# The Clinical Value of Diffusion-Weighted Imaging in Combination With T2-Weighted Imaging in Diagnosing Prostate Carcinoma: A Systematic Review and Meta-Analysis

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**OBJECTIVE.** We aimed to explore the role of diffusion-weighted imaging (DWI) in combination with T2-weighted imaging (T2WI) in detecting prostate carcinoma through a systematic review and meta-analysis.

**MATERIALS AND METHODS.** The MEDLINE, EMBASE, Cancerlit, and Cochrane Library databases were searched for studies published from January 2001 to July 2011 evaluating the diagnostic performance of T2WI combined with DWI in detecting prostate carcinoma. We determined sensitivities and specificities across studies, calculated positive and negative likelihood ratios, and constructed summary receiver operating characteristic curves. We also compared the performance of T2WI combined with DWI with T2WI alone by analyzing studies that had also used these diagnostic methods on the same patients.

**RESULTS.** Across 10 studies (627 patients), the pooled sensitivity of T2WI combined with DWI was 0.76 (95% CI, 0.65–0.84), and the pooled specificity was 0.82 (95% CI, 0.77–0.87). Overall, the positive likelihood ratio was 4.31 (95% CI, 3.12–5.92), and the negative likelihood ratio was 0.29 (95% CI, 0.20–0.43). In seven studies in which T2WI combined with DWI and T2WI alone were performed, the sensitivity and specificity of T2WI combined with DWI were 0.72 (95% CI, 0.67–0.82) and 0.81 (95% CI, 0.76–0.86), respectively, and the sensitivity and specificity of T2WI alone were 0.62 (95% CI, 0.55–0.68) and 0.77 (95% CI, 0.71–0.82), respectively.

**CONCLUSION.** T2WI combined with DWI may be a valuable tool for detecting prostate cancer in the overall evaluation of prostate cancer, compared with T2WI alone. High-quality prospective studies of T2WI combined with DWI to detect prostate carcinoma still need to be conducted.

**Keywords:** diffusion-weighted imaging, meta-analysis, prostate carcinoma, systematic review, T2-weighted imaging

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Prostate cancer is a leading cause of morbidity and mortality among men in the United States [1]. At present, serum prostate-specific antigen (PSA) levels and digital rectal examination are the mainstays of clinical detection of prostate cancer. Abnormal findings are followed up by transrectal ultrasound–guided biopsy. MRI provides incremental value to biopsy and digital rectal examination for prostate cancer localization [2]. It can aid in many aspects of prostate cancer management, from initial detection to treatment planning and follow-up. The sensitivity and specificity of T2-weighted imaging (T2WI) for prostate cancer vary widely, because of differences in imaging techniques, reference standards, criteria for defining disease involvement on MRI, and interobserver variability [3]. Functional imaging techniques are being developed to complement conventional MRI in the detection and staging of prostate cancer. In particular, diffusion-weighted imaging (DWI) is an unenhanced technique that can be easily acquired and processed and that increases the accuracy for tumor localization compared with the use of T2WI alone [4].

Recent studies have reported that DWI combined with T2WI has improved diagnostic performance over T2WI alone. However, the diagnostic performances that were evaluated in these prior studies varied depending on many factors, such as the field strength of the MRI scanner, the b value used, and the reference standard that was used in each study. Signal-to-noise ratio will also affect detectability, particularly with a low signal-to-noise ratio technique such as DWI. Moreover, disease stage, lesion size, and presence of hemorrhage from previous biopsy may influence the diagnostic performance as well.

Because a large number of studies exploring the role of T2WI combined with DWI in detecting prostate carcinoma have been pub-

lished, a comprehensive systematic review would be useful to synthesize the currently available bulk of information. The objective of this review was to assess the overall diagnostic value of T2WI combined with DWI in detecting prostate carcinoma with a meta-analysis, which, to our knowledge, had not previously been published.

## Materials and Methods

### *Search Strategy*

We performed a comprehensive computer literature search to identify articles about the diagnostic performance of T2WI combined with DWI in detecting prostate carcinoma. The MEDLINE and EMBASE databases were searched for articles published from January 2001 to July 2011 with the following terms or MeSH subject headings: "diffusion magnetic resonance" or "diffusion-weighted magnetic resonance images" or "DW-MRI" or "DW magnetic resonance images" and "T2-weighted imaging" and "prostate" or "prostate" and "carcinoma" or "carcinoma." Other databases, such as Cancerlit and Cochrane Library, were also searched for relevant articles from the same period. Reference lists of included studies and review articles were manually searched.

### *Studies Selection*

Two investigators, who were blinded to the journal, author, institution, and date of publication, independently checked retrieved articles. According to a standardized data extraction form, we read all the abstracts to get the potentially eligible articles and then we retrieved the full text of these articles to determine whether they were exactly eligible.

The inclusion criteria were as follows: first, articles had to be published in English. Second, T2WI combined with DWI had to be used to evaluate prostate carcinoma. Third, for sextant basis statistics, sufficient data had to be presented to calculate the true-positive, false-negative, false-positive, and true-negative values. Fourth, 10 or more patients had to be included. Fifth, to ensure the quality of study design, only the article of which the number of the answer "yes" for the 14 questions in Quality Assessment of Diagnostic Accuracy Studies quality assessment tool [5] was more than nine was included. Finally, when data or subsets of data were presented in more than one article, the article with most details or the most recent article was chosen. The authors of abstracts and studies not reporting with sufficient data were contacted to request additional information.

### *Data Extraction and Quality Assessment*

The same two investigators who performed the database searches also performed the relevant data extraction independently. To resolve disagreement between reviewers, a third reviewer assessed all discrepant items, and the majority opinion was used for analysis. Relevant studies were further examined with Quality Assessment of Diagnostic Accuracy Studies criteria again. To perform accuracy analyses, we extracted data on characteristics of studies and patients, measurements performed, and results. For each report, we extracted the following items: author, journal, year of publication, country of origin, sample size, description of study population (age), study design (prospective, retrospective, or unknown), patient enrollment (consecutive or not), inclusion and exclusion criteria, reasons for exclusions from the analysis, and number of experts who assessed and interpreted the results of MRI. We also recorded whether there was any mention of blinding of MRI measurements to the histopathologic and clinical results or to other diagnostic methods used (e.g., PSA). For each study, we recorded the number of true-positive, false-positive, true-negative, and false-negative findings for T2WI combined with DWI in diagnosing prostate cancer.

### *Data Synthesis and Analysis*

Data on the diagnostic performance of T2WI combined with DWI were combined quantitatively across eligible studies. Data were used to construct 2 × 2 contingency tables, with true-positive, true-negative, false-positive, and false-negative results. We computed sensitivity and specificity. Pooled sensitivity and specificity with 95% CIs were obtained. A value of 0.5 was added to all cells of studies that contained a count of zero to avoid potential problems in odds calculations for studies with sensitivities or specificities of 100%. Positive and negative likelihood ratios (LRs) were derived as functions of these summary estimates. We also used the derived estimates of sensitivity, specificity, and respective variances to construct a summary receiver operating characteristic (ROC) curve. The area under the ROC curve was used as an alternative global measure of test performance [6–8].

Heterogeneity was assessed by using the LR chi-square test and the $I^2$ index. The $I^2$ index is a measure of the percentage of total variation across all studies resulting from heterogeneity beyond chance. A value over 50% indicates heterogeneity [9]. For the LR chi-square test, $p$ less than 0.05 was considered as having apparent heterogeneity. If heterogeneity existed, a random-effect model was used for the primary meta-analysis to obtain a summary estimate for sensitivity with 95% CIs. The threshold effect was one important extra source of variation in meta-analysis. If the threshold effect exists, an inverse correlation appears; combining study results in these cases involves fitting an ROC curve, which is better than pooling sensitivities and specificities. To judge whether the threshold effect existed, we plotted the sensitivity and specificity for T2WI combined with DWI on an ROC plane. Moreover, we also calculated the Spearman correlation coefficient (between the logit of sensitivity and logit of specificity) for T2WI combined with DWI. If no threshold effect existed in the meta-analysis, metaregression analysis was then performed to explore other sources of heterogeneity in the studies for T2WI combined with DWI. We applied single-factor metaregression analysis by adding study design (prospective or retrospective), patient enrollment (consecutive or not), whether the MRI reviewer was blinded to other test results and clinical data, b value (b ≥ or < 1000 s/mm$^2$), image analysis used (native DWI or apparent diffusion coefficient [ADC] map), and coil used (pelvic phased-array coil or combination of an endorectal coil and a phased-array coil).

Subgroup analyses were also performed according to patient enrollment type (consecutive vs nonconsecutive or not reported), blinding (yes vs no or not reported), study design (prospective vs retrospective), b value (b ≥ vs b < 1000 s/mm$^2$), image analysis (native DWI vs ADC map), and coil (pelvic phased-array coil vs combination of an endorectal coil and a phased-array coil). Publication bias was assessed visually by using Deeks funnel plot asymmetry test, which is a scatterplot of the inverse of the square root of the effective sample size ($1 / ESS^{1/2}$) versus the diagnostic log odds ratio.

All the statistical computations were performed using Stata/SE software (version 11.1, StataCorp) and Meta-DiSc (version 1.4, Javier Zamora), which is freeware used to perform systematic reviews of studies of evaluation of diagnostic and screening tests. $p$ values less than 0.05 were considered to be statistically significant.

## Results

### *Literature Search and Selection of Studies*

After the comprehensive computerized search was performed and reference lists were extensively cross-checked, our search yielded 162 primary studies, of which 147 were excluded after reviewing the title and abstract. Seven articles were excluded after reviewing the full article for the following reasons: first, the aim of the articles was not to reveal the diagnostic value of T2WI combined with DWI for identification and characterization of prostate cancer [10]. Second, the researchers in the articles did not have enough data that could be used to construct or calculate true-positive, false-positive, true-negative, and false-negative results [11]. Third, the study was not published in English [12]. Fourth, results presented in the article were from a combination of

**TABLE 1: Principal Characteristics of Eligible Studies**

| Study | Year | No. of Patients | Design | Patient Age (y), Mean (Range) | Patient Enrollment | Coil | Use of Native DWI Alone Versus Use of Either ADC Map Alone or Both Native DWI and ADC Map | b Value (s/mm²) | Reviews | Blind | Magnet Field Strength (T) | PSA Level (ng/mL), Mean (Range) | Interval Between MRI and Radical Prostatectomy |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Yağci et al. [17] | 2011 | 43 | Prospective | 66 (49–79) | Consecutive | Integrated coil | ADC map | 800 | 1 | Blind | 1.5 | 9.1 (1.4–120) | 7 days |
| Rosenkrantz et al. [18] | 2011 | 42 | Retrospective | 62 (47–76) | Consecutive | Pelvic phased-array coil | Native DWI | 1000 | 2 | Blind | 1.5 | 6.2 (1.3–32.5) | 19 (1–39) days |
| Katahira et al. [19] | 2011 | 201 | Retrospective | 70 (43–79) | Consecutive | Pelvic phased-array coil | Native DWI | 1000 | 3 | Not | 1.5 | 8.6 (2.61–114) | Within 2 months |
| Kitajima et al. [20] | 2010 | 53 | Retrospective | 69 (56–84) | Consecutive | Pelvic phased-array coil | Both native DWI and ADC maps | 1000 | 2 | Blind | 3 | 11.1 (4.2–112.1) | 22 (10–41) days |
| Kajihara et al. [21] | 2009 | 23 | Retrospective | 68 (29–78) | Not documented | Pelvic phased-array coil | Native DWI | 2000 | 6 | Blind | 1.5 | 12.6 (4.0–28.1) | Within 3 weeks |
| Lim et al. [22] | 2009 | 52 | Retrospective | 65 (48–76) | Not documented | Combination of an endorectal coil and a phased-array coil | ADC map | 1000 | 3 | Blind | 1.5 | 10.5 (1.2–79.6) | 11 (2–38) days |
| Yoshimitsu et al. [23] | 2008 | 37 | Retrospective | 66 (56–75) | Not documented | Pelvic phased-array coil | ADC map | 1000 | 2 | Not documented | 1.5 | 11.9 (0.7–54.8) | 2.5 weeks |
| Haider et al. [24] | 2007 | 49 | Prospective | 61 (46–75) | Not documented | Combination of an endorectal coil and a phased-array coil | ADC map | 600 | 1 | Blind | 1.5 | 5.375 (0.9–26) | 15 (2–77) days |
| Tanimoto et al. [25] | 2007 | 83 | Prospective | 67 (53–87) | Consecutive | Pelvic phased-array coil | ADC maps | 1000 | 2 | Not documented | 1.5 | 19.4 (4.3–332.1) | Within 4 months |
| Morgan et al. [26] | 2007 | 44 | Prospective | 68 (52–80) | Consecutive | Endorectal coil | ADC map | 800 | 2 | Blind | 1.5 | 9.8 (6.95–14.6) | 15 (1–90) days |

Note—ADC = apparent diffusion coefficient, DWI = diffusion-weighted imaging, PSA = prostate-specific antigen.

many diagnostic methods to detect prostate cancer that could not be differentiated for assessment of single test [13, 14]. Fifth, the data were not based on sextant basis analysis [15]. Finally, there was one article for which we only had the abstract [16]. Thus, a total of 10 studies [17–26] with 627 patients, who fulfilled all of the inclusion criteria, were considered for the analysis (Table 1). The detailed procedure of study selection in the meta-analysis is shown in Figure 1.

### *Study Description, Study Quality, and Publication Bias*

We conducted all analyses on the basis of sextant basis data analysis. There were a total of 627 patients in the included studies, and their ages ranged from 29 to 87 years. The median number of participants per study was 63 (range, 23–201 participants). The average PSA level was 10.46 ng/mL (range, 0.7–332.1 ng/mL). The median PSA level was 10.15 ng/mL. Of all 10 studies, six studies [18–23] enrolled patients retrospectively; four studies [17, 24–26] enrolled patients prospectively. Six studies [17–20, 25, 26] enrolled patients in a consecutive manner; the others [21–24] were not enrolled in a consecutive manner, or the manner of enrollment was unknown. There were seven studies [17, 18, 20–22, 24, 26] in which the MRI reviewer was blinded to other test results and clinical data. Six studies [18–21, 23, 25] used pelvic phased-array coils, whereas three studies [17, 22, 24] used an endorectal coil and a phased-array coil combined, and one study used an endorectal coil only [26]. There were three studies [18, 19, 21] in which images were analyzed by native DWI, six studies [17, 22–26] were interpreted by ADC map, and the other one [20] was interpreted by both native DWI and ADC map. Table 1 shows the principal characteristics of the 10 studies included in the meta-analysis. The nonsignificant slope of Deeks funnel plot asymmetry tests indicated that no significant bias was found ($p = 0.90$).

### *Diagnostic Accuracy of T2WI Combined With DWI*

The pooled sensitivity for T2WI combined with DWI was 0.76 (95% CI, 0.65–0.84), and the pooled specificity was 0.82 (95% CI, 0.77–0.87). Using the fitted summary ROC curve, the overall area under the ROC curve was 0.84 (95% CI, 0.80–0.87), indicating good diagnostic accuracy [27]. Results for sensitivity in individual studies ranged from 45% to 100%. The highest sensitivity (100%) occurred in an individual study [21]. Results for specificity ranged from 64% to 94%. The highest specificity (94%) occurred in an individual study [20]. LR syntheses gave an overall positive LR of 4.31 (95% CI, 3.12–5.92) and negative LR

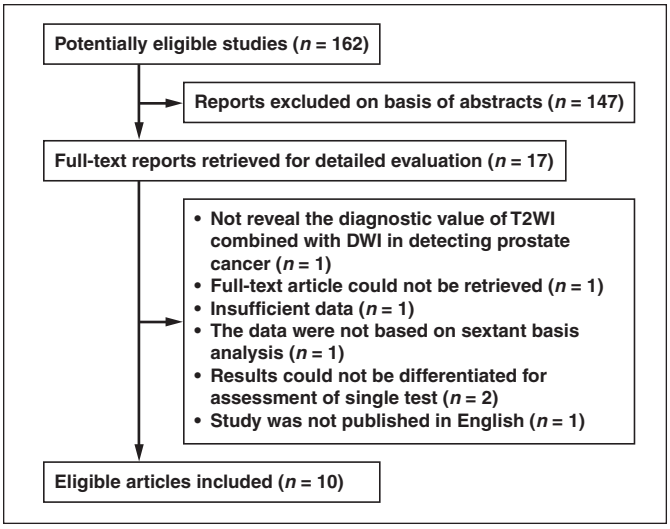


**Fig. 1**—Flowchart for reports included in meta-analysis. DWI = diffusion-weighted imaging, T2WI = T2-weighted imaging.

of 0.29 (95% CI, 0.20–0.43). Forest plots of the sensitivity and specificity of T2WI combined with DWI in the detection of prostate carcinoma cancer are shown in Figure 2.

### *Heterogeneity Assessing and Metaregression Analysis*

The heterogeneity in sensitivity and specificity tests was highly significant ($p < 0.05$; $I^2 > 50\%$). It was confirmed that there was strong evidence of between-study heterogeneity (Fig. 2).

We plotted the sensitivity and specificity for T2WI combined with DWI on an ROC plane and found that it did not show a curvilinear pattern. A summary ROC curve is shown in Figure 3. The Spearman correlation coefficient (between the logit of sensitivity and logit of specificity) for T2WI combined with DWI was 0.32 ($p = 0.23$). These two results show that no threshold effect existed in this meta-analysis. Metaregression analysis showed that patient enrollment and MRI reviewer blinding to other test results and clinical data were the most important variable sources of heterogeneity for sensitivity and specificity, respectively ($p < 0.01$) (Table 2).

### *Subgroup Analysis and Comparison Against Other Diagnostic Methods*

The results of subgroup analysis are presented in Table 2. Nonconsecutive or unknown

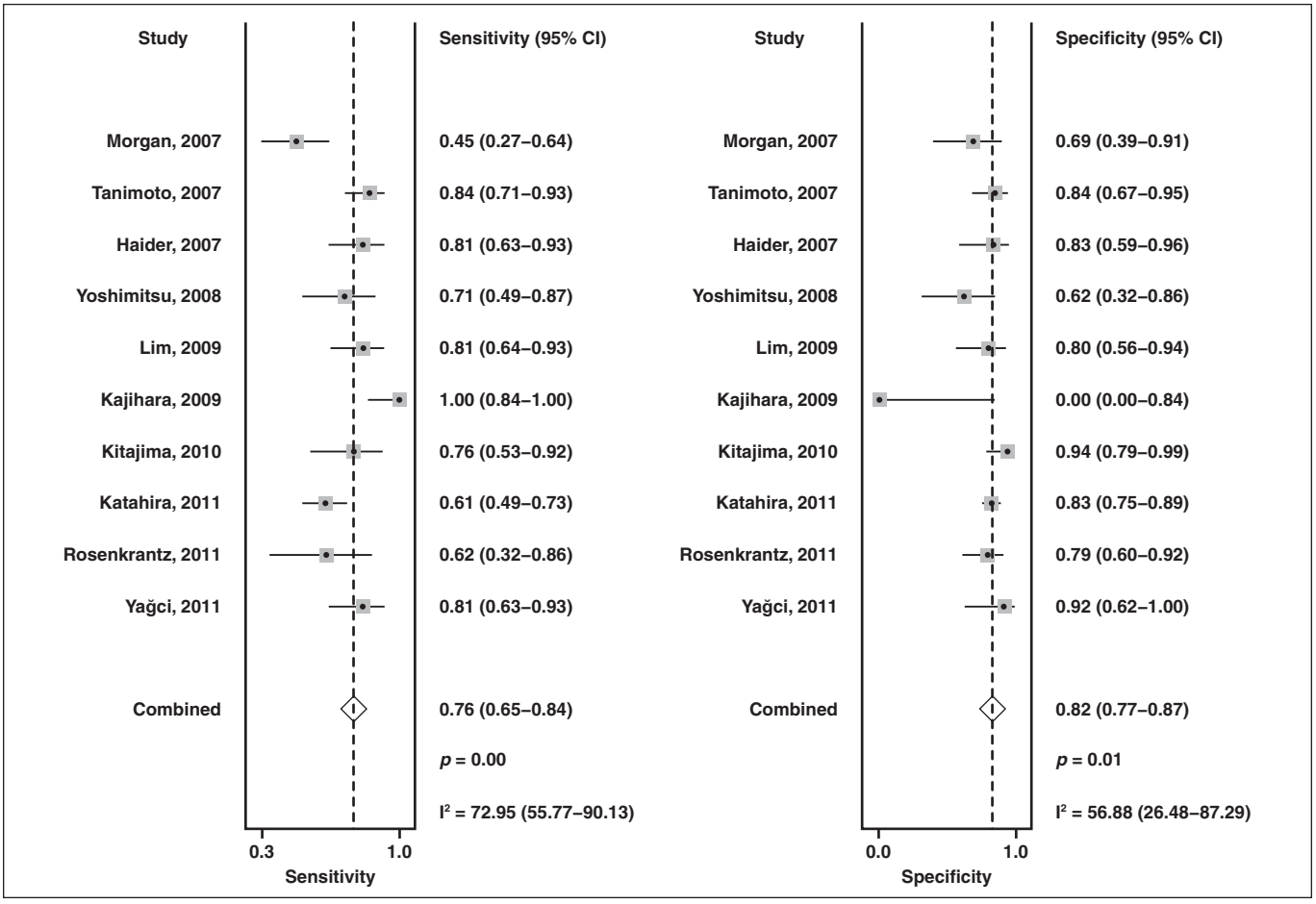


**Fig. 2**—Forest plot of pooled sensitivity and specificity of T2-weighted imaging (T2WI) combined with diffusion-weighted imaging (DWI) in detecting prostate carcinoma. Summary sensitivity and specificity of T2WI combined with DWI were 0.76 (95% CI, 0.65–0.84) and 0.82 (95% CI, 0.77–0.87), respectively. $I^2$ index is measure of percentage of total variation across all studies due to heterogeneity beyond chance. $I^2$ value greater than 50% indicates heterogeneity.

patient enrollment yielded the highest results for sensitivity (0.78; 95% CI, 0.68–0.86). Blinded and consecutively designed studies had the highest specificity among the studies (0.84 [95% CI, 0.76–0.90] and 0.84 [95% CI 0.79–0.88], respectively).

The comparison of T2WI combined with DWI with T2WI alone is shown in Table 3. The sensitivity and specificity of T2WI combined with DWI were 0.72 (95% CI, 0.67–0.82) and 0.81 (95% CI, 0.76–0.86), respectively, and the sensitivity and specificity of T2WI alone were 0.62 (95% CI, 0.55–0.68) and 0.77 (95% CI, 0.71–0.82), respectively. Positive and negative LRs of T2WI combined with DWI were 3.30 (95% CI, 2.23–4.89) and 0.34 (95% CI, 0.22–0.52), respectively, and those of T2WI alone were 2.27 (95% CI, 1.60–3.23) and 0.54 (95% CI, 0.46–0.65), respectively.

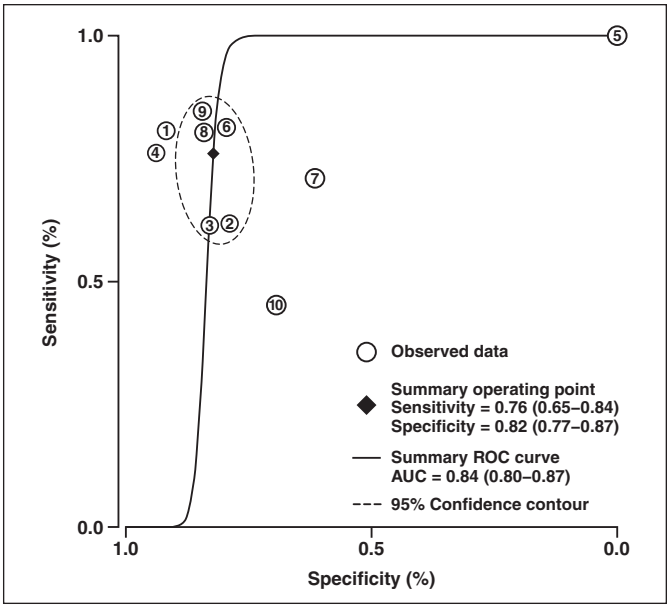


**Fig. 3**—Summary receiver operating characteristic (ROC) curves of T2-weighted imaging combined with diffusion-weighted imaging in detection of prostate carcinoma for 10 included studies. Numbers in parentheses are 95% CIs. AUC = area under ROC curve.

## Discussion

Accurate tumor detection and estimation of tumor extent in prostate cancer is essential to facilitate focal treatment planning [28–32]. Conventional MRI, which is typically performed using T2WI, has established that prostate cancer is characterized by low T2 signal intensity replacing the normally high T2 signal intensity in the peripheral zone [33]. However, the presence of decreased T2 signal intensity in the peripheral zone is of limited sensitivity, because some prostate tumors are isointense. This finding is also of limited specificity, because there are other possible causes of low T2 signal intensity in the peripheral zone, including hemorrhage, scarring, prostatitis, atrophy, cryosurgery, hormonal therapy, and effects of radiation therapy.

**TABLE 2: Diagnostic Accuracy of T2-Weighted Imaging Combined With Diffusion-Weighted Imaging (DWI) in Detecting Prostate Cancer**

| Study Characteristics | References | Summary Sensitivity (95% CI) | *p* | Summary Specificity (95% CI) | *p* | Positive LR (95% CI) | Negative LR (95% CI) |
|---|---|---|---|---|---|---|---|
| Total | [17–26] | 0.76 (0.65–0.84) | 0.00 | 0.82 (0.77–0.87) | 0.01 | 4.31 (3.12–5.92) | 0.29 (0.20–0.43) |
| Design | | | 0.23 | | 0.02 | | |
| Prospective | [17, 24–26] | 0.74 (0.66–0.81) | | 0.83 (0.78–0.90) | | 3.85 (1.75–8.48) | 0.30 (0.13–0.67) |
| Retrospective | [18–23] | 0.69 (0.61–0.76) | | 0.82 (0.77–0.87) | | 3.41 (2.20–5.29) | 0.40 (0.30–0.53) |
| Patient enrollment | | | 0.00 | | 0.30 | | |
| Consecutive | [17–20, 24–26] | 0.69 (0.62–0.75) | | 0.84 (0.79–0.88) | | 3.85 (2.33–6.36) | 0.37 (0.23–0.58) |
| Nonconsecutive and unclear | [21–24] | 0.78 (0.68–0.86) | | 0.77 (0.63–0.87) | | 3.07 (1.62–5.81) | 0.30 (0.19–0.47) |
| Blinding | | | 0.52 | | 0.00 | | |
| Blind | [17, 18, 20–22, 24, 26] | 0.72 (0.64–0.79) | | 0.84 (0.76–0.90) | | 3.92 (2.17–7.10) | 0.34 (0.20–0.56) |
| Nonblind or unclear | [19, 23, 25] | 0.71 (0.66–0.81) | | 0.81 (0.75–0.87) | | 3.28 (1.93–5.56) | 0.36 (0.20–0.64) |
| b value (s/mm$^2$) | | | 0.72 | | 0.08 | | |
| ≥ 1000 | [17, 24, 26] | 0.73 (0.66–0.79) | | 0.83 (0.78–0.87) | | 3.66 (2.46–5.42) | 0.34 (0.24–0.49) |
| < 1000 | [18–23, 25] | 0.69 (0.58–0.78) | | 0.81 (0.67–0.92) | | 3.46 (1.11–10.75) | 0.35 (0.13–0.92) |
| Native DWI or ADC map used | | | 0.28 | | 0.09 | | |
| Native DWI | [18, 19, 21] | 0.71 (0.63–0.78) | | 0.82 (0.76–0.88) | | 3.43 (2.37–5.00) | 0.47 (0.35–0.63) |
| ADC map | [17, 22–26] | 0.75 (0.68–0.81) | | 0.80 (0.71–0.87) | | 3.28 (1.91–5.65) | 0.31 (0.18–0.55) |
| Coil | | | 0.45 | | 0.06 | | |
| Pelvic phased-array coil | [18–21, 23, 25] | 0.74 (0.64–0.78) | | 0.83 (0.78–0.88) | | 3.64 (2.27–5.86) | 0.36 (0.24–0.53) |
| Combination of an endorectal coil and a phased-array coil | [17, 22, 24] | 0.77 (0.69–0.90) | | 0.84 (0.71–0.93) | | 4.79 (2.53–9.08) | 0.23 (0.15–0.35) |

Note— LR = likelihood ratio , ADC = apparent diffusion coefficient,.

**TABLE 3: Comparison of Diagnostic Accuracy of T2-Weighted Imaging (T2WI) Combined With Diffusion-Weighted Imaging (DWI) With T2WI Alone for Selected Studies [17, 19, 22–26]**

| Diagnostic Methods Compared | Summary Sensitivity (95% CI) | Summary Specificity (95% CI) | Positive LR (95% CI) | Negative LR (95% CI) |
|---|---|---|---|---|
| T2WI alone | 0.62 (0.55–0.68) | 0.77 (0.71–0.82) | 2.27 (1.60–3.23) | 0.54 (0.46–0.65) |
| T2WI combined with DWI | 0.72 (0.67–0.82) | 0.81 (0.76–0.86) | 3.30 (2.23–4.89) | 0.34 (0.22–0.52) |

Note—LR = likelihood ratio.



DWI can add valuable information about tissue at the cellular level to the information from conventional T1-weighted imaging and T2WI [34]. Furthermore, reduced diffusion of water in prostate cancer has been attributed to the increased cellularity of malignant lesions, with reduction of the extracellular space and restriction of the motion of a larger portion of water molecules to the intracellular space. Therefore, DWI provides an important quantitative biophysical parameter that can be used to differentiate benign from malignant prostate tissue [35].

Recent studies [22, 36, 37] have found that DWI and ADC mapping can increase the sensitivity (54–98%) and specificity (58–100%) of MRI in detecting prostate cancer when DWI is used in conjunction with T2WI. In this meta-analysis, we explored the ability of T2WI combined with DWI to detect prostate cancer, which included data from 627 patients. Here, we have shown that T2WI combined with DWI has high specificity (82%) and relatively lower sensitivity (76%) in detecting prostate cancer. Our results, together with those of previous reports, show that T2WI combined with DWI is a potentially accurate method of detecting prostate cancer.

In the subgroup analysis, we found that DWI using a b value of more than 1000 s/mm$^2$ in the detection of prostate cancer had high pooled sensitivity and specificity. The b value reflects the strength of the diffusion-sensitizing gradients. Correctly assigning the b value for DWI is critical, because it directly affects the ability to detect water molecule diffusion. At a high b value, DWI represents the molecular diffusion of water almost exclusively. In this meta-analysis, most of the included studies used b values of 1000 s/mm$^2$ [18–23, 25]. Higher b values may provide better characterization of prostate cancer and treatment response in experimental mouse models [38]. Qayyum [39] has suggested the use of b values higher than 1000 s/mm$^2$ because of the inherently high T2 signal of the prostate gland. On the other hand, Kitajima et al. [40] performed a comparison of the native DWI maps and found that increasing b values from 1000 to 2000 s/mm$^2$ did not confer an additional benefit for lesion detection. Kim et al. [41] performed comparisons of the ADC maps and reported that DWI at 3 T using a b value of 1000 s/mm$^2$ was more sensitive and more accurate in localizing prostate cancer than DWI performed using a b value of 2000 s/mm$^2$. However, Fütterer et al. [42] found that the optimal b value was determined by considering the ADC value of the prostate tissue. In a diffusion experiment, the optimal b value for any tissue should be such that the b value multiplied by the ADC is equal to 1. The ADC of interest in their study was $1.220 \times 10^{-3}$ mm$^2$/s for the central zone and $1.610 \times 10^{-3}$ mm$^2$/s for the peripheral zone. The average ADC is $1.415 \times 10^{-3}$ mm$^2$/s. The optimal b value is calculated as follows: $1 / (1.415 \times 10^{-3}) = 706.7$ s/mm$^2$. They chose the b value of 700 s/mm$^2$, which is within 1% of the theoretical optimal value. The subgroup analysis also compared pelvic phased-array coil with integrated endorectal-pelvic phased-array coils, which resulted in superior quality for the combination of both coils. Improved results could be explained by the use of an integrated endorectal-pelvic phased-array coil, which resulted in a significant improvement of anatomic details and visibility of the prostate anatomy compared with pelvic phased-array coil alone.

To explore sources of heterogeneity in the studies for T2WI combined with DWI, not only the diagnostic threshold analysis but also the metaregression analysis was performed. Because no threshold effect was found in these studies, the heterogeneity for T2WI combined with DWI was caused by other factors, such as study characteristics. The results of metaregression analysis indicate that patient enrollment and the MRI reviewer being blinded to other test results and clinical data were found to be the most important variable sources of heterogeneity for sensitivity and specificity, respectively.

We should acknowledge some limitations of this meta-analysis. First, we did not perform analyses according to the location of prostate cancer because this would have required lesion-based data. It is commonly known that approximately 75% of prostate cancers originate from the peripheral zone; 5–10% of cancers originate from the transitional zone. Furthermore, detection of transition zone tumors is challenging in hypertrophied prostates, although some recent studies have shown the utility of T2WI and DWI in this regard.

Second, the interpretation of MRI scans was performed qualitatively in the majority of the studies, and in many studies blinding was either unclear or absent. Thus, there is a risk of subjective interpretation, but it is more likely to be in favor of MRI, and its diagnostic accuracy might be even lower.

Third, bias was considered. To avoid selection bias, not only the MEDLINE and EMBASE databases but also the ScienceDirect, SpringerLink, SciVerse Scopus, and Cochrane Library libraries were searched for relevant articles. To minimize bias in the selection of studies and in data extraction, reviewers who were blinded to the journal, author, institution, and date of publication independently selected articles on the basis of inclusion criteria.

Fourth, with the limited number of studies available, we attempted to examine publication bias by using Deeks funnel plot, and no publication bias was found. However, potential publication bias may still exit, because small studies with optimistic results may be published more easily than small studies with unfavorable results. Larger studies with optimistic results may also be published more easily than larger studies with unfavorable results, but this difference usually is smaller. Moreover, we only included studies published in English, which might invoke the so-called "Tower of Babel" bias, which refers to the fact that investigators working in a language other than English could be sending only studies with positive results to international journals. Although certain less-qualified studies would be neglected by limiting the publication language to English, the Tower of Babel bias would make it possible that studies with negative results could have been left out.

Finally, although the Quality Assessment of Diagnostic Accuracy Studies tool was used to

ensure that all the selected articles were high-quality articles, there were still many retrospectively designed studies included in this meta-analysis, which may affect the quality of articles. Thus, high-quality prospective studies of the combination of T2WI plus DWI in detecting prostate carcinoma are of worth.

In conclusion, T2WI combined with DWI is superior to T2WI alone in the detection of prostate cancer. High-quality prospective studies regarding the combination of T2WI plus DWI in detecting prostate carcinoma still need to be conducted.

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