More Than Detection of Adenocarcinoma – Indications and Findings in Prostate MRI in Benign Prostatic Disorders

Bildgebung jenseits des Karzinoms – Indikationen und Befunde der MRT im Rahmen benigner Prostataveränderungen

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ABSTRACT

Background Multiparametric MRI of the prostate has become a fundamental tool in the diagnostic pathway for prostate cancer and is recommended before (or after negative) biopsy to guide biopsy and increase accuracy, as a staging examination (high-risk setting), and prior to inclusion into active surveillance. Despite this main field of application, prostate MRI can be utilized to obtain information in a variety of benign disorders of the prostate.

Methods Systematic bibliographical research with extraction of studies, national (German) as well as international guidelines (EAU, AUA), and consensus reports on MRI of benign disorders of the prostate was performed. Indications and imaging findings of prostate MRI were identified for a) imaging the enlarged prostate, b) prostate MRI in prostatic artery embolization, c) imaging in prostatitis and d) imaging in congenital anomalies.

Results and Conclusions Different phenotypes of the enlarged prostate that partly correlate with severity of symptoms are discussed. We provide an overview of the different types of prostatitis and possible imaging findings, highlighting abscesses as a severe complication. The most common congenital anomalies of the prostate are utricular cysts, whereas anomalies like aplasia, hypoplasia, and ectopia are rare disorders. Knowledge of indications for imaging and imaging appearance of these conditions may improve patient care and enhance differential diagnosis.

Key Points:
- Current guidelines do not implement indications for mpMRI apart from prostate carcinoma.
- MRI can distinguish different anatomical phenotypes of prostatic enlargement.
- Prostatic artery embolization represents a valuable treatment option in cases of symptomatic benign prostatic enlargement.
- Different forms of prostatitis exist and may mimic prostate carcinoma in MRI.
- MRI can be used to evaluate anatomical prostate anomalies.

ZUSAMMENFASSUNG

Hintergrund Die multiparametrische MRT der Prostata bildet einen der Grundsteine im diagnostischen Vorgehen zur Erkennung des Prostatakarzinoms. Sie wird vor Biopsie (oder nach negativer Biopsie mit fortbestehendem Karzinomer-
Introduction

In recent years, multiparametric MRI of the prostate (mpMRI) has successively been implemented in the process of clinically significant prostate cancer detection [1], active surveillance [2], and relapse diagnosis [3]. National and international guidelines recommend mpMRI in combination with consecutive MRI-guided targeted and systematic biopsy in order to minimize false-negative results in biopsy-naïve patients [4]. There is also consensus for the indication of mpMRI prior to targeted biopsy after previous negative systematic biopsy and prior to placing a patient under active surveillance [4–6]. Further indications for mpMRI are the evaluation of local tumor expansion and extraprostatic infiltration, staging of high-risk tumors prior to therapy [5], evaluation of tumor extent prior to focal therapy [5] and image-guided radiotherapy [IGRT] [7]. The diagnostic accuracy of mpMRI for the detection of clinically significant cancer has been extensively studied. A recent meta-analysis reports a pooled sensitivity of 87% and a pooled specificity of 74% for the standardized reporting lexicon for mpMRI [8], PI-RADS (prostate imaging reporting and data system), with version 2.1 being the most recent edition [9].

Despite this major field of application, prostate MRI can be employed as a diagnostic modality for various other, benign conditions. In this review, we provide an overview of the use of prostate MRI for enlarged prostate imaging, prostate artery embolization imaging, prostatitis imaging, and imaging of congenital anomalies. If applicable, we refer to recommendations of (German) national guidelines and international guidelines (EAU and AUA). We do not review the imaging of malignancies other than adenocarcinoma as these entities have been discussed in detail before [10].

Imaging the enlarged prostate

Definitions and guidelines for imaging

In this manuscript, we follow the terminology used in the German S5e guideline "Diagnostic and differential diagnosis of benign prostate syndrome (BPS)”. An update of the guideline is currently in progress. The term benign prostate syndrome (BPS) refers to the triad of lower urinary tract symptoms (LUTS), benign prostatic enlargement (BPE), and bladder outlet obstruction (BOO) [11]. BPE is defined as an increase in prostate volume (> 25 ml, although different cut-off values have been proposed) due to benign prostatic hyperplasia (BPH). BPH is a histopathological diagnosis and is commonly used incorrectly synonymously with BPS, although only 25–50% of patients with BPH will eventually develop LUTS over time. Additionally, BPH is often used incorrectly for an enlarged prostate diagnosed with imaging alone. BOO is defined as a reduced rate of urine flow and an increase in detrusor pressure, irrespective of cause [12]. Benign prostatic obstruction (BPO) represents BOO due to BPE [13].

LUTS comprise both irritative symptoms such as high frequency of urination or urge incontinence and obstructive symptoms like decreased peak urine velocity or terminal dribbling. LUTS can be caused by pathologies other than BPE/BOO, e. g. by infection, structural anatomical aberrations or neurogenic disorders. For a comprehensive review of LUTS, refer to the guidelines of the National Institute for Health and Care Excellence (NICE) [14]. English-speaking countries specify the diagnosis of LUTS due to BOO on the basis of BPO/BPE by referring to "LUTS suggestive of BPH" [11, 12]. Only in 50% of cases will BPH eventually result in BPE [14]. On the other hand, BPE is not a necessary condition for BPO (patients with small prostates may suffer from symptoms due to musculostromal hyperplasia) [15].

Anlageanomalien wie die glanduläre Aplasie, Hypoplasie und Ektopie gehören zu den selteneren Erscheinungsbildern. Die Kenntnis über Bildgebungsinformation und die bildmorphologischen Charakteristika der genannten Erkrankungen können zur Verbesserung der Patientenversorgung und genaueren Differenzialdiagnostik beitragen.

Kernaussagen:

- Aktuelle Leitlinien implizieren keine Indikationen für die multi-parametrischen MRT der Prostata außerhalb der Diagnostik des Prostatakarzinoms.
- Eine Differenzierung verschiedener anatomischer Phänotypen der benignen Prostatavergrößerung ist mittels MRT möglich.
- Prostataarterienembolisation stellt eine effektive Therapieoption im Rahmen einer symptomatischen Prostatavergrößerung dar.
- Verschiedene Formen der Prostatitis kommen als Differenzialdiagnose des Prostatakarzinoms in der MRT infrage.
- Anomalien der Prostata oder Samenblasen können mittels MRT dargestellt werden.
Typical indications for imaging in the assessment of BPS are measurement of prostate size and examination of the presence of an intravesical prostatic lobe, for which guidelines suggest transrectal (TRUS) or transabdominal suprapubic ultrasound [13]. It is explicitly stated that cross-sectional imaging can be employed when already available [12]. However, the acquisition of new cross-sectional images of the prostate is currently not implemented in the diagnostic algorithm of LUTS/BPS [12].

MRI offers excellent soft tissue contrast and different prostatic zones can be reliably distinguished and accurately measured [16]. Quantification of the exact prostate volume, exclusion of prostate cancer prior to therapy of an enlarged prostate and detection of pathologies leading to LUTS are promising use cases for mpMRI that have not yet been implemented in current guidelines. It is recommended to estimate prostate volume by measurement of the maximum longitudinal and anterior-posterior diameter on a mid-sagittal image and measurement of the maximum transverse diameter on axial images with the ellipsoid formula \((D_1 \times D_2 \times D_3 \times 0.52)\) [9]. Furthermore, manual and automated segmentation [17] may be employed.

Classification of phenotype

The zonal anatomy of the prostate (differentiating transition zone, peripheral zone, central zone, periurethral glands, and anterior fibromuscular stroma) has been established by McNeal [18]. In the case of an enlarged prostate, Wasserman proposed a phenotypical classification, taking into account in which part (or combination of parts) the enlargement originates [15]. The MRI classification [15] is based on an ultrasound classification [19]. Subtypes of BPH phenotypes may lead to specific symptoms – the AUA has suggested additional research in "disease ‘phenotypes’ and [...] better disease definitions (e.g. [...] patient phenotypes relative to urological symptom profiles)" [15]. We provide an overview of proposed phenotypes in ▶ Fig. 1. The reported distribution of Wasserman types was 63 % type 1 and 31 % type 3 (after exclusion of type 0 cases) in Wasserman et al. 2015 [15]. According to the authors and to our own clinical experience, Wasserman type 2 occurs more infrequently. The majority of patients can thus be described with only two phenotypes, compare to ▶ Fig. 2. When enlarged, the transition zone is referred to as lateral lobes and the periurethral glands as the median (retrourethral) lobe [19].

Two different tissues contribute to hyperplasia of the prostate and therefore to symptoms of BOO on the basis of BPH: glandular/epithelial tissue and stromal tissue [19]. Predominant hyperplasia of glandular tissue leads to mechanical compression of the urethra and the bladder neck, referred to as the static effect. Hyperplasia of stromal tissue leads to an increase in muscle tone, referred to as the dynamic effect [19]. There is evidence that MRI can distinguish between these forms of hyperplasia, with epithelial hyperplastic changes having a high signal in T2-weighted images and stromal hyperplastic changes having a low signal [20], refer to ▶ Fig. 3. Although this knowledge could hypothetically influence treatment options (e.g., better response to 5α-receptor antagonists in cases with predominantly stromal hyperplasia), this approach has not been sufficiently investigated.

Over the past two decades, an intravesical protrusion of enlarged prostatic tissue has been proven to be a clinically relevant morphological feature [21]. For example, a trial without a catheter in the case of acute urinary retention related to BPE is more likely to fail when intravesical protrusion is > 10 mm [22]. The extent of intravesical protrusion (> 10 mm versus ≤ 10 mm) is correlated with the severity of BOO in cases with BPE [23], compare to ▶ Fig. 4a. A protrusion > 10 mm also predicts poorer response to treatment with tamsulosin in patients with LUTS due to BPO compared to patients with a protrusion ≤ 10 mm [24]. Measurement of intravesical prostatic protrusion (IPP) is mentioned in the current EAU guideline [13] as a potentially "feasible option to infer BPO in men with LUTS", and "the role of IPP as a non-invasive alternative to pressure flow studies (PFS) in the assessment of male LUTS remains under evaluation" [13]. AUA guidelines refer to ultrasound-based evaluation of IPP as optional during the clinical workup [12].
Several studies investigated the correlation of the prostatic urethral angle (PUA) with symptoms due to BOO/LUTS in cases with BPE. PUA is defined as the angle between the proximal and distal part of the prostatic urethra measured on a mid-sagittal image, compare to Fig. 4b. The angulation point is the proximal part of the verumontanum [25]. A common quantification tool for the severity of symptoms in BPS is the international prostatic symptoms score (IPSS). Two studies that assessed PUA in MRI (mid-sagittal T2-weighted images) did not demonstrate a significant correlation of PUA with the IPSS score [26] – with one study acknowledging the usage of an endorectal coil as a possible source of bias due to deformation of the prostate and the prostatic urethra [27]. Other studies using ultrasound as imaging modality reported significant associations of PUA with IPSS, BOO severity, and peak urine flow rate [25, 28, 29]. A commonly reported cut-off value for an increased PUA is $\geq 35^\circ$ [25]. PUA measurement is mentioned in the EAU guidelines as an experimental diagnostic tool for noninvasive pressure-flow testing [13]. However, there is also a strong recommendation not to offer noninvasive testing as an alternative to PFS for the diagnosis of BOO.

Fig. 2 a Wasserman prostate type 1, enlargement of the transition zone only. b Wasserman prostate type 2, enlargement of the retrourethral lobe only. c Wasserman prostate type 3, enlargement of the transition zone and the retrourethral lobe. The majority of patients will either have a type 1 or type 3 phenotype.

Fig. 3 a Axial T2w. b Coronal T2w. Glandular hyperplastic changes of the transition zone have high signal intensity (solid arrows), stromal hyperplastic changes have low signal intensity (dashed arrows).

Fig. 4 a Intravesical prostatic protrusion (IPP, dashed line) is measured perpendicular from the assumed normal bladder floor (white line) on a mid-sagittal image. b The prostatic urethral angle (PUA) is the angle between the proximal and distal part of the prostatic urethra (white lines) measured on a mid-sagittal image.
Performing multiparametric MRI of the prostate before a planned prostatic artery embolization (PAE) serves to detect clinically significant prostate cancer, to determine the size of the prostate, and to visualize the zonal anatomy. Preprocedural imaging of the prostatic arteries helps interventional radiologists to reduce procedure time and the risk of embolization of surrounding organs [30]. Vessel imaging can be performed with DSA combined with cone-beam CT, CT angiography, or MR angiography [30–32].

If there are PI-RADS 3–5 findings in the patient’s prostate, these have to be clarified before PAE by biopsy. The size of the prostate and certain characteristics of the zonal anatomy are prognostic factors for the clinical success of PAE, which should be addressed in the pre-procedure informed consent discussion. The larger the total prostate and the transition zone, the better the clinical success [33]. With an ROC analysis, a threshold value of 39 mL for the total prostate volume was calculated as a guide for a minimum size of the prostate to be treated [33]. Patients with a dominant transition zone and large BPH nodes benefit more from PAE than patients without a dominant transition zone and large BPH nodes [34]. The calculation of the quotient of transition zone volume/total prostate volume showed better clinical success for values > 0.45 with a sensitivity of 85 % and a specificity of 75 % [35]. It was also shown that the size of the median lobe is positively correlated with the clinical success of PAE [36]. IPP is significantly reduced by PAE [37]. Measurement of IPP and PUA is mentioned in the current position paper of the German Society of Interventional Radiology (DeGIR) on PAE in the pre-procedure evaluation. Measurement in follow-up exams is possible in the case of special interest [38].

One day after PAE the anatomy in the transition zone can be delineated more poorly on T2w images than before PAE [39]. In addition, T1w hyperintensities are found as surrogate markers for hemorrhagic necrosis in almost half of cases [39]. Furthermore, the diffusion-weighted and the DCE-MRI images show further signs of ischemia with diffusion restriction and severely reduced vascularization [39], compare to ▶ Fig. 5. 6 months after PAE, the changes seen in the diffusion-weighted and DCE-MRI images are less distinct and signs of fibrotic remodeling, especially of the transition zone, can be found on T2w images [39]. Parameters that enable an inference from the initial MRI changes 1 day after PAE to the clinical outcome could not be identified [39]. However, another study showed that 87 % of patients with clinical success of PAE had ischemic areas on DCI-MRI images [40]. Furthermore, when evaluating an MRI examination of the prostate after PAE, the continually decreasing volume of the prostate after successful embolization should be taken into account and seems to have reached the nadir after 6 months [41]. After 12 months, morphological stability is reached [38]. The DeGIR position paper states useful clinical control intervals of 1–3 months, 6 months, and...


Imaging in prostatitis

Prostatitis can be divided into three subgroups according to symptoms and etiology. Patients with acute bacterial prostatitis (ABP) usually suffer from abruptly-onsetting voiding symptoms, diffuse perineal pain (which may be associated with defecation) and fever. Chronic bacterial prostatitis (CBP) is defined by pain in the perineal region for a period of three months or more. Lastly, chronic pelvic pain syndrome (CPPS) describes a non-bacterial form of chronic prostatitis with similar symptoms [42].

European guidelines recommend distinguishing bacterial prostatitis from CPPS according to the National Institute of Diabetes, Digestive and Kidney diseases (NIDDK) and National Institutes of Health (NIH) classification [43]. Although it is a very common diagnosis, bacterial infection is only proven in around 10 % of prostatitis cases [44]. E. coli are the predominant pathogens in patients with acute bacterial prostatitis [45]. Chronic bacterial prostatitis is caused by a wider spectrum of pathogens, including atypical bacteria. One study found that in 74.2 % of patients with symptoms of chronic prostatitis there was an underlying infectious etiology. Although E. coli is often regarded as the most common pathogen, the authors found infections with C. trachomatis in 37.2 %, T. vaginalis in 10.5 % and U. urealyticum in 5 % of the cases, whereas E. coli accounted for only 6.6 % [46]. CPPS per definition is an abacterial condition with a mostly unknown etiology with immunological dysfunction, neuropathic pain, and difficult to detect infections such as interstitial cystitis, as well as other possibilities being discussed.

There are no recommendations on a standardized diagnostic algorithm, but the diagnostic basis consists of urine dipstick testing (U-Stix), mid-stream urine culture, and DRE [47]. Dipstick testing for nitrite and leukocytes has a positive predictive value of 95 % and a negative predictive value of 70 % in patients with ABP [48]. On DRE, the prostate may appear swollen and tender. Additionally, blood cultures in the case of fever and prostate-specific antigen levels can be taken into consideration. When testing for CBP, the four-glass Meares and Stamey test is established as the diagnostic tool of choice [49]. It is furthermore suggested to take urethral samples in order to rule out atypical pathogens such as C. trachomatis and others [46].

Transrectal ultrasound (TRUS) can be helpful to detect complications such as endoprostatic abscesses but is not recommended as a first-line diagnostic tool for prostatitis due to its limited sensitivity [50]. PSA levels are only increased in 60 % of ABP and 20 % of CBP and therefore offer “no practical diagnostic information in prostatitis” [51]. In MR imaging, prostatitis can occur as a focal or diffuse pattern of low T2 signal intensity with low to moderate diffu-
tion restriction and corresponding early avid contrast enhancement [52]. ▶ Fig. 6 provides an example case of ABP. First-line therapy consists of oral application of culture-guided antibiotic treatment. In cases of ABP an empirical regiment until pathogen identification or parenteral antibiotic treatment of systemically-ill patients can be considered [53].

Prostatic abscesses are severe complications in prostatitis and, according to EAU guidelines, can be detected by TRUS or "imaging studies", thus including MRI. Vice versa, prostatic microabscesses can indicate prostatitis when other imaging criteria are missing. Similar to manifestations in other locations, endoprostatic abscesses appear as mostly circumscribed lesions with a T2w-hyperintense signal, peripheral contrast enhancement, and diffusion restriction [54], compare to ▶ Fig. 7. Treatment can either be conservative when abscesses remain under 1 cm in diameter or interventional (e.g. aspiration, drainage) in the case of greater abscesses [55].

Granulomatous prostatitis [GP] is a rare type of prostatic inflammation (1–3% of cases of benign prostatic inflammation) due to a variety of causes. While primary GP is often idiopathic, secondary causes may be urinary tract infections, surgical interventions, biopsy, and BCG instillation – an established treatment option for superficial urothelial bladder carcinoma. When dealing with nonspecific GP, which represents most cases, the disease is mainly self-limiting and requires only symptomatic treatment [56–58]. GP occurs both in young and old patients, with the greatest prevalence between 50–70 years and a mean age of 62–63 years [59, 60]. Incidence rates of prostatitis are highest between the third and fifth decades of life and from the seventh decade onwards [61]. Imaging shows either a diffuse or nodular
low T2 signal compared to normal tissue, sometimes with extra-capular extensions, diffusion restriction, and early, often pro-longed peripheral contrast enhancement [57, 62], compare to Fig. 8. Histopathologically, lesions appear as centrally caseating necrosis corresponding to low signal intensities in the center of the lesions in post-contrast imaging [62]. Small cystic compo-nents within the lesions are described in a few cases. The disease can be barely distinguishable from malignancies as radiological features are overlapping [57]. Hence, follow-up examinations and histopathological confirmation through biopsy in unclear cases to rule out PCa appear to be adequate diagnostic pathways, although guidelines do not offer specific recommendations.

Although mpMRI has a high sensitivity for prostate cancer detection, it sometimes lacks specificity, partly due to the above-mentioned conditions. A recent study found that quantitative imaging analysis of mpMRI could reliably differentiate prostatitis, from prostate cancer [64]. For example, the prostate gland connected with testicular feminization, ambiguous genitalia, epispadias or hypospadias (Fig. 9).

Congenital anomalies of the prostate

The prostate gland and the bulbourethral glands develop from the urogenital sinus, whereas the seminal vesicles (SV) and the ejaculatory duct (ED) arise from the Wolffian ducts. There are no guidelines (EAU, AUA) for the evaluation of prostatic congenital anomalies. Imaging in those cases remains a physician’s individual decision.

Congenital anatomic anomalies of the prostate gland such as agenesis, hypoplasia, cysts and ectopia are rare conditions. Just like anomalies of the seminal vesicles, they often appear in combination with other anomalies of the urogenital system [64]. For example, agenesis of the prostate gland can be associated with testicular feminization, ambiguous genitalia, epispadias or hypospadias (Fig. 9).

Congenital prostatic cysts originate from either the Müllerian or the Wolffian duct. Anomalies originating from the Müllerian duct are utricular cysts and Müllerian duct cysts, usually located in the prostatic midline. ED and SV cysts on the other hand arise from the Wolffian duct and mostly occur off-midline. ED and SV cysts represent rather uncommon conditions and shall not be discussed further in this article. Another pathology associated with the Wolffian duct is Zinser’s syndrome (ipsilateral ejaculatory duct obstruction, seminal vesicle cysts, and renal agenesis). For further details on the differential diagnosis (including periprostatic lesions like Cowper’s duct cysts) of prostatic cystic lesions, refer to [65].

Uricular cysts are focal, often pear-shaped dilatations within the prostatic utricle (a remnant of the Müllerian duct) and therefore show continuity with the pars prostatica of the urethra. They are located in a median plane within the prostatic gland, compare to Fig. 10. Müllerian duct cysts (results of failed focal regression of the Müllerian duct) show no communication with the prostatic urethra, may extend beyond the prostate gland, can grow to large diameters with consecutive irritative urinary symptoms, and typically arise behind the Colliculus seminalis. Uricular cysts and Müll-
Müllerian duct cysts may be indistinguishable on imaging. Whereas urotelial cysts are associated with various genitourinary abnormalities, Müllerian duct cysts usually appear without such associations [65]. Rarely, the otherwise incidental findings may become symptomatic due to infection, urinary retention, bleeding, and impaired fertility [10]. In those cases, MRI of the prostate can be employed for visualization of complex anatomical variants and offers additional information.

In contrast to neoplasms and abscesses, benign cystic lesions show a homogeneous T2 hyperintense signal, a simple internal structure, and no restriction in diffusion-weighted imaging.

Summary

In addition to the detection of clinically significant cancer, prostate MRI can be utilized to obtain information for a variety of benign disorders. In this review, we discuss the use of prostate MRI for imaging of the enlarged prostate, imaging related to prostatic artery embolization, and imaging in prostatitis. We also briefly address imaging in congenital anomalies. Especially in the workup of an enlarged prostate and prostatitis, prostate MRI does not play a central role at the moment according to EAU and AUA guidelines. However, we believe that additional knowledge of clinically significant findings unrelated to established indications for MRI examinations offers additional value for patient care.

Conflict of Interest

The authors declare that they have no conflict of interest.

References
