Staging and Grading

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There is a staging graph below

Blood in the urine is the most common indication that something is wrong. Often one will experience pain or difficulty upon urination, frequency of urination, or have irritation along with urgency. After symptoms and/or urinalysis have indicated a cause for concern, the next steps for staging would most likely include some or all of the following diagnostic procedures;

Cystoscopy, bladder wash cytology, biopsy and/or bladder mapping , IVP, Ultra Sonography, pathology tests. Bone scans and CT scans may be used, though doctors will use their judgement, and don’t usually prescribe them if the cancer appears to be non-muscle-invasive. MRI’s have been shown to be helpful in experimental studies, but are also not usually used for initial staging. PET scans have been shown to be very helpful and even more accurate that CT or MRI in diagnosing distant metastases, but they are not yet approved for bladder cancer diagnostics and have potential drawbacks when trying to stage local disease (see imaging studies). Although these new imaging modalities have been shown to be helpful in some instances, they cannot replace cystoscopy for detection of small tumors.

The stage refers to how far a cancer has progressed anatomically, while the grade refers to cell appearance (differentiation) and DNA make up. Stage is determined by the depth to which the tumor has penetrated the bladder wall, and assessment of invasion of lymph nodes and other surrounding organs and tissues.

Tumors that pose a high risk for progression and death are multifocal (multiple tumors in more than one area of the bladder) Ta lesions, tumors with associated carcinoma in situ (also written as Tis or CIS), and T1 lesions. Eventually, one-half of these high-risk patients will require a cystectomy, and one-third are at risk of dying from bladder cancer over 15 to 20 years. More info on risk factors can be found here: non-muscle-invasive bladder cancer

For an excellent first-hand report of the importance of correct staging, read Ken Z's experience in the "Tales from the Trenches" section of this website.

The grade is determined by pathology tests, showing how abnormal or aggressive the cells of biopsy specimens appear , and how closely a tumor resembles normal tissue of its same type. Differentiation is another term used to describe the degree of an abnormal cell’s resemblence to it’s normal counterpart. Tumor cells are described as well differentiated when they look much like normal cells of the same type and are able to carry out some functions of normal cells. Poorly differentiated and undifferentiated tumor cells are disorganized and abnormal looking. As a general rule, the grade of a tumor corresponds to its rate of growth or aggressiveness. An undifferentiated or high-grade tumor grows more quickly than a well differentiated or a low-grade one. A large tumor can be low grade,a small tumor can be high grade.Carcinoma in situ is a potentially dangerous and usually high grade tumor, and CIS patients are at greater risk for progression and must be monitored closely.

The World Health Organization (WHO) classification recognizes three grades of urothelial carcinoma. Grade 1 represents well-differentiated papillary tumors with limited atypia and mitoses. At the other end, Grade 3 lesions show a marked

increase in the cell layers and cell size, and noticeable pleomorphism and mitoses are prominent. Tumor grade appears to correlate significantly with the natural history of transitional cell carcinoma. The higher the grade of the diagnosis, the higher the incidence of death from the disease within two years.

Bimannual examination in order to detect palpable masses is another important part of clinical staging. The presence of a mass palpable on bimanual examination is of prognostic value and incorporation of this feature with microscopic tumor invasion may enhance the usefulness of clinical staging.1

Pathology tests can also be done which anlayse various biomarkers/prognostic indicators . These findings combined with results of all diagnostic procedures perfomed can help to best define treatment strategies. Biopsy alone cannot always accurately assess the depth of invasion, thus the grade as determined in the path lab is an intergral part of staging.

Many different factors can effect the course of treatment, and every case is unique; the extent of tumor invasion, large or multi focal tumors, ureter obstruction, rare histological cell type, carcinoma in situ, compromised renal function are important prognosis factors. If a person is not a good surgical candidate, or has concomittant medical problems, this may also substantially influence which treatment strategy is recommended as well as the prognosis.

Out of all patients with bladder cancer, about 50% belong to the low-risk group, 35% to the intermediate group, and 15% to the high-risk group. Patients belong to the low-risk group if they have a single primary or recurrent Ta grade 1 or Ta grade 2 lesion, or the high-risk group if they have multiple primary or recurrent T1 grade 3 lesions and/or if the tumour(s) are larger than 3 cm. In between there are patients with multiple but less than seven Ta grade 1 or Ta grade 2 lesions: they have an intermediate prognosis. 2 See also: risk graph

Clinical staging, including nuclear imaging, often underestimates the extent of tumor invasion, particularly in cancers that are less differentiated and more deeply invasive. In a study which reviewed accuracy of staging in 130 cystectomy patients, the overall clinical staging error was 61.5%, with 41.5% of the cancers understaged. Of the patients with Carcinoma in situ, 60% were found to be of greater extent than pT1 tumors. The authors stated that clinical errors in classification are common and impair the evaluation of neoadjuvant treatments. This supports an aggressive approach when these patients do not respond promptly to intravesical chemotherapy. 3

Although cystoscopy is a very reliable follow up tool, it also has a small margin of error. Unfortunately there is no reliable test which is accurate enough to detect microscopic metastases. A biopsy can detect cancerous cells in tissues removed, but this is an invasive, expensiveand uncomfortable method of follow up, and not always feasible nor advisable on a regular basis, as the re-seeding of cancer cells through biopsy procedures and transurethral resection (‘TUR’-the removal of tumor through a scope inserted into the urethra) is a valid concern.

The future holds promise, however, as new urine marker tests and biomarkers have potential to help with earlier detection and screening.

For an article which contains clear diagrams explaining the staging of bladder tumors, see: Staging and Grading of Bladder Cancer from Associated Urologists Inc.: http://www.associatedurologists.com/bladder.html

The American Joint Committee on Cancer (AJCC) has designated staging by TNM classification to define bladder cancer:

T=Tumor, N+Nodes involved, M=metastasis

TX
Primary tumor cannot be assessed

T0
No evidence of primary tumor

Ta
Noninvasive papillary carcinoma

Tis
Carcinoma in situ: "flat tumor"

T1
Tumor invades subepithelial connective tissue

T2
Tumor invades muscle

T2a
Tumor invades superficial muscle (inner half)

T2b
Tumor invades deep muscle (outer half)

T3
Tumor invades perivesical tissue

T3a
Microscopically

T3b
Macroscopically (extravesical mass)

T4
Tumor invades any of the following: prostate, uterus, vagina, pelvic wall, or abdominal wall.

T4a
Tumor invades the prostate, uterus, vagina

T4b
Tumor invades the pelvic wall, abdominal wall

N=nodes M=mets

Stage 0
Tis or Ta, N0, M0

Stage I
T1, N0, M0

Stage II
T2a, N0, M0 or T2b, N0, M0

Stage III
T3a, N0, M0 or T3b, N0, M0 or T4a, N0, M0

Stage IV
T4b, N0, M0, any T, N1-N3, M0, or any T, any N, M1

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