Prostate Cancer Diagnosis and Staging

Updated: Jan 14, 2019
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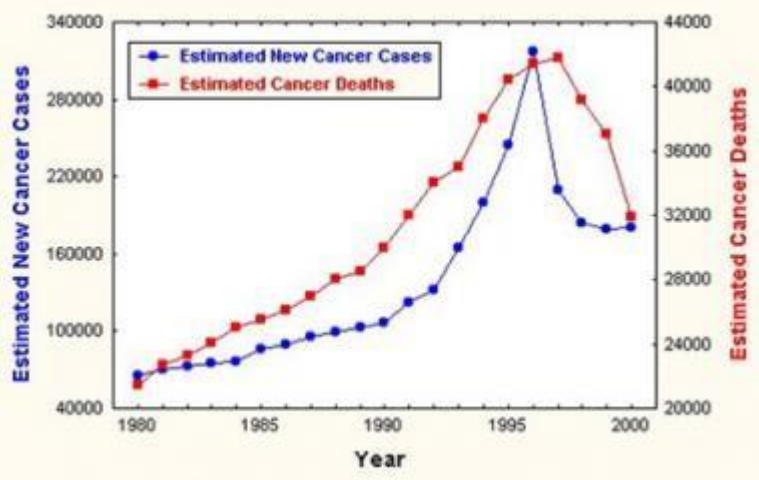
Practice Essentials

Prostate cancer is the most common noncutaneous cancer in men, making the diagnosis and staging of this cancer of great medical and public interest. Although prostate cancer can be slow growing, the disease nonetheless accounts for almost 10% of cancer-related deaths in males, with thousands of men dying of prostate cancer each year (see the image below).



Estimated incidence of and mortality from prostate cancer. Courtesy of the American Cancer Society.

Signs and symptoms

With the advent of PSA screening, patients report the following local symptoms:

- No symptoms (47%)
- Urinary frequency (38%)
- Urinary urgency (10%)
- Decreased urine stream (23%)
- Hematuria (1.4%)

Metastatic symptoms of prostate cancer include the following:

- Weight loss and loss of appetite
- Bone pain, with or without pathologic fracture
- Lower extremity pain and edema
- Uremic symptoms

Diagnosis

Laboratory studies

- PSA screening: Controversy exists regarding PSA level cutoffs and reference ranges
- DRE: Serial examinations are best; clues to the patient's condition in conjunction with PSA levels include presence of a nodule, as well as asymmetry, texture difference(s), and bogginess of the prostate, seminal vesicles, and adjacent organs
- Biopsy and histologic examination: These aid in the diagnosis and help to determine the Gleason score; a biopsy can also help differentiate a cyst or calculus from cancer foci

Imaging studies

- Computed tomography (CT) scanning: To assess extension into the bladder and lymph nodes for staging the cancer or for considering pretreatment lymph node sampling
- Endorectal magnetic resonance imaging (MRI): To localize cancer within the prostate and seminal vesicles; to help in local staging
- Bone scanning: To evaluate bone metastasis
- MRI: To determine the etiology of questionable lesions found on bone scans
- Transrectal ultrasonography: To examine the prostate for hypoechoic areas, which are commonly associated with cancers but are not specific enough for diagnostic purposes

Men with PSA levels above 10 ng/mL, high-grade histology (Gleason score of ≥7), or physical findings suggesting stage T3 disease should probably undergo a staging CT scan and bone scan. Neither CT scanning nor MRI can be used to determine if lymph nodes are reactive or contain malignant deposits, unless the nodes are significantly enlarged and a percutaneous biopsy can be performed.

Staging

Staging of prostate cancer is based on the following five key pieces of information[6] :

- The extent of the primary tumor (T category)
- Whether the cancer has spread to nearby lymph nodes (N category)
- The absence or presence of distant metastasis (M category)
- The PSA level at the time of diagnosis
- The Grade Group, based on prostate biopsy (or surgery)

Overview

Prostate cancer is the most common noncutaneous cancer in men, making the diagnosis and staging of this cancer of great medical and public interest. Although prostate cancer can be slow growing, the disease nonetheless accounts for almost 10% of cancer-related deaths in mens, with thousands dying from prostate cancer each year.

With the development of prostate-specific antigen (PSA) screening, however, prostate cancer is being diagnosed earlier in the disease course than it was prior to PSA examination.

Currently, most cases of prostate cancer are found because of abnormalities in a screening PSA level or findings on digital rectal examination (DRE) rather than because of symptoms (see Prostate-Specific Antigen). In addition, prostate cancer can be an incidental pathologic finding when tissue is removed during transurethral resection to manage obstructive prostatic symptoms (see Benign Prostatic Hypertrophy).

The American Cancer Society (ACS) estimated that 240,890 new cases of prostate cancer were diagnosed in the United States in 2011 and that 33,720 men died of the disease in that year. (See the chart below.) Comparable ACS estimates for 2019 are 174,650 new cases and 31,620 deaths.[7]

Age- and race-related demographics

Prostate cancer is rarely diagnosed in men younger than 40 years, and it is uncommon in men younger than 50 years.

Prevalence rates of prostate cancer remain significantly higher in African-American men than in white men, while the prevalence in Hispanic men is similar to that of white men. Hispanic men and African-American men tend to present with more advanced disease, a situation that is most likely related to external (eg, income, education, insurance status) and cultural factors. In addition, African-American men generally have higher levels of testosterone, which may contribute to the higher incidence of carcinoma in that population.[8, 9]

Mutations that appear specific to, or more common in, African-American patients have been identified in aggressive prostate tumors. Further research will be needed to determine whether these mutations factor into the racial differences in incidence and clinical outcome that are seen in prostate cancer.[10]

Differentials

Differential diagnoses of prostate cancer include the following:

- Benign prostatic hypertrophy
- Calculi
- Prostatic cysts
- Prostatic tuberculosis
- Prostatitis

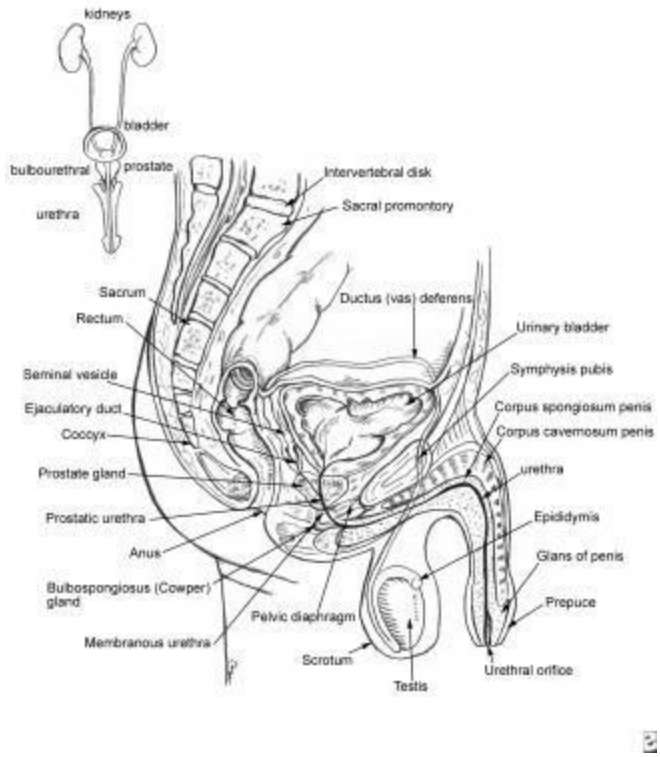
Patient education

Because of the advent of PSA screening, a greater number of men now require education about prostate cancer, including the risk of progression and how the disease is diagnosed, staged, and treated. A study by Hall et al found that 80% of primary care physicians discussed PSA screening with their male patients, with 64.1% encouraging the screening.[11]

For patient education information, see the Men's Health Center and the Cancer Center, as well as Prostate Cancer.

Relevant Anatomy

The prostate lies below the bladder and encompasses the prostatic urethra. It is surrounded by a capsule and is separated from the rectum by a layer of fascia termed the Denonvilliers aponeurosis. The position of the prostate in the male genitourinary tract is shown in the image below.



Relevant anatomy of the male pelvis and genitourinary tract.

The blood supply to the base of the bladder and prostate is from the inferior vesical, which is derived from the internal iliac. The capsular branches of the inferior vesical artery help to identify the pelvic plexus arising from the S2-S4 and T10-T12 nerve roots.

The neurovascular bundle lies on either side of the prostate on the rectum. It is derived from the pelvic plexus and is important for erectile function.

Prostate Cancer Symptoms

Local symptoms

In the pre-PSA era, patients with prostate cancer commonly presented with local symptoms. Urinary retention developed in 20-25% of these patients, back or leg pain developed in 20-40%, and hematuria developed in 10-15%. Currently, with PSA screening, 47% of cases are diagnosed in asymptomatic patients. In symptomatic patients, te most common complaints are urinary frequency (38%), decreased urine stream (23%), urinary urgency (10%), and hematuria (1.4%). However, none of these symptoms is unique to prostate cancer; each can arise from various other ailments.

Metastatic symptoms

Metastatic symptoms include weight loss and loss of appetite; bone pain, with or without pathologic fracture (because prostate cancer, when metastatic, has a strong predilection for bone); and lower extremity pain and edema due to obstruction of venous and lymphatic tributaries by nodal metastasis. Uremic symptoms can occur from ureteral obstruction caused by local prostate growth or retroperitoneal adenopathy secondary to nodal metastasis.

Prostate-Specific Antigen Screening

Elevated PSA level

PSA is a single-chain glycoprotein that has chymotrypsinlike properties. The upper limit of normal for PSA is 4ng/mL. Some advocate age-related cutoffs, such as 2.5ng/mL for the fifth decade of life, 3.5ng/mL for the sixth decade of life, and 4.5ng/mL for the seventh decade of life. Others advocate race-specific reference ranges. Using data from screening studies, some have advocated upper limits of normal of 2.5ng/mL instead of 4ng/mL.

If the physician believes that an elevated PSA level may be due to infection, 4-6 weeks of antibiotics are provided, and then the

PSA level is rechecked.

PSA velocity

PSA velocity is an important concept. A PSA velocity of lower than 0.75ng/mL/y has traditionally been used to prompt a prostate biopsy. However, evidence suggests in men younger than 50 years, a PSA velocity of 0.6 ng/mL/y may be more appropriate.

Percentage of free PSA

The measurement of bound and free PSA can help to differentiate mildly elevated PSA levels caused by cancer from elevated levels resulting from benign prostatic hyperplasia. The lower the ratio of free-to-total PSA, the higher the likelihood of cancer. (Free PSA is reported as a percentage.) For example, among men with greater than 25% free PSA, only 8% are found to have cancer at prostate biopsy.

In contrast, more than half of men with less than 10% free PSA are found to have cancer at biopsy. While cutoffs may be used, the percentage of free PSA is usually employed as an additional factor in making an informed recommendation for or against biopsy. Generally, these percentages are useful in patients who have a PSA level in the range of 4-10ng/mL.

This information is most useful in men with very large glands or in whom 1 biopsy result has already been negative. In healthy men with a PSA level of 4-10ng/mL, many recommend biopsy without the additional free-PSA test or consider a trial of antibiotic therapy for 4-6 weeks before repeating the PSA test. (If antibiotic therapy quickly lowers the PSA level to within the reference range, the cause of the prior elevation is less likely to be prostate cancer, and the PSA test should be repeated within a few months.)

Prostate Health Index testing

The Prostate Health Index (PHI) test is a diagnostic blood test that combines free and total PSA and the (-2) pro-PSA isoform (p2PSA). The PHI test is intended to reduce the number of unnecessary prostate biopsies in PSA-tested men. In prospective multicenter studies, the PHI test has outperformed free and total PSA for detection of prostate cancer and has improved prediction of clinically significant prostate cancer in men with a PSA of 2 or 4 ng/mL to 10 ng/mL.[17]

Digital Rectal Examination

DREs are examiner dependent, and serial examinations are best. Various factors are considered when a DRE is performed. A nodule is important, but findings such as asymmetry, difference in texture, and bogginess are important clues to the patient's condition and should be considered in conjunction with the PSA level. Change in texture over time can offer important clues about the need for intervention.

Pay careful attention to the prostate’s consistency, along with the seminal vesicles and adjacent organs. Such observation can be help to detect the disease’s spread to other structures, the results of which can be as follows:

- Overdistention of the bladder due to outlet obstruction
- Lower extremity lymphedema
- Supraclavicular adenopathy
- Lower extremity deep venous thrombosis
- Cancer cachexia
- Neurologic findings secondary to cord compression - Other subtle neurologic findings, such as paresthesias or wasting, are uncommon

Cysts and stones cannot be accurately differentiated from cancer based on DRE findings alone; therefore, maintain a high index of suspicion if the DRE results are abnormal.

If cancer is detected, the DRE findings form the basis of clinical staging of the primary tumor using the TNM staging system.

In most patients who are diagnosed with prostate cancer, however, the DRE results are normal and the PSA readings are abnormal.

Biopsy Studies

Physical examination findings alone cannot reliably differentiate a cyst or calculus from cancer foci. Therefore, a biopsy is warranted in these circumstances, to aid in the diagnosis and to determine the Gleason score.

Before the biopsy, antibiotics are administered and an enema is often provided, with a short course of antibiotics administered

after the biopsy as well. Coagulation tests are not routinely performed, but patients are instructed to stop aspirin and nonsteroidal anti-inflammatory drugs (NSAIDs) 10 days prior to the biopsy. Many, but not all, physicians use lidocaine prior to the biopsy.

The number of biopsy specimens that should be obtained is debated. Sextant- versus 12- versus 18-core biopsy protocols are published in the literature. The 12- or 18-core protocols yield more specimens from the lateral regions and usually sample the transition zone. Several studies have demonstrated an increase in the cancer detection rate, but others have not. The NCCN recommends extended-pattern biopsy with six sextant cores and six cores from the lateral peripheral zone, along with lesion-directed sampling of palpable nodules and sites corresponding to suspicious images.[3]

In men with a negative biopsy result, epigenetic profiling with the ConfirmMDx assay (MDxHealth, Irvine, CA) may help to distinguish patients who have a true negative biopsy from those at risk for occult cancer. ConfirmMDx is a commercially available assay that assesses methylation markers of prostate cancer (GSTP1, APC, and RASSF1) to distinguish histologically benign biopsy cores from patients diagnosed with no cancer, low-volume cancer (Gleason score 6), or higher-volume cancer (Gleason score 7). The assay has a negative predictive value of 90%, but a positive predictive value of only 28%.[18]

PCA3 is a prostate-specific, non-coding messenger RNA biomarker that is detectable in urine sediments obtained after three strokes of prostatic massage during DRE. A urine test for PCA3 (Progensa PCA3) is commercially available. Currently, the main indication for PCA3 testing is to help determine whether repeat biopsy is needed after an initially negative biopsy. A negative result, considered together with clinical and other laboratory information, would argue against repeat biopsy.[17]

In patients with a persistently elevated PSA level in the face of negative biopsy results, the literature supports repeating the biopsy once or twice. Among cancer cases, 31% were detected on repeat biopsy and 39% were detected if the PSA value was greater than 20ng/mL. If all of the biopsy results are negative, a repeat round of biopsies has been suggested when the PSA increases by 25% from the level at which the last biopsies were performed.

According to European guidelines, indications for repeat biopsy after a previously negative biopsy are as follows[17] :

- Rising and/or persistently elevated PSA
- Suspicious findings on DRE (5-30% cancer risk)
- Atypical small acinar proliferation (ie, atypical glands suspicious for cancer; 40% risk
- High-grade prostatic intraepithelial neoplasia (HGPIN) at ≥3 biopsy sites (~30% risk)
- A few atypical glands immediately adjacent to HGPIN (~50% risk)

The guidelines recommend that repeat biopsies after negative biopsies be performed with MRI targeting.

Further workup depends on the clinical staging. A higher clinical stage of cancer determined by DRE findings, PSA level, and Gleason score (as determined by biopsy) correlates with an increased risk of extraprostatic spread, and these tests are considered key factors in determining the staging workup and predicting patient prognosis.

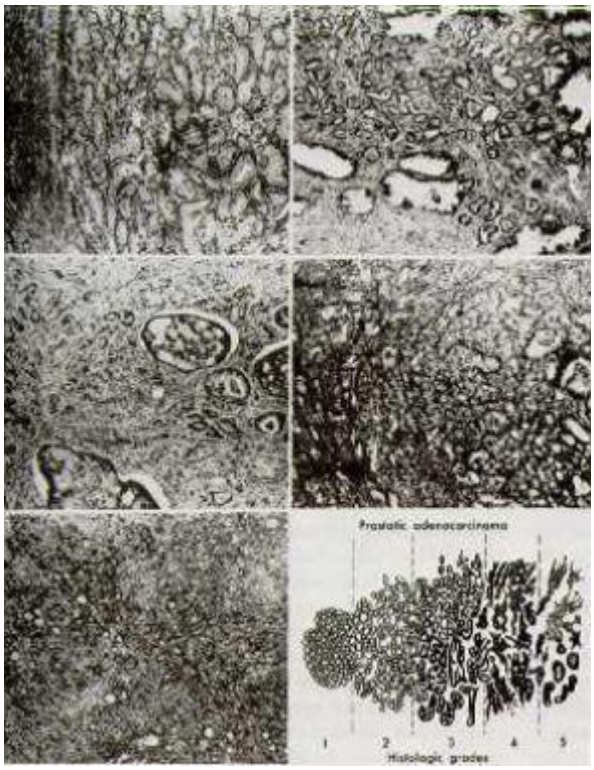
Bul et al studied the factors predicting reclassification from low-risk to higher-risk prostate cancer in men undergoing active surveillance and found a significant association between an increase in risk classification and the number of initial positive biopsy cores obtained. However, patient age, clinical stage, total number of biopsy cores, and PSA did not significantly influence the outcome. (Although a PSA doubling time of under 3y also had a significant link to reclassification to higher risk.[19])

Histologic Findings

Gleason score

The most commonly used system for classifying the histologic characteristics of prostate cancer is the Gleason scoring system, which uses the glandular architecture within the tumor.

The predominant pattern and the second-most common pattern (seen in the image below) are each given a grade of between 1 and 5. The Gleason score is the sum of these 2 grades. Scoring based on the 2 most common patterns is an attempt to factor in the considerable heterogeneity within cases of prostate cancer. In addition, this scoring method was found to be superior for predicting disease outcomes compared with using the individual grades alone.



Histologic scoring system (the Gleason scoring system) showing the 2 most common patterns seen on biopsy specimens in prostate cancer.

Grades are based on the extent to which the epithelium assumes a normal glandular structure. A grade of 1 indicates a near-normal pattern, and grade 5 indicates the absence of any glandular pattern (less malignant to more malignant). This scheme of grading histologic features greatly depends on the skill and experience of the pathologist and is subject to some degree of individual variation.

Gleason scores range as follows:

- Score of 2-4 - Considered low grade or well differentiated
- Score of 5-7 - Considered moderate grade or moderately differentiated
- Score of 8-10 - Considered high grade or poorly differentiated

Although the change in glandular architecture represented by the Gleason score is currently the most widely used and correlative histologic parameter, it is not the only histologic change that can be observed in prostate cancers. Indeed, notable changes in cell and nuclear morphology, neuroendocrine differentiation, and vascularity can be observed and may have great prognostic significance.

Grade groups

The grade grouping system was introduced in 2013, and has been adopted by the NCCN. Like the Gleason score, the Grade Group is derived from needle-core biopsies in patients with suspected prostate cancer or analysis of a radical-prostatectomy specimen. However, in contrast with the three risk tiers defined by the Gleason score, the Grade Group distinguishes five risk groups based on the core with the worst grade, as follows:

- Grade Group 1 - Gleason 3+3
- Grade Group 2 - Gleason 3+4
- Grade Group 3 - Gleason 4+3
- Grade Group 4 – Gleason 8
- Grade Group 5 - GS 9-10

In a study of 8052 patients, grade grouping at biopsy and radical prostatectomy demonstrated better discrimination of recurrence-free survival between individual risk groups than Gleason score risk groups, with Grade Groups 2, 3, 4, and 5 each incrementally associated with increased risk.[20]

Perineural invasion

Perineural invasion is an indicator of invasiveness and is considered in terms of which side should possibly undergo a nerve-sparing procedure, as well as whether a patient might benefit more from high- or low-risk brachytherapy.

Prostatic intraepithelial neoplasia

Prostatic intraepithelial neoplasia (PIN) represents the putative precancerous end of the morphologic continuum of cellular proliferations within prostatic ducts, ductules, and acini.

Two grades of PIN are identified. Low-grade PIN is mild dysplasia. High-grade PIN encompasses moderate and severe dysplasia. High-grade PIN is considered by most to be a precursor of invasive carcinoma. Men with high-grade PIN alone can be started on finasteride and monitored closely.

The continuum that culminates in high-grade PIN and early invasive cancer is characterized by basal cell layer or basement membrane disruption, progressive loss of secretory differentiation markers, increasing nuclear and nucleolar abnormalities, increasing proliferative potential, and increasing variation in deoxyribonucleic acid (DNA) content (aneuploidy).

Clinical studies suggest that PIN predates a carcinoma by 10 or more years.[21] The clinical importance of recognizing PIN is based on its strong association with carcinoma. Studies claim that men with high-grade PIN in a prostate biopsy specimen have a 35-50% chance of being diagnosed with prostate cancer after a subsequent biopsy.[22] Atypical small acinar proliferation (ASAP) has also been associated with higher cancer detection rates.

The identification of PIN in prostate biopsy specimens warrants further searching for concurrent invasive carcinoma. In most men, this means repeat biopsies if the PSA level changes significantly. The same may also be true for ASAP findings after biopsy.

Evaluation of findings

Men with PSA levels below 10ng/mL and low- or moderate-grade histology (Gleason score < 7) with no findings or minimal findings on physical examination may proceed to surgery or brachytherapy without further studies.

CT Scanning, MRI, and Bone Scanning

Men with PSA levels above 10 ng/mL, high-grade histology (Gleason score of 7 or higher), or physical findings that suggest stage T3 disease should probably undergo a staging computed tomography (CT) scan and bone scan. CT scanning is the one modality with evidence-based guidelines. The CT scan can be used to evaluate extension into the bladder and lymph nodes to help stage the patient's cancer or to consider lymph node sampling prior to treatment.

According to the National Comprehensive Cancer Network (NCCN), technetium-99m-methyl diphosphonate (MDP) bone scan is indicated in the initial evaluation of patients at high risk for skeletal metastases, as indicated by any of the following[23] :

- T1 disease, PSA ≥20
- T2 disease, PSA ≥10
- Gleason score ≥8
- T3/T4 disease
- Symptoms suggestive of osseous metastasis

The NCCN recommends pelvic CT or magnetic resonance imaging (MRI) in patients with any of the following:

- T3 disease
- T4 disease
- T1-T2 diseaes and nomogram-indicated probability of lymph node involvement >10%

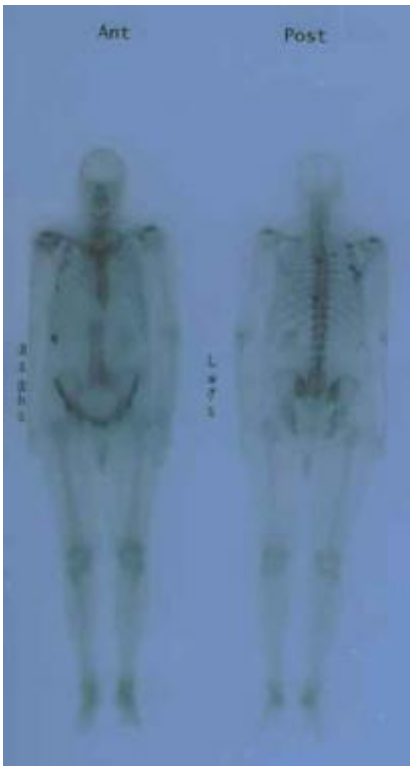
Conventional endorectal MRI is helpful for localizing cancer within the prostate and seminal vesicles and for local staging. Dynamic, contrast-enhanced MRI and MR spectroscopic imaging are complementary in local staging, but their use is currently limited to a research setting.

Diffusion-weighted MRI appears to improve detection of transition-zone prostate cancer. In a retrospective study of 156 prostate cancer patients before they underwent radical prostatectomy, the addition of diffusion-weighted endorectal magnetic resonance imaging (MRI) to T2-weighted imaging improved not only the detection of transition zone prostate cancer but also the evaluation of tumor aggressiveness.[24] At the (individual) patient and sextant (localization) levels, there was improvement in the areas under the receiver operating characteristic curves. There was also an inverse correlation between tumor apparent diffusion coefficients and tumor Gleason scores in the transition zone.[24]

Guidelines from the NCCN[23] and the European Association of Urology[17] note that evidence supports the use of multi-parametric MRI (mpMRI)—that is, the combination of T2-weighted images with diffusion-weighted imaging, dynamic contrast enhanced imaging, or H1-spectroscopy—in prostate cancer staging. The advantages of mpMRI include the following[23] :

- Detection of large and poorly differentiated tumors (ie, Gleason score ≥7)
- T staging: Detection of extracapsular extension, with high negative predictive values in low-risk men
- N staging: MpMRI is equivalent to CT scan
- M staging: MpMRI outperforms bone scan and targeted x-rays for M staging, with 98-100% sensitivity and specificity

Although MRI is superior to bone scanning in evaluating bone metastasis, it is impractical for routine total-body surveys. Instead, it is used to determine the etiology of questionable lesions found on bone scans. Bone-scan examples are seen below.



Anterior and posterior bone scans of a patient with prostate cancer, with metastasis to the 12th rib and thoracic spine represented by the increased uptake of isotope.

Neither CT scanning nor MRI can be used to determine if lymph nodes are reactive or contain malignant deposits, unless the nodes are significantly enlarged and a percutaneous biopsy can be performed.

Despite the wealth of literature regarding the lack of use that imaging studies have in men with low-risk disease, more than one third of patients with low-risk prostate cancer in a SEER (Surveillance, Epidemiology, and End Results program)-Medicare analysis underwent imaging studies.[25]

Other Imaging Modalities

PET scanning

There is increasing interest in using metabolic activity to detect cancer foci. Positron emission tomography (PET) scanning uses glucose analogue 18 F-fluorodeoxyglucose (18 F-FDG) to detect cancer, but studies thus far have been disappointing for prostate cancer detection.

C-choline PET scanning fused with CT imaging shows more promise but is not yet the standard of care.

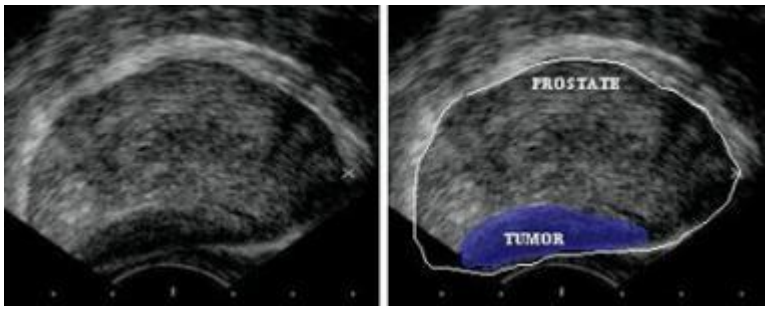
Fluciclovine F 18 (Axumin) was approved in May 2016 for PET imaging in men with suspected prostate cancer recurrence. Approval was based on a comparative trial with 11C-choline. Sensitivities for 11C-choline and fluciclovine F 18 were 32% vs 37%, specificities 40% vs 67%, accuracies 32% vs 38%, and positive predictive values (PPVs) 90% vs 97%.[26] A second trial observed the diagnostic performance of fluciclovine PET/CT in recurrent prostate cancer was superior to that of CT and fluciclovine PET/CT provided better delineation of prostatic from extraprostatic recurrence.[27]

ProstaScint scanning

Likewise, there is renewed interest in ProstaScint scans fused with MRI or CT images. ProstaScint scanning involves the use of a murine monoclonal antibody that reacts with prostate-specific membrane antigen to identify cancer in the prostate and in metastatic deposits.

TRUS

Transrectal ultrasonography (TRUS) is used to examine the prostate for hypoechoic areas, which are commonly associated with cancers but are not specific enough for diagnostic purposes. An example of a hypoechoic lesion is seen below.



Transrectal sonogram of the prostate showing a hypoechoic lesion in the peripheral zone of the gland that is suggestive of cancer.

Staging of Prostate Cancer

The American Joint Committee on Cancer (AJCC) tumor/node/metastasis (TNM) classification and staging system for cancer are provided below.[34]

Primary tumor

Clinical tumor staging is as follows:

- TX - Primary tumor cannot be assessed
- T0 - No evidence of primary tumor
- T1 - Clinically inapparent tumor not palpable
- T1a - Tumor incidental histologic finding in 5% or less of tissue resected
- T1b - Tumor incidental histologic finding in more than 5% of tissue resected
- T1c - Tumor identified by needle biopsy (because of elevated PSA level); tumors found in 1 or both lobes by needle biopsy but not palpable
- T2 - Tumor is palpable and confined within prostate
- T2a - Tumor involves up to half of one lobe
- T2b - Tumor involves more than half of one lobe but not both lobes
- T2c - Tumor involves both lobes
- T3 - Extraprostatic tumor that is not fixed or does not invade adjacent structures
- T3a - Extracapsular extension (unilateral or bilateral)
- T3b - Tumor invading seminal vesicle(s)
- T4 - Tumor fixed or invading adjacent structures other than seminal vesicles (eg, bladder neck, external sphincter, rectum, levator muscles, pelvic wall)

Pathologic tumor staging is as follows (note that there is no pathologic T1 classification):

- pT2 - Organ confined
- pT3 - Extraprostatic extension
- pT3a - Extraprostatic extension (unilateral or bilateral) or microscopic invasion of the bladder neck
- pT3b - Seminal vesicle invasion
- pT4 - Tumor is fixed or invades adjacent structures other than seminal vesicles (eg, external sphincter, rectum, bladder, levator muscles, pelvic wall)

Regional lymph nodes

Clinical lymph node staging is as follows:

- NX - Regional lymph nodes not assessed
- N0 - No regional lymph node metastasis
- N1 - Metastasis in one or more regional lymph nodes

Pathologic lymph node staging is as follows:

- pNX - Regional nodes not sampled
- pN0 - No positive regional nodes
- pN1 - Metastases in regional node(s)

Regional lymph nodes are assessed via surgical removal or through biopsy of the pelvic lymph nodes, including the obturator chain. The surgical boundaries include the bifurcation of the common iliac, the obturator nerve, and the node of Cloquet.

Distant metastasis

Distant metastasis staging is as follows:

- M0 - No distant metastasis
- M1 - Distant metastasis
- M1a - Nonregional lymph node(s)
- M1b - Bone(s)
- M1c - Other site(s), with or without bone disease

Stage groupings

Staging of prostate cancer is based on the following five key pieces of information[6] :

- The extent of the primary tumor (T category)
- Whether the cancer has spread to nearby lymph nodes (N category)
- The absence or presence of distant metastasis (M category)
- The PSA level at the time of diagnosis
- The Grade Group, based on prostate biopsy (or surgery); see Histologic Findings, above.

Table. Prognostic Groups for Prostate Cancer (Open Table in a new window)

Group	Tumor	Node	M	PSA (ng/mL)	Grade Group
Stage I	cT1a-c	N0	M0	< 10	1
	cT2a	N0	M0	< 10	1
	pT2	N0	M0	< 10	1
Stage IIA	cT1a-c	N0	M0	10 to < 20	1
	cT2a	N0	M0	10 to < 20	1
	pT2	N0	M0	10 to < 20	1

	cT2c	N0	M0	< 20	1
Stage IIB	T1-2	N0	M0	< 20	2
Stage IIC	T1-2	N0	M0	< 20	3
	T1-2	N0	M0	< 20	4
Stage IIIA	T1-2	N0	M0	≥ 20	1-4
Stage IIIB	T3-4	N0	M0	Any	1-4
Stage IIIC	Any T	N0	M0	Any	5
Stage IVA	Any T	N1	M0	Any	Any
Stage IVB	Any T	Any N	M1	Any	Any

Risk classification

Guidelines from the European Society for Medical Oncology (ESMO) recommend classifying localized prostate cancer as follows, in order to guide prognosis and therapy[5] :

- Low risk: T1–T2a and Gleason score ≤6 and PSA ≤10
- Intermediate risk: T2b and/or Gleason score 7 and/or PSA 10-20
- High risk: ≥T2c or Gleason score 8-10 or PSA >20

The ESMO recommends that patients with intermediate- or high-risk disease have nodal staging using CT, MRI, choline positron emission tomography/CT (PET/CT), or pelvic nodal dissection. Patients with intermediate- or high-risk disease should be staged for metastases using technetium bone scan and thoracoabdominal CT scan, whole-body MRI, or choline PET/CT.[5]

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