REVIEW

New trends in Prostate Cancer Imaging

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Abstract

Successful imaging of prostate cancer remains a major goal in everyday clinical practice. The widely adapted imaging techniques are limited by their low specificity and sensitivity especially for identification of lymph node or bone metastasis. A novel imaging technique with better outcomes would provide a significant aid and possibly increase the overall survival of patients suffering from prostate cancer. We review the literature about this interesting topic in an effort to clarify the value of these methods (if any) and their role in prostate cancer diagnosis.

Introduction

Prostate cancer (PCA) is one of the most common cancers of the male population and its successful imaging remains one of the most difficult to achieve, goal of urology. The words of P.C. Walsh: “The invention that will have the most impact in urology will be the development of an accurate imaging technique that finds cancer inside the prostate” 1 inspired many researchers in order to optimize the existing modalities or even invent new ones. The methods we have at our disposal today (digital rectal examination, PSA, and ultrasound guided biopsies) have several limitations since they can diagnose only 20-50% of prostate cancers with large detection rates of clinically insignificant tumors 2,3. Similarly detection rates of lymph node metastasis with the use of computed tomography (CT) or magnetic resonance imaging (MRI) are as low as 30%. The above mentioned data support the need for the development of a novel, more precise imaging method for diagnosis and staging of prostate cancer. In this article we are reviewing the literature for any recently introduced refinements and improvements of existing imaging methods or any novel approaches and test their value in the everyday clinical practice.

Material and Methods

We reviewed the literature for articles concerning imaging modalities for the diagnosis and staging of prostate cancer. The search was limited in articles which had at least an abstract written in English and were indexed in PubMed from 2000-2015.

Key words

Prostate Cancer; Imaging; mpMRI; PSMA

Citation


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The keywords that were used in our search were imaging, prostate cancer, mpMRI and PET scan. We studied all the relevant articles and we analyzed the ones with the biggest series.

**Ultrasound**

Until recently transrectal ultrasound was the most common and effective method for the initial approach of PCa despite its extremely low sensitivity and specificity. In an attempt to increase the diagnostic rates of this easy and relatively inexpensive method some improvements were developed. One of them is three-dimensional ultrasound. This method, that utilizes appropriate software to convert ultrasound images into a three-dimensional environment, yielded satisfactory results in recent studies.

In the diagnosis of PCa reported sensitivity and specificity reach 85% and 41% respectively, but these rates rise significantly to 84% and 96% respectively when identifying locally advanced disease. Although the number of patients is not large enough to draw safe conclusions, this method can be an easy, low-cost alternative for diagnosing locally advanced disease. Another method based on ultrasound imaging, called Histoscanning, which was firstly reported by Braeckman J et al and Simmons LA et al. utilized computer algorithm analysis of ultrasound images. According to the authors the above mentioned method can identify tumors with volume lesser than 0.5 ml while its negative predictive value is almost 100% with correspondingly high rates of sensitivity. As expected the conclusions of these studies were limited by their retrospective nature and by the low number of patients, however, their results remain promising.

Other attempts reported in the literature such as the administration of PDE5 inhibitors with concomitant utility of Doppler Mode of the ultrasound, and a new prostate elastography (Shear Wave Elastography), both yielding controversial results. Regarding the standard method of ultrasound guided prostate biopsies (12 cores), efforts were made to optimize it with fusion of MRI and ultrasound images, in order to identify and target more easily suspicious for malignancy areas. The PCa diagnosis rates with this method reached 72%, improving significantly the ones offered by the standard one.

**Multi-Parametric Magnetic Resonance Imaging (mpMRI)**

There is a growing body of literature concerning the role of mpMRI in prostate cancer diagnosis. This modality consists of two or three different magnetic imaging methods, each one providing a score which sums up in the final examination score (PI-RADS score). The techniques used are the high-resolution T2 (T2 weighted images T2WI), the Diffusion weighted Imaging (DWI), the MR spectroscopic imaging (MRSI) and Dynamic MRI (DCE-MRI). Each of them solely has its advantages and disadvantages but their combination increases the sensitivity and specificity of the final result.

The first and most popular method for magnetic imaging of prostate is T2WI MRI. Despite its high sensitivity, when used alone is not sufficient to diagnose PCa due to several drawbacks. Firstly it exhibits low specificity due to the fact that benign prostatic hyperplasia in this sequence can be easily confused with PCa. Another disadvantage is that bleeding of prostate (eg after prostate biopsy) may mimic PCa whereas imaging of the central zone of the prostate can potentially be misleading. Due
to these disadvantages it is recommended to avoid MRI of the prostate with this sequence for 4-6 weeks after the prostate biopsy, or add T1 sequence images in order to preclude hemorrhage. The second more popular method of prostate magnetic resonance imaging is the DCE MRI which is superior to T2W imaging although it sets more strongly the suspicion of PCa its results are not specific. Even though it can identify a suspicious lesion with volume <0.5 ml, its value increases as the tumor size increases. Another important part of multiparametric MRI is DWI MRI. This method uses apparent diffusion coefficient (ADC) maps that give characteristically low values when PCa is present. These values have been associated with tumor aggressiveness and can potentially be of significant value in an active surveillance setting. However its major disadvantage is its susceptibility to artifacts that can potentially affect final interpretation of results. Finally adjunctive method in mpMRI is the MRSI which recognizes the citrate and choline levels in tissue examination and therefore can confirm the existence or not of cancer within the prostate. More specifically, the PCa exhibits lower citrate and higher choline levels compared to normal prostate tissue, and recent studies correlate these results with the Gleason Score (GS) and hence tumor aggressiveness.

The interpretation of mpMRI results are based on Prostate Imaging Reporting and Data System (PI-RADS) score which was validated from two large studies recently published. According to this score, patients with values 1-2 have very little chance of having clinically significant prostate cancer, score 4-5 means that PCa existence is very likely and score 3 represents the gray zone area. However it is important to note that due to heterogeneity in results reporting, no specific instructions for its interpretation have been published. Attempts have been made to improve the value of the above mentioned score by developing a second version but its value is far from being proven. In conclusion mpMRI is earning steadily its place in the diagnosis of PCa even though currently EAU guidelines recommend it before deciding a repeated prostate biopsy with negative prior biopsy, and also for the local staging in high risk patients or patients with locally advanced PCa.

**PET Scan**

The role of the PET Scan in urology and in prostate cancer is still quite limited. Although staging methods widely adapted do not offer high sensitivity and specificity, the cost of PET Scan still remain a major drawback for further utilization of this method in the diagnosis of prostate cancer. With the development of new detectors however (more specific for PCa) this situation seems to be changing. A sufficiently studied targeting agent, is the prostate specific membrane antigen (PSMA) based on which the PSMA PET scan was created. PSMA utilizes mainly radiisotope (68) Ga which binds to PSMA and is expressed in more than 90% of PCa. Main advantages of this imaging method are that PSMA expression is particularly increased in advanced and metastatic PCa and its improved sensitivity in identifying metastatic disease compared to CT, MRI or bone scan.

A recent study which followed patients scheduled for radiotherapy, after first time diagnosis or relapses of PCa and concluded that PSMA PET Scan dramatically changed the therapeutic approach of 50% of them. Recently a relatively big study of 100 patients concluded that 68 Ga-PSMA-PET has a high clinical impact on staging and radiation therapy in patients with biochemically recurrent PCa even at low serum PSA levels (1 ng/ml). The growing body of literature was included in a large meta-analysis of 1,309 patients by Perera et al which demonstrated the excellent rates of detection of cancer spread in late stage prostate cancer. On per patient analysis, the sensitivity and specificity of 68Ga-PSMA PET were both 80% and on per lesion analysis the rates were 80% and 97% respectively. These encouraging results led Eiber and al to study the results of the combination mpMRI and PSMA Pet scan in detecting lymph node and distant metastasis. The PSMA PET scan is a promising diagnostic method but until results from large studies are published its use remain experimental. In summary the basic characteristics of available modalities are shown at Table 1.

**Conclusion**

There are enough data in the literature for optimized or novel imaging modalities but only mpMRI seem to probe its value in prostate cancer diagnosis and screening. Nevertheless new data, concerning this important issue, are been continuously published and may alter the way that we diagnose and treat prostate cancer in the near future.

**Conflicts of interest**

The authors declared no conflict of interest.
Η επιτυχής απεικονιστική διάγνωση του καρκίνου του προστάτη αποτελεί έναν δύσκολο να επιτευχθεί στόχο ακόμα και σήμερα. Οι μέχρι σήμερα ευρέως χρησιμοποιούμενες μέθοδοι χαρακτηρίζονται από χαμηλή ευαισθησία και ειδικότητα ειδικά στην ανεύρεση λεμφαδενικών ή οστικών μεταστάσεων. Η ανάγκη για την ανάπτυξη μιας νέας απεικονιστικής μεθόδου η οποία και θα καλύψει το κενό δίνοντας καλύτερα αποτελέσματα είναι μεγάλη και προς αυτήν την κατεύθυνση πολλοί ερευνητές έχουν δημοσιεύσει την εμπειρία τους με καινούριες μεθόδους. Το παρόν άρθρο ανασκοπεί την βιβλιογραφία σε μια προσπάθεια να ξεκαθαριστεί αν υπάρχει κάποια μέθοδος που μπορεί να πλησιάσει στην επίτευξη του παραπάνω στόχου αλλά και αν αυτή μπορεί να χρησιμοποιηθεί στην καθημερινή πράξη.

**Περίληψη**

Λέξεις ευρετηριασμού

καρκίνος του προστάτη, απεικονιστικές μέθοδοι, mpMRI, Pet Scan

**References**

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