European Journal of Radiology 95 (2017) 46–55

Contents lists available at ScienceDirect

European Journal of Radiology

journal homepage: www.elsevier.com/locate/ejrad

Research article

Diagnostic performance of MRI for prediction of muscle-invasiveness of bladder cancer: A systematic review and meta-analysis

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ARTICLE INFO

Keywords:
Bladder cancer
Muscle-invasive bladder cancer
Local staging
Magnetic resonance imaging
Systematic review
Meta-analysis

ABSTRACT

Purpose: To review the diagnostic performance of ≥1.5-T MRI for local staging of bladder cancer.
Methods: MEDLINE and EMBASE were searched up to February 21, 2017. We included diagnostic accuracy studies published since 2000 that used ≥1.5-T MRI for local staging (≥T2 [muscle-invasive]) in patients with bladder cancer, using pathology as the reference standard. The methodological quality was assessed using Quality Assessment of Diagnostic Accuracy Studies-2. Sensitivity and specificity were pooled and plotted in a hierarchical summary receiver operating characteristics plot. Sensitivity analyses using several clinically relevant covariates were performed.
Results: 24 studies (1774 patients) were included. Pooled sensitivity was 0.92 (95% CI 0.88–0.95) with specificity of 0.87 (95% CI 0.78–0.93). Sensitivity analyses showed that sensitivity estimates were comparable and consistently high across all subgroups, but specificity estimates were variable. Studies using 3-T scanners had higher specificity (0.93 [95% CI 0.86–0.98]) than those using 1.5-T scanners (0.83 [95% CI 0.74–0.98]). Studies using multiparametric MRI (conventional + ≥2 functional sequences) showed the highest accuracy with sensitivity and specificity of 0.94 (95% CI 0.89–1.00) and 0.95 (95% CI 0.89–0.98), respectively.
Conclusions: MRI shows good diagnostic performance for predicting muscle-invasiveness of bladder cancer. Multiparametric 3-T MRI seems to improve both sensitivity and specificity.

1. Introduction

In bladder cancer, determining the depth of invasion is of paramount importance. Management options differ considerably for muscle-invasive bladder cancer (MIBC) with stage T2 or higher and non-MIBC with stage T1 or lower. MIBC is usually treated with radical cystectomy, or a combination of radiation and/or chemotherapy while non-MIBC can be managed with transurethral resection (TUR) [1,2]. Therefore, it would be valuable if preoperative imaging studies can accurately assess the depth of invasion of bladder cancer.

During the past two decades, there has been great interest in the use of magnetic resonance imaging (MRI) for local staging of bladder cancer paralleling advances in MRI technique (i.e., widespread use of scanners with magnet strength of ≥1.5 T). Variable techniques including conventional T1- (T1WI) and T2-weighted imaging (T2WI) and more advanced sequences such as contrast-enhanced (CE) MRI and diffusion-weighted imaging (DWI) has shown promising results for determining the depth of invasion [3–5]. However, in clinical practice, TUR followed by pathological investigation is used for local staging, and current guidelines state that due to (1) the variability of diagnostic performance for local staging using MRI in the literature (73% to 96%) and (2) insufficient data on the use of advanced MRI techniques (i.e., DWI), no recommendations can be made regarding their use in the management of bladder cancer [6,7]. In this clinical context, a comprehensive review of the existing literature on the diagnostic performance of MRI in local staging of bladder cancer may be needed to ascertain the role of MRI.

Therefore, we performed a systematic review and meta-analysis to evaluate the diagnostic performance of contemporary MRI for local staging of bladder cancer with focus on the prediction of muscle-invasiveness.

Abbreviations: MIBC, muscle-invasive bladder cancer; TUR, transurethral resection; MRI, magnetic resonance imaging; T1WI, T1-weighted imaging; T2WI, T2-weighted imaging; CE, contrast-enhanced; DWI, diffusion-weighted imaging; PRISMA, Preferred Reporting Items for Systematic Reviews and Meta-Analyses; QUADAS-2, Quality Assessment of Diagnostic Accuracy Studies-2; HSROC, hierarchical summary receiver operating characteristic

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http://dx.doi.org/10.1016/j.ejrad.2017.07.021
Received 27 April 2017; Received in revised form 30 June 2017; Accepted 25 July 2017

2. Materials and methods

The current meta-analysis was written according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines. The research question for the purpose of this meta-analysis was formulated based on the following PICOS criteria [8]: What is the diagnostic performance of ≥1.5-T MRI for local staging in patients with bladder cancer, as compared with pathological results in original articles published since 2000?

2.1. Literature search

A computerized search of MEDLINE and EMBASE databases up to February 21, 2017 was performed to identify relevant studies. The search query combined synonyms for bladder cancer, MRI, staging, and diagnostic accuracy as the following: (bladder OR urothelial OR papillary OR transitional) AND (cancer OR carcinoma OR tumor OR tumour OR neoplasm) AND (MRI OR MR OR "magnetic resonance") AND (stage OR staging OR TNM) AND (sensitivity OR specificity OR accuracy OR "predictive value"). References of the identified papers were screened to expand the scope of literature search. The search was not limited to any particular language.

2.2. Study selection

2.2.1. Inclusion criteria

We included studies that met the following PICOS criteria (10): (a) patients diagnosed with bladder cancer; (b) MRI used as the index test for local staging (assessment of stage ≥T2 [MIBC]); (c) pathology based on cystectomy or TUR for comparison; (d) sufficient information for reconstruction of 2 × 2 tables regarding sensitivity and specificity; and (e) publication type of original articles.

2.2.2. Exclusion criteria

The exclusion criteria were as follows: (1) study population of less than 10 patients; (2) publication type other than original articles (i.e., review articles, letters, editorials, conference abstracts, and etc.); (3) MRI used for assessment of bladder cancer, but focusing on other topics (i.e., treatment response, local staging but not MIBC vs non-MIBC, nodal or distant metastasis staging); (4) studies using < 1.5-T MRI scanners; (5) studies published before 2000; (6) overlapping patient population; and (7) insufficient data for reconstruction of 2 × 2 tables. When multiple studies with overlapping study population were present, we only included the study with the largest study population. Authors of the studies were contacted when 2 × 2 tables could not be reconstructed for diagnostic accuracy studies.

The literature search and study selection process was independently performed by two reviewers and disagreements were resolved by consensus.

2.3. Data extraction and quality assessment

The following data with regards to patient/tumor, study, and MRI characteristics were extracted from the selected studies by using a standardized form:

(1) Patient and tumor characteristics—number of patients, ethnicity of study population, mean age and range of patients, number of tumors, prevalence of stage ≥T2 tumors, and histological subtypes (only urothelial carcinoma vs inclusion of other subtypes)

(2) Study characteristics—origin of study (authors, institution, and duration of patient recruitment), publication year, study design (i.e., prospective, multi-center, and consecutive enrollment), reference standard (based on cystectomy or TUR), interval between MRI and reference standard, blinding between MRI interpretation and pathological assessment, and characteristics of readers (number, consensus reading, and experience)

(3) MRI characteristics—scanner manufacturer and model, magnet field strength (1.5- or 3.0-T), type of MRI sequences used, their corresponding technical parameters, whether preparation for bladder distension was performed or not, whether MRI was performed before or after a prior TUR or biopsy, and whether criteria for staging was explicitly provided.

The methodological quality of the included studies was assessed using the Quality Assessment of Diagnostic Accuracy Studies-2 (QUADAS-2) tool [9]. Data extraction and quality assessment was performed independently by two reviewers with disagreements resolved via consensus.

2.4. Data synthesis and analysis

Two x two tables were reconstructed from the included studies to calculate their sensitivity and specificity. If several different diagnostic performance values were provided within a single study (i.e., several types of MRI sequences or multiple independent readers), we selected the result with the highest accuracy to be representative of the study.

Summary estimates of sensitivity and specificity were calculated with hierarchical logistic regression modelling including bivariate and hierarchical summary receiver operating characteristic (HSROC) modelling [10,11]. These results were plotted using HSROC curves with 95% confidence and prediction regions. Publication bias was evaluated using visual analysis of the Deeks' funnel plot and calculating the p value using Deeks' asymmetry test [12].

Heterogeneity was assessed with the following methods: (1) Cochran's Q-test with $p < 0.05$ indicating that heterogeneity was present; (2) Higgins I^2 test with the degree of heterogeneity interpreted using the following criteria: inconsistency index (I^2) = 0%–40%, heterogeneity might not be important; 30%–60%, moderate heterogeneity may be present; 50%–90%, substantial heterogeneity may be present; and 75%–100%, considerable heterogeneity [13]; and (3) testing for a threshold effect (positive correlation between sensitivity and false positive rate) between the included studies. In order to explore the cause of heterogeneity, sensitivity analyses using several covariates were performed.

The "metandi" and "midas" modules in Stata 10.0 (StataCorp LP, College Station, TX, USA) and "mada" package in R software version 3.2.1 (R Foundation for Statistical Computing, Vienna, Austria) were used for statistical analyses with $p < 0.05$ indicating statistical significance.

3. Results

3.1. Literature search

The systematic literature search initially yielded 1062 articles. After removing 387 duplicates, screening of the 675 titles and abstracts yielded 70 potentially eligible original articles. Full-text reviews were performed and 46 studies were excluded due to the following: less than 10 patients ($n = 1$), not in field of interest ($n = 4$), used < 1.5-T MRI ($n = 24$), published before 2000 ($n = 11$), insufficient data to reconstruct 2 × 2 tables ($n = 3$), and shared study population with other studies ($n = 3$). Ultimately, 24 studies including 1774 patients evaluating the diagnostic performance of MRI for local staging of bladder cancer were included in this meta-analysis [3–5,14–34]. The study selection process is shown in Fig. 1.

3.2. Characteristics of included studies

The patient characteristics are summarized in Table 1. The size of the study population ranged from 19 to 362 patients. The patients were of Asian ethnicity in 13 studies and non-Asian in the other 11. The mean age of the patients ranged from 61.3 to 72.1 years. The number of bladder cancers ranged from 20 to 362. The prevalence of stage ≥T2