Is power Doppler US a good predictor of prostate cancer aggressiveness?

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**Abstract**

**Purpose.** To determine the value of Power Doppler US for the diagnosis of prostate cancer and in the prediction of cancer aggressiveness.

**Patients and methods.** One hundred and five consecutive patients with PSA > 4 ng/ml and/or abnormal digital rectal exam underwent power Doppler US prior to biopsy. In addition to biopsies directed to suspicious lesion on US, 10 to 12 standard sextant biopsies were obtained. Histologic results were correlated to imaging findings.

**Results.** A hypervascular lesion (enlarged, irregular, serpentine or disorganized vessels) was present at power Doppler US in 34 patients and corresponded to cancer in 28 cases. Nineteen cancers showed no detectable abnormality on power Doppler US. Cancer was present in 271 of 1093 cores. After correlation with results from sextant prostate biopsy, power Doppler showed a sensitivity of 44%, specificity of 96%, positive predictive value of 84% and negative predictive value of 80%. Positive results on power Doppler US were strongly correlated with higher Gleason scores.

**Conclusion.** Power Doppler US may contribute to the evaluation of prostate cancer aggressiveness and direct biopsies to more aggressive foci.

**Key words:** Prostate. Cancer. Doppler. Biopsy.

**Materials and methods**

Between June 2006 and December 2007, 105 consecutive patients referred for US guided prostate biopsy underwent power Doppler US. All patients had a PSA level >4ng/ml and/or an abnormality on DRE.

**Prostate carcinoma is a real public health problem since it is the most frequent cancer in males, and the third leading cause of cancer related death after lung and colon cancer (1). The aging population and patient screening are responsible for a continuous increase in its incidence. US guided transrectal prostate biopsy provides histological proof. On average, 12 samples are collected, but more extensive protocols (12-18 biopsies) and saturation prostate biopsy (>18 biopsies) may be considered in patients with high suspicion of prostate cancer and negative initial biopsies (2). Results from DRE, PSA level, Gleason score, percentage of grades 4 and 5 and number and percentage of invaded cores all correspond to prognostic factors that will influence management (3). Pretreatment nomograms integrating these prognostic factors predict the statistical risk of tumor extension or recurrence as a function of treatment (4). Imaging plays a crucial role for guidance of transrectal biopsies and pretreatment staging. Since the year 2000, MRI is used for tumor detection and localization especially after negative biopsies and for post-treatment follow-up and detection of recurrent current (5). The role of power Doppler US in prostate carcinoma has been the subject of several publications (6-9). It improves, in spite of some false negative results, the sensitivity of endorectal US, demonstrates tumor vascularity, detects capsular extension and aids for imaging guided biopsy. Are false negative results on Doppler US related to well-differentiated tumors of low growth potential? The purpose of this study was to determine the value of power Doppler US in the detection of prostate cancer and evaluation of its aggressiveness.

**Résumé**

L’écho-Doppler puissance est-il un bon témoin de l’agressivité du cancer de la prostate ?

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**Objectifs.** Déterminer la valeur de l’écho-Doppler puissance (EDP) dans le diagnostic et l’évaluation de l’agressivité du cancer de la prostate.

**Patients et méthodes.** Cent cinq consécutifs présentant un PSA supérieur à 4 ng/ml et /ou un toucher rectal (TR) pathologique ont bénéficié d’un EDP avant une série de biopsie. En plus des biopsies dirigées sur les zones suspectes à l’EDP, 10 à 12 biopsies ont été réalisées en sextant. Les résultats histopathologiques ont été corréls aux données de l’imagerie.

**Résultats.** Une anomalie caractérisée par une zone hypervasculaire (vaisseaux hypertrophés, irréguliers, sinueux ou désorientés) était présente à l’EDP chez 34 patients et correspondait à un cancer dans 28 cas. Dix-neuf cancers ne présentaient aucune anomalie à l’examen EDP. Une anomalie caractérisée par une zone hypervasculaire était présente à l’EDP chez 34 patients et correspondait à un cancer dans 28 cas. Dix-neuf cancers ne présentaient aucune anomalie à l’examen EDP.

**Conclusions.** L’EDP peut contribuer à l’évaluation de l’agressivité du cancer de la prostate et diriger les tirs biopsiques sur les foyers les plus agressifs.

Informed consent was obtained prior to Doppler US and biopsy. Antibiotic prophylaxis (Ciprofloxacin 500 mg) over 3 days was prescribed along with a rectal enema 1 hour prior to biopsy.

Power Doppler US and biopsies were performed in all patients in the left lateral decubitus. All examinations were performed using a Toshiba nemio (Toshiba medical systems, Japan) unit equipped with a multi-frequency end fire type rectal probe (4–7.5 MHz) set to detect slow flow. Doppler gain was set as high as possible without background noise (85%). The PRF was between 4 and 6 kHz. Filtration was set at maximum. First, morphological images were obtained of the prostate in the transverse plane from seminal vesicles to apex. Prostate volumetry using the ellipsoid method was calculated. Prostate lesions, essentially hypoechoic foci, were recorded.

Doppler evaluation was obtained from transverse images of the peripheral zone only. Areas of abnormal intraprostatic hypervascularity (irregular, tortuous or disorganized vessels) were detected within hypoechoic lesions using power Doppler. In patients with no hypoechoic lesion, the entire peripheral zone was interrogated at power Doppler to detect areas of focal or diffuse vascular asymmetry. Doppler was considered positive or negative based on the presence or absence of vascular abnormality. The unifocal or multifocal nature and location were recorded.

Prior to biopsy, periprostatic anesthesia was achieved by injecting 10 ml of Lidocaine 1% next to the neurovascular bundles. First, suspicious hypoechoic lesions and hypervascular foci were biopsied, followed by six sextant biopsies and 4 to 6 biopsies of the lateral peripheral zone (2 biopsies were obtained at the apex for glands over 50 g). Biopsies were performed using an automated 18G biopsy gun. Cores were fixed in formalin then sent to the pathology lab.

US findings were correlated to histology results and to prostatectomy specimens. Data were analyzed per patient and per sextant. Patients with at least one positive biopsy corresponding to a positive area on Doppler US were considered true positive (TP) and patients with negative Doppler US and biopsy were considered true negative (TN). Patients with positive biopsy without Doppler abnormality were considered false negative (FN) and patients with Doppler abnormality but negative biopsy were considered false positive (FP). Patients with FN and FP areas without TP area were considered unclassifiable (UNC).

Sensitivity, specificity, positive and negative predictive values for cancer diagnosis were determined, and the degree of significance was calculated with the chi 2 test (p<0.05).

Results

Mean patient age was 71 years (56 to 91 years), the median PSA level was 13 ng/ml (2.6 to 166 ng/ml) and the median prostate volume was 49 g (17 to 280 g). Post-biopsy follow-up was uneventful in all patients.

“Per patient” analysis

Forty-seven percent of prostate carcinomas (44%) were detected. From 105 patients, 34 showed lesions on power Doppler US (32%). Biopsy of the lesions was positive in 28 patients. The 6 false positive results corresponded to prostatitis with lymphoplasmacytic infiltration in 3 cases and prostatic adenomitis in 3 cases. A prostate with large central zone extending into the peripheral zone would explain the presence of central zone glandular tissue at the distal end of medial cores. From 47 patients with prostate carcinoma, 19 (40%) had a negative power Doppler US examination (fig. 1).

Standard biopsies detected 45 prostate cancers, whereas cancers were only detected on directed biopsies.

Sensitivity, specificity, PPV and NPV of power Doppler US are summarized in table I.

“Per sextant” analysis

From a total of 1093 biopsies, 271 were positive, corresponding to 184 sextants. Sextant per sextant analysis of Doppler US results showed that from a total of 630 sextants, 97 demonstrated an abnormality with associated cancer in 82 cases, and 533 demonstrated no abnormality including 431 without cancer. These results showed a sensitivity of 44% for power Doppler with specificity of 96%, PPV of 84% and NPV of 80%.

Gleason scores

Correlation between power Doppler findings and Gleason scores showed that 86% of hypervascular lesions on power Doppler had a Gleason score ≥7 compared to 26% of non-vascular malignant nodules. The presence of abnormal vessels was significantly correlated to the degree of cellular differentiation of the lesion (p<0.001).

All five patients with negative DRE and absence of lesions on Doppler US had a Gleason score 5–6. Only 4 (4%) of the 102 malignant foci not visible at power Doppler US showed extracapsular spread at biopsy compared to 19 (23%) of those visible on power Doppler US.

Discussion

Prostate cancer detection is based on DRE and yearly PSA screening. The increasing use of PSA screening over the last few years has resulted in a decrease in the mortality rate from prostate cancer (10). On the other hand, it would be responsible for the diagnosis of clinically insignificant prostate cancer, sometimes not detected on prostatectomy specimens. In addition, up to 15% of aggressive cancers with Gleason scores ≥7 would not be detectable by PSA (11).

Table I

Diagnostic accuracy of power Doppler US in the detection of prostate cancer, analysis per patient (Se: sensitivity, Spe: specificity, PPV: positive predictive value, NPV: negative predictive value).

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<td>28</td>
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<td>6</td>
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Fig. 1: Nodule in the left median sextant, hypoechoic with normal vessels. (PSA: 8.4 ng/ml, positive biopsies in the left median sextant, Gleason score: 6, no extracapsular extension).

Fig. 2: Hypoechoic hypervascular tumor.
A B mode US: hypoechoic nodule.
B Hypervascularity on the right on power Doppler US. (PSA: 16ng/ml, positive biopsies in the 3 right sextants, Gleason score: 9, extracapsular extension).
Prostate cancer is characterized by increased vascularity compared to normal prostate tissue due to neoangiogenesis and/or growth of vascular capacity of the existing parenchyma (12). It has been demonstrated that aggressive behavior and risk of metastasis were related to this increased density of capillaries (13, 14). A correlation between tumor vascularization and survival has also been reported by several groups (15, 16). This tumor neoangiogenesis explains the interest in dynamic gadolinium enhanced MRI for detection of the hypervascularity and its morphological and quantitative assessment. Cancer enhances earlier, more intensely and more rapidly with faster washout compared to normal peripheral zone tissue. This technique has improved the efficacy of MRI for diagnosis and expended its role in pre-treatment staging for tumor detection and volumetric assessment prior to biopsy (17). Tumor hypervascularity, the result of neoangiogenesis, may also be detected by power Doppler US, a technique that is less expensive and more readily available than MRI (fig. 2). Hypervascularity in regions of benign adenomatous change may be mistaken for cancer hypervascularity in the central zone, reducing the value of Doppler US in the evaluation of this zone (18). In all cases, additional anterior core biopsies are only obtained after initial negative peripheral zone biopsies, irrespective of findings on Doppler US. Our results demonstrate that Doppler US shows an excellent specificity and good PPV and NPV for the detection of tumors. Several groups have reported similar results (19-21).

A comparison of power Doppler US results and Gleason scores shows a strong correlation between aggressive behavior and vascularity. This relationship, previously described by Nelson (22) underscores the ability of power Doppler US to detect more aggressive tumors and better direct biopsies especially since prostate cancer frequently is multifocal.

Of the seven patients treated with radical prostatectomy, the correlation between power Doppler US findings and the histological specimen was excellent in 4 cases. Two patients, in addition to the primary tumor site, showed a tumor focus in the transition zone with Gleason score of 5 and 6 not identified on biopsies. The last patient had capsular extension of tumor not detected on biopsy and a small contralateral tumor focus with Gleason score of 8.

Conclusion

Due to its ability to detect the more aggressive foci of prostate tumor, power Doppler US improves directed biopsies, which may in turn improve patient management.

Conflict of interest

The authors disclose no conflict of interest.

References


