Diagnostic Value of CT in Detecting Peripheral Zone Prostate Cancer

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OBJECTIVE. The purpose of this study was to identify the sensitivity of contrast-enhanced CT in detecting high-grade prostate adenocarcinoma.

MATERIALS AND METHODS. A retrospective analysis included 100 patients with prostate cancer proven by biopsy between January 2010 and December 2017 who underwent staging CT of the abdomen and pelvis within 3 months of diagnosis. The control subjects were 100 randomly selected aged-matched male outpatients with no known history of malignancy who underwent contrast-enhanced CT of the abdomen and pelvis in the same time period as the patients with cancer. Two readers, blinded to both groups, independently assessed the likelihood of prostate cancer on the basis of the CT finding of focal abnormally increased peripheral enhancement in the prostate. Binary classification of sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) was used to assess the diagnostic utility of CT versus the reference standard of transrectal ultrasound–guided biopsy.

RESULTS. Eighty-three of 100 patients with biopsy-proven prostate cancer and 92 of 100 control subjects were correctly identified (sensitivity, 0.83; specificity, 0.92; PPV, 0.91; NPV, 0.84). There was no significant difference in diagnostic accuracy among subjects with different Gleason scores. Interrater agreement on both the cancer and control patients was 0.76 as assessed by Cohen kappa statistic.

CONCLUSION. Incidental detection of a focal area of increased enhancement in the periphery of the prostate at contrast-enhanced CT may represent a clinically significant cancer and deserves further workup with prostate-specific antigen measurement and correlation with clinical risk factors for prostate cancer.

Although many studies have shown the high sensitivity of multiparametric MRI (mpMRI) in detecting clinically significant prostate cancer [1, 2], contrast-enhanced CT (CECT) has been used mainly to look for nodal and distant metastases for disease staging. CT has had almost no role in prostate cancer detection or primary tumor staging [3]. On the basis of anecdotal observation at our institution, focal increased enhancement in the peripheral zone of the prostate is frequently seen during staging CT. We noticed that this area often correlates with the focus of cancer seen in mpMRI. Results of a few small studies have suggested high sensitivity of CECT in the detection of high-grade prostate cancer as abnormal focal enhancement in the prostate [4–6]. Jia et al. [5] found that this enhancement could be observed as early as 9 years before the diagnosis of prostate cancer. It seems that CT does offer some value in detecting prostate cancer in the peripheral zone, which is particularly useful when the cancer is an incidental finding in patients in whom prostate cancer is not suspected. The purpose of this study was to identify the sensitivity of CT in the detection of prostate cancer.

Materials and Methods
This retrospective study was approved by our institutional ethics review board. The requirement for written informed consent was waived in view of the retrospective nature of the study.

Study Population
From the electronic clinical database at our facility, we identified 159 consecutively registered patients with newly diagnosed prostate cancer between January 2010 and December 2017. The following inclusion criteria were applied to select the participants in the study population: prostate cancer diagnosed at our institution by means...
TABLE 1: Patient Demographics and Histopathologic Data (n = 100)

<table>
<thead>
<tr>
<th>Demographic Information and Biopsy Result</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (y) (^{a})</td>
<td>69 (49–90)</td>
</tr>
<tr>
<td>Prostate-specific antigen level at time of TRUS biopsy (ng/mL) (^{a})</td>
<td>18 (5.3–91)</td>
</tr>
<tr>
<td>Prevalence of Gleason scores in TRUS biopsy (^{b})</td>
<td></td>
</tr>
<tr>
<td>3 + 3</td>
<td>2 (2)</td>
</tr>
<tr>
<td>3 + 4</td>
<td>39 (39)</td>
</tr>
<tr>
<td>4 + 3</td>
<td>28 (28)</td>
</tr>
<tr>
<td>4 + 4</td>
<td>18 (18)</td>
</tr>
<tr>
<td>4 + 5</td>
<td>11 (11)</td>
</tr>
<tr>
<td>5 + 4</td>
<td>2 (2)</td>
</tr>
</tbody>
</table>

Note—TRUS = transrectal ultrasound.

\(^{a}\)Data are mean with range in parentheses.

\(^{b}\)Data are absolute count with percentage in parentheses.

of transrectal ultrasound--guided biopsy; biopsy finding of prostate cancer with Gleason score \(\geq 6\) \((3 + 3)\); staging CECT of the abdomen and pelvis within 3 months of the diagnosis of prostate cancer; and staging CT before any treatment of prostate cancer. The exclusion criteria were as follows: locally invasive prostate cancer or intraabdominal metastases, including lymphadenopathy, present at CT \((n = 9)\); severe prostatic hypertrophy causing severe thinning of the peripheral zone (prostatic volume cutoff, \(\geq 100\) mL) \((n = 7)\); substantial prostatic calcification \((n = 5)\) or hip arthroplasty \((n = 18)\) causing beam-hardening artifact severe enough to interfere with image interpretation, indwelling Foley catheter \((n = 7)\); and history of other malignancy \((n = 13)\). The final study population comprised 100 patients, whose characteristics are summarized in Table 1.

The control subjects were 100 randomly selected male patients without a history of prostate or other cancer who underwent outpatient CECT of the abdomen and pelvis between January 2010 and December 2017 at our institution. The following inclusion criteria were applied: age between the minimum and maximum ages of the study patients \((mean, 67\ years; range, 55–86\ years)\) and no known history of malignancy. The exclusion criteria were as follows: marked prostatic hypertrophy with prostate volume \(\geq 100\) mL, because it markedly thins and distorts the peripheral zone of the prostate, making it difficult to visualize let alone adequately assess; marked prostatic calcification or hip arthroplasty affecting image interpretation; and genitourinary problems, such as infection, surgery, or trauma as indicated on the CT requisition form, that might affect enhancement of the prostate.

**Imaging Analysis**

One fellowship-trained attending abdominal radiologist \((13\ years’ experience)\) and one radiology fellow \((6\ years’ experience)\) in abdominal imaging served as reader 1 and reader 2. Both readers were blinded to all clinical information and pathology results and independently reviewed the CT images of the randomized study subjects and control subjects. This review was performed 2 months after case selection and focused solely on the prostate. The images were reviewed predominately in the axial plane; coronal images were used occasionally in an adjunctive role. Image review was conducted with a narrow window setting to help highlight any focal enhancing areas from the background prostate parenchyma.

In the venous phase of CT, the peripheral zone of the prostate should have homogeneously low attenuation compared with the central gland, owing to higher water content, which also causes T2 hyperintensity on MR images (Fig. 1). Each reader was asked whether one or more areas of abnormal focal enhancement, irrespective of the size and morphologic features of the area or lesion, could be subjectively identified in the peripheral zone of the prostate, which could potentially suggest the presence of cancer. In cases of discrepancies, consensus opinion was recorded for analysis. Quantitative assessment was performed by measuring the attenuation in Hounsfield units of the focal lesions and the normal hyperdense adjacent peripheral zone of the prostate. The mean attenuation difference between the focal lesions and normal prostatic parenchyma was calculated. No attempt was made to compare the CT findings with prostate MRI findings because the purpose of the study was to determine whether it is possible to prospectively detect or suspect clinically significant prostate cancer by use of CECT alone.

**Statistical Analysis**

The Cohen kappa statistic was used to assess agreement between the two raters on CT findings in both patients with cancer and matched control subjects. Under the null hypothesis, it was expected that the reviewers would classify one-half of CT findings correctly. Using a null hypothesis that the probability of detecting prostate cancer is 0.5, exact binomial probabilities were calculated to determine the probability of observing the outcome or a more extreme outcome. Binary classification of sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) was used to assess the diagnostic utility of CT versus the reference standard of transrectal ultrasound--guided biopsy.

**Results**

We correctly identified 83% \((83/100)\) of patients with biopsy–proven prostate cancer and 92% \((92/100)\) of the control subjects who did not have known prostate cancer \((sensitivity, 0.83; specificity, 0.92; PPV, 0.91; NPV, 0.84)\). The accuracy was 0.875 \((95\% CI, 0.821–0.917; p < 0.0001)\). Both binomial tests had \(p\) values less than 10\(^{-10}\). Between the two readers, the kappa coefficient was 0.76 and the McNemar test \(p\) value, 0.11. Examples of focal enhancement of the prostate are shown in Figure 2. There was no significant difference in the detection of focal enhancement (presumed cancer) among Gleason score...
categories (Table 2). Examples of focal enhancement of cancers with different Gleason scores are shown in Figure 3.

We found that the mean CT attenuation of focal enhancing lesions was 80 HU (range, 60–138 HU) and that of the normal adjacent peripheral zone was 40 HU (range, 17–56 HU). The mean attenuation difference between the focal lesion and the normal parenchyma was 40 HU (range, 23–100 HU).

Seventeen percent (17/100) of biopsy-proven prostate cancers were not detected during imaging analysis. Among these false-negative cases, we found that 53% of patients (9 of 17) had bilateral and multifocal disease as opposed to 29% (24 of 83) in the group with true-positive group findings.

Eight of 100 (8%) control subjects had positive scores for abnormal enhancement. Among these eight subjects, three had normal PSA levels within 6 months of CT; two had clinically documented urinary tract infection within 1 month before CT (but not indicated on the CT requisition forms) (Fig. 4); one had a PSA level of 9.6 ng/mL (documented 3 months after CT) but no urologic assessment at that point; and two had no PSA levels available in the electronic medical record within 2 years before or after the CT.

Discussion

Prostate cancer will be diagnosed in approximately 11.2% of men at some point during their lifetime, according to the Surveillance, Epidemiology, and End Results database [7]. Digital rectal examination, PSA level with associated parameters (e.g., free PSA), mpMRI, and transrectal ultrasound–guided biopsy are the main diagnostic tools for the evaluation of prostate cancer [3, 8, 9]. CT is considered lacking in sensitivity and specificity for the detection of localized prostate cancer owing to its poor soft-tissue contrast [3, 10].

The clinical behavior of prostate cancer ranges from indolent to highly aggressive with high morbidity and mortality. Tumors with Gleason score ≥ 7, tumor volume > 0.5 cm³, or extraprostatic extension are considered clinically significant and warrant therapy [11]. Approximately 70% of prostate cancers arise from the peripheral zone of the prostate because the peripheral zone contains most of the prostatic glandular tissue [12]. As a result, random transrectal ultrasound–guided biopsy of the prostate usually focuses on the peripheral zone.

Normal peripheral zone of the prostate has homogeneously low attenuation on CECT. Given that peripheral zone prostate cancer exhibits increased enhancement on contrast-enhanced mpMR images, it is expected that the area containing the tumor would also have abnormally increased enhancement on CT [13]. The value of CT in the detection of prostate cancer has been studied by other groups with varied methods. Prando and Wallace [6] performed a small retrospective study that included 25 patients with proven prostate cancer and found that CT revealed cancer in 22 (88%) patients. Glazer et al. [4] asked 10 blinded radiologists to assess patients with higher-grade prostate cancer (≥ Gleason 4 + 3), lower-grade prostate cancer (≥ Gleason 3 + 4), or no prostate cancer on CT images. They found that focal enhancement in the peripheral zone on routine venous phase CT images was specific and predictive of higher-grade (≥ Gleason 4 + 3) prostate cancer. Jia et al. [5] compared CT, mpMRI, and pathology findings of 27 patients with prostate cancer and found high concordance between abnormalities detected with CT and MRI.

Our results show that venous phase CECT has sensitivity, specificity, PPV, and NPV of 83%, 92%, 91%, and 84%, respectively, for detecting high-grade prostate cancer, and, rather significantly, these results are concordant with those in the aforementioned studies. The detection rates of prostate cancer for the two readers were similar irrespective of the severity of prostate cancer, that is, Gleason score. This finding is concordant with that of Rosenkrantz et al. [14], who found no
association between prostate cancer detection with contrast-enhanced MRI and tumor grade. Our finding, however, contrasts to the findings of Glazer et al. [4], who found that CT had higher specificity for detecting Gleason 4 + 3 and greater cancers than for detecting Gleason 3 + 4 and lower cancers. Two factors might have contributed to the discrepancy between the two studies. First, the random nature of prostate biopsy may have missed the highest Gleason grade cancer in the prostate. Second, the high prevalence of prostate cancer occurring synchronously in multiple locations in the gland might have decreased our ability to detect a single focus of abnormal enhancement in these situations.

Our interrater agreement was high with a kappa coefficient of 0.76. This suggests that a general radiologist should easily recognize focal abnormal enhancement in the prostate. This should minimize the number of false-positive interpretations in prospective readings, thereby avoiding unnecessary workup and patient anxiety.

With regard to our false-negative rate of 17%, because this group had considerably more bilateral and multifocal disease, we speculate that multifocality and bilaterality could make it more difficult to detect an abnormality than would unilateral or unifocal disease.

Eight (8%) control subjects had positive scores for abnormal focal enhancement. Two patients had urinary tract infections within 1 month before CT, which might have caused prostatitis and, therefore, abnormal enhancement in the prostate. For the other six control patients, the positive score might have been due to interpretation error, undiagnosed prostatitis, or prostate carcinoma.

There were limitations in our study. First, the population had a high prevalence of prostate cancer in that 100 of 200 (50%) patients in the population had confirmed prostate cancer. It is likely that in a general population the PPV and NPV would decrease owing to a lower prevalence of prostate cancer. Second, because we excluded patients with clinically significant prostatic hypertrophy, prostate calcifications, and hip arthroplasty, our findings cannot be applied to these patient populations.

**Conclusion**

Because prostate cancer is a common condition and because an increasing number of people are undergoing CT in their lifetime, incidental detection of a focal area of increased enhancement in the periphery of the prostate at CECT, although by no means diagnostic, may represent a clinically significant cancer and deserves further workup with PSA measurement and correlation with clinical risk factors for prostate cancer.

**References**


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