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Original Article

Role of Magnetic Resonance Imaging in the Detection of Local Prostate Cancer Recurrence after External Beam Radiotherapy and Radical Prostatectomy

L.M. Wu *, J.-R. Xu *, H.Y. Gu *, J. Hua *, J. Zhu *, J. Chen *, W. Zhang *, J. Hu †

* *Department of Radiology, Renji Hospital, Shanghai Jiao Tong University School of Medicine, Shanghai, China*
† *Department of Radiology, Wayne State University, Detroit, MI, USA*

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Abstract

Aims: To carry out a meta-analysis to assess the effectiveness of magnetic resonance imaging (MRI) during the follow-up of patients with prostate cancer after undergoing external beam radiotherapy (EBRT) or radical prostatectomy.
Materials and methods: MEDLINE, EMBASE and other databases were searched for relevant original articles published from January 1995 to October 2011. Methodological quality was assessed using the Quality Assessment of Diagnostic Accuracy Studies (QUADAS) tool. Pooled estimation and subgroup analysis data were obtained by statistical analysis.
Results: Fourteen of 768 initially identified studies were included in the meta-analysis. Seven studies examining patient after radical prostatectomy had a pooled sensitivity and specificity on the patient level of 82% (95% confidence interval 78–86%) and 87% (95% confidence interval 81–92%), respectively. In the subgroup analysis, compared with T2-weighted imaging (T2WI), dynamic contrast-enhanced (DCE) MRI showed higher pooled sensitivity (85%, 95% confidence interval 78–90%) and specificity (95%, 95% confidence interval 88–99%). DCE MRI combined with magnetic resonance spectroscopic imaging (1H-MRSI) had the highest pooled sensitivity (92%, 95% confidence interval 83–97%). Nine studies examining men after EBRT had a pooled sensitivity and specificity on the patient level of 82% (95% confidence interval 75–88%) and 74% (95% confidence interval 64–82%), respectively. Compared with T2WI, DCE MRI showed higher pooled sensitivity (90%, 95% confidence interval 77–97%) and specificity (81%, 95% confidence interval 64–93%). DCE combined with 1H-MRSI had the highest pooled specificity (90%, 95% confidence interval 56–100%). The pooled sensitivity and specificity on sextant analysis was 58% (95% confidence interval 53–64%) and 85% (95% confidence interval 82–88%), respectively. DCE MRI showed the highest pooled sensitivity: 71% (95% confidence interval 60–80%).
Conclusion: A limited number of small studies suggest that MRI can accurately detect local recurrences after EBRT and radical prostatectomy. DCE MRI is particularly accurate. The addition of MRSI to DCE MRI can significantly improve the diagnostic accuracy of local prostate cancer recurrence. The eventual role of 1H-MRSI alone remains controversial and needs to be defined further.

Key words: Meta-analysis; MRI; recurrent prostate cancer; systematic review

Introduction

In patients with prostate cancer, tumour recurrence after radical prostatectomy or external beam radiotherapy (EBRT) is a critical issue because it may greatly influence the subsequent therapeutic strategy and patient management. Typically, patients are followed up after treatment with serial measurements of their serum prostate-specific antigen (PSA) levels. According to the guidelines, a PSA increase over a threshold of 0.2 ng/ml later than 6–12 months after radical prostatectomy suggests treatment failure with a high risk of local recurrence [1], whereas a PSA increase within a shorter period correlates with distant metastasis progression. For EBRT, biochemical failure (increasing PSA level after a nadir level) is seen in about 50% of patients after 5 years, depending on the pre-treatment risk factors [2]. In patients with biochemical failure after treatment, a diagnostic imaging procedure is often carried out to distinguish between local cancer recurrence and distant spread of disease [3,4]. This information influences further therapeutic decisions.

Transrectal ultrasound-guided sextant biopsy is the current reference standard for the detection of local recurrence of prostate cancer in patients with biochemical

Author for correspondence: Jian-Rong Xu, Department of Radiology, Renji Hospital, Shanghai Jiao Tong University School of Medicine, No. 1630, Dongfang Road, Pudong, Shanghai 200127, China. Tel: +86-21-58752345; Fax: +86-21-68738344.
E-mail address: xujianr@yeah.net (J.-R. Xu).

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failure, but it is invasive and may fail to depict some tumours because only a small fraction of the gland is sampled. Computed tomography is not widely used for the detection of local recurrence because of the low accuracy of this technique in the differentiation of local recurrence from postsurgical scarring [5]. Immunoscintigraphy [6] and carbon 11 choline positron emission tomography-computed tomography [7] have been introduced as innovative imaging modalities for the detection of disease relapse, but their role is still incompletely defined. An accurate non-invasive alternative that enabled assessment of the recurrence of prostate cancer would be preferable.

Magnetic resonance imaging (MRI), with its inherent superior contrast and spatial resolution, looks promising for the evaluation of local recurrence of prostatic cancer [8,9]. Recently, several studies [10,11] have shown that MRI has emerged as an exciting modality for the local detection and characterisation of recurrent prostate cancer. As many investigations have explored the role of MRI in detecting local prostate cancer recurrence after radical prostatectomy or EBRT, a comprehensive systematic review would be useful to summarise the currently available bulk of information. The objective of this study was to assess the overall diagnostic value of MRI in detecting local prostate cancer recurrence with a meta-analysis, which to our knowledge, had not previously been studied.

Materials and Methods

Literature Search

A comprehensive literature search of studies on human subjects (patients) was carried out by one observer to identify articles about the diagnostic performance of MRI in the detection of local prostate cancer recurrence after radical prostatectomy or EBRT. The MEDLINE and EMBASE databases from January 1995 to October 2011 were used for English articles with the following keywords: ('MRI OR magnetic resonance imaging') AND ('prostate cancer or tumour') AND (sensitivity OR specificity OR false negative OR false positive OR diagnosis OR detection OR accuracy). Other databases, such as Scopus and the Cochrane Database of Systematic Reviews were also checked for relevant articles with similar keywords. All review articles, letters, comments and case reports were eliminated. For articles found to be eligible on the basis of their title, abstracts were then selected to further determine suitability for inclusion in this study.

Inclusion and Exclusion Criteria

Two reviewers (Wu LM, who had previous experience in data extraction from more than 10 meta-analyses, and Xu JR, who had experience in data extraction for retrospective and prospective studies) independently reviewed all eligible articles for the following inclusion criteria: (a) articles were reported in English; (b) MRI was used to identify and characterise local residual or recurrent prostate; (c) a histopathological analysis and clinical follow-up were used as the reference standard; (d) the quality of the study design, only the studies in which the number of answers 'yes' for the 14 questions in the Quality Assessment of Diagnostic Accuracy Studies (QUADAS) quality assessment tool [12] was greater than nine were included. If the number of answers 'no' or 'unclear' was larger than four, the report was excluded; (e) sufficient data were reported to construct 2 × 2 contingency tables. Although we would have preferred to include only large studies to increase the statistical power of the analyses, a minimal sample size of five patients was chosen because most studies involving patients with recurrent prostate cancer have small samples. The authors of abstracts and studies not reporting with sufficient data were contacted to for additional information.

Data Extraction and Quality Assessment

The same two investigators who carried out the database searches also carried out the relevant data extraction independently. In order to resolve disagreement between reviewers, a third reviewer assessed all discrepant items, and the majority opinion was used for the analysis. Relevant studies were further examined with QUADAS criteria again. To carry out accuracy analyses, we extracted data on the characteristics of studies and patients, measurements carried out and results. For each report, we extracted the following items: author; journal; sample size; description of study population (age); study design (prospective, retrospective or unknown); patient enrolment (consecutive or not); inclusion and exclusion criteria, reasons for exclusions from the analysis and number of experts who assessed and interpreted the results of the MRI. We also recorded whether there was any mention of blinding of MRI measurements to the histopathological and clinical results and/or to other diagnostic methods used.

Data Synthesis and Analysis

Meta-Disc allows the exploration of heterogeneity with a variety of statistics, including the chi-squared test and the I^2 index. The I^2 index is a measure of the percentage of total variation across studies due to heterogeneity beyond chance, a value over 50% indicates heterogeneity. For chi-squared tests, $P < 0.05$ 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% confidence intervals. We only used the random effect model provided by the software. For each study, we recorded the number of true positive (TP), false positive (FP), true negative (TN) and false negative (FN) findings for MRI in diagnosing recurrent prostate cancer. If TPs, FPs, FNs and TNs were not reported directly, we calculated them from the following formulas: sensitivity = TP/(FN + TP), specificity = TN/(FP + TN), positive predictive value (PPV) = TP/(TP + FP), negative predictive value (NPV) = TN/(TN + FN), TP + FP + FN + TN = sample size (n). Data on the diagnostic performance of MRI were combined quantitatively across eligible studies and they were used to construct 2 × 2 contingency tables, with TP, TN, FP and FN