## Reference Study Type Patients/Events Study Objective (Purpose of Study) Study Results
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1. Siegel RL, Miller KD, Jemal A. Cancer Statistics, 2017. CA Cancer J Clin. 2017;67(1):7-30. Review/Other-Dx N/A To estimate the numbers of new cancer cases and deaths that will occur in the United States in the current year and compile the most recent data on cancer incidence, mortality, and survival. Mortality data were collected by the National Center for Health Statistics. In 2017, 1,688,780 new cancer cases and 600,920 cancer deaths are projected to occur in the United States. For all sites combined, the cancer incidence rate is 20% higher in men than in women, while the cancer death rate is 40% higher. However, sex disparities vary by cancer type. For example, thyroid cancer incidence rates are 3-fold higher in women than in men (21 vs 7 per 100,000 population), despite equivalent death rates (0.5 per 100,000 population), largely reflecting sex differences in the "epidemic of diagnosis." Over the past decade of available data, the overall cancer incidence rate (2004-2013) was stable in women and declined by approximately 2% annually in men, while the cancer death rate (2005-2014) declined by about 1.5% annually in both men and women. From 1991 to 2014, the overall cancer death rate dropped 25%, translating to approximately 2,143,200 fewer cancer deaths than would have been expected if death rates had remained at their peak. Although the cancer death rate was 15% higher in blacks than in whites in 2014, increasing access to care as a result of the Patient Protection and Affordable Care Act may expedite the narrowing racial gap; from 2010 to 2015, the proportion of blacks who were uninsured halved, from 21% to 11%, as it did for Hispanics (31% to 16%). Gains in coverage for traditionally underserved Americans will facilitate the broader application of existing cancer control knowledge across every segment of the population.

* See Last Page for Key

Revised 2017

van der Pol/Sahni

Page 1
## EVIDENCE TABLE

<table>
<thead>
<tr>
<th>Reference</th>
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<tr>
<td>2. Zhang J, Gerst S, Lefkowitz RA, Bach A. Imaging of bladder cancer. Radiol Clin North Am. 2007;45(1):183-205.</td>
<td>Review/Other-Dx</td>
<td>N/A</td>
<td>Review article on advances in imaging of bladder cancer.</td>
<td>CT urography can be used as a one-stop-shop examination to evaluate the entire urinary system. The overall accuracy of 83% can be achieved by CT for local staging and 73%-92% for nodal evaluation. MRI has the potential to become the modality of choice in staging all pelvic malignancies. Dynamic contrast-enhanced MR yields higher accuracy than other imaging techniques. Differentiation of post-treatment changes in the bladder from tumor, however, still can be difficult.</td>
<td>4</td>
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<tr>
<td>3. Amling CL. Diagnosis and management of superficial bladder cancer. Curr Probl Cancer. 2001;25(4):219-278.</td>
<td>Review/Other-Dx</td>
<td>N/A</td>
<td>Review of diagnosis and staging of superficial bladder cancer; includes demographics and epidemiology.</td>
<td>TCC accounts for greater than 90% of all bladder cancers; 70% of TCC present as superficial tumors; the remainder are invasive; 15%-20% of superficial tumors will progress to muscle invasion.</td>
<td>4</td>
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<tr>
<td>5. Shinagare AB, Ramaiya NH, Jagannathan JP, Fennessy FM, Taplin ME, Van den Abbeele AD. Metastatic pattern of bladder cancer: correlation with the characteristics of the primary tumor. AJR Am J Roentgenol. 2011;196(1):117-122.</td>
<td>Review/Other-Tx</td>
<td>150 patients</td>
<td>To evaluate the metastatic pattern of muscle-invasive bladder cancer and to correlate the findings with the characteristics of the primary tumor.</td>
<td>The TCC group consisted of 94 (63%) patients and the atypical histologic features group of 56 (37%) patients. The most common metastatic sites were lymph nodes (104 patients, 69%), bone (71 patients, 47%), lung (55 patients, 37%), liver (39 patients, 26%), and peritoneum (24 patients, 16%). Patients with tumors of a more advanced T category had shorter metastasis-free intervals (P=0.001). There was no significant difference in the metastatic patterns of tumors in the different T categories. Patients with atypical histologic features had a shorter median metastasis-free interval (3 months; range, 0-29 months) than patients with TCC (12 months; range, 0-192 months) (P=0.0001). Patients with atypical histologic features had a significantly higher incidence of peritoneal metastasis (P=0.0002).</td>
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# Pretreatment Staging of Muscle-Invasive Bladder Cancer

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<td>6. Roth B, Wissmeyer MP, Zehnder P, et al.</td>
<td>Observational-Dx</td>
<td>60 consecutive cystectomy patients</td>
<td>To use SPECT combined with CT plus intraoperative gamma probe verification to map the primary lymphatic landing sites of the bladder.</td>
<td>A median of 4 (range: 1-14) radioactive lymph nodes were detected per site and patient. Ninety-two percent of all lymph nodes were found distal and caudal to where the ureter crosses the common iliac arteries. Eight percent were found proximal to the ureter-iliaic crossing, none without simultaneous detection of additional radioactive lymph nodes within the endopelvic region. Extended pelvic lymph node dissection (PLND) resected 92% of all primary lymphatic landing sites; limited PLND resected only 52%. A few lymph nodes may have been missed despite preoperative SPECT/CT, intraoperative gamma probe verification, and extended backup PLND. Multimodality SPECT/CT plus intraoperative gamma probe show the template of the bladder's primary lymphatic landing sites to be larger than is often thought. PLND limited to the ventral portion of the external iliac vessels and obturator fossa removes only about 50% of all primary lymphatic landing sites, whereas extended PLND along the major pelvic vessels, including the internal iliac, external iliac, obturator, and common iliac region up to the uretero-iliaic crossing, removes about 90%.</td>
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<td>Lodde M, Lacombe L, Friede J, Morin F, Saourine A, Fradet Y. Evaluation of fluorodeoxyglucose positron-emission tomography with computed tomography for staging of urothelial carcinoma. BJU Int. 2010;106(5):658-663.</td>
<td>Observational- Dx</td>
<td>70 patients</td>
<td>To investigate the role of FDG-PET combined with CT and forced diuresis, in the staging and follow-up of urothelial carcinoma.</td>
<td>For the detection of primary urothelial bladder cancer, FDG-PET/CT was slightly more sensitive than CT (85% vs 77%) but less specific (25% vs 50%). For the detection of pelvic node metastasis FDG-PET/CT was more sensitive than CT (57% vs 33%) with a specificity of 100% for both imaging techniques. In 20 patients, extrapelvic FDG-PET/CT images showed suspected disease at the first evaluation. Urothelial carcinoma progressed in 9/10 patients who had synchronous multiple PET-positive retroperitoneal or mediastinal lymph nodes, and in only 2/9 with unique hyperactive lesions in the lung. FDG-PET/CT also detected a pT1G3 urothelial carcinoma of the renal pelvis and all bone metastases detected by bone scintigraphy.</td>
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<td>Saokar A, Islam T, Jantsch M, Saksena MA, Hahn PF, Harisinghani MG. Detection of lymph nodes in pelvic malignancies with Computed Tomography and Magnetic Resonance Imaging. Clin Imaging. 2010;34(5):361-366.</td>
<td>Observational- Dx</td>
<td>30 consecutive patients</td>
<td>To compare conventional contrast-enhanced MRI to contrast-enhanced helical CT for their ability to detect pelvic lymph nodes in patients with known primary bladder or prostate malignancy.</td>
<td>CT detected 189 nodes, and MRI detected 271 nodes. This difference was statistically significant in the external iliac (CT/MRI=73/87 nodes), obturator (CT/MRI=48/75 nodes), and internal iliac (CT/MRI=24/46 nodes) nodal chains. Based on size, the number of nodes detected by CT and MRI were as follows: 1–5 mm, CT/MRI=91/166; 6–10 mm, CT/MRI=91/98; N10 mm, CT/MRI=7/7 nodes. MRI detected significantly more lymph nodes in the size range of 1–5 mm.</td>
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<tr>
<td>9. Thoeny HC, Froehlich JM, Triantafyllou M, et al. Metastases in normal-sized pelvic lymph nodes: detection with diffusion-weighted MR imaging. Radiology. 2014;273(1):125-135.</td>
<td>Observational-Dx</td>
<td>120 Patients</td>
<td>To prospectively assess the diagnostic performance of diffusion-weighted (DW) magnetic resonance (MR) imaging in the detection of pelvic lymph node metastases in patients with prostate and/or bladder cancer staged as N0 with preoperative cross-sectional imaging.</td>
<td>A total of 4846 lymph nodes were resected in 120 patients. Eighty-eight lymph node metastases were found in 33 of 120 patients (27.5%). Short-axis diameter of these metastases was less than or equal to 3 mm in 68, more than 3 mm to 5 mm in 13, more than 5 mm to 8 mm in 5; and more than 8 mm in 2. On a per-patient level, the three readers correctly detected metastases in 26 (79%; 95% CI: 64%, 91%), 21 (64%; 95% CI: 45%, 79%), and 25 (76%; 95% CI: 60%, 90%) of the 33 patients with metastases, with respective specificities of 85% (95% CI: 78%, 92%), 79% (95% CI: 70%, 88%), and 84% (95% CI: 76%, 92%). Analyzed according to hemipelvis, lymph node metastases were detected with histopathologic examination in 44 of 240 pelvic sides (18%); the three readers correctly detected these on DW MR images in 26 (59%; 95% CI: 45%, 73%), 19 (43%; 95% CI: 27%, 57%), and 28 (64%; 95% CI: 47%, 78%) of the 44 cases.</td>
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## Pretreatment Staging of Muscle-Invasive Bladder Cancer

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<td>12. Zaid HB, Patel SG, Stimson CJ, et al. Trends in the utilization of neoadjuvant chemotherapy in muscle-invasive bladder cancer: results from the National Cancer Database. Urology. 2014;83(1):75-80.</td>
<td>Observational-Dx</td>
<td>5692 Patients</td>
<td>To evaluate variation in neoadjuvant chemotherapy (NAC) use among patients with &gt;10x clinical T2 (cT2) bladder cancer and determine changes in staging at radical cystectomy (RC) associated with therapy.</td>
<td>A total of 5692 patients met our inclusion criteria, 962 (16.9%) of whom received NAC. A multivariable logistic regression model revealed several factors that negatively influenced receipt of NAC: increasing age, lower patient income, and treatment at a nonacademic institution (P &lt;.01). Higher clinical stage and fewer comorbid conditions were associated with higher likelihood of receiving NAC (P &lt;.01). The overall use of NAC increased from 7.6% in 2006 to 20.9% in 2010 (P &lt;.01). Those receiving NAC were significantly more likely to be downstaged at RC (31.2% vs 7.6%, P &lt;.01), with 10.6% achieving complete pathologic downstaging.</td>
<td>3</td>
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<tr>
<td>13. Griffiths G, Hall R, Sylvester R, Raghavan D, Parmar MK. International phase III trial assessing neoadjuvant cisplatin, methotrexate, and vinblastine chemotherapy for muscle-invasive bladder cancer: long-term results of the BA06 30894 trial. J Clin Oncol. 2011;29(16):2171-2177.</td>
<td>Experimental-Tx</td>
<td>976 Patients</td>
<td>To present the long-term results of the international multicenter randomized trial that investigated the use of neoadjuvant cisplatin, methotrexate, and vinblastine (CMV) chemotherapy in patients with muscle-invasive urothelial cancer of the bladder treated by cystectomy and/or radiotherapy.</td>
<td>He previously reported possible survival advantage of CMV is now statistically significant at the 5% level. Results show a statistically significant 16% reduction in the risk of death (hazard ratio, 0.84; 95% CI, 0.72 to 0.99; P = .037, corresponding to an increase in 10-year survival from 30% to 36%) after CMV.</td>
<td>1</td>
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<tr>
<td>15. Beyersdorf D, Zhang J, Schoder H, Bochner B, Hricak H. Bladder cancer: can imaging change patient management? Curr Opin Urol. 2008;18(1):98-104.</td>
<td>Review/Other-Dx</td>
<td>N/A</td>
<td>To discuss the impact of technical advances in CT, MRI, and PET on management of patients with bladder cancer.</td>
<td>CT and MRI can visualize bladder cancer and perivesical infiltration, but MRI is superior for evaluation of the depth of invasion in the bladder wall.</td>
<td>4</td>
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<tr>
<td>16. American College of Radiology. ACR Appropriateness Criteria®: Hematuria. Available at: <a href="https://acsearch.acr.org/docs/69490/Narrative/">https://acsearch.acr.org/docs/69490/Narrative/</a>.</td>
<td>Review/Other-Dx</td>
<td>N/A</td>
<td>Evidence-based guidelines to assist referring physicians and other providers in making the most appropriate imaging or treatment decision for hematuria.</td>
<td>No results stated in abstract.</td>
<td>4</td>
</tr>
<tr>
<td>17. American College of Radiology. ACR Appropriateness Criteria®: Post-Treatment Surveillance of Bladder Cancer. Available at: <a href="https://acsearch.acr.org/docs/69364/Narrative/">https://acsearch.acr.org/docs/69364/Narrative/</a>.</td>
<td>Review/Other-Dx</td>
<td>N/A</td>
<td>Evidence-based guidelines to assist referring physicians and other providers in making the most appropriate imaging or treatment decision for post-treatment surveillance of bladder cancer.</td>
<td>No results stated in abstract.</td>
<td>4</td>
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</table>

* See Last Page for Key

Revised 2017

van der Pol/Sahni

Page 6
# Pretreatment Staging of Muscle-Invasive Bladder Cancer

## EVIDENCE TABLE

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<tr>
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<td>18.</td>
<td>MacVicar AD. Bladder cancer staging. BJU Int. 2000;86 Suppl 1:111-122.</td>
<td>Review/Other-Dx</td>
<td>N/A Review bladder cancer staging.</td>
<td>CT remains the mainstay of bladder cancer staging. CT cannot detect individual layers of the bladder wall and an important role of CT is to distinguish those tumors confined to the bladder wall from those spreading into the perivesical fat. CT has difficulty in tumor near the dome and trigone of the bladder and invasion with adjacent organs. MRI established an important imaging method for staging of bladder carcinoma and has the potential of becoming the investigation of choice. More accurate than CT in both local staging and lymph node metastases. MRI is the preferred technique for follow up imaging in patients post-cystectomy and radiation therapy.</td>
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<td>19.</td>
<td>Cohan RH, Caoili EM, Cowan NC, Weizer AZ, Ellis JH. MDCT Urography: Exploring a new paradigm for imaging of bladder cancer. AJR Am J Roentgenol. 2009;192(6):1501-1508.</td>
<td>Review/Other-Dx</td>
<td>N/A To review the epidemiology, staging, and treatment of bladder cancer; to discuss the role of MDCT urography for the evaluation of patients with known or suspected bladder cancer; and to address the role of MDCT urography in patients who require follow-up imaging after a diagnosis of bladder cancer has been made.</td>
<td>MDCT urography now has a large role in the evaluation of patients with known and suspected bladder cancer. However, its precise role has not been established. Because many bladder neoplasms will not be detected by MDCT urography and more research is needed to determine the optimal technique for diagnosing bladder cancer, the authors think that MDCT urography cannot replace cystoscopy at present.</td>
<td>4</td>
</tr>
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<td>20.</td>
<td>Vikram R, Sandler CM, Ng CS. Imaging and staging of transitional cell carcinoma: part 1, lower urinary tract. [Review] [37 refs]. AJR Am J Roentgenol. 192(6):1481-7, 2009 Jun.</td>
<td>Review/Other-Dx</td>
<td>N/A To discuss the epidemiology, pathologic characteristics, and patterns of tumor spread of bladder carcinomas. The authors illustrate and focus on the role of imaging in the diagnosis, staging, and surveillance of TCC.</td>
<td>The hallmark of TCC is multiplicity and recurrence. Cystoscopy is the method of choice for evaluation of the primary tumor in patients with bladder carcinoma. Imaging acts as an adjunct to accurately stage disease in these patients. Nearly 2%-4% of patients with bladder cancer develop upper tract TCC. Hence, surveillance of the upper tract, in which imaging plays a central role, is an important component in the management of TCC.</td>
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<td>21.</td>
<td>Barentsz JO, Ruijs SH, Strijk SP. The role of MR imaging in carcinoma of the urinary bladder. AJR Am J Roentgenol. 1993;160(5):937-947.</td>
<td>Review/Other-Dx</td>
<td>N/A To review the role of MRI in TCCB.</td>
<td>MRI and clinical staging are complementary for staging urinary bladder cancer; in superficial tumors, clinical staging, including transurethral resection, is the best technique. For invasive tumors, MR imaging is the best technique for staging.</td>
<td>4</td>
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</table>

* See Last Page for Key

Revised 2017

van der Pol/Sahni

Page 7
<table>
<thead>
<tr>
<th>Reference</th>
<th>Study Type</th>
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<td>22. Paik ML, Scolieri MJ, Brown SL, Spirnak JP, Resnick MI. Limitations of computerized tomography in staging invasive bladder cancer before radical cystectomy. J Urol. 2000;163(6):1693-1696.</td>
<td>Observational-Dx</td>
<td>82 consecutive cases</td>
<td>To determine the accuracy of staging CT findings, usefulness before planned extirpative surgery and impact or surgical management of this disease.</td>
<td>Overall accuracy in staging 54.9%. Understaging: 39%. Overstaging: 6.1%. Extraskeletal Spread: False positive: 4.9% False negative: 20.7% Lymph node involvement: False negative: 20.7% Preoperative CT altered planned surgical management 3.7%. Staging CT of the abdomen and pelvis in patients with invasive bladder carcinoma has limited accuracy, mainly because of its inability to detect microscopic or small volume extraskeletal tumor extension and lymph node metastases. CT tends to under stage advanced disease and failed to alter surgical management in nearly all of our cases.</td>
<td>3</td>
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<tr>
<td>23. Tritschler S, Mosler C, Straub J, et al. Staging of muscle-invasive bladder cancer: can computerized tomography help us to decide on local treatment? World J Urol. 2012;30(6):827-831.</td>
<td>Observational-Dx</td>
<td>276 patients</td>
<td>To assess the power of multi-detector row computerized tomography (MDCT) in daily routine as a basic staging procedure for the decision on local treatment of patients with bladder cancer.</td>
<td>Accuracy of MDCT in predicting pathological tumour stage was 49% (kappa coefficient, 0.23; P &lt; 0.001). Overstaging occurred in 23.4%, and understaging occurred in 24.7%. Accuracy in predicting lymph node metastases was 54% (kappa coefficient, 0.04; P = 0.297). Overstaging and understaging occurred in 8.3 and 29.4%, respectively. Significantly more ileal conduits were performed in patients with high postoperative pathological tumour stages (P = 0.04) and positive lymph nodes (P = 0.013). In contrast, there was no correlation between preoperative CT tumour/nodal stage and the number of removed lymph nodes (P = 0.44 and P = 0.732, respectively), and between preoperative tumour stage and type of urinary diversion (P = 0.126).</td>
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<td>24. Tritschler S, Mosler C, Tilki D, Buchner A, Stief C, Graser A. Interobserver variability limits exact preoperative staging by computed tomography in bladder cancer. Urology. 2012;79(6):1317-1321.</td>
<td>Observational-Dx</td>
<td>276 Patients</td>
<td>To evaluate the agreement between radiologic staging of bladder cancer using multidetector row computed tomography (CT) and histopathologic staging and estimate the influence of interobserver variability of the CT findings as a potential limitation of this imaging modality.</td>
<td>Preoperative CT scans were available for 276 patients who underwent radical cystectomy. The accuracy of the primary and reference radiologists in predicting the correct local tumor stage was 49% (kappa 0.23, P &lt; .001) and 51% (kappa 0.24, P &lt; .001), respectively. The accuracy in predicting the presence of lymph node metastases was 54% (kappa 0.04, P = .297) and 58% (kappa 0.15, P = .011). The agreement between both radiologists was fair with regard to the local tumor stage (kappa 0.23, P &lt; .001) and the presence of lymph node metastases (kappa 0.35, P &lt; .001).</td>
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<td>25. Yuan JB, Zu XB, Miao JG, Wang J, Chen MF, Qi L. Laparoscopic pelvic lymph node dissection system based on preoperative primary tumour stage (T stage) by computed tomography in urothelial bladder cancer: results of a single-institution prospective study. BJU Int. 2013;112(2):E87-91.</td>
<td>Observational-Tx</td>
<td>63 Patients</td>
<td>To study prospectively the clinical value of preoperative spiral computed tomography (CT) staging of primary tumours in deciding the extent of pelvic lymph node dissection (PLND) during laparoscopic radical cystectomy (RC) in the management of bladder cancer (BC).</td>
<td>All patients were divided into five categories according to their CTx stages: three at CT1, seven at CT2a, 38 at CT2b, seven at CT3b, and eight at CT4a. All 63 procedures were completed successfully without any conversion to open surgery. The mean estimated blood loss was 450 mL, and 14 patients (22.2%) had postoperative lymphatic leakage. Each case was pathologically confirmed as transitional cell carcinoma with negative margins at the urethral and ureteric stumps. None of the patients with a low CTx stage (CT1-CT2a) had positive lymph nodes above the level of the common iliac artery bifurcation. There was no jump lymph node metastasis, and no positive lymph node was detected above the level of aortic bifurcation in all cases.</td>
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<td>26. Horn T, Zahel T, Adt N, et al. Evaluation of Computed Tomography for Lymph Node Staging in Bladder Cancer Prior to Radical Cystectomy. Urol Int. 2016;96(1):51-56.</td>
<td>Observational-Dx</td>
<td>231 Patients</td>
<td>To retrospectively evaluate the value of CT for lymph node (LN) staging in bladder cancer.</td>
<td>LN metastases were found in 59 of 231 patients (25.5%). On a patient-based level, sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV) and accuracy were 52.6, 93.6, 73.2, 85.6 and 83.4%, respectively. Using the field-based approach, a total of 1,649 anatomical fields were evaluable, of which 114 fields showed malignancy (6.9%). On a field basis, sensitivity, specificity, PPV, NPV and accuracy were 30.2, 98, 51.5, 94.5 and 93.3%, respectively. Concerning local staging (pT category), the overall accuracy was 78%; overstaging occurred in 6% and understaging in 16%.</td>
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<td>27. Wang D, Zhang WS, Xiong MH, Yu M, Xu JX. Bladder tumors: dynamic contrast-enhanced axial imaging, multiplanar reconstruction, three-dimensional reconstruction and virtual cystoscopy using helical CT. Chin Med J (Engl). 2004;117(1):62-66.</td>
<td>Observational-Dx</td>
<td>42 patients</td>
<td>To evaluate clinical applications of helical CT dynamic contrast-enhanced axial imaging, MPR, 3D reconstruction and virtual cystoscopy in bladder tumors (benign and malignant). Results were compared with the findings of conventional cystoscopy and surgery in a double-blinded mode.</td>
<td>Sensitivity in detecting bladder tumors: 90.8% axial. 76.9% 3D. 95.4% CT virtual cystoscopic. Axial CT 87.7% accurate in preoperative staging of bladder cancer, 76.9% for Ta-T2 and 94.7% for T3-T4. Axial able to detect pathologic lymph nodes in 6/7 patients. MPR useful in demonstrating origin and extravesical invasion of tumors and relation to ureter. CT virtual cystoscopy could not provide extravesical information. The combination of axial, MPR, 3D and CT virtual cystoscopic images with helical CT can provide comprehensive information on bladder tumor.</td>
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### Pretreatment Staging of Muscle-Invasive Bladder Cancer

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<td>28. Rajesh A, Sokhi H, Fung R, Mulcahy KA, Bankart MJ. Role of whole-body staging computed tomographic scans for detecting distant metastases in patients with bladder cancer. J Comput Assist Tomogr. 2011;35(3):402-405.</td>
<td>Observational-Dx</td>
<td>201 patients</td>
<td>To establish the incidence of distant metastases on whole-body CT scans in patients with newly diagnosed bladder cancer and to determine whether there is a significant difference in the incidence of metastases in patients with superficial and muscle invasive cancers.</td>
<td>Of 201 patients, 11 (5.5%) were found to have distant metastases on CT. In univariable models, staging was not associated with either age (odds ratio, 0.98; 95% confidence interval, 0.92-1.04; P = 0.4) or sex (Fisher exact test, P = 0.07). Mean (SD) age was 74.1 (10.5) years. There was a significant association between staging and metastasis (odds ratio, 19.9; 95% confidence interval, 3.2-infinity; P = 0.0003). Of the patients, 7% of males had metastases versus 0% of the females. Staging CT scans for assessment of distant metastatic disease in patients with newly diagnosed bladder cancer can be restricted to patients with muscle invasive disease.</td>
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<td>30. Kawashima A, Vrtiska TJ, LeRoy AJ, Hartman RP, McCollough CH, King BF, Jr. CT urography. Radiographics. 2004;24 Suppl 1:S35-54; discussion S55-38.</td>
<td>Review/Other-Dx</td>
<td>N/A</td>
<td>Review of the role of CT urography in the evaluation of patients with urologic disease.</td>
<td>Neither excretory urography nor CT is as sensitive as cystoscopy. Gross urothelial tumor of the bladder can be detected. Ureteral obstruction caused by bladder cancer often a sign a muscle-invasive tumor. CT urography up to 97% sensitive in the detection of intrinsic urothelial lesions throughout the tract.</td>
<td>4</td>
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## EVIDENCE TABLE

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<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>
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<tbody>
<tr>
<td>31. Jinzaki M, Matsumoto K, Kikuchi E, et al. Comparison of CT urography and excretory urography in the detection and localization of urothelial carcinoma of the upper urinary tract. AJR Am J Roentgenol. 2011; 196(5):1102-1109.</td>
<td>Observational-Dx</td>
<td>104 patients and 552 urinary tract segments</td>
<td>To compare the accuracy of CTU and excretory urography for the detection and localization of upper urinary tract urothelial carcinoma.</td>
<td>Upper urinary tract urothelial carcinoma was diagnosed in 77 (14%) segments of 46 (44%) patients. Per-patient sensitivity, specificity, overall accuracy, and area under the receiver operating characteristic curves for detecting carcinomas with CTU (93.5% [43/46], 94.8% [55/58], 94.2% [98/104], and 0.963, respectively) were significantly greater than those for excretory urography (80.4% [37/46], 81.0% [47/58], 80.8% [84/104], and 0.831, respectively) (P=0.041, P=0.027, P=0.001, and P&lt;0.001, respectively). Per-segment sensitivity and overall accuracy for the localization of upper urinary tract urothelial carcinoma were significantly greater with CTU (87.0% [67/77] and 97.8% [540/552]) than with excretory urography (41.6% [32/77] and 91.5% [505/552]) (P&lt;0.0001).</td>
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<td>32. Vikram R, Sandler CM, Ng CS. Imaging and staging of transitional cell carcinoma: part 2, upper urinary tract. AJR Am J Roentgenol. 2009; 192(6):1488-1493.</td>
<td>Review/Other-Dx</td>
<td>N/A</td>
<td>To discuss the epidemiology, pathologic characteristics, and patterns of tumor spread. The authors also illustrate and discuss the role of imaging in the diagnosis, staging, and surveillance of TCC of the renal pelvis and the ureter.</td>
<td>The hallmark of TCC is multiplicity and recurrence. Nearly 2%-4% of patients with bladder cancer develop upper tract TCC; but 40% of patients with upper tract TCC develop bladder cancer. Diagnosis of upper tract TCC is heavily dependent on imaging. Understanding the appearances of upper tract TCC on the different imaging techniques used is important in the accurate interpretation of imaging studies. Newer techniques such as CTU are now increasingly used instead of conventional excretory urography in the surveillance of the upper tract in patients with bladder cancer.</td>
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* See Last Page for Key

Revised 2017 van der Pol/Sahni
Page 12
### Pretreatment Staging of Muscle-Invasive Bladder Cancer

#### EVIDENCE TABLE

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<tr>
<th>Reference</th>
<th>Study Type</th>
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<td>34. Wang HJ, Pui MH, Guo Y, et al.</td>
<td>Observational-Dx</td>
<td>39 Patients</td>
<td>To determine an optimal multiparametric MRI protocol for characterizing tumors of low versus high grade and differentiating tumors as T1 versus T2 for preoperative staging of bladder urothelial carcinoma.</td>
<td>A total of 49 category T1 and T2 lesions were analyzed. The average ADC of 11 low-grade tumors (1.141 +/- 0.164 x 10(-3) mm(2)/s) was significantly (p &lt; 0.05) higher than that of 20 high-grade malignant tumors (0.766 +/- 0.091 x 10(-3) mm(2)/s). Neither reader considered T1 tumors as probably having muscle invasion (category T2) in the T2-weighted plus DWI image sets or the T2-weighted plus DWI plus DCE-MRI image sets. Using the T2-weighted plus DCE-MRI sets, the two readers overstaged 13 and 15 of 36 tumors by misdiagnosing category T1 as T2. With the cutoff ADC value of 0.899 x 10(-3) mm(2)/s, the sensitivity and specificity for differentiating high- and low-grade bladder urothelial carcinoma were 100% and 95%.</td>
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<td>35. El-Assmy A, Abou-El-Ghar ME, Mosbah A, et al.</td>
<td>Observational-Dx</td>
<td>106 patients</td>
<td>To evaluate the clinical feasibility of DWI-MRI in detection and staging of urinary bladder tumor and to compare DWI-MRI with the T2-weighted technique.</td>
<td>In DWI staging accuracy was 63.6% and 69.6% in differentiating superficial from invasive tumors and organ-confined from non-organ-confined tumors, respectively. On a stage by a stage basis, DWI accuracy was 63.6% (21/33), 75.7% (25/33), 93.7% (30/32) and 87.5% (7/8) for stages T1, T2, T3 and T4, respectively. In the T2-weighted technique, the overall staging accuracy was only 39.6% and accuracy for differentiating superficial from invasive tumors and organ-confined from non-organ-confined tumors was 6.1% and 15.1%, respectively. DWI is superior to T2-weighted MRI in staging of organ-confined tumors =T2) and both techniques are comparable in the evaluation of higher-stage tumors.</td>
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* See Last Page for Key

Revised 2017

van der Pol/Sahni

Page 13
### EVIDENCE TABLE

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<th>Reference</th>
<th>Study Type</th>
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<td>36. Takeuchi M, Sasaki S, Ito M, et al. Urinary bladder cancer: diffusion-weighted MR imaging--accuracy for diagnosing T stage and estimating histologic grade. Radiology. 2009; 251(1):112-121.</td>
<td>Observational-Dx</td>
<td>40 patients with 52 bladder tumors</td>
<td>To prospectively evaluate the ability of DWI-MRI to be used to determine the T stage of bladder cancer and to measure the correlation between the ADC and histologic grade.</td>
<td>The overall accuracy of T stage diagnosis was 67% for T2-weighted images alone, 88% for T2-weighted plus DWI, 79% for T2-weighted plus contrast-enhanced images, and 92% for all 3 image types together. The overall accuracy, specificity, and A(z) for diagnosing T2 or higher stages were significantly improved by adding DWI (P&lt;.01). The mean ADC of G3 tumors was significantly lower than that of G1 and G2 tumors (P&lt;.01).</td>
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<td>37. Wu LM, Chen XX, Xu JR, et al. Clinical value of T2-weighted imaging combined with diffusion-weighted imaging in preoperative T staging of urinary bladder cancer: a large-scale, multiobserver prospective study on 3.0-T MRI. Acad Radiol. 2013;20(8):939-946.</td>
<td>Observational-Dx</td>
<td>362 Patients</td>
<td>To prospectively assess the incremental value of diffusion-weighted imaging (DWI) combined with T2-weighted images (T2WI) in determining the T stage of bladder cancer by using pathologic findings as the reference standard.</td>
<td>For differentiating Tis to T1 tumors from T2 to T4 tumors, the AUCs for T2WI and DWI (0.97 for observer 1 and 0.96 for observer 2) were greater than those for the DWI alone (0.92 for observer 1 and 0.90 for observer 2) (P &lt; .05). Observer 3 had similar AUCs for T2WI and DWI compared to DWI alone. The accuracy of T2WI and DWI (observer 1, 98%; observer 2, 96%; observer 3, 92%) was greater than that of DWI alone (observer 1, 92%; observer 2, 90%; observer 3, 87%) for all observers (P &lt; .05). The specificity of T2WI and DWI (observer 1, 100%; observer 2, 98%; observer 3, 93%) was greater than that of DWI alone (observer 1, 92%; observer 2, 90%; observer 3, 87%) for all observers (P &lt; .05). Sensitivity was not improved even when T2WI and DWI were used. For differentiating Tis to T2 Tumors from T3 to T4 Tumors, the overall accuracy, specificity, and AUC for diagnosing T2 or higher stages were not significantly improved by combiningT2WI and DWI.</td>
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<td>38. Kobayashi S, Koga F, Yoshida S, et al.</td>
<td>Observational-Dx</td>
<td>104 Patients</td>
<td>To investigate the diagnostic performance of diffusion-weighted magnetic resonance imaging (DW-MRI) in bladder cancer and the potential role of apparent diffusion coefficient (ADC) values in predicting pathological bladder cancer phenotypes associated with clinical aggressiveness.</td>
<td>In detecting patients with bladder cancer, DW-MRI exhibited high sensitivity equivalent to that of T2W-MRI (&gt;90%). Interobserver agreement was excellent for DW-MRI (kappa score, 0.88) though moderate for T2W-MRI (0.67). ADC values were significantly lower in high-grade (vs. low-grade, P &lt; 0.0001) and high-stage (T2 vs. T1 vs. Ta, P &lt; 0.0001) tumours. At a cut-off ADC value determined by partition analysis, clinically aggressive phenotypes including muscle-invasive bladder cancer (MIBC) and high-grade T1 disease were differentiated from less aggressive phenotypes with a sensitivity of 88%, a specificity of 85% and an accuracy of 87%.</td>
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<td>39. Daneshmand S, Ahmadi H, Huynh LN, Dobos N.</td>
<td>Observational-Dx</td>
<td>122 Patients</td>
<td>To evaluate the accuracy of dynamic gadolinium-enhanced magnetic resonance imaging (DGE-MRI) to detect extravesical bladder cancer (BC) and lymph node-positive disease in patients with invasive BC.</td>
<td>A total of 122 patients (72 men) with a mean age of 67.8 years were included. Pathologic examination revealed invasive BC in 80/122 (65.5%), including stage pT4 in 15/122 (12.3%), pT3 in 27/122 (22.1%), and pT2 in 38/122 (31.1%), and 27 patients (22.1%) had node-positive disease. The interobserver agreement for T and N staging according to the kappa score was 0.44 and 0.49, respectively. The sensitivity, specificity, and accuracy of DGE-MRI in differentiating lymph node-negative organ-confined from nonorgan-confined BC was 87.5%, 47.6%, and 74% and for the detection of positive nodal disease was 40.7%, 91.5%, and 80.3%, respectively.</td>
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<th>Study Objective (Purpose of Study)</th>
<th>Study Results</th>
<th>Study Quality</th>
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</thead>
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<td>40. Rajesh A, Sokhi HK, Fung R, Mulcahy KA, Bankart MJ. Bladder cancer: evaluation of staging accuracy using dynamic MRI. Clin Radiol. 2011;66(12):1140-1145.</td>
<td>Observational-Dx</td>
<td>100 Patients</td>
<td>To assess the accuracy of magnetic resonance imaging (MRI) in staging bladder cancer and to assess whether dynamic gadolinium-enhanced sequences have any added benefit in staging.</td>
<td>On a stage-by-stage basis, tumours were correctly staged using MRI in 63% of patients (observed agreement=0.63, weighted kappa=0.57). The sensitivity and specificity of MRI to differentiate between superficial ((\leq) T1) from invasive ((\geq) T2) disease was 78.2 and 93.3%. The observed agreement for this group was 85% (kappa=70%; p&lt;0.0001). The sensitivity and specificity of MRI to differentiate between organ-confined ((\leq) T2) from non-organ confined ((\geq) T3) disease was 90.5 and 60%. The observed agreement for this group was 89% (kappa=30%; p&lt;0.01). Gadolinium-enhanced images improved staging in only three patients.</td>
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<td>41. Rabie E, Faeghi F, Izadpanahi MH, Dayani MA. Role of Dynamic Contrast-Enhanced Magnetic Resonance Imaging in Staging of Bladder Cancer. J Clin Diagn Res. 2016;10(4):TC01-05.</td>
<td>Observational-Dx</td>
<td>45 Patients</td>
<td>To evaluate the accuracy of dynamic gadolinium-enhanced MRI in staging of bladder cancer through differentiating superficial tumours from invasive tumours and organ-confined tumours from non-organ-confined tumours and investigate the benefits of DCE-MRI in diagnosis of tumor progression steps.</td>
<td>The most common stage that was seen in pathology and MRI findings was T3b. Kappa agreement coefficient between MRI and pathology was 0.7 (p=0.001). The accuracy of MRI in differentiating superficial tumours ((\leq)T1) from invasive tumours ((\geq) T2a), and organ-confined tumours ((\leq)T2b) from non-organ-confined tumours ((\geq) T3b) was 0.97 and 0.84, respectively. The overall accuracy of MRI was 0.77 (p&lt;0.001). Totally, 10 cases of disagreement between MRI and pathological staging were found, eight (80%) of which were overestimated and two cases (20%) underestimated. MRI detection rate was 0% in stage Ta, 100% in stage T1, 66.7% in stage T2, 86.7% in stage T3, and 100% in stage T4. The sensitivity and specificity of MRI in differentiating superficial tumours from invasive tumours were 0.97 and 1, respectively, and in differentiating organ-confined tumours from non-organ-confined tumours were 0.94 and 0.77, respectively. The Spearman's correlation coefficient between the signal enhancement slope of time-intensity curves and tumour stages was 0.88 (p&lt;0.001).</td>
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<th>Patients/Events</th>
<th>Study Objective (Purpose of Study)</th>
<th>Study Results</th>
<th>Study Quality</th>
</tr>
</thead>
<tbody>
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<td>42. Ghafoori M, Shakiba M, Ghiasi A, Asvadi N, Hosseini K, Alavi M. Value of MRI in local staging of bladder cancer. Urol J. 2013;10(2):866-872.</td>
<td>Observational-Dx</td>
<td>86 Patients</td>
<td>To evaluate the accuracy of magnetic resonance imaging (MRI) in bladder cancer staging as well as differentiating superficial from invasive tumors and organ-confined from non-organ-confined tumors.</td>
<td>The most common stage determined by both MRI and pathology was T2a. Considering stages in details, the kappa agreement coefficient between MRI and pathology was 0.8 (P &lt; .0001). Combining groups a and b in each stage, the kappa agreement coefficient between MRI and pathology was 0.87 (P &lt; .0001). Considering stages in details, we had 22 (20.3%) mismatches in staging between MRI and pathology; 10 (45.5%) were underestimation and 12 (54.5%) were overestimation. Combining groups a and b in each stage, we had 14 (13%) mismatch cases; 6 (46.2%) were underestimation and 8 (53.8%) were overestimation. The detection rate of MRI was 0% in stage Ta, 80% in stage T1, 88.1% in stage T2, 81.2% in stage T3, and 100% in stage T4. The sensitivity and specificity of MRI in differentiating superficial from deep tumors were 0.98 and 0.82, respectively. The sensitivity and specificity of MRI in differentiating organ-confined from non-organ-confined tumors were 0.93 and 0.94, respectively.</td>
<td>2</td>
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<tr>
<td>43. Gupta N, Sureka B, Kumar MM, Malik A, Bhushan TB, Mohanty NK. Comparison of dynamic contrast-enhanced and diffusion weighted magnetic resonance image in staging and grading of carcinoma bladder with histopathological correlation. Urol Ann. 2015;7(2):199-204.</td>
<td>Observational-Dx</td>
<td>60 Patients</td>
<td>To evaluate and compare accuracy of Dynamic contrast enhanced (DCE) and Diffusion weighted (DW) MRI for preoperative T staging of urinary bladder cancer and find correlation between apparent diffusion coefficient (ADC) and maximum enhancement with histological grade.</td>
<td>The extent of agreement between the radiologic staging and histopathological staging was relatively greater with the DW-MRI (kappa=0.669) than DCE-MRI (kappa=0.619). The sensitivity, specificity, and accuracy are maximum and similar for stage T4 tumors in both DCEMRI (100.0, 96.2 and 96.7) and DW-MRI (100.0, 96.2 and 96.7) while minimum for stage T2 tumors - DCEMRI (83.3, 72.2, and 76.7) and DW-MRI (91.7, 72.2, and 80).</td>
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### Pretreatment Staging of Muscle-Invasive Bladder Cancer

#### EVIDENCE TABLE

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<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>44. Nguyen HT, Pohar KS, Jia G, et al. Improving bladder cancer imaging using 3-T functional dynamic contrast-enhanced magnetic resonance imaging. Invest Radiol. 2014;49(6):390-395.</td>
<td>Observational-Dx</td>
<td>36 Patients</td>
<td>To assess the capability of T2-weighted magnetic resonance imaging (T2W-MRI) and the additional diagnostic value of dynamic contrast-enhanced MRI (DCE-MRI) using multitransmit 3 T in the localization of bladder cancer.</td>
<td>The sensitivity, specificity, and accuracy of the localization with T2W-MRI alone were 81% (29/36), 63% (5/8), and 77% (34/44) for observer 1 and 72% (26/36), 63% (5/8), and 70% (31/44) for observer 2. With additional DCE-MRI available, these values were 92% (33/36), 75% (6/8), and 89% (39/44) for observer 1 and 92% (33/36), 63% (5/8), and 86% (38/44) for observer 2. Dynamic contrast-enhanced MRI significantly (P&lt;0.01) improved the sensitivity and accuracy for observer 2. For the 23 patients treated with chemotherapy, DCE-MRI also significantly (P&lt;0.02) improved the sensitivity and accuracy of bladder cancer localization with T2W-MRI alone for observer 2. Scores of kappa were 0.63 for T2W-MRI alone and 0.78 for additional DCE-MRI. Of 7 subcentimeter malignant tumors, 4 (57%) were identified on T2W images and 6 (86%) were identified on DCE maps. Of 11 malignant tumors within the bladder wall thickening, 6 (55%) were found on T2W images and 10 (91%) were found on DCE maps.</td>
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<td>45. Liedberg F, Bendahl PO, Davidsson T, et al. Preoperative staging of locally advanced bladder cancer before radical cystectomy using 3 tesla magnetic resonance imaging with a standardized protocol. Scand J Urol. 47(2):108-12, 2013 Apr.</td>
<td>Observational-Dx</td>
<td>53 Patients</td>
<td>To compare tumour stage at MRI with pathological tumour stage in the cystectomy specimen.</td>
<td>MRI overestimated tumour stage in 23 out of 47 patients (49%), whereas six patients (13%) were understaged. In the three groups of patients (those with the same stage group at MRI as in the cystectomy specimen, overestimated tumour stage and understaged patients), the time interval between transurethral resection of the bladder (TURB) and MRI did not differ significantly.</td>
<td>2</td>
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</tbody>
</table>

* See Last Page for Key

Revised 2017

van der Pol/Sahni

Page 18
### EVIDENCE TABLE

<table>
<thead>
<tr>
<th>Reference</th>
<th>Study Type</th>
<th>Patients/Events</th>
<th>Study Objective (Purpose of Study)</th>
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<td>46. Shariat SF, Palapattu GS, Karakiewicz PI, et al. Discrepancy between clinical and pathologic stage: impact on prognosis after radical cystectomy. Eur Urol. 2007;51(1):137-149; discussion 149-151.</td>
<td>Observational-Dx</td>
<td>778 Patients</td>
<td>To compare clinical and pathologic staging in a large, contemporary, consecutive series of patients who were treated with radical cystectomy and pelvic lymphadenectomy, and determined the effect of stage discrepancy on outcomes.</td>
<td>Pathologic upstaging occurred in 42% of patients, and pathologic downstaging occurred in 22%. Forty percent of patients with non-muscle-invasive clinical stage had muscle-invasive pathologic stage. Thirty-six percent of patients with organ-confined clinical stage had non-organ-confined pathologic stage (&gt; or =pT3N0 or pTanyN-positive). Patients with higher clinical stage were more likely to be upstaged to non-organ-confined disease (p&lt;0.001). Patients were stratified into three groups: pathologically upstaged, same clinical and pathologic stage, and pathologically downstaged. When adjusted for the effects of standard postoperative features, upstaged patients were at a significantly higher risk of disease recurrence and bladder cancer-specific death than patients who had the same pathologic and clinical stage, who in turn were at significantly higher risk than downstaged patients. This observation remained true within each clinical stage strata. Within each pathologic stage strata, clinical stage did not substratify into different risk groups.</td>
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<td>47. Klein L, Pollack HM. Computed tomography and magnetic resonance imaging of the female lower urinary tract. [Review] [73 refs]. Radiol Clin North Am. 30(4):843-60, 1992 Jul.</td>
<td>Review/Other-Dx</td>
<td>N/A</td>
<td>To review the use of CT and MRI of female lower urinary tract.</td>
<td>Both CT and MR imaging are able to accurately stage bladder carcinoma, with MR imaging able to distinguish between superficial and deep muscle invasion of tumor. CT and MR are also the studies of choice for evaluating retroperitoneal fibrosis, which often affects the urinary tract; MR imaging is often able to detect the presence of active inflammation and occasionally rule out a malignant cause. MR imaging holds promise for the evaluation of stress urinary incontinence and urethral disease. Although diseases of the distal ureter continue to be most accurately diagnosed by intravenous urography and retrograde studies, CT and MR imaging may serve a helpful secondary role.</td>
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<td>48. Yoshida S, Koga F, Kawakami S, et al. Initial experience of diffusion-weighted magnetic resonance imaging to assess therapeutic response to induction chemoradiotherapy against muscle-invasive bladder cancer. Urology. 2010; 75(2):387-391.</td>
<td>Observational- Dx</td>
<td>20 patients</td>
<td>To investigate the feasibility of DWI-MRI in predicting therapeutic response to low-dose chemoradiotherapy against muscle-invasive bladder cancer.</td>
<td>Pathologic examination of cystectomy specimens revealed pathologic complete response in 13 (65%) of the 20 patients. The sensitivity/specificity/accuracy of T2-weighted, DCE, and DWI in predicting pathologic response was 43%/45%/44%, 57%/18%/33%, and 57%/92%/80%, respectively. Despite comparable sensitivity, DWI was significantly superior in specificity and accuracy to T2-weighted (P=.03 and .02, respectively) and DCE (P=.002 for both).</td>
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<td>49. Takahashi N, Kawashima A, Glockner JF, et al. Small (&lt;2-cm) upper-tract urothelial carcinoma: evaluation with gadolinium-enhanced three-dimensional spoiled gradient-recalled echo MR urography. Radiology. 2008;247(2):451-457.</td>
<td>Observational- Dx</td>
<td>110 patients; 11 patients with 23 upper-tract urothelial carcinomas &lt; 2 cm</td>
<td>To retrospectively evaluate the detection of small (&lt;2-cm) urothelial tumors by using gadolinium-enhanced 3D spoiled gradient-recalled echo (GRE) MR urography.</td>
<td>Of 23 tumors, 17 (74%) were detected by using at least one sequence, eight (35%) were detected with T2-weighted imaging, 15 (65%) were detected on nephrographic phase images, and 15 (65%) were detected on excretory phase images. Two lesions each were detected only on either nephrographic or excretory phase images. Detectability was significantly higher on nephrographic and excretory phase images compared with T2-weighted images (P &lt; .05). Gadolinium-enhanced 3D spoiled GRE MR urography helped detect 74% of small urothelial carcinomas. Nephrographic and excretory phase images are essential for helping detect small urothelial carcinomas.</td>
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<td>50. Goodfellow H, Viney Z, Hughes P, et al. Role of fluorodeoxyglucose positron emission tomography (FDG PET)-computed tomography (CT) in the staging of bladder cancer. BJU Int. 2014;114(3):389-395.</td>
<td>Observational-Dx</td>
<td>233 Patients</td>
<td>To determine whether to use (18) F-fluorodeoxyglucose positron emission tomography (FDG PET) scans in the preoperative staging of bladder cancer (BC).</td>
<td>The PET scan was able to detect metastatic disease outside of the pelvis with a sensitivity of 54% compared with 41% for the staging CT (N = 207). Both scans had similar specificities of 97% and 98%. There were 13 PET avid lesions not visualised on the corresponding staging CT scans. These proved to be metastatic BC (six patients), a synchronous primary colonic cancer (one), colonic adenomas (one), basal cell tumour of the parotid gland (one) and inflammatory lesions (four). The sensitivity and specificity of the CT scans for pelvic LN involvement was 45% and 98%, respectively (N = 93). Using a combination of the PET and CT scan, the sensitivity for detecting metastatic disease in LNs increased to 69% with a 3% reduction in specificity to 95%.</td>
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<td>51. Nayak B, Dogra PN, Naswa N, Kumar R. Diuretic 18F-FDG PET/CT imaging for detection and locoregional staging of urinary bladder cancer: prospective evaluation of a novel technique. Eur J Nucl Med Mol Imaging. 2013;40(3):386-393.</td>
<td>Observational-Dx</td>
<td>25 Patients</td>
<td>To evaluate the potential application of diuretic (18)F-FDG PET/CT in improving detection and locoregional staging of urinary bladder tumours.</td>
<td>Of the 25 patients, CECT detected a primary tumour in 23 (sensitivity 92 %), while (18)F-FDG PET/CT was positive in 24 patients (sensitivity 96 %). Mean size and maximum standardized uptake value of the bladder tumours were 3.33 cm (range 1.6-6.2) and 5.3 (range 1.3-11.7), respectively. Of the 25 patients, only 10 patients underwent radical cystectomy based on disease status on TURBT. Among those ten patients, nine had locoregional metastases. Among the nine patients who had positive lymph nodes for metastasis on histopathology, CECT and PET/CT scan had a sensitivity of 44 and 78 %, respectively. (18)F-FDG PET/CT was found to be superior to CECT in the detection of the primary tumour and locoregional staging (p &lt; 0.05).</td>
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<td>52. Soubra A, Hayward D, Dahm P, et al.</td>
<td>Observational-Dx</td>
<td>78 Patients</td>
<td>To assess the diagnostic accuracy of 18F-fluorodeoxyglucose with positron emission tomography and computed tomography (FDG-PET-CT) to predict nodal metastases in patients with bladder cancer (BC) scheduled to undergo radical cystectomy (RC).</td>
<td>For detecting nodal metastases in 78 patients, the sensitivity of FDG-PET-CT was 0.56 (95% CI 0.29-0.80) and the specificity, 0.98 (95% CI 0.91-1.00). Pooled sensitivity and specificity for detecting lymph node metastasis were 0.57 and 0.95, respectively. Positive likelihood ratio was 9.02. All lesions that were suspicious for distant metastasis were found to be positive on biopsy.</td>
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<td>53. Pichler R, De Zordo T, Fritz J, et al. Pelvic Lymph Node Staging by Combined 18F-FDG-PET/CT Imaging in Bladder Cancer Prior to Radical Cystectomy.</td>
<td>Observational-Dx</td>
<td>70 Patients</td>
<td>To evaluate the diagnostic accuracy of contrast-enhanced computed tomography (CT) and 18F-fluorodeoxyglucose (18F-FDG) positron emission tomography (PET) alone, or combined for preoperative pelvic LN staging.</td>
<td>Metastatic LNs were confirmed in 53 (2.8%) of 1906 resected LNs in 11 (15.7%) patients. Sensitivity, specificity, and accuracy were 54.5%, 89.8%, and 84.3% for 18F-FDG-PET alone; 45.5%, 91.5%, and 84.3% for CT (LNs &gt; 8 mm) alone; and 27.3%, 96.6%, and 85.7% for CT (LNs &gt; 10 mm) alone, respectively. Combined 18F-FDG-PET/CT resulted in a nonsignificant increase of diagnostic accuracy using a cutoff &gt; 8 mm for LN evaluation (63.6%, 86.4%, and 82.9%, respectively). A significant improvement of sensitivity to 63.6% was achieved only when LNs &gt; 10 mm were considered suspicious (P = .046), but this reduced specificity to 88.1% (P = .025).</td>
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<td>54. Kibel AS, Dehdashti F, Katz MD, et al. Prospective study of [18F]fluorodeoxyglucose positron emission tomography/computed tomography for staging of muscle-invasive bladder carcinoma. J Clin Oncol. 2009; 27(26):4314-4320.</td>
<td>Observational-Dx</td>
<td>43 chemotherapy-naive patients</td>
<td>To report a prospective study of FDG-PET/CT in patients undergoing radical cystectomy for cT2-3N0M0 urothelial carcinoma of the bladder.</td>
<td>Median follow-up was 14.9 months (range, 0.4 to 46.1 months). One patient who did not undergo lymphadenectomy was excluded from the pathology data analysis (n=42), whereas another patient who failed to return for follow-up was excluded from survival analysis (n=42). FDG-PET/CT demonstrated a PPV of 78% (7/9), a NPV of 91% (30/33), sensitivity of 70% (7/10), and specificity of 94% (30/32). Recurrence-free survival, disease-specific survival, and OS were all significantly poorer in the patients with positive FDG-PET/CT than in those with negative FDG-PET/CT.</td>
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<td>55. Apolo AB, Riches J, Schoder H, et al.</td>
<td>Observational-Dx</td>
<td>57 patients</td>
<td>To investigate the value of FDG-PET/CT imaging in the management of patients with advanced bladder cancer.</td>
<td>135 individual lesions were evaluable in 47 patients for the organ-based analysis. Overall sensitivity and specificity were 87% (95% CI, 76% to 94%) and 88% (95% CI, 78% to 95%), respectively. In the patient-based analysis, malignant disease was correctly diagnosed in 25 of 31 patients, resulting in a sensitivity of 81% (95% CI, 63% to 93%). FDG-PET/CT was negative in 15 of 16 patients without malignant lesions for a specificity of 94% (95% CI, 71% to 100%). Pre- and post-PET surveys revealed that FDG-PET/CT detected more malignant disease than conventional CT/MRI in 40% of patients. Post-PET surveys showed that clinicians changed their planned management in 68% of patients based on the FDG-PET/CT results. FDG-PET/CT has excellent sensitivity and specificity in the detection of metastatic bladder cancer and provides additional diagnostic information that enhances clinical management more than CT/MRI alone. FDG-PET/CT scans may provide better accuracy in clinical information for directing therapy.</td>
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<tr>
<td>56. Kollberg P, Almquist H, Blackberg M, et al.</td>
<td>Review/Other-Dx</td>
<td>103 Patients</td>
<td>To evaluate the clinical use of [(18)F]fluorodeoxyglucose-positron emission tomography/computed tomography (FDG-PET/CT) in addition to conventional preoperative radiological investigations in a defined group of patients with high-risk muscle-invasive bladder cancer.</td>
<td>Compared to CT alone, FDG-PET/CT provided more supplemental findings suggesting malignant manifestations in 48 (47%) of the 103 patients. The additional FDG-PET/CT findings led to an altered provisional treatment plan in 28 out of 103 patients (27%), detection of disseminated bladder cancer and subsequent cancellation of the initially intended cystectomy in 16 patients, and identification of disseminated disease and treatment with induction chemotherapy before radical cystectomy in 12 patients.</td>
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## Pretreatment Staging of Muscle-Invasive Bladder Cancer

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<tr>
<td>57. Mertens LS, Fioole-Bruining A, Vegel E, Vogel WV, van Rhijn BW, Horenblas S. Impact of (18) F-fluorodeoxyglucose (FDG)-positron-emission tomography/computed tomography (PET/CT) on management of patients with carcinoma invading bladder muscle. BJU Int. 2013;112(6):729-734.</td>
<td>Review/Other-Tx</td>
<td>96 Patients</td>
<td>To evaluate the clinical impact of (18) F-fluorodeoxyglucose (FDG)-positron-emission tomography/computed tomography (PET/CT) scanning, compared with conventional staging with contrast-enhanced CT imaging (CECT).</td>
<td>The median (range) interval between CECT and FDG-PET/CT was 0 (0-29) days. In 21.9% of the patients, stage on FDG-PET/CT and CECT were different. Upstaging by FDG-PET/CT was more frequent than downstaging (19.8 vs 2.1%). Clinical management changed for 13.5% of patients as a result of FDG-PET/CT upstaging. In eight patients, FDG-PET/CT detected second primary tumours. This led to changes of bladder cancer treatment in another four of 96 patients (4.2%). All the management changes were validated by tissue confirmation of the additional lesions.</td>
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<tr>
<td>58. Picchio M, Treiber U, Beer AJ, et al. Value of 11C-choline PET and contrast-enhanced CT for staging of bladder cancer: correlation with histopathologic findings. J Nucl Med. 2006;47(6):938-944.</td>
<td>Observational-Dx</td>
<td>27 patients</td>
<td>To compare the diagnostic accuracy of contrast enhanced CT with 11C-choline PET for the staging of bladder cancer.</td>
<td>The presence of residual bladder cancer (pTa-pT4) was correctly detected in 21/25 histologically tumor-positive patients (84%) by CT and in 24/25 patients (96%) by 11C-choline PET. Lymph node involvement was correctly detected in 4/8 patients (50%) by CT and in 5/8 patients (62%) by 11C-choline PET. The median size of the 3 nodes with false-negative PET results was 9 mm (range, 6-21 mm), and the median size of the metastatic lesions within the lymph nodes was 3 mm (range, 1-15 mm). CT resulted in 6 (22%) false-positive lymph nodes, whereas none was demonstrated by 11C-choline PET; these data indicated a significantly higher accuracy of PET than of CT (P&lt;0.01). Both modalities missed a small peritoneal metastasis verified by histologic evaluation. No positive results were obtained from bone scintigraphy.</td>
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* See Last Page for Key

Revised 2017

van der Pol/Sahni

Page 24
<table>
<thead>
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<th>Reference</th>
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<th>Study Objective (Purpose of Study)</th>
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<tr>
<td>59. Brunocilla E, Ceci F, Schiavina R, et al. Diagnostic accuracy of (11)C-choline PET/CT in preoperative lymph node staging of bladder cancer: a systematic comparison with contrast-enhanced CT and histologic findings. Clin Nucl Med. 2014;39(5):e308-312.</td>
<td>Observational-Dx</td>
<td>26 Patients</td>
<td>To evaluate the role of C-choline PET/CT in the preoperative evaluation of the nodal involvement of patients with bladder carcinoma (BC) suitable for radical cystectomy and extended pelvic lymph node dissection in comparison with contrast-enhanced CT (CECT) using the pathologic specimen as reference standard.</td>
<td>Seven of 26 patients (26.9%) showed nodal metastases at pathologic analysis. Overall, 844 LNs were evaluated, and 38 of them (4.5%) showed metastatic involvement. On a patient-based analysis, C-choline PET/CT showed a sensitivity of 42% and specificity of 84%, whereas, CECT showed a sensitivity of 14% and specificity of 89%. On a region-based analysis, C-choline PET/CT showed a sensitivity of 11% and specificity of 82%, whereas CECT showed a sensitivity of 5% and specificity of 80%. On a lesion (LN)-based analysis, C-choline PET/CT showed a sensitivity of 10% and specificity of 64%, whereas CECT showed a sensitivity of 2% and specificity of 63%.</td>
<td>3</td>
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<tr>
<td>60. Ceci F, Bianchi L, Graziani T, et al. 11C-choline PET/CT and bladder cancer: lymph node metastasis assessment with pathological specimens as reference standard. Clin Nucl Med. 2015;40(2):e124-128.</td>
<td>Observational-Dx</td>
<td>59 Patients</td>
<td>To evaluate the potential role of C-choline-PET/CT in nodal assessment in patients with bladder cancer (BCa) using the pathological specimen as reference standard.</td>
<td>C-choline-PET/CT overall detection rate was 62.7% (37/59 patients). On a regional-based analysis, C-choline-PET/CT was considered positive for primary cancer and/or local relapse in bladder bed in 54.2% of the patients (32/59). Pathological LN uptake was reported in 23.7% of the patients (14/59) and systemic choline deposit (bone or lung) in 11.8% of the patients (7/59). Considering LN metastasis detection, compared with histological analysis, C-choline-PET/CT showed in the whole population a sensitivity, specificity, positive predictive value, negative predictive value, and accuracy of 59%, 90%, 71%, 84%, and 81%, respectively. No other investigated factors reached statistical significance.</td>
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<td>61. Golan S, Sopov V, Baniel J, Groshar D. Comparison of 11C-choline with 18F-FDG in positron emission tomography/computerized tomography for staging urothelial carcinoma: a prospective study. J Urol. 2011;186(2):436-441.</td>
<td>Observational-Tx</td>
<td>20 Patients</td>
<td>To compare the value of using 11C-choline with the well investigated 18F-FDG tracer in this setting.</td>
<td>A total of 51 lesions showed abnormal tracer activity. The positive predictive value for all detected lesions was 84.7% for 11C-choline positron emission tomography/computerized tomography and 90.7% for 18F-FDG positron emission tomography/computerized tomography. The corresponding positive predictive values for extravesical lesions were 79.4% and 88.2%, respectively. Discrepant findings between the tracers were noted at 11 sites. 18F-FDG positron emission tomography/computerized tomography correctly identified 4 extravesical metastases missed by choline positron emission tomography/computerized tomography in the absence of a contrary observation. Mean maximum standardized uptake and lesion-to-background ratio at extravesical sites were significantly higher for FDG.</td>
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<td>62. Kuroda M, Meguro N, Maeda O, et al. Stage specific follow-up strategy after cystectomy for carcinoma of the bladder. Int J Urol. 2002;9(3):129-133.</td>
<td>Observational-Dx</td>
<td>351 patients</td>
<td>To develop a stage specific follow-up strategy after cystectomy for bladder cancer.</td>
<td>The risk of metastases was related to the pathologic stage of the primary tumor. Recurrences in patients with pT3 or higher were found earlier and more frequently than those with pT2 or lower. A stage-driven follow-up strategy for monitoring patients after radical cystectomy can reduce medical expenses while efficiently detecting recurrences and complications.</td>
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<td>65. Brismar J, Gustafson T. Bone scintigraphy in staging of bladder carcinoma. Acta Radiol. 1988;29(2):251-252.</td>
<td>Observational-Dx</td>
<td>71 consecutive cases 458 staging bone scans</td>
<td>To evaluate the efficacy of bone scanning in staging of bladder cancer.</td>
<td>4.6% positive (2.8% true, 1.7% false). In only four (0.9%) was surgery avoided because of the results, “scintigraphy thus has no place in the routine preoperative staging of bladder carcinoma”.</td>
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* See Last Page for Key

Revised 2017

van der Pol/Sahni
Page 26
## Pretreatment Staging of Muscle-Invasive Bladder Cancer

### EVIDENCE TABLE

<table>
<thead>
<tr>
<th>Reference</th>
<th>Study Type</th>
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<td>66. Braendengen M, Winderen M, Fossa SD. Clinical significance of routine pre-cystectomy bone scans in patients with muscle-invasive bladder cancer. Br J Urol. 1996;77(1):36-40.</td>
<td>Observational-Dx</td>
<td>91 patients</td>
<td>To evaluate the clinical significance of bone scans taken routinely before total cystectomy in patients with bladder cancer of clinical stage =T2.</td>
<td>Of the 91 patients, 37 (41%) developed skeletal bone metastases after cystectomy, unrelated to the clinical T category. In 35 patients, the pre-cystectomy bone scan showed pathological uptake of isotope which was interpreted by the specialist in nuclear medicine as suspicious of (13 patients) or probably caused by (22 patients) skeletal metastases. In either circumstance, the clinician decided that total cystectomy was precluded, particularly as most of the changes could be explained radiologically as being degenerative. In the individual patient, there was no clinically useful correlation between the findings on the precystectomy bone scan and the clinical course of disease, nor if serum alkaline phosphatase level was included as an additional predictive factor. The findings of a routine preoperative bone scan are usually unable to identify patients with bladder cancer of stage =T2 who will not be cured by total cystectomy. Unless further investigations, particularly MRI, can be performed, the findings of a routine pre-operative bone scan are usually unable to identify patients with bladder cancer of stage &gt; or = T2 who will not be cured by total cystectomy.</td>
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* See Last Page for Key

Revised 2017

van der Pol/Sahni

Page 27
<table>
<thead>
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<th>Reference</th>
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<tr>
<td>67. Taher AN, Kotb MH. Bone metastases in muscle-invasive bladder cancer. J Egypt Natl Canc Inst. 2006;18(3):203-208.</td>
<td>Observational-Dx</td>
<td>179 patients</td>
<td>To address the necessity of incorporating isotopic bone scan in the routine staging work-up of muscle invasive bladder cancer patients, the authors analyzed the data in their files to determine the incidence of bone metastasis in such patients. The rate of subsequent development of bone metastasis along the natural history of the disease was also investigated.</td>
<td>Amongst the 179 patients, 26 (14.5%) had bone metastasis on presentation, a finding that showed a statistically significant correlation with the increasing depth of muscle invasion; 61.5% of the metastatic cases had deep muscle invasion, 19.2% had superficial muscle invasion and there was no muscle invasion in 7.7% (p=0.000). Transitional cell carcinoma was the pathology in 92.3% of those patients, while only 7.7% had squamous cell carcinoma (p=0.036). The cumulative 3-year incidence of bone-metastasis in the non metastatic patients after treatment mounted to 19.4 +/- 4.4%. The cumulative 3-year bone metastasis incidence in the 153 patients was higher with increasing clinical stage; 8.4 +/- 8% for c-stage 2 and 49.1 +/- 18.5% for c-stage 4 (p=0.046). As for the p-category of the tumor in the 130 patients who underwent operation, the incidence increased with higher p-stages (p=0.006). Though pelvic nodal involvement was not associated with statistically significant increase in the incidence of bone metastases, yet when incorporated as one of the 3 risk factors (grade&gt;3, p (3) 4a and lymph node positive at surgery) according to which patients were grouped, there was a statistically significant difference in the incidence between patients with no risk factors, only 1 and 2 or more factors (p=0.021). CONCLUSION: Meticulous search for bone metastasis alone or as a component of distant failure in the newly diagnosed bladder cancer patients is crucial to offer them the proper management and avoid undue radical surgical procedures. Thus bone scan is suggested to be performed routinely in patients with evidence of muscle invasion.</td>
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<tr>
<td>68. Fang YC, Chou YH, Hsu CC, Chang T. Staging of bladder cancer by transabdominal real-time ultrasound. Zhonghua Yi Xue Za Zhi (Taipei). 1993;52(1):21-25.</td>
<td>Observational-Dx</td>
<td>214 patients staged for bladder cancer</td>
<td>To stage TCCB with abdominal US vs pathological specimens.</td>
<td>Overall accuracy 78.5%; 9.8% overstaging; 11.7% understaging: stage A=87%, stage B=60.5% (23/38); stage C=41.2% (7/17) and stage D=83.3% (10/12). There was no strong correlation between tumor grading and staging, except that most of the grade I lesions were at stage A (30/31, 97%). The preoperative local staging of urinary bladder cancer by real-time US might be of great value to determine the management planning and prognosis of the patients.</td>
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<td>69. Tadin T, Sotosek S, Rahelic D, Fuckar Z. Diagnostic accuracy of ultrasound T-staging of the urinary bladder cancer in comparison with histology in elderly patients. Coll Antropol. 2014;38(4):1123-1126.</td>
<td>Observational-Dx</td>
<td>156 Patients</td>
<td>To evaluate diagnostic accuracy of ultrasound T-staging (UTS) of UBC in dthe group of elderly patients.</td>
<td>In 152 elderly patients referred to transabdominal ultrasound examination in two different facilities (76 each) due to various symptoms (primarily painless gross or microscopic haematuria) UBC was diagnosed. Initial UTS at the moment of detection was performed and compared with final histological T-staging (HTS). A high level of conformity between UTS and HTS was detected. In a total of 152 patients with UBC there were 115 (75.66%) patients with complete match between the UTS and HTS, 24 (15.79%) patients with minimal variation within one stage, and 13 (8.55%) patients with one stage difference between the UTS and HTS. The best result was established for the stage T1, where the accuracy was 94.5%. In other stages the accuracy was between 84.9% and 91.8%. The Youden's index for all the stages was over 0.6. UTS has a high diagnostic accuracy, especially for stages T1 and T2.</td>
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<td>70. Ozden E, Turgut AT, Yesil M, Gogus C, Gogus O. A new parameter for staging bladder carcinoma: ultrasonographic contact length and height-to-length ratio. J Ultrasound Med. 2007;26(9):1137-1142.</td>
<td>Observational-Dx</td>
<td>57 patients</td>
<td>To investigate the value of tumor-bladder wall contact length, tumor height, and height-to-length ratio for preoperative staging of bladder carcinoma.</td>
<td>Statistically significant differences were found for contact length and height-to-length ratio between superficial and invasive tumor groups. These parameters were also effective for differentiating superficial or deep muscle invasion. The US measurements of contact length of the tumor with the bladder wall and height-to-length ratio may be useful for staging bladder carcinoma by verification of these findings in larger groups of patients.</td>
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* See Last Page for Key

Revised 2017

van der Pol/Sahni

Page 29
<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>
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<td>71. Wagner B, Nesslauer T, Bartsch G, Jr., Haumann RE, Gottfried HW. Staging bladder carcinoma by three-dimensional ultrasound rendering. Ultrasound Med Biol. 2005;31(3):301-305.</td>
<td>Observational- Dx</td>
<td>63 patients</td>
<td>To assess value and limitations of 3D US rendering in bladder cancer staging.</td>
<td>Superficial tumors correctly staged in 66% of cases; lamina propria invasive tumors correctly staged in 83% of cases; muscle invasive tumors correctly staged in 100% of cases; overall accuracy was 79%. 3D US rendering is most valuable to discriminate between superficial stages pT1. This new technique might improve staging of bladder cancer.</td>
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<td>72. Caruso G, Salvaggio G, Campisi A, et al. Bladder tumor staging: comparison of contrast-enhanced and gray-scale ultrasound. AJR Am J Roentgenol. 2010;194(1):151-156.</td>
<td>Observational- Dx</td>
<td>34 patients</td>
<td>To evaluate the effectiveness of contrast-enhanced sonography in comparison with conventional sonography in differentiating muscle-infiltrating and superficial neoplasms of the urinary bladder.</td>
<td>Final pathologic staging revealed 25 superficial tumors (Ta-T1 disease) and nine muscle-infiltrating tumors (&gt;T1). Conventional sonography depicted five of nine muscle-infiltrating tumors, and contrast-enhanced sonography depicted all nine. The diagnostic performance of contrast-enhanced sonography approached that of the reference standard (area under the receiver operating characteristic curve, 0.996), but the diagnostic performance of gray-scale US was worse (area under curve, 0.613). Study showed that contrast-enhanced sonography is better than conventional sonography for differentiating muscle-infiltrating and superficial neoplasms of the urinary bladder.</td>
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<td>73. Akdas A, Turkeri L, Ersev D, Ersev A, Kullu S. Transurethral ultrasonography, fiberoptic cystoscopy and bladder washout cytology in the evaluation of bladder tumours. Int Urol Nephrol. 1992;24(5):503-508.</td>
<td>Observational- Dx</td>
<td>104 patients</td>
<td>To evaluate the accuracy of TUUS, fiber optic cystoscopy and cytology in the evaluation of bladder tumors.</td>
<td>TUUS: overall accuracy in diagnosis and T staging = 96.5%; Ta and T1=96.2%; T2=100.0%; T3=91.7%; T4=100.00%. The efficacy of TUUS was found to be high enough for routine employment in the evaluation of the bladder tumors. Fiberoptic cystoscopy in conjunction with washout cytology as a combination relatively easy to perform can be used especially for follow-up purposes of the bladder tumors.</td>
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<td>74. Saga Y, Numata A, Tokumitsu M, et al. Comparative study of novel endoluminal ultrasonography and conventional transurethral ultrasonography in staging of bladder cancer. Int J Urol. 2004;11(8):597-601.</td>
<td>Observational- Dx</td>
<td>19 patients</td>
<td>To assess the feasibility and usefulness of ELUS in bladder cancer staging and compare to TUUS.</td>
<td>ELUS and TUUS equally useful in detecting muscle invasion in bladder cancer, with an accuracy of 84% compared to CT (44%) and MRI (82%); ELUS superior to TUUS in visualizing intramural ureter.</td>
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<td>75. Tomita Y, Kobayashi K, Saito T, Tanikawa T, Kimura M, Takahashi K. Use of miniature ultrasonic probe system for intravesical ultrasonography for transitional cell cancer of the urinary tract. Scand J Urol Nephrol. 2000;34(5):313-316.</td>
<td>Review/Other-Dx</td>
<td>17 patients</td>
<td>To describe the use of a miniature ultrasonic probe (MUP) system for intravesical ultrasonography for staging of urinary bladder and/or ureteral tumors.</td>
<td>Using the MUP, each tumor could be scanned under simultaneous cystoscopic observation to choose the optimal probe position. However, in 4 of 17 patients optimal scanning could not be obtained because of large tumors and poor US penetration or because of tumor localization at the anterior dome which did not allow an appropriate scanning plane for staging. Of 13 evaluable patients, 5 with no interruption or folding of the low-echoic muscle layer were diagnosed as having a superficial tumor, and this was confirmed histopathologically in all but one case. All 8 cases evaluated as having invasive tumors demonstrated muscle invasion histologically. The MUP can be more easily manipulated than a conventional probe.</td>
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<td>76. Anderson TS, Regine WF, Kryscio R, Patchell RA. Neurologic complications of bladder carcinoma: a review of 359 cases. Cancer. 2003;97(9):2267-2272.</td>
<td>Observational-Dx</td>
<td>359 patients</td>
<td>To review cases of patients with bladder carcinoma to determine nature and frequency of neurologic complications.</td>
<td>52 patients had neurologic complications. 7 (2%) had lumbosacral plexopathies, 6 (2%) had metastatic epidural spinal cord compression. Non-metastastic complications were more common (metabolic encephalopathies in 24 patients (7%), peripheral neuropathies in 9 patients (2.5%), cerebral infarctions in 6 patients (2%), and seizures in 5 patients (1%). Study shows that neurologic complications are relatively uncommon. Local extension into peripheral nerves or bone, rather than hematogenous dissemination, is the most common cause of neurologic complications resulting from bladder carcinoma.</td>
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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

Dx = Diagnostic
Tx = Treatment