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Review

Value of DCE-MRI for staging and response evaluation in rectal cancer: A systematic review

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ABSTRACT

Purpose: Aim was to perform a systematic review to evaluate the clinical value of dynamic contrast-enhanced (DCE) MRI in rectal cancer.

Methods and materials: A systematic search was performed on Pubmed, Embase and the Cochrane library. Studies that evaluated DCE-MRI for tumour aggressiveness, primary staging and restaging after chemoradiation (CRT) were included. Information on population, DCE technique, DCE parameters and outcome (angiogenesis, staging and response) were extracted.

Results: 19 studies were identified; 10 evaluated quantitative analyses, 6 semiquantitative analyses and 3 evaluated both. 8 studies evaluated correlation between DCE-parameters and angiogenesis or tumour aggressiveness, 11 studies evaluated response prediction pre- and post-CRT. Semiquantitative washin parameters showed a significantly positive correlation with angiogenesis, while for quantitative analyses conflicting results were found. Conflicting results were also reported for the correlation between DCE parameters and tumour aggressiveness: both higher and lower vascularity in more aggressive tumours are reported, while some studies report no correlation. Six studies showed a predictive value of Ktrans for response. A high Ktrans pre-CRT was significantly correlated with a complete/good response, but the reported pre-CRT Ktrans varied substantially (0.36-1.93). After CRT a reduction in Ktrans of 32%-36% was significantly associated with response. For semiquantitative analyses pre-CRT late slope was reported to be significantly lower in good responders, however only few studies exist on semiquantitative analyses of post-CRT DCE-MRI.

Conclusion: DCE-MRI in rectal cancer is promising mainly for prediction and assessment of response to CRT, where a high pre-CRT Ktrans and a decrease in Ktrans are significantly predictive for response.

1. Introduction

Over the past years many improvements in rectal cancer imaging have been made. Since the routine implementation of MRI for rectal cancer staging, several new imaging techniques have been explored to improve MRI based staging of rectal cancer even further. One of the more recent additions in the MR spectrum of imaging in rectal cancer is dynamic contrast-enhanced (DCE) MRI. With this technique the vascularity of a tumour can be assessed which can provide valuable information about tumour aggressiveness and the degree of angiogenesis and may aid in (re) staging of rectal tumours. DCE-MRI is already used in breast imaging and prostate cancer to identify malignant tumours based on specific enhancement patterns [1–5]. There is also evidence that DCE-MRI can be of help in predicting and assessing response to neo-adjuvant treatment[6–9]. In rectal cancer several studies have been performed to evaluate the clinical value and diagnostic performance of DCE-MRI for primary staging and response assessment after neo-adjuvant treatment. These studies report conflicting results: some show great diagnostic potential for DCE MRI [7,8,10–12], while others find no significant results.

Therefore, the objective of this study is to systematically review the

Abbreviations: VEGF, vascular endothelial growth factor; EGFR, epidermal growth factor receptor; MVD, microvessel density; MVA, microvessel area; MVC, microvessel count; Ktrans, volume rate constant; Ve, volume of extracellular space; Kep, (or K21) constant flow rate; SITC, signal-intensity-time curve; TTP, time to peak; Amplitude A, volume of contrast agent uptake (equivalent to max peak enhancement); Erise, relative enhancement during rapid rise; Emax, maximal enhancement; SLP, steepest slope; ERpeak, peak enhancement ratio; Tfirst-enhance, first enhancement time; MSD, maximum signal difference; WII, wash-in intercept; WOI, wash-out intercept; WIS, wash-in slope; WOS, wash-out slope; TIC, time intensity curve

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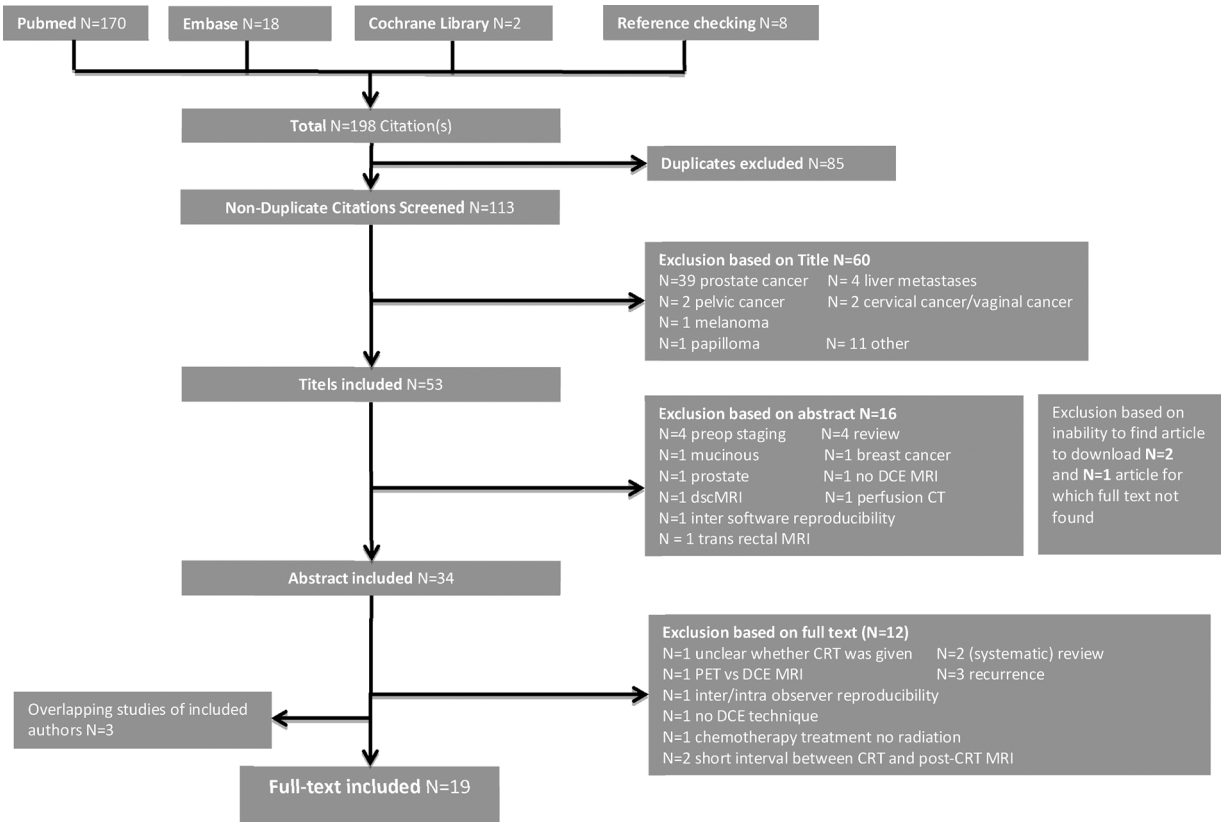

Fig. 1. PRISMA flowchart describing the identification and inclusion of studies.

evidence on DCE-MRI for use in rectal cancer and determine its diagnostic value in assessing tumour aggressiveness and staging and for prediction of complete response before and after treatment.

2. Materials and methods

A literature search was done in Pubmed, the Cochrane Library and Embase with (a combination of) the following keywords with the use of MeSH terms [13]: “Rectal Neoplasms”; “Rectal cancer”; “Dynamic contrast enhanced magnetic resonance imaging”; “DCE MRI”; “Sensitivity and Specificity”; “Sensitivity”; “Specificity”; “Neoadjuvant Therapy” and “Neoadjuvant chemoradiotherapy”.

No language restriction was used during this literature search. Inclusion criteria were: (1) inclusion of patients with biopsy proven rectal cancer, (2) a dynamic contrast-enhanced MRI was performed, (3) purpose of the study was to assess the value of DCE-MRI parameters for evaluation of (a) tumour aggressiveness, (b) primary tumour staging or (c) response to neoadjuvant treatment, (4) 1.5T or 3T scanner.

Exclusion criteria were: (1) review articles, case series or case reports, (2) studies that performed only a 4-phase post-contrast scan, (3) recurrent rectal cancer, (4) inclusion of predominantly mucinous tumours ($>$ 5% of the population), (5) the use of transrectal MRIs and (6) short interval ($<$ 4 weeks) between CRT and post-CRT MRI (as this does not lead to downstaging and response cannot be evaluated). In case of overlapping publications from one study group, the publication with the largest sample size was used and (if available) any additional data that was presented in the smaller study was also used.

Two independent reviewers (RAPD and MM) performed a systematic search for eligible studies. Each reviewer first checked all titles and then abstracts for eligibility. Thereafter, all eligible studies were read and studied in full by both reviewers to decide which studies met all the inclusion criteria.

Consensus was reached in case of disagreement. References of the included studies were checked for additional eligible studies by one reader (RAPD). When there was doubt about inclusion, a decision was made by consensus between the two readers. The following data were extracted from the studies: (a) number, gender and age of patients, (b) details on the index test, (c) studied DCE parameters, (d) study design, (e) degree of blinding and (f) main study outcomes: results regarding angiogenesis, staging or response after CRT and (g) details on the reference standard. If reported, results regarding diagnostic performance (e.g. accuracy, sensitivity and specificity) were also extracted. All included studies were assessed using the QUADAS-2 checklist for quality assessment of diagnostic accuracy studies [14]. Because of the heterogeneity of the studies and their outcomes a meta-analysis was not performed.

2.1. Identification of eligible studies

In total, 19 studies were included. The literature search yielded a total of 113 papers after duplicates were removed. Based on title 60 articles were excluded because they either did not focus on rectal cancer and/or DCE-MRI. 19 articles were excluded based on the abstract because they were not relevant to the study question [15–33]. The remaining 34 papers were studied in full text. Twelve were excluded for the following reasons: one studied inter/intra observer reproducibility of DCE MRI and the effect of slice selection [34]; one studied the correlation between DCE MRI and PET-CT [35]; two concerned a (systematic) review [12,36]; for one study it was unclear whether patients received CRT [37]; one study used a combination of four different sequences to produce a dynamic image [38]; one study had only chemotherapy as treatment [39]; two studies had a short interval between CRT and post-CRT MRI of only three weeks [6,40]; and three studied DCE MRI in recurrent rectal cancer [41–43]. This left a total of 22 papers for potential inclusion[7–11,44–60] In these 22 papers 5 papers were included that had largely overlapping study populations. These papers came from two author groups [8,9,45,46,57]. Fig. 1 shows the flowchart for study identification and inclusion.