Pro Index | Journal of Science in Medicine and Life
Volume: 2 Issue: 11 Year: 2024
ISSN: 2992-9202 | http://journals.proindex.uz

Modern Interpretation of Early Diagnosis of Prostate Cancer

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Abstract: On average, 70% of the normal prostate is composed of glandular elements and the remaining 30% is fibromuscular stroma. The glandular tissue of the prostate is usually composed of internal glands, which include the transition zone and periureteral glandular tissue, and external glands, which occupy the peripheral and central zones. TRUS can distinguish the transition zone, which is usually located anteriorly as a hypoechoic area, from the peripheral zone, which is echogenic and has a uniform echotexture compared to the rest of the gland. On the other hand, in healthy adult men, the central zone differs little from the peripheral zone. The transition zone is the main site of hyperplastic changes and makes up the majority of the prostate tissue in older men. It may be the site of development of about 20% of all prostate cancers. It should be noted that 1 to 5% of prostate cancers are located in the central zone. The peripheral zone, the main site of development of chronic prostatitis, causes about 70% of prostate cancer. On the other hand, cancer lesions in the transition zone are unlikely to be distinguished from BPH nodules by TRUS.

Key points: Anterior fibromuscular tissue, capsule, periprostatic adipose tissue, periprostatic lymph nodes, neurovascular bundles, ejaculatory ducts.

SONOGRAPHIC ANATOMY

The average dimensions of the normal adult prostate are 4.0-4.5 cm, 2.5-3.0 cm, and 3.0-4.0 cm in the transverse, anteroposterior, and craniocaudal directions, respectively. This gland is surrounded by a thin pseudocapsule that is almost indistinguishable from the surrounding fascial planes. Anatomically, the neurovascular bundles penetrating the prostate capsule are of great importance, as they represent the main weak point of the capsular apparatus and are likely to be involved in the tumor process. The picture of a normal gland on TRUS depends on age. While younger men experience less hyperplasia of the glandular tissue, older men develop BPH and the prostate becomes a larger gland with a more rounded shape.

Scantechnik

Nowadays, biplane sensors along with end and side sensors allow multiplane imaging in semicoronal, axial and sagittal projections during transrectal scanning of the prostate. Technically, 5 to 8 MHz transducers provide high accuracy for the peripheral part of the gland, which is very important for accurate sample selection during biopsy. Air bubble artifacts affect image quality. This can be avoided by using ultrasound gel applied to a latex condom placed on the transducer. A self-enema before the procedure helps to remove gases and debris, another factor that can cause TRUS image distortion. A simultaneous digital rectal examination can be helpful in identifying suspicious findings on physical examination related to TRUS abnormalities. Many specialists prefer the left lateral decubitus position because it is well tolerated. In summary, a full bladder allows a clear view of the base of the prostate, which helps in better visualization of the prostate. However, according to the authors, clinical practice shows that the bladder should not be over-distended, as this may lead to urinary incontinence during biopsy.

TRUS examination of the prostate begins with a systematic scan in the transverse or semicoronal plane, starting at the level of the seminal vesicles adjacent to the base of the prostate and continuing to the apical plane, which visualizes the gland. zones. Then, an examination is performed in the sagittal plane to detect lobular asymmetry and confirm suspicious lesions detected on axial or coronal scans. Prostatic and extraprostatic structures evaluated in a systematic approach are shown in Table 1. It should be noted that the ellipsoid formula allows you to calculate the size of the prostate using diameters along orthogonal axes:

Anatomical structures evaluated by TRUS

external gland

internal gland

Anterior fibromuscular tissue

capsule

Periprostatic adipose tissue

Periprostatic lymph nodes

neurovascular bundles

ejaculatory ducts

seminal vesicles

rectal wall

urethra

In patients diagnosed with prostate cancer, an assessment of prostate size may be necessary to prescribe appropriate therapy. Appropriate assessment can also be helpful in the treatment of patients with undiagnosed cancer, as it can direct therapy to patients with symptoms of lower urinary tract obstruction. The transrectal ultrasound approach of the prostate also allows the operator to perform various diagnostic and therapeutic interventions for prostate cancer due to its significantly higher accuracy compared to other ultrasound examination methods.

PROSTATE CANCER

PCa is the second leading cause of cancer-related death in men. This disease not only represents a major medical problem but also poses a major public health problem due to its high economic cost. Although early detection of the disease is important for adequate treatment, small foci of cancer can be found alongside significant tumor lesions. Nowadays, the main tools for diagnosing the disease are digital rectal examination, serum prostate-specific antigen (PSA) level and TRUS-guided prostate biopsy. Currently, the positive predictive value of prostate biopsy based on digital rectal examination, PSA and TRUS results is low and results in a significant number of unnecessary biopsies. Therefore, there is a clear need to improve the accuracy of prostate cancer diagnostic methods.

The most common indication for a TRUS of the prostate is for diagnostic evaluation in suspected prostate cancer. It appears that early detection of prostate cancer is closely related to reducing mortality, as detection in the early stages of the disease is often the only chance for treatment. Before diagnostic tools such as digital rectal examination, TRUS and PSA testing were widely used to detect the disease at an early stage, prostate cancer was often diagnosed at an advanced stage, resulting in patients dying earlier. Although a serum total PSA (TPSA) level above 4 ng/mL may indicate the presence of prostate cancer, patients with BPH and inflammatory prostate disease may also have elevated serum total PSA levels. The lack of specificity of serum total PSA for PCa screening inevitably led to further efforts to find an ideal protocol combining PSA, TRUS and digital rectal examination to improve specificity without compromising sensitivity. Although TRUS

is considered the best method for ultrasound guidance in biopsies, its low positive predictive value in the diagnosis of malignant tumors is an important disadvantage.

Since its first clinical introduction in the 1960s, there have been steady improvements in TRUS technology. Although there is a consensus on the use of TRUS for assessing prostate size and ultrasound for biopsy, its limited value for accurate detection of early-stage PCa and detection of local tumor spread still precludes its use. However, grayscale ultrasound can clearly define the zonal anatomy of the prostate, and the gland can be easily distinguished by TRUS from periprostatic tissue, including the rectum, neurovascular bundles, and adipose tissue.

Classically, a hypoechoic lesion in the peripheral zone may indicate a malignant process, but PCa may have less hypoechoic or hyperechoic features.

Prostate cancer. Transverse grayscale TRUS image shows a poorly defined, slightly hypoechoic mass in the subcapsular zone (arrow) of the left lobe, which was histologically confirmed as adenocarcinoma.

(A) Transverse grayscale TRUS image with no obvious lesion in the peripheral zone. (B) Transverse color Doppler TRUS image of the same patient shows an area of vascular enhancement in the right peripheral zone (arrow), which was the only histopathologically identified feature of adenocarcinoma. Due to its isoechoic nature, the tumor was invisible on grayscale TRUS.

Currently, the use of other, less specific features is required for the diagnosis of prostate cancer, since a significant proportion of detected prostate cancers are isoechoic. In this context, the following features may be helpful: asymmetry, echotexture, or glandular edge. Accordingly, a nonspecific irregular echo or a bulging or discontinuous capsular contour may indicate the presence of PCa. However, about half of PCa lesions are not visible on grayscale ultrasound. In addition, some types of pathologies, for example, BPH, prostatitis, atrophy, hematoma, ductal ectasia, and intraepithelial neoplasia, can mimic the picture of prostate cancer on grayscale ultrasound. Another challenge in the assessment of PCa is that it is predominantly multifocal; a single circular formation may also occur, but this pattern is less common. Morphologically, only 30% of PCa may occur as a single nodule, a lesion with an infiltrative component occurs in about 50% of patients, and the infiltrative pattern predominates in the remaining 20%. Ultrasound examination shows advanced prostate cancer with diffuse hypoechoic and heterogeneous peripheral echotexture, which is isoechoic or hyperechoic compared to normal prostate tissue.

ULTRASONOGRAPHY OF THE PROSTATE:

Prostate cancer. (A) Transverse grayscale TRUS image shows a round hypoechoic mass in the right peripheral zone (arrow). Neither color (B) nor power Doppler TRUS (C) showed a significant increase in blood flow, suggesting the neovascularization characteristics of PCa. (D) Transverse TRUS image shows the trajectory of the needle used to obtain a biopsy sample from the above lesion.

Prostate cancer. (A, B) Grayscale transverse and longitudinal TRUS images showing a localized nodule in the right peripheral zone (arrows in A and B). (C, D) Transverse and longitudinal power Doppler TRUS images (arrows C and D) showed vascular enhancement in the lesion.

Prostate cancer. (A) Transverse grayscale TRUS image shows diffuse heterogeneous parenchymal echotexture with irregular capsular contour and marked posterior extracapsular extension. The lesion has a marked protrusion and is located close to the rectal wall, suggesting infiltration of cancerous tissue. Transverse color (B) and power (C) Doppler TRUS images show increased blood supply to the affected area. (D) Whole-body scan of the same patient shows multiple areas of increased growth in the axial skeleton, suggestive of abnormal osteoblastic activity and consistent with a metastatic lesion.

Smaller cancers usually have a hypoechoic appearance, while tumor extension may result in an isoechogenic lesion or a heterogeneous echogenic lesion. There are no specific ultrasound features for transition zone cancers, but they differ from peripheral zone cancers in that they are clinically

less aggressive. Therefore, routine biopsy is the only way to detect transition zone cancers. The concurrent presence of BPH may be a limiting factor in TRUS evaluation of the prostate, as the mixed signal reflection or peripheral compression effect may mask prostate cancer.

In addition to adenocarcinoma, the most common histological form of prostate cancer, ultrasound features of rare prostate tumors have also been described. An adenomatous cyst of the prostate can present with several identical small cysts. Comedocarcinoma, the most dangerous form of PC, appears sonographically as a cancerous hypoechoic zone interspersed with numerous heterogeneous small hypoechoic foci. Lymphomas, on the other hand, show the appearance of large hypoechoic masses in the transitional and peripheral zones on ultrasound. In summary, soft tissue masses invading the bladder and prostate can present as rhabdomyosarcoma, which develops in childhood.

Although the use of TRUS in PCa diagnosis is limited, some TRUS findings can detect extracapsular extension. These findings include local protrusions or irregularities of the prostatic capsule and hypoechoic lines in the plane of the periprostatic fat. However, TRUS cannot detect extracapsular spread of small microscopic collections of tumor cells.

COLOR DOPLEROGRAPHY

Doppler ultrasound is a tool for assessing local blood flow, which is closely related to tissue function and vitality. In color Doppler, the color palette depends on the direction of blood flow and the direction of the sensor when receiving the signal, with the flow to the sensor shown in red and the flow from the sensor shown in blue. On the other hand, with the accelerated growth rate, the increase in blood supply requirements of cancer tissue is more obvious than that of normal tissue, which may cause significant changes in local hemodynamics. This affects the ability to detect and identify cancer using color Doppler ultrasound. Color Doppler ultrasound can detect an increase in the number of dilated and atypical blood vessels, which is due to angiogenesis and increased blood flow in tumor tissue. Technically, increased blood flow can be detected by spectral analysis using pulsed Doppler, which detects waves that represent shifts in frequency or velocity, or by color Doppler, which displays a spectrum of colors that represent the average range of frequency or velocity shifts. red blood cells in the bloodstream.

Previously, it was believed that color Doppler sonography was the best diagnostic of prostate cancer because it allowed to determine the diffuse, local and surrounding nature of blood flow. Later, it was found that the technique had low specificity for adequate evaluation. In addition, hypoechoic lesions and hypervascularity, which are indicative of PCa, do not correlate. However, the color Doppler signal has been shown to correlate well with the stage and type of PCa, as well as the risk of recurrence after treatment, which is crucial in determining the behavior and aggressiveness of PCa. Accordingly, color Doppler sonography has proven useful to differentiate low-risk hypovascular tumors from high-risk hypervascular tumors, since the latter group is associated with hypervascularity and represents a higher stage of Gleason tumor, which represents a high risk of Simta extension. Targeted biopsy relies exclusively on high-frequency color or power Doppler imaging because of the theoretical risk of missing a significant number of tumors. In addition to quantifying blood flow, color Doppler ultrasound can calculate microvascular density (distribution of microvessels), which may be useful for assessing blood flow in the prostate. Naturally, microvessel density was higher in metastatic tumors, which is typical for PCa. Since core biopsy underestimates Gleason histology, microvessel density can be used as an indicator of disease prognosis. Technical limitations of color Doppler imaging for prostate assessment include angle dependence of Doppler flow, intraprostatic noise simulating flow enhancement, and inadequate detection techniques at low flow rates.

POWER-DOPPLEROGRAPHIE

Power Doppler has a lower angle dependence than color Doppler and provides information about the presence and intensity of flow signals. The advantage of the technique is to detect slow flow in small tumor vessels and even subtle changes in blood flow. However, it is not possible to predict the direction of flow using this method. Power Doppler ultrasound, which has three to four times the

sensitivity for detecting prostate cancer, also helps in the differential diagnosis of BPH and prostate cancer. However, this technique has rarely been reported to be superior to color Doppler in detecting PCa. Although power Doppler can help determine an appropriate site for prostate biopsy by identifying areas of local hypervascularity, it is not considered superior to color Doppler and is only useful for targeted biopsy when the number of biopsies is limited by the prostate. Combined grayscale ultrasonography and TRUS-guided color Doppler biopsy are not sensitive enough to obviate the need for routine biopsy. A recent study has shown that measuring the spectral waveform of prostatic capsular and urethral arteries using power Doppler ultrasound may be helpful in differentiating prostate cancer from benign hypertrophy. The researchers also hypothesized that increasing the number of biopsies limited to abnormal spectral Doppler index values would increase the diagnostic efficiency in detecting PCa.

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