<td>Of 69 cases, 38 were intratesticular lesions and 31 were extratesticular lesions. MRI and US diagnoses were discordant in 21 (55.32%) intratesticular and 19 (61.3%) extratesticular lesions. MRI diagnosis was malignant after an indeterminate US in 0 and 4 (12.9%) intratesticular and extratesticular lesions, respectively. MRI diagnosis was benign after an indeterminate US in 18 (47.43%) and 14 (45.2%) intratesticular and extratesticular lesions, respectively. A malignant US diagnosis was reversed to benign MRI diagnosis in 1 (2.6%) intratesticular and 1 (3.2%) extratesticular lesion. In no case was a benign lesion on US read as malignant on MRI in either group. The cohort of patients with intratesticular lesions received a mean clinical and radiographic follow up of 2.49 +/- 1.97 and 1.85 +/- 1.46 years, respectively. The patients with extratesticular lesions received a mean clinical and radiographic follow up of 1.30 +/- 1.08 and 2.00 +/- 1.28 years, respectively. In no case did repeat imaging change the diagnosis after initial MRI and US evaluation.</td>
<td>3</td>
</tr>
<tr>
<td>49. Fernandez EB, Colon E, McLeod DG, Moul JW. Efficacy of radiographic chest imaging in patients with testicular cancer. <em>Urology</em> 1994; 44(2):243-248; discussion 248-249.</td>
<td>Observational-Dx</td>
<td>362 patient records (119 excluded); 201 had both CXR and chest CT; 24 CXR alone; 20 CT of the chest alone</td>
<td>To determine the efficacy of CT of the chest and CXR in the initial staging process of testicular GCTs.</td>
<td>CXR alone is preferable for initial chest staging in all patients with seminomas and in patients with NSGCT with negative findings on CTA. Chest CT remains of slight benefit for patients with clinical stage II and greater NSGCT and to evaluate further suspicious CXR findings in any patient, although it appears not to be necessary in patients who have clinical stage I disease determined by CTA. These findings have important cost-saving implications.</td>
<td>3</td>
</tr>
<tr>
<td>50. Steinfeld AD, Macher MS. Radiologic staging of chest in testicular seminoma. <em>Urology</em> 1990; 36(5):428-430.</td>
<td>Review/Other-Dx</td>
<td>N/A</td>
<td>To review the benefits of CXR, conventional planar tomography, and computerized axial tomography in evaluating patients with stages I and II testicular seminoma.</td>
<td>Routine use of computerized axial tomography or conventional planar tomography is not indicated in staging.</td>
<td>4</td>
</tr>
</tbody>
</table>
### Staging of Testicular Malignancy

#### EVIDENCE TABLE

<table>
<thead>
<tr>
<th>Reference</th>
<th>Study Type</th>
<th>Patients/Events</th>
<th>Study Objective (Purpose of Study)</th>
<th>Study Results</th>
<th>Study Quality</th>
</tr>
</thead>
<tbody>
<tr>
<td>51. Meyer CA, Conces DJ. Imaging of intrathoracic metastases of nonseminomatous germ cell tumors. <em>Chest Surg Clin N Am</em> 2002; 12(4):717-738.</td>
<td>Review/Other-Dx</td>
<td>N/A</td>
<td>To review the imaging of intrathoracic metastases of NSGCT.</td>
<td>CT is the workhorse of staging for testicular cancer. The addition of FDG-PET is useful in assessing thoracic masses in select, high-risk patients.</td>
<td>4</td>
</tr>
<tr>
<td>52. Horan G, Raqique A, Robson J, Dixon AK, Williams MV. CT of the chest can hinder the management of seminoma of the testis; it detects irrelevant abnormalities. <em>Br J Cancer</em> 2007; 96(6):882-885.</td>
<td>Observational-Dx</td>
<td>182 consecutive patients</td>
<td>Retrospective review to evaluate the role of chest CT in the initial staging of testicular seminomatous GCTs.</td>
<td>24 patients had abnormal abdominal CT findings. 158 had normal abdominal CT findings but, on initial staging, chest CT reported abnormalities in 13 patients, which, on further follow-up CT were deemed to be irrelevant to the diagnosis of seminoma. There was a further patient with a normal CT abdomen in whom chest CT detected obvious metastatic disease, which was seen on CXR. Overall 18 cases required additional investigations and follow-up for abnormalities subsequently found to be benign. There was a false-positive rate of 10% for initial staging with chest CT. This is the largest reported series of staging CT chest in testicular seminoma. In all patients with normal abdominal CT, normal CXR and abnormal chest CT, subsequent follow-up investigations demonstrated that the lung lesions were incidental findings. Study concludes that for patients with normal abdominal CT findings and thereby presumed low stage tumors, any abnormality in the chest CT should not necessarily influence management or delay treatment.</td>
<td>3</td>
</tr>
<tr>
<td>53. Gietema JA, Meinardi MT, Sleijfer DT, Hoekstra HJ, van der Graaf WT. Routine chest X-rays have no additional value in the detection of relapse during routine follow-up of patients treated with chemotherapy for disseminated nonseminomatous testicular cancer. <em>Ann Oncol</em> 2002; 13(10):1616-1620.</td>
<td>Review/Other-Dx</td>
<td>353 consecutive patients</td>
<td>To evaluate all patients with disseminated testicular cancer treated with chemotherapy at the University Hospital Groningen.</td>
<td>None of over 10,000 CXR was positive. Yield was very low. Routine CXR has no additional value in the detection of tumor relapses during follow-up after chemotherapy in the subset of patients who present their disseminated nonseminomatous testicular cancer with increased tumor markers and are in complete response after treatment. In order to save valuable resources, CXR can be omitted from the follow-up schedule after chemotherapy for marker-positive nonseminomatous testicular cancer in complete response.</td>
<td>4</td>
</tr>
</tbody>
</table>

* See Last Page for Key

2016 Review

Yacoub/Oto

Page 17
### Reference Study Type Patients/ Events Study Objective (Purpose of Study) Study Results Study Quality

<table>
<thead>
<tr>
<th>Reference</th>
<th>Study Type</th>
<th>Patients/ Events</th>
<th>Study Objective (Purpose of Study)</th>
<th>Study Results</th>
<th>Study Quality</th>
</tr>
</thead>
<tbody>
<tr>
<td>54. Cremerius U, Effert PJ, Adam G, et al. FDG PET for detection and therapy control of metastatic germ cell tumor. <em>J Nucl Med</em> 1998; 39(5):815-822.</td>
<td>Observational-Dx</td>
<td>87 total patients: 54 PET, 33 CT</td>
<td>To examine the use of FDG-PET for detection and therapy control of metastatic germ cell cancer as compared to CT.</td>
<td>While sensitivities of PET and CT did not differ markedly, PET was significantly more specific than CT. FDG-PET is superior to CT for assessment of residual disease after chemotherapy for germ cell cancer.</td>
<td>3</td>
</tr>
<tr>
<td>55. Cremerius U, Wildberger JE, Borchers H, et al. Does positron emission tomography using 18-fluoro-2-deoxyglucose improve clinical staging of testicular cancer? Results of a study in 50 patients. <em>Urology</em> 1999; 54(5):900-904.</td>
<td>Observational-Dx</td>
<td>50 patients</td>
<td>To compare PET and CT for staging in unselected patients with germ cell cancer.</td>
<td>PET: 87% sensitivity, 97% specificity. CT: 73% sensitivity, 94% specificity. PET is superior to CT for staging. FDG-PET has the potential to improve clinical staging of testicular cancer. However, PET, as well as CT, is limited in the detection of small retroperitoneal lymph node metastases.</td>
<td>3</td>
</tr>
<tr>
<td>56. de Wit M, Brenner W, Hartmann M, et al. [18F]-FDG-PET in clinical stage I/II non-seminomatous germ cell tumours: results of the German multicentre trial. <em>Ann Oncol</em> 2008; 19(9):1619-1623.</td>
<td>Observational-Dx</td>
<td>72 patients</td>
<td>To determine the predictive values of FDG-PET in primary staging in patients with newly diagnosed NSGCT clinical stage I/II.</td>
<td>The prevalence of nodal involvement was 26%. Correct nodal staging by FDG-PET was achieved in 83% compared with correct CT staging in 71%. CT had a sensitivity and specificity of 41% and 95%, respectively. PPV and NPV were 87% and 67%, respectively. FDG-PET had a sensitivity and specificity of 66% and 98%, respectively. PPV was 95%. The primary end point was not reached, with an NPV of 78%. FDG-PET as a primary staging tool for NSGCT yielded only slightly better results than CT. Both methods had a high specificity while false-negative findings were more frequent with CT. FDG-PET is mostly useful as a diagnostic tool in case of questionable CT scan.</td>
<td>2</td>
</tr>
<tr>
<td>57. Hain SF, O'Doherty MJ, Timothy AR, Leslie MD, Partridge SE, Huddart RA. Fluorodeoxyglucose PET in the initial staging of germ cell tumours. <em>Eur J Nucl Med</em> 2000; 27(5):590-594.</td>
<td>Observational-Dx</td>
<td>31 patients</td>
<td>A retrospective study to determine if FDG-PET is useful for staging testicular cancer.</td>
<td>The PPV was 100%. The NPV was 76%. It may be concluded that FDG-PET is capable of detecting metastatic disease at diagnosis that is not identified by other imaging techniques. These preliminary results are sufficient to suggest that a large prospective study should be performed to evaluate the role of FDG-PET in primary staging of disease.</td>
<td>3</td>
</tr>
</tbody>
</table>
**Staging of Testicular Malignancy**

**EVIDENCE TABLE**

<table>
<thead>
<tr>
<th>Reference</th>
<th>Study Type</th>
<th>Patients/Events</th>
<th>Study Objective (Purpose of Study)</th>
<th>Study Results</th>
<th>Study Quality</th>
</tr>
</thead>
<tbody>
<tr>
<td>58. Lassen U, Daugaard G, Eigted A, Hojgaard L, Damgaard K, Rorth M. Whole-body FDG-PET in patients with stage I non-seminomatous germ cell tumours. <em>Eur J Nucl Med Mol Imaging</em> 2003; 30(3):396-402.</td>
<td>Observational-Dx</td>
<td>46 patients</td>
<td>To compare FDG-PET and CT in patients with stage I NSGCT.</td>
<td>The sensitivity, specificity and accuracy of PET were 70%, 100% and 93%, respectively. The sensitivity of detecting small retroperitoneal metastases was 88%. The negative and PPV were 92% and 100%, respectively, whereas the NPV of standard staging procedures was 78%. FDG-PET thus seems to be superior to conventional staging (<em>P</em>=0.06) in stage I NSGCT. This noninvasive method may improve the overall management of patients with NSGCT.</td>
<td>2</td>
</tr>
<tr>
<td>59. Spermon JR, De Geus-Oei LF, Kiemeney LA, Witjes JA, Oyen WJ. The role of (18)fluoro-2-deoxyglucose positron emission tomography in initial staging and re-staging after chemotherapy for testicular germ cell tumours. <em>BJU Int</em> 2002; 89(6):549-556.</td>
<td>Review/Other-Dx</td>
<td>50 patients</td>
<td>To investigate the role of FDG-PET in the initial staging of clinical stage I and II NSGCT and in re-staging NSGCT after chemotherapy.</td>
<td>FDG-PET performed equally well with CT on initial staging but was superior to CT on restaging. It could be useful to predict fibrotic residual mass in NSGCT in those patients with no teratoma component in their primary tumor.</td>
<td>4</td>
</tr>
<tr>
<td>60. Ambrosini V, Zucchini G, Nicolini S, et al. 18F-FDG PET/CT impact on testicular tumours clinical management. <em>Eur J Nucl Med Mol Imaging</em> 2014;41(4):668-673.</td>
<td>Observational-Dx</td>
<td>56 patients</td>
<td>To evaluate the clinical impact of FDG-PET/CT in patients with testicular tumor.</td>
<td>On a scan basis, 51 seminoma and 70 nonseminoma cases were reviewed. Of the 121 cases, 32 were found to be true-positive, 74 true-negative, 8 false-positive and 6 false-negative by PET/CT. PET/CT showed good sensitivity and specificity for seminoma lesion detection (92% and 84%, respectively), but its sensitivity was lower for nonseminoma forms (sensitivity and specificity 77% and 95%, respectively). The PET/CT scan influenced the clinical management of 47/51 seminomas (in 6 chemotherapy was started/continued, in 3 RT was started/continued, in 2 surgery of secondary lesions was performed, and in 36 clinical surveillance was considered appropriate), and 59/70 nonseminoma (in 18 therapy/surgery was started/continued, and in 41 clinical surveillance was considered appropriate).</td>
<td>3</td>
</tr>
</tbody>
</table>
## Staging of Testicular Malignancy

### EVIDENCE TABLE

<table>
<thead>
<tr>
<th>Reference</th>
<th>Study Type</th>
<th>Patients/Events</th>
<th>Study Objective (Purpose of Study)</th>
<th>Study Results</th>
<th>Study Quality</th>
</tr>
</thead>
<tbody>
<tr>
<td>61. Bachner M, Loriot Y, Gross-Goupil M, et al. 2-(1)fluoro-deoxy-D-glucose positron emission tomography (FDG-PET) for postchemotherapy seminoma residual lesions: a retrospective validation of the SEMPET trial. <em>Ann Oncol</em> 2012; 23(1):59-64.</td>
<td>Observational-Dx</td>
<td>127 PET studies</td>
<td>A retrospective validation of FDG-PET recommendations in the evaluation of postchemotherapy seminoma residuals in a larger group of patients.</td>
<td>Of 127 eligible PET studies, 69% were true negative, 11% true positive, 6% false negative, and 15% false positive. Authors compared PET scans carried out before and after a cut-off level of 6 weeks after the end of the last chemotherapy cycle. PET sensitivity, specificity, NPV, and PPV were 50%, 77%, 91%, and 25%, respectively, before the cut-off and 82%, 90%, 95%, and 69% after the cut-off. PET accuracy significantly improved from 73% before to 88% after the cut-off (<em>P</em>=0.032). The study confirms the high specificity, sensitivity, and NPV of FDG-PET for evaluating postchemotherapy seminoma residuals. When carried out at an adequate time point, FDG-PET remains a valuable tool for clinical decision-making in this clinical setting and spares patients unnecessary therapy.</td>
<td>3</td>
</tr>
</tbody>
</table>

* See Last Page for Key
<table>
<thead>
<tr>
<th>Reference</th>
<th>Study Type</th>
<th>Patients/Events</th>
<th>Study Objective (Purpose of Study)</th>
<th>Study Results</th>
<th>Study Quality</th>
</tr>
</thead>
<tbody>
<tr>
<td>62. Becherer A, De Santis M, Karanikas G, et al.</td>
<td>Observational-Dx</td>
<td>54 patients</td>
<td>Multicenter study. To prospectively examine whether FDG-PET can improve the prediction of viable tumor in post-chemotherapy seminoma residuals. <em>Eur J Radiol</em> 2005; 54(2):284-288.</td>
<td>After adequate chemotherapy, there were 74 CT-documented residual masses ranging in size from 1 to 11 cm (median, 2.2 cm). Their dignities were confirmed histologically in 13 lesions, or by follow-up CT in 61 lesions. 4 of 47 lesions &lt;3 cm and 11/27 lesions ≥3 cm were viable. PET was true positive in 1 lesion &lt;3 cm and in 11 lesions ≥3 cm, false negative in 3 lesions &lt;3 cm, and true negative in 59 lesions (43 lesions &lt;3 cm). No PET scan was false positive. In detecting viability the sensitivity and specificity was 73% (95% CI, 44-88), and 73% (59-83), respectively, for CT (&lt; or &gt; or ≥3 cm); and 80% (51-95), and 100% (93-100), respectively, for PET (specificity, (P&lt;0.001)). In post-chemotherapy seminoma residuals, a positive PET is highly predictive for the presence of viable tumor. The specificity of PET is significantly higher than that of CT when using a ≥3 cm cut-off. A negative PET scan is excellent for the exclusion of disease in lesions ≥3 cm, with a somewhat higher sensitivity than CT. PET can contribute to the management of residual seminoma lesions, especially in terms of avoiding unnecessary additional treatment for patients with lesions ≥3 cm.</td>
<td>2</td>
</tr>
</tbody>
</table>
## Staging of Testicular Malignancy

### EVIDENCE TABLE

<table>
<thead>
<tr>
<th>Reference</th>
<th>Study Type</th>
<th>Patients/Events</th>
<th>Study Objective (Purpose of Study)</th>
<th>Study Results</th>
<th>Study Quality</th>
</tr>
</thead>
<tbody>
<tr>
<td>63. Hinz S, Schrader M, Kempensteffen C, et al. The role of positron emission tomography in the evaluation of residual masses after chemotherapy for advanced stage seminoma. <em>J Urol</em> 2008; 179(3):936-940; discussion 940.</td>
<td>Observational-Dx</td>
<td>20 patients</td>
<td>Prospective multicenter trial to analyze the accuracy of preoperative PET for predicting viable tumor residuals in patients with seminoma. CT and FDG-PET were performed before surgical resection for residual or recurrent masses in patients who had undergone chemotherapy for stage IIb, IIc or III seminoma.</td>
<td>Of the patients, 18 presented with residual masses and 2 had recurrent masses following chemotherapy. Histopathological assessment revealed viable tumor in 3 patients and benign lesions in 17. All patients with viable tumor were identified correctly by PET. No false-negative results were observed but 9 patients had false-positive PET results. This resulted in a NPV of 1 (95% CI, 0.63-1) and a PPV of 0.25 (95% CI, 0.05-0.57) for FDG-PET. The data indicate that FDG-PET is capable of excluding viable disease in residual masses, even those exceeding 3 cm. Therefore, it may be considered an additional tool to improve patient counseling. However, the decision to perform surgical resection of the residual mass should not be based exclusively on a positive PET image since false-positive results appear to be common.</td>
<td>3</td>
</tr>
<tr>
<td>64. De Santis M, Becherer A, Bokemeyer C, et al. 2-18fluoro-deoxy-D-glucose positron emission tomography is a reliable predictor for viable tumor in postchemotherapy seminoma: an update of the prospective multicentric SEMPET trial. <em>J Clin Oncol</em> 2004; 22(6):1034-1039.</td>
<td>Observational-Dx</td>
<td>51 patients</td>
<td>Prospective multicenter study to define clinical value of FDG-PET as a predictor for viable residual tumor in postchemotherapy seminoma residuals.</td>
<td>19 cases with residual lesions &gt;3 cm and 35 (95%) of 37 with residual lesions ≤3 cm were correctly predicted by FDG-PET. The specificity, sensitivity, PPV, and NPV of FDG-PET were 100%, 80%, 100%, and 96%, respectively, vs 74%, 70%, 37%, and 92%, respectively, for CT discrimination of the residual tumor by size (&gt;3 cm/≤3 cm). This investigation confirms that FDG-PET is the best predictor of viable residual tumor in postchemotherapy seminoma residuals and should be used as a standard tool for clinical decision making in this patient group.</td>
<td>3</td>
</tr>
<tr>
<td>65. Treglia G, Sadeghi R, Anrunziata S, Caldarella C, Bertagna F, Giovanella L. Diagnostic performance of fluorine-18-fluorodeoxyglucose positron emission tomography in the postchemotherapy management of patients with seminoma: systematic review and meta-analysis. <em>Biomed Res Int.</em> 2014;2014:852681.</td>
<td>Meta-analysis</td>
<td>9 studies including 375 scans</td>
<td>To analyze published data about the diagnostic performance of FDG-PET and PET/CT in the postchemotherapy management of patients with seminoma.</td>
<td>9 studies including 375 scans were selected. The pooled analysis provided the following results: sensitivity 78% (95% CI: 67%-87%), specificity 86% (95% CI: 81%-89%), PPV 58% (95% CI: 48%-68%), NPV 94% (95% CI: 90%-96%), and accuracy 84% (95% CI: 80%-88%). The area under the curve was 0.90. A better diagnostic accuracy of FDG-PET or PET/CT in evaluating residual/recurrent lesions &gt;3 cm compared to those &lt;3 cm was found.</td>
<td>M</td>
</tr>
</tbody>
</table>

* See Last Page for Key

2016 Review Yacoub/Oto Page 22
## Staging of Testicular Malignancy

### EVIDENCE TABLE

<table>
<thead>
<tr>
<th>Reference</th>
<th>Study Type</th>
<th>Patients/Events</th>
<th>Study Objective (Purpose of Study)</th>
<th>Study Results</th>
<th>Study Quality</th>
</tr>
</thead>
<tbody>
<tr>
<td>66. Oechsle K, Hartmann M, Brenner W, et al. [18F]Fluorodeoxyglucose positron emission tomography in nonseminomatous germ cell tumors after chemotherapy: the German multicenter positron emission tomography study group. <em>J Clin Oncol</em> 2008; 26(36):5930-5935.</td>
<td>Observational-Dx</td>
<td>121 patients</td>
<td>Prospective multicenter study to evaluate the accuracy of FDG-PET for the prediction of histology compared with CT and serum tumor markers.</td>
<td>Prediction of tumor viability with FDG-PET was correct in 56%, which did not reach the expected clinically relevant level of 70%, and was not better than the accuracy of CT (55%) or serum tumor markers (56%). Sensitivity and specificity of FDG-PET were 70% and 48%. The PPVs were not significantly different (55%, 61%, and 59% for CT, serum tumor markers, and PET, respectively). Judging only vital carcinoma as a true malignant finding, the NPV increased to 83% for FDG-PET. The presence of vital carcinoma and mature teratoma is common (55%) in residual masses in patients with NSGCT, and CT and serum tumor markers cannot reliably predict absence of disease. In contrast to prior studies, this prospective trial, which is the only with histologic confirmation in all patients, demonstrated that FDG-PET is unable to give a clear additional clinical benefit to the standard diagnostic procedures, CT and serum tumor markers, in the prediction of tumor viability in residual masses.</td>
<td>2</td>
</tr>
<tr>
<td>67. Sanchez D, Zudaire JJ, Fernandez JM, et al. 18F-fluoro-2-deoxyglucose-positron emission tomography in the evaluation of nonseminomatous germ cell tumours at relapse. <em>BJU Int</em> 2002; 89(9):912-916.</td>
<td>Observational-Dx</td>
<td>15 patients</td>
<td>To compare the performance of FDG-PET and CT in the follow-up of NSGCT in the retroperitoneum.</td>
<td>11 patients either presented with retroperitoneal disease or this did not disappear after chemotherapy. The results of both examinations coincided in 18 cases and were contradictory in the other 7, the difference being statistically significant (<em>P</em>=0.042).</td>
<td>3</td>
</tr>
<tr>
<td>68. Huddart RA, O'Doherty MJ, Padhani A, et al. 18fluorodeoxyglucose positron emission tomography in the prediction of relapse in patients with high-risk, clinical stage I nonseminomatous germ cell tumors: preliminary report of MRC Trial TE22--the NCRI Testis Tumour Clinical Study Group. <em>J Clin Oncol</em> 2007; 25(21):3090-3095.</td>
<td>Observational-Dx</td>
<td>116 total registered patients: 111 underwent PET scans; 87 proceeded to surveillance</td>
<td>To examine whether an FDG-PET scan could identify patients without occult metastatic disease for whom surveillance is an attractive option.</td>
<td>For 12 months follow-up, 33/87 patients on surveillance relapsed (1-year relapse-free rate, 63%; 90% CI, 54% to 72%). Relapse rate among PET negative patients is high. Results indicate that FDG PET scanning is not sufficiently sensitive to identify patients at low risk of relapse in this setting.</td>
<td>2</td>
</tr>
</tbody>
</table>

* See Last Page for Key

Yacoub/Oto

Page 23
<table>
<thead>
<tr>
<th>Reference</th>
<th>Study Type</th>
<th>Patients/Events</th>
<th>Study Objective (Purpose of Study)</th>
<th>Study Results</th>
<th>Study Quality</th>
</tr>
</thead>
<tbody>
<tr>
<td>69. Braga FJ, Arbex MA, Haddad J, Maes A. Bone scintigraphy in testicular tumors. Clin Nucl Med 2001; 26(2):117-118.</td>
<td>Review/Other-Dx</td>
<td>28 patients</td>
<td>To identify the role of bone scan in staging and restaging bone disease in testicular cancer.</td>
<td>Early detection of metastases is very important to ensure the efficacy of RT and chemotherapy. Bone scintigraphy may play an important role in such cases and seems to be more sensitive than conventional radiography. Testicular tumor metastases should be considered when iliac involvement is observed. Paget's disease should be included in a differential diagnosis.</td>
<td>4</td>
</tr>
<tr>
<td>70. Nakamoto Y, Osman M, Wahl RL. Prevalence and patterns of bone metastases detected with positron emission tomography using F-18 FDG. Clin Nucl Med 2003; 28(4):302-307.</td>
<td>Review/Other-Dx</td>
<td>403 patients</td>
<td>A retrospective study to report the prevalence and imaging characteristics of bone metastases detected with FDG-PET compared with bone scans in the same patients.</td>
<td>FDG-PET is superior to bone scan in detecting bone lesions. The most frequent pattern of detectable bone metastases with FDG-PET imaging was multiple foci of intense uptake. PET revealed more lesions than did bone scanning, independent of the type of cancer or location of bone involvement, in patients who were accurately diagnosed by FDG-PET imaging.</td>
<td>4</td>
</tr>
</tbody>
</table>
### Evidence Table Key

**Study Quality Category Definitions**

- **Category 1** The study is well-designed and accounts for common biases.
- **Category 2** The study is moderately well-designed and accounts for most common biases.
- **Category 3** There are important study design limitations.
- **Category 4** The study is not useful as primary evidence. The article may not be a clinical study or the study design is invalid, or conclusions are based on expert consensus. For example:
  - a) the study does not meet the criteria for or is not a hypothesis-based clinical study (e.g., a book chapter or case report or case series description);
  - b) the study may synthesize and draw conclusions about several studies such as a literature review article or book chapter but is not primary evidence;
  - c) the study is an expert opinion or consensus document.

- **M** = Meta-analysis

### Abbreviations Key

- **CI** = Confidence interval
- **CT** = Computed tomography
- **CXR** = Chest radiograph
- **FDG-PET** = Fluorine-18-2-fluoro-2-deoxy-D-glucose-positron emission tomography
- **GCT** = Germ cell tumor
- **MRI** = Magnetic resonance imaging
- **NPV** = Negative predictive value
- **NSGCT** = Nonseminomatous germ cell tumors
- **PPV** = Positive predictive value
- **RT** = Radiation therapy
- **TM** = Testicular microlithiasis
- **US** = Ultrasound

Dx = Diagnostic
Tx = Treatment