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Original article

Diagnostic performance of MRI for assessment of response to neoadjuvant chemoradiotherapy in oesophageal cancer

S. E. Vollenbrock[1,8] , F. E. M. Voncken[2], J. M. van Dieren[3], D. M. J. Lambregts[1], M. Maas[1], G. J. Meijer[6], L. Goense[6,7] , S. Mook[6], K. J. Hartemink[4], P. Snaebjornsson[5], L. C. ter Beek[1], M. Verheij[2], B. M. P. Aleman[2], R. G. H. Beets-Tan[1,8] and A. Bartels-Rutten[1]

Departments of [1]Radiology, [2]Radiation Oncology, [3]Gastrointestinal Oncology, [4]Surgery and [5]Pathology, Netherlands Cancer Institute–Antoni van Leeuwenhoek Hospital, Amsterdam, Departments of [6]Radiation Oncology and [7]Surgery, University Medical Center Utrecht, Utrecht, and [8]GROW School for Oncology and Developmental Biology, Maastricht University, Maastricht, the Netherlands
Correspondence to: Dr S. E. Vollenbrock, Department of Radiology, Netherlands Cancer Institute–Antoni van Leeuwenhoek Hospital, Plesmanlaan 121, 1066 CX, Amsterdam, the Netherlands (e-mail: s.vollenbrock@nki.nl)

Background: Patients with a pathological complete response (pCR) after neoadjuvant chemoradiotherapy (nCRT) for oesophageal cancer may benefit from non-surgical management. The aim of this study was to determine the diagnostic performance of visual response assessment of the primary tumour after nCRT on T2-weighted (T2W) and diffusion-weighted (DW) MRI.

Methods: Patients with locally advanced oesophageal cancer who underwent T2W- and DW-MRI (1·5 T) before and after nCRT in two hospitals, between July 2013 and September 2017, were included in this prospective study. Three radiologists evaluated T2W images retrospectively using a five-point score for the assessment of residual tumour in a blinded manner and immediately rescored after adding DW-MRI. Histopathology of the resection specimen was used as the reference standard; ypT0 represented a pCR. Sensitivity, specificity, area under the receiver operating characteristic (ROC) curve (AUC) and interobserver agreement were calculated.

Results: Twelve of 51 patients (24 per cent) had a pCR. The sensitivity and specificity of T2W-MRI for detection of residual tumour ranged from 90 to 100 and 8 to 25 per cent respectively. Respective values for T2W + DW-MRI were 90–97 and 42–50 per cent. AUCs for the three readers were 0·65, 0·66 and 0·68 on T2W-MRI, and 0·71, 0·70 and 0·70 on T2W + DW-MRI ($P = 0.441$, $P = 0.611$ and $P = 0.828$ for readers 1, 2 and 3 respectively). The κ value for interobserver agreement improved from 0·24–0·55 on T2W-MRI to 0·55–0·71 with DW-MRI.

Conclusion: Preoperative assessment of residual tumour on MRI after nCRT for oesophageal cancer is feasible with high sensitivity, reflecting a low chance of missing residual tumour. However, the specificity was low; this results in overstaging of complete responders as having residual tumour and, consequently, overtreatment.

Introduction

A standard therapy with curative intent for patients with locally advanced oesophageal cancer consists of neoadjuvant chemoradiotherapy (nCRT) followed by surgery. nCRT improves survival compared with surgery alone (5-year survival rate 47 *versus* 33 per cent respectively)[1]. In 25–30 per cent of patients with oesophageal cancer, the resection specimen shows no residual tumour cells (ypT0) after nCRT[2,3], also known as a pathological complete response (pCR). Patients with a pCR have an excellent prognosis, with a 5-year recurrence-free survival rate of 62 per cent[4,5], which is better than that of patients

with vital tumour cells in the resection specimen (no pCR). The high postoperative morbidity and mortality rates after oesophagectomy raise the question of whether non-surgical management (watch and wait) is a safe alternative treatment option in patients with oesophageal cancer who have a clinical complete response (cCR)[6].

To implement non-surgical treatment for advanced oesophageal cancer it is critical to accurately identify pCR. CT and fluorodeoxyglucose (FDG) PET/CT are both inaccurate in discriminating residual disease from pCR owing to the presence of wall thickening and/or radiation oesophagitis[7–13]. The same is true for endoscopic

ultrasonography (EUS), which has an accuracy of only 36 per cent for ypT determination[14,15]. Endoscopic response evaluation after nCRT is hampered by the fact that it provides information only on the luminal side of the oesophagus[16], whereas residual cancer cells are located beneath the mucosal layer in a subset of patients[17,18]. Even deeper bite-on-bite biopsies combined with EUS and fine-needle aspiration of suspicious lymph nodes yielded a negative predictive value (NPV) of only 45 per cent for detecting tumours with a tumour regression grade (TRG) of 2 or higher[11]. Previous retrospective cohort studies[19−22] reported on patients with a cCR after neoadjuvant treatment who did not have surgery but underwent serial response assessments including endoscopy, EUS, CT and/or FDG-PET/CT. Among those assessed as having a cCR who did undergo oesophagectomy, residual tumour was found in 28–33 per cent of patients[19−21].

In a propensity-based matching study[22], after a median follow-up of 51·1 months, local recurrence had developed more frequently among patients with a cCR who underwent a watch-and-wait approach than in those who had surgical treatment.

The limitations of the current response assessment tools warrant investigation of other imaging techniques. In rectal cancer, MRI can aid in the diagnosis of a cCR after nCRT[23,24]. Although MRI of the oesophagus is technically more challenging, owing to oesophageal motility and motion of the surrounding heart and diaphragm, advances in technology now enable the acquisition of high-resolution magnetic resonance (MR) images. Previous studies[25−29] on response prediction with MRI in oesophageal cancer focused on quantitative diffusion-weighted (DW) MRI parameters. However, visual response assessment on T2-weighted (T2W) and

Fig. 1 MRI of a patient with locally advanced oesophageal cancer that showed a pathological complete response to neoadjuvant chemoradiotherapy
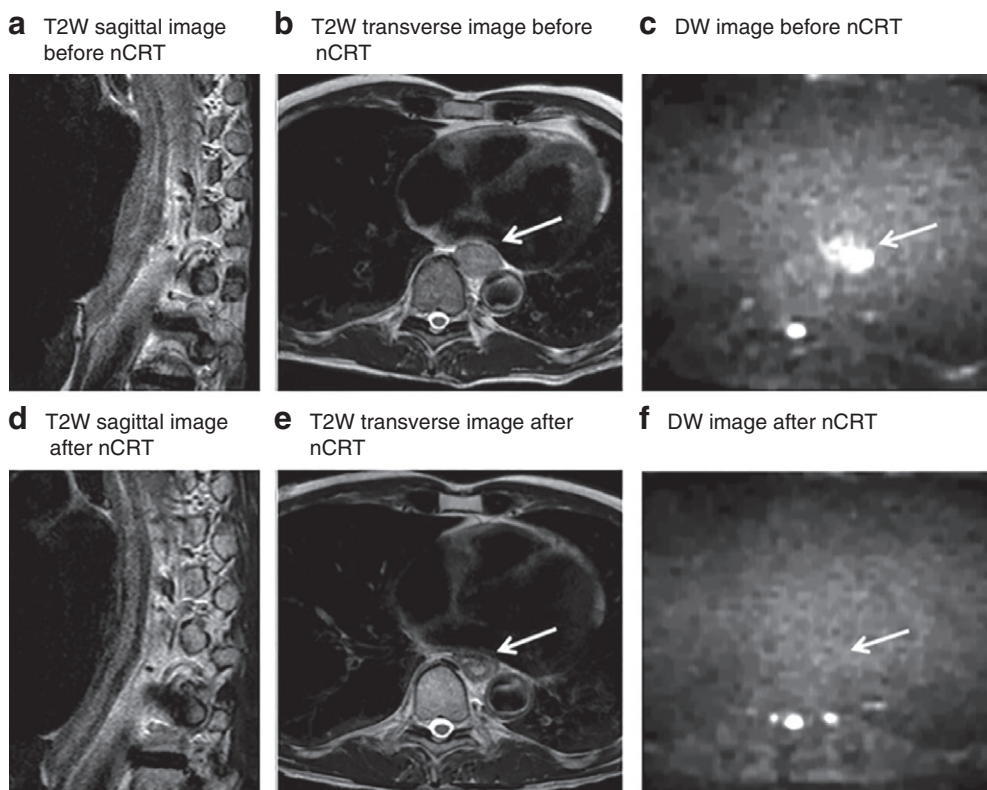
Images from a 55-year-old man with a cT3N0 lower oesophageal squamous cell carcinoma, and a complete pathological response after neoadjuvant chemoradiotherapy (nCRT) and oesophagectomy (tumour regression grade 1, ypT0 N0). **a–c** T2-weighted (T2W) sagittal (**a**) and transverse (**b**) images before chemoradiotherapy show a hyperintense oesophageal wall, accompanied by a hyperintense signal on diffusion-weighted (DW) imaging (**c**). **d–f** T2W sagittal (**d**) and transverse (**e**) images after nCRT show a hypointense oesophageal wall, indicating fibrosis; no high signal remained on the corresponding DW image (**f**). Arrows mark (initial) tumour location.

functional DW-MRI in rectal cancer yielded higher sensitivity for detecting residual tumour compared with quantitative assessment[30]. The performance of visual response assessment on MRI in oesophageal cancer is as yet unknown. The aim of this study was to determine the diagnostic performance of visual response assessment of the primary oesophageal tumour after nCRT on T2W-MRI and functional DW-MRI.
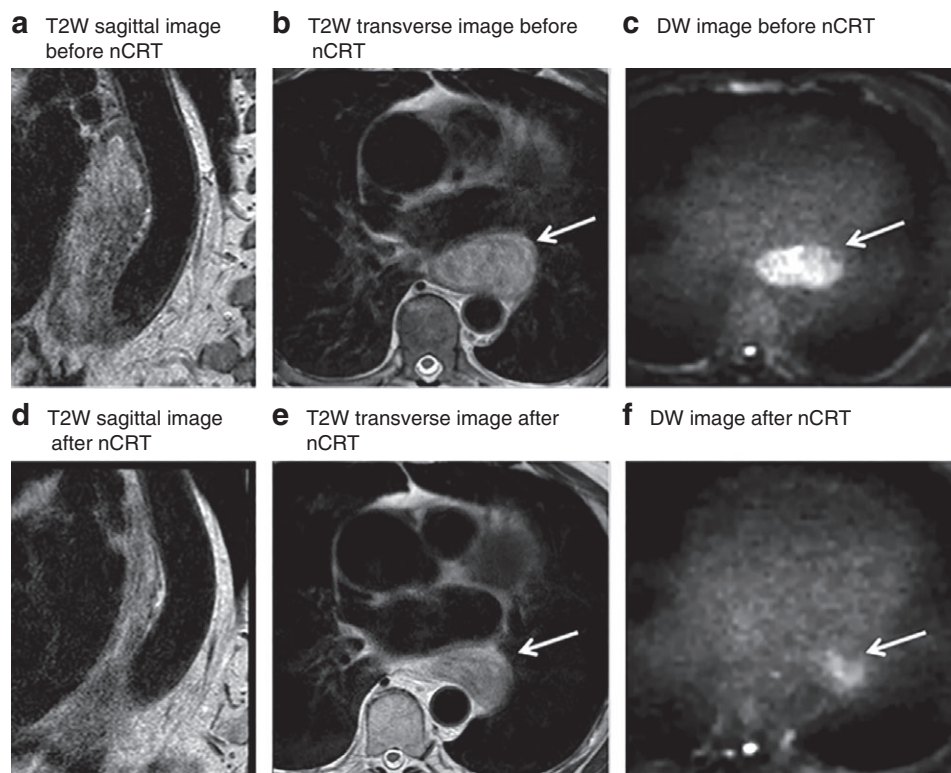
Methods

Patients diagnosed with locally advanced oesophageal cancer were enrolled prospectively and data were analysed retrospectively. The study was approved by the local medical ethics committees and registered at ClinicalTrials.gov (NCT02139488 and NCT02125448). Written informed consent to participate was obtained from the patients. Patients underwent MRI before and after nCRT between July 2013 and September 2017. Inclusion criteria

were: biopsy-proven locally advanced, non-metastatic oesophageal cancer; 5 weeks of nCRT (total of 41·4 Gy in 23 fractions, with weekly administration of carboplatin and paclitaxel) followed by oesophagectomy; and maximum of 21 days between preoperative MRI and surgery. Patients were excluded if MRI quality was judged insufficient by at least two radiologists. Causes of insufficient image quality were severe motion artefacts leading to blurred T2W images, and lack of, or only slight, diffusion restriction in the spleen as a surrogate marker of inadequate DW images.

Image acquisition

Imaging was performed on a 1·5-T MRI scanner (Achieva or Ingenia; Koninklijke Philips, Best, the Netherlands), using Torso-XL (16 channel) or anterior/posterior (28 channel) receiver coils respectively (supplied by Koninklijke Philips). The MRI protocol consisted of T2W multislice turbo spin-echo sequences in transverse

Fig. 2 MRI of a patient with locally advanced oesophageal cancer that showed pathological residual tumour after chemoradiotherapy and surgery

a T2W sagittal image before nCRT

b T2W transverse image before nCRT

c DW image before nCRT

d T2W sagittal image after nCRT

e T2W transverse image after nCRT

f DW image after nCRT

Images from a 78-year-old man with a cT2 N0 lower oesophageal adenocarcinoma, who had residual tumour after neoadjuvant chemoradiotherapy (nCRT) and oesophagectomy (tumour regression grade 5, ypT2 N0). T2-weighted (T2W) sagittal (**a,d**) and transverse (**b,e**) images before (**a,b**) and after (**d,e**) nCRT both show a hyperintense oesophageal wall. The corresponding b = 800 diffusion-weighted (DW) images before (**c**) and after (**f**) nCRT demonstrate a clear hyperintense signal, highly suspicious for tumour. Arrows mark tumour location.

(slice thickness 4 mm) and sagittal (slice thickness 3 mm) planes. A respiratory navigator was positioned on the diaphragm, and to reduce motion artefacts, images were acquired only during expiration[31]. A DW echo-planar imaging sequence was acquired in the transverse direction with b = 0, b = 200 and b = 800 s/mm^2, and a slice thickness of 4 mm. The transverse T2W and DW sequences were angled in identical planes. Detailed MRI sequence parameters are provided in *Table S1* (supporting information).

Image evaluation

Images were analysed independently by three expert radiologists, who were blinded to tumour characteristics (location, histology, TNM stage[32]) and clinical outcomes. The radiologists first judged images of the primary tumour area acquired by T2W-MRI and DW-MRI before nCRT. They then scored the images obtained by T2W-MRI after nCRT for the likelihood of residual tumour. Finally, still in the same reading session, DW-MR images of b = 800 s/mm^2 were added and the scoring was repeated. A five-point confidence level score (CLS) was used, derived from previous studies in rectal cancer (CLS1, definitely complete response; 2, probably complete response; 3, inconclusive; 4, probably residual tumour; 5, definitely residual tumour)[23].
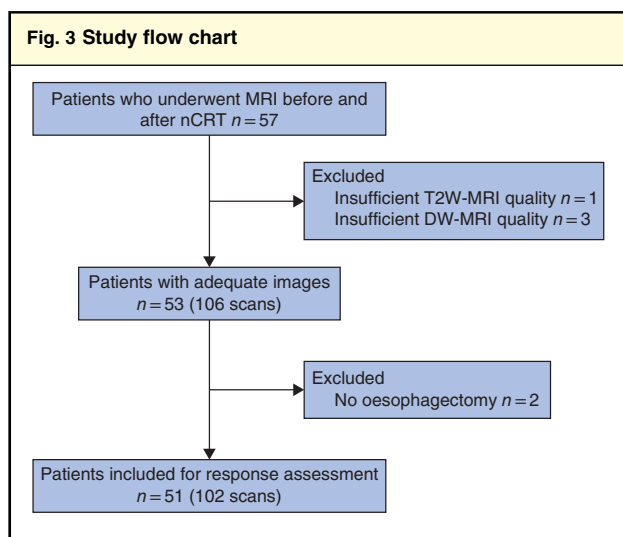
MRI criteria

A complete response of the primary tumour on T2W-MRI was defined by a normalized oesophageal wall or only a thin hypointense signal (indicating fibrosis) without distortion of the wall; on DW-MRI, a complete response of the primary tumour was defined by the absence of high signal on images of b = 800 s/mm^2 in the irradiated tumour bed. On T2W-MRI, a residual mass with persistent iso-intense signal or the presence of mixed hyperintense and hypointense signals within the tumour bed were considered signs of residual tumour; on DW-MRI, the presence of high signal within the tumour bed indicated residual tumour. These criteria are illustrated in *Figs 1* and *2*.

Table 1 Patient and tumour characteristics			
	Hospital 1 (*n* = 32)	**Hospital 2** (*n* = 19)	**Total** (*n* = 51)
Age (years)*	64 (53–72)	64 (60–68)	64 (56–72)
Sex ratio (M : F)	23 : 9	16 : 3	39 : 12
Tumour location			
Upper oesophageal	0	1	1 (2)
Middle oesophageal	3	3	6 (12)
Lower oesophageal	15	11	26 (51)
Gastro-oesophageal junction	14	4	18 (35)
Histological tumour type			
Adenocarcinoma	28	14	42 (82)
Squamous cell carcinoma	4	5	9 (18)
Grade of differentiation			
Well differentiated	2	0	2 (4)
Moderately differentiated	15	10	25 (49)
Poorly differentiated	14	3	17 (33)
Undifferentiated	0	2	2 (4)
Unknown	1	4	5 (10)
Clinical T category†			
cT1	1	0	1 (2)
cT2	8	4	12 (24)
cT3	23	14	37 (73)
cT4a	0	1	1 (2)
Clinical N category†			
cN0	15	4	19 (37)
cN1	6	8	14 (27)
cN2	9	7	16 (31)
cN3	2	0	2 (4)
Radicality of resection			
R0	32	18	50 (98)
R1	0	1	1 (2)
Mandard grade			
TRG 1	6	6	12 (24)
TRG 2	10	7	17 (33)
TRG 3	12	4	16 (31)
TRG 4	3	1	4 (8)
TRG 5	1	1	2 (4)

Values in parentheses are percentages unless indicated otherwise; *values are median (i.q.r.). †According to the seventh edition of the TNM classification[32]. Hospital 1, Netherlands Cancer Institute; hospital 2, University Medical Center Utrecht. TRG, tumour regression grade.

Fig. 3 Study flow chart

Patients who underwent MRI before and after nCRT *n* = 57

Excluded
Insufficient T2W-MRI quality *n* = 1
Insufficient DW-MRI quality *n* = 3

Patients with adequate images *n* = 53 (106 scans)

Excluded
No oesophagectomy *n* = 2

Patients included for response assessment *n* = 51 (102 scans)

nCRT, neoadjuvant chemoradiotherapy; T2W, T2-weighted; DW, diffusion-weighted.

Fig. 4 Receiver operating characteristic curves for assessment of residual tumour after neoadjuvant chemoradiotherapy using T2-weighted MRI and T2-weighted combined with diffusion-weighted MRI
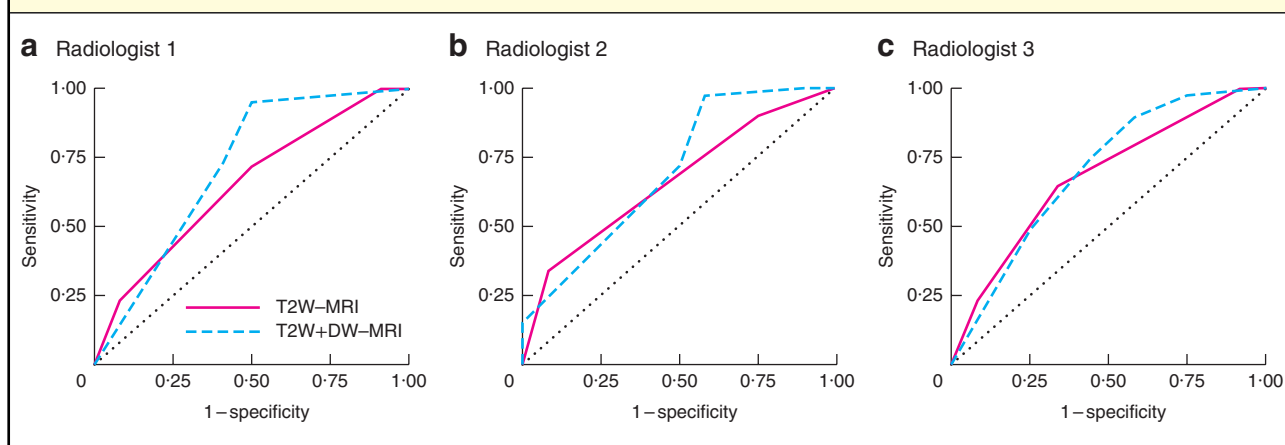
a Reader 1, **b** reader 2 and **c** reader 3. T2W, T2-weighted; DW, diffusion-weighted. Comparison of areas under the curve for T2W-MRI *versus* T2W + DW-MRI: **a** $P = 0.441$, **b** $P = 0.611$, **c** $P = 0.828$ (DeLong test[33]).

Table 2 Diagnostic performance for assessment of residual tumour

	T2W-MRI			T2W + DW-MRI		
	Reader 1	Reader 2	Reader 3	Reader 1	Reader 2	Reader3
Sensitivity (%)	100	90	90	95	97	90
	(89, 100)	(75, 97)	(75, 97)	(81, 99)	(85, 100)	(75, 97)
Specificity (%)	8	25	25	50	42	42
	(0, 40)	(7, 57)	(7, 57)	(22, 78)	(17, 71)	(17, 71)
PPV (%)	78	80	80	86	84	83
	(64, 88)	(64, 90)	(64, 90)	(71, 94)	(70, 93)	(68, 92)
NPV (%)	100	43	43	75	83	56
	(6, 100)	(12, 80)	(12, 80)	(36, 96)	(37, 99)	(23, 85)
True-positive	39	35	35	37	38	35
False-positive	11	9	9	6	7	7
True-negative	1	3	3	6	5	5
False-negative	0	4	4	2	1	4
Accuracy (%)	78	75	75	84	84	78
AUC*	0·65	0·66	0·68	0·71	0·70	0·70
	(0·47, 0·83)	(0·49, 0·83)	(0·51, 0·86)	(0·52, 0·90)	(0·52, 0·88)	(0·51, 0·88)

Values in parentheses are 95 per cent confidence intervals. Residual tumour (tumour regression grade 2–5 in resected primary tumour) was considered the positive outcome. T2W, T2-weighted; DW, diffusion-weighted; PPV, positive predictive value; NPV, negative predictive value; AUC, area under the receiver operating characteristic curve. *Comparison of T2W-MRI *versus* T2W + DW-MRI: $P = 0.441$, $P = 0.611$ and $P = 0.828$ for readers 1, 2 and 3 respectively (DeLong test[33]).

Reference standard

Histopathological examination of the resection specimen was performed by dedicated gastrointestinal pathologists at the two centres. The resection specimen was evaluated in accordance with the seventh edition of the UICC protocol for ypTNM classification[32]. The TRG of the resected primary tumour was assessed according to Mandard and colleagues[3]. The tumour bed was embedded completely for histopathological analysis. A pCR was defined as ypT0 (TRG 1) and residual tumour as ypT1–4 (TRG 2–5).

Statistical analysis

Before undertaking the analyses, dichotomization between CLS2 (probably complete response) and CLS3

(inconclusive) was decided as the cut-off, to minimize the risk of missing residual disease. Receiver operating characteristic (ROC) curves were constructed and areas under the curve (AUCs) calculated to evaluate the performance of the three radiologists on T2W-MRI only and on T2W + DW-MRI, with histologically confirmed residual tumour as the positive outcome. Sensitivities, specificities, positive predictive values (PPVs) and NPVs were calculated with 95 per cent confidence intervals. AUCs on T2W-MRI and T2W + DW-MRI were compared by means of the DeLong test[33]. $P < 0.050$ was considered statistically significant. The possible change in the number of uncertainties was analysed by comparing the number of equivocal scores (CLS3). Interobserver agreement between radiologists was calculated using quadratic weighted κ values (0–0·20, poor; 0·21–0·40, fair; 0·41–0·60, moderate; 0·61–0·80, good; and 0·81–1·00 excellent agreement)[34]. Statistical analyses were done using SPSS® version 22 (IBM, Armonk, New York, USA) and Stata® version 11 (StataCorp, College Station, Texas, USA).

Results

Six of 57 patients were excluded: four had insufficient MRI quality, one patient had distant metastases after completion of nCRT and therefore did not undergo surgical resection, and one patient was deemed to have unresectable disease at surgical exploration. Therefore, 51 patients were evaluated (*Fig. 3*). Of the 51 included patients, 42 (82 per cent) were diagnosed with adenocarcinoma and nine (18 per cent) with squamous cell carcinoma. *Table 1* shows baseline patient and tumour characteristics at both institutes that participated in the study. Transhiatal oesophagectomy was performed in 24 patients (47 per cent) and transthoracic oesophagectomy in 27 (53 per cent), followed by gastric conduit reconstruction with cervical anastomosis in all patients. The median interval between the last radiation fraction and oesophagectomy was 59 (range 24–75) days.

It was 47 (17–65) days between the last radiation fraction and MRI, and 11 (4–21) days from post-nCRT MRI until oesophagectomy.

On histopathological assessment, a pCR of the primary tumour (ypT0, TRG 1) was found in 12 of 51 patients (24 per cent). In one of these patients, the disease was confirmed as ypT0N1, which was regarded a complete response of the primary tumour area (ypT0) in this study. The pCR rate was five of nine (56 per cent) for squamous cell carcinomas and seven of 42 (17 per cent) for adenocarcinomas. The remaining 39 patients had residual tumour, which was graded as TRG 2 in 17 of 51 patients (33 per cent), TRG 3 in 16 (31 per cent), TRG 4 in four (8 per cent) and TRG 5 in two patients (4 per cent).

Diagnostic performance

ROC curves for the assessment of residual tumour after nCRT are shown in *Fig. 4*. AUCs on T2W-MRI were 0·65 for reader 1, 0·66 for reader 2 and 0·68 for reader 3. After addition of DW-MRI, AUCs were 0·71, 0·70 and 0·70 respectively ($P = 0.441$, $P = 0.611$ and $P = 0.828$). The sensitivity for detection of residual tumour ranged from 90 to 100 per cent on T2W-MRI alone, and from 90 to 97 per cent after addition of DW-MRI. Specificity ranged from 8 to 25 per cent on T2W-MRI alone, and from 42 to 50 per cent after addition of DW-MRI (*Table 2*). The numbers of MRI-positive and -negative tests per TRG stage for response assessment on T2W + DW-MRI are shown in *Table 3*.

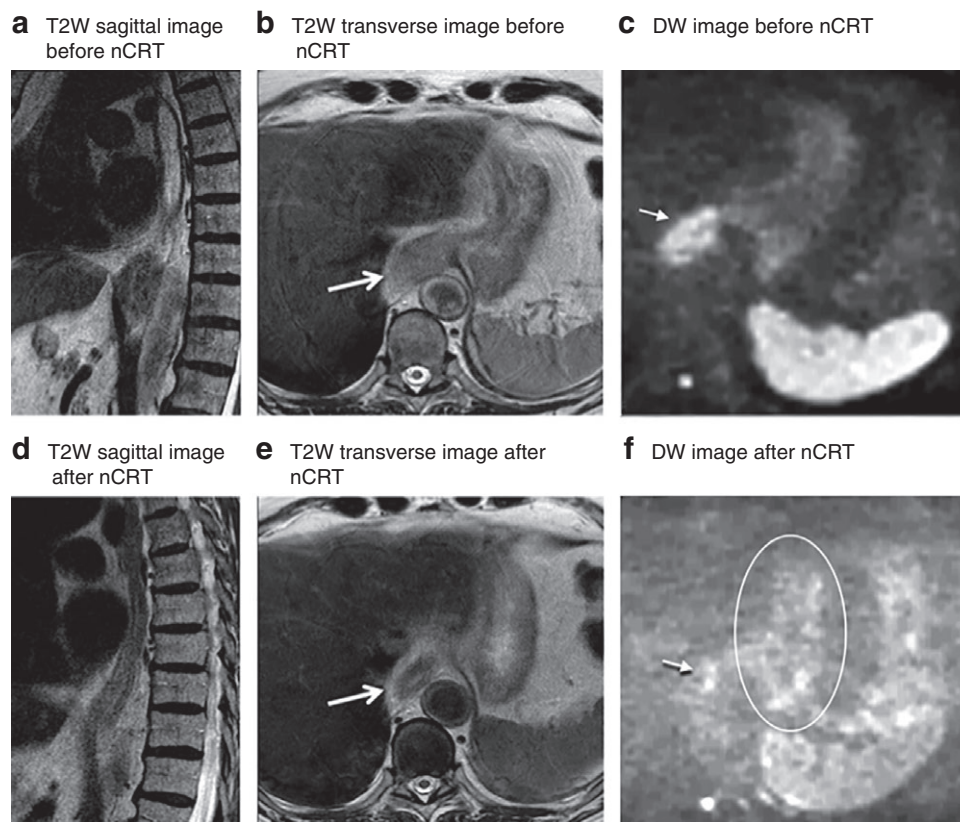### Equivocal (confidence level 3) scores

Readers 1, 2 and 3 assigned 16, 30 and 15 equivocal scores (CLS3) respectively on T2W-MRI, which decreased to 9, 11 and 9 equivocal scores after the addition of DW-MRI.

Table 3 Number of test-positive and test-negative patients according to tumour regression grade for response assessment on T2-weighted combined with diffusion-weighted MRI

	No. of patients					
	Reader 1		Reader 2		Reader 3	
Mandard grade	MRI-positive	MRI-negative	MRI-positive	MRI-negative	MRI-positive	MRI-negative
TRG 1	6	6	7	5	7	5
TRG 2	16	1	16	1	15	2
TRG 3	15	1	16	0	14	2
TRG 4	4	0	4	0	4	0
TRG 5	2	0	2	0	2	0

TRG, tumour regression grade according to Mandard and colleagues[3]; MRI-positive, clinical residual tumour; MRI-negative, clinical complete response.

Fig. 5 MRI of a patient with locally advanced oesophageal cancer located at the gastro-oesophageal junction

a T2W sagittal image before nCRT   **b** T2W transverse image before nCRT   **c** DW image before nCRT

d T2W sagittal image after nCRT   **e** T2W transverse image after nCRT   **f** DW image after nCRT

Images from an 80-year-old man with a cT3 N0 squamous cell carcinoma located at the gastro-oesophageal junction. Histopathology after oesophagectomy showed residual tumour (tumour regression grade 2, ypT1a N0). **a–c** T2-weighted (T2W) sagittal (**a**) and transverse (**b**) images before neoadjuvant chemoradiotherapy (nCRT) show a thick hyperintense wall, accompanied by a hyperintense signal on diffusion-weighted (DW) imaging (**c**). **d–f** After nCRT, the T2W images (**d,e**) show shrinkage of the wall with a mixed hyperintense and hypointense signal, which was assigned a confidence level score of 3 by all readers. The DW image (**f**) shows spots of hyperintense signal in the primary tumour area (arrow), which is suspicious for residual tumour and was therefore assigned a confidence level score of 4 by all readers. The area within the circle indicates normal stomach wall, which also shows small hyperintense areas on DW imaging. Arrows indicate tumour location.

Fig. 5 shows an example of a tumour for which all readers assigned an equivocal score on T2W-MRI, whereas a correct diagnosis of residual tumour (CLS4 for all 3 readers) was made after addition of DW-MRI.

Interobserver agreement

Interobserver agreement was fair to moderate on T2W-MRI alone (quadratic weighted $\kappa = 0.24$, 0.55 and 0.41), and increased to moderate to good on T2W + DW-MRI (quadratic weighted $\kappa = 0.55$, 0.71 and 0.61).

Discussion

This study has shown that preoperative response assessment after nCRT for oesophageal cancer performed visually on (DW-)MRI has promising overall diagnostic performance, with AUCs in the range $0.65-0.71$. The sensitivity of DW-MRI for detection of residual tumour was high (over 90 per cent), indicating that the chance of missing residual tumour was small. Addition of images obtained by functional DW-MRI to the anatomical T2W-MRI protocol did not influence the overall diagnostic performance to a great extent, but had a positive impact on the specificity and NPV for most readers. Moreover, addition of DW sequences led to improved interobserver agreement and a reduction in the number of equivocal scores, indicating increased confidence of the readers. MRI showed promising visualization of the primary oesophageal tumour bed after nCRT in oesophageal cancer and could thereby improve current response assessment strategies. The main

drawback was the poor specificity of MRI in this unimodal approach, which in clinical practice would result in over-staging of complete responders as having residual tumour and, consequently, overtreatment. Therefore, exploration of response assessment including MRI, but also other diagnostic modalities, after nCRT for locally advanced oesophageal cancer is warranted.

The present study evaluated oesophageal MRI for the assessment of complete response of the primary tumour by visual interpretation of morphology on T2W-MRI and restrictive signals on DW-MRI. Previous studies[26,27,29] on this subject did not perform visual assessment, but focused on quantitative DW-MRI. These studies found that an increase in the apparent diffusion coefficient (ADC, a quantitative measure of the magnitude of diffusion) dur-ing nCRT, compared with before nCRT, is a predictor of response. Furthermore, an increase in ADC after nCRT compared with the baseline value seemed to be predictive of gross tumour response, defined as TRG 1–2[28,29] or TRG 1–3[25]. However, the results reported for the pre-operative selection of complete response (TRG 1 only) using ADC values were poor[26,29]. In contrast, in the present study, preoperative visual response assessment on DW-MRI after nCRT had high sensitivity for the detection of residual tumour. Moreover, the cut-off was predefined and can therefore be used prospectively, whereas in the aforementioned studies exploring ADC values, the optimal cut-offs were defined retrospectively which limits their use.

A recent study[11] of clinical assessment with endoscopy/EUS, in which bite-on-bite biopsies and fine-needle aspirates were obtained after nCRT, yielded a specificity of 72 per cent for detection of residual tumour, which is higher than the specificity in the present study. However, the reported sensitivity of 77 per cent was lower than values of over 90 per cent in the present study. Combined with clinical examination and endoscopy, (DW-)MRI has led to the safe selection of patients with rectal tumours for a watch-and-wait policy after nCRT[35]. Combining (DW-)MRI and endoscopy/EUS will poten-tially result in accurate assessment of pCR after nCRT for oesophageal cancer without missing residual disease.

The specificity for detection of residual tumour improved from 8–25 to 42–50 per cent after adding DW-MRI in the present study. This specificity is, however, still low. One potential explanation for the overstaging of a pCR as residual tumour is the occurrence of small punctate foci of hyperintensity at the former tumour bed on images obtained with b = 800 DW-MRI (implying restricted diffusion, which raises the suspicion of tumour). These false-positive foci were observed in patients with a tumour of the gastro-oesophageal junction and may

be explained by the fact that the normal stomach wall also shows small hyperintensities on DW-MRI, or by the presence of radiation-induced inflammation. Prolonging the interval between the end of radiotherapy and MRI may result in resolution of inflammation. Furthermore, prolonging the interval between radiation and surgery may lead to an increase in pCR rates. A recent analysis in oesophageal cancer[36] showed that a longer interval between nCRT and surgery increased pCR rates, without increasing the frequency of postoperative complications.

This study had a relatively large sample size compared with previous response studies in oesophageal cancer; how-ever, validation in a larger cohort is required. This will also allow subgroup analyses of squamous cell carcinoma and adenocarcinoma. Another potential limitation is that ADC maps were not included in the response evalua-tion, although the readers could always refer to the T2W images to rule out, for example, shine-through effects caused by fluid in the oesophageal lumen. Furthermore, lymph node response was not assessed for two reasons. The differentiation between benign and malignant lymph nodes on oesophageal T2W-MRI remains challenging as non-enlarged nodes may harbour malignant cells, whereas reactive (benign) nodes may be enlarged[37,38]. DW-MRI can detect lymph nodes, but all lymph nodes have a high signal on DW images. In patients with T0 N1 rectal cancer, MRI showed poor performance for detection of lymphadenopathy[39]. Second, the field of view (FOV) of MRI in this study focused on the primary tumour and did not comprise the complete craniocaudal perioesophageal area owing to imaging time restrictions. Hence, lymph nodes outside this FOV could not be assessed. There-fore, this study focused on tumour detection at the pri-mary tumour bed only (TRG 1, ypT0). Other response assessment tools are needed for the detection of lymph node metastases after nCRT, such as EUS.

To overcome the limitations of the present study and further increase specificity without decreasing sensitivity for the preoperative detection of residual tumour in oesophageal cancer, larger studies are needed. The multicentre observational PRIDE (Preoperative Image-guided Identification of Response to Neoadjuvant Chemoradiotherapy in Esophageal Cancer) study[40] was initiated to explore the combination of multiple diagnostic modalities in assessing the response of the primary tumour and lymph nodes to chemoradiotherapy. This study aims to develop an optimal multimodal response prediction model focusing on clinical (endoscopy and EUS) and radiological (MRI and FDG-PET/CT) assessment combined with patient-specific parameters (such as circulating tumour DNA) for oesophageal cancer.

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Supporting information

Additional supporting information can be found online in the Supporting Information section at the end of the article.