Staging Carcinoma of the Prostate

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For patients with carcinoma of the prostate, staging is crucial in determining the severity of the disease, its prognosis, and how therapy will be guided. The staging categories, staging methods and their applications, and the impact of staging on therapeutic results and patient management are discussed herein.

**Staging Systems**

The most widely used staging nomenclature is the modified Whitmore-Jewett system. Most urologists are familiar with this system as it is commonly used in clinical situations and has been widely discussed in the literature. Stage A represents the incidental finding of carcinoma, usually discovered after transurethral prostatectomy for obstruction. In stage A-1 less than 5% of the resected tissue is neoplastic and well differentiated, whereas in stage A-2 greater than 5% of the tissue is neoplastic and/or poorly differentiated. In stage B the lesion is palpable and confined to the prostate gland. In stage B-1 the nodule is confined to less than one lobe and is surrounded by normal prostate tissue, whereas in stage B-2 the palpable nodule is more extensive, usually involving one or more lobes, though still within the confines of the prostate gland. In stage C the carcinoma extends beyond the prostate, but without distant metastases. Minimal extracapsular extension is seen in stage C-1, and stage C-2 consists of bulky tumor with bladder outlet and/or ureteral obstruction. Distant metastases characterize stage D. In stage D-1 pelvic lymph node metastases are found by surgery or by needle biopsy. In stage D-2 distant metastatic disease is evident, usually in the bones, whereas stage D-3 indicates a relapse following endocrine therapy.

The tumor, node, metastasis (TNM) staging system, which is preferred in many parts of the world including Europe, has the advantage of describing the status of the local disease as well as the extent of the nodal involvement and distant disease. While most urologists and oncologists prefer the modified Whitmore-Jewett system to the TNM system, some combination of these two systems will ultimately provide a universal staging system (1).

**Serum Studies**

Following the histologic diagnosis of prostatic adenocarcinoma, serum studies are necessary for accurate staging of the disease. These include prostatic acid phosphatase (PAP), alkaline phosphatase, and prostate specific antigen (PSA).

While serum studies are essential to the staging process, idiosyncrasies of each of these biochemical parameters have limited specificity in describing the precise status of the neoplasm. Interpretation of acid phosphatase levels in individual patients is difficult because results may be normal both in patients with cancer confined to the prostate gland and in up to 30% of patients with metastatic disease. Conversely, some patients with benign prostatic hypertrophy (BPH), as well as those with nonprostatic disease such as osteitis deformans (Paget disease), multiple myeloma, or blood dyscrasias may have elevated serum acid phosphatase. Furthermore, patients who have had recent urethral instrumentation or palpation of a benign prostate gland may exhibit transient (24 to 48 hr) elevation of PAP. Compared to enzymatic assays for measuring PAP, radioimmunoassays and counterimmunoelectrophoresis are more sensitive, but the frequent occurrence of false-positive results makes these tests unacceptable for screening purposes.

Elevation of alkaline phosphatase in patients with carcinoma of the prostate is associated with metabolic bone repair in an area of osseous metastasis as well as with liver disease. The serum alkaline phosphatase level is particularly useful in documenting response to endocrine therapy in patients with skeletal metastases (2).

PSA has recently been evaluated as a marker in BPH and in localized and disseminated carcinoma of the prostate. Thus, in patients with BPH, PSA levels greater than 4 µg/L (normal = 0 to 4 µg/L) were noted in 20% of patients and levels greater than 10 µg/L were noted in another 3% to 5% of patients. In localized carcinoma of the prostate, PSA levels greater than 4 µg/L were noted in 60% of patients and levels greater than 10 µg/L were noted in 30% to 50% of patients. In active stage D-2 disease, PSA levels greater than 4 µg/L occurred in 98% of patients.

Comparison of PAP levels in control patients and in those with BPH and carcinoma of the prostate stages A through D demonstrates that while not much difference exists between BPH and stages A and B prostate carcinoma, PSA levels progressively increase with advancing stages of carcinoma of the prostate. Thus, as noted by Ercole et al (3), PAP is elevated in 10% of patients with stage A, 24% with stage B, 53% with stage C, and 92% with stage D disease. Since significant elevations of PAP are found in patients with BPH, PAP is not recommended for screening but is a useful marker in monitoring patients with a known diagnosis of carcinoma of the prostate.

Comparison of PAP and PSA in carcinoma of the prostate is of interest. In a recent study, PAP and PSA were studied in 136 con...
Understaging

Understaging occurs in a significant percentage of patients with prostate carcinoma, with the clinical stage typically lower than the true pathologic stage. In patients presumed to have stage A-1, B-1, and B-2 carcinoma, the frequency of both microscopic and macroscopic local tumor invasion in radical prostatectomy specimens was from 15% to 30%. In clinical stages A-2, B-1, and B-2, significant percentages of capsular invasion, seminal vesicle invasion, and lymph node metastasis were found. According to Epstein et al (5), in patients with presumed A-1 disease, based on transurethral prostatectomy, subsequent radical prostatectomy revealed an 86% incidence of significant residual disease and in many cases large volume residual disease. Interestingly, no correlation existed between the amount of neoplasm found on the transurethral specimen, or its grade, and subsequent volume of tumor in the radical specimen.

Radiologic Studies

Radiologic studies used in the staging of prostate carcinoma include chest x-ray, bone scans and skeletal x-rays, intravenous pyelograms, lymphangiography, prostatic ultrasound, computed tomography (CT), and magnetic resonance imaging (MRI). Pulmonary metastases are usually depicted by a streaking rather than a nodular appearance. Rib metastases may also be seen. Intravenous pyelograms may show bladder floor elevation or in more advanced cases ureteral obstruction or deviation. Many bone scans show some degree of abnormality. In prostate cancer bony involvement is axial and occurs as well in the pelvis. However, metastases must be differentiated from prior fractures and arthritis. When in doubt, a bone biopsy is necessary. Skeletal x-rays in the area of the bone scan abnormality will depict typical changes characteristic of blastic prostate cancer metastases. Lymphangiography is tedious to perform and has been replaced by CT and MRI studies for patients with prostate carcinoma. Lymph node assessment, which is particularly important in the preoperative staging of patients with prostate carcinoma, is done by either CT-guided needle biopsy or by pelvic lymphadenectomy.

Prostatic ultrasound is useful in demonstrating capsular involvement, periprostatic extension, and seminal vesicle invasion (6). These areas can be selectively sampled in patients in whom stage C disease is suspected. Since most patients with stage C disease are candidates for radiation therapy or hormonal therapy and not radical prostatectomy, an ultrasound-guided biopsy of this area is imperative. Similarly, the pelvic CT scan is useful in showing the prostatic capsule and the possibility of disruption. MRI has also been useful in staging involvement of the bladder neck and seminal vesicles (7). At Henry Ford Hospital we prefer to use the ultrasound-guided perineal needle biopsy, although transrectal ultrasound-guided biopsies are also performed. A study of 27 patients with biopsy-proven prostate carcinoma compared the sensitivity of MRI and ultrasound to each other and to CT in staging the disease. Sonography was superior to MRI for detection of intraglandular carcinoma and capsular disruption, whereas MRI was superior to both sonography and CT for evaluating seminal vesicle invasion and was slightly better than CT for detecting lymphadenopathy (8).

Conclusions

Errors are inherent in all staging procedures. Once staging data are obtained and assembled, the urologist must discuss with the patient and his family the pros and cons of external radiation therapy and radical prostatectomy for the treatment of stage A-1, A-2, B-1, and B-2 disease. Both modalities have been considered equal in the treatment of prostate carcinoma. However, based on results obtained with the recently introduced nerve-sparing technique, I prefer that young and otherwise healthy patients with localized, early stage prostatic carcinoma be treated by radical prostatectomy rather than with external radiation therapy.

References