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Research Article

Diffusion-weighted imaging to predict longer-term response in Crohn's disease patients commencing biological therapy: results from the MOTILITY trial

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Abstract

Objectives: Predicting longer-term response to biological therapy for small bowel Crohn's disease (SBCD) is an unmet clinical need. Diffusion-weighted magnetic resonance (MR) imaging (DWI) may indicate disease activity, but its predictive ability, if any, is unknown. We investigated the prognostic value of DWI for 1 year response or remission (RoR) in SBCD patients commencing biologic therapy, including incremental value over C-reactive protein (CRP) and faecal calprotectin (FC).

Methods: A subset of participants in a prospective, multicentre study investigating the predictive ability of motility MRI for 1-year RoR in patients starting biologic therapy for active SBCD, underwent additional DWI at baseline and post-induction (12-30 weeks). CRP and FC were collected in a subgroup. RoR at 1 year was evaluated using clinical and morphological MR enterography (MRE) parameters. We calculated sensitivity and specificity to predict RoR and quality of life (QoL) at 1 year, comparing apparent diffusion coefficient (ADC) value, Clermont score, and CRP using multivariable logistic regression.

Results: A total of 25 participants were included (mean 36.9 years, 32% female). ADC changes and Clermont score had poor sensitivity (30.0% [95% CI, 6.7-65.2] and 40.0% [95% CI, 12.2-73.8], respectively) and poor-to-modest specificity (50.0 [95% CI, 27.2-72.8] and 65.0% [95% CI, 40.8-84.6]) for RoR. None of Clermont score, CRP, or FC predicted QoL.

Conclusions: DWI has inadequate sensitivity and specificity for RoR at 1 year. There is no significant incremental prognostic value of DWI over CRP and FC to predict RoR and/or QoL at 1 year.

Advances in knowledge: Early post-induction DWI has no prognostic value for RoR at 1 year.

Keywords: Crohn's disease; diffusion magnetic resonance imaging; prognosis; biological therapy; quality of life.

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Introduction

An increasing number of biological drugs have revolutionized management of small bowel Crohn's disease (SBCD). Current standard of care is to suppress inflammation, aiming to heal bowel, which prevents cumulative, irreversible bowel damage and reduces hospitalization and surgery.[1] Despite widespread use of biologics for SBCD, only 36% to 40% of treated patients achieve remission at 1 year. Moreover, this is unpredictable; we cannot tell in advance which patients are most likely to exhibit RoR, and vice versa.[2]

Cross-sectional imaging, notably magnetic resonance enterography (MRE) and intestinal ultrasound, plays a central role for management of Crohn's disease, staging disease, assessing activity, and monitoring therapeutic response.[3] Although there are several validated morphological MRE parameters of disease activity, including bowel wall thickening and mural T2 signal intensity, these change relatively slowly in response to treatment, and there is limited evidence they can predict longer-term response.[4-7] Functional MRE parameters are an alternative to purely structural assessments. These aim to provide objective markers of disease activity and treatment response and may also have prognostic value. Diffusion-weighted imaging (DWI) is one such functional MRE sequence and is included increasingly in routine MRE protocols.

DWI provides information on tissue composition by capturing differential Brownian motion of water molecules within tissues using specific pulse sequences.[8] When this random motion is impeded (eg, by tissue hypercellularity in active inflammation), DWI in that bowel segment increases ("diffusion restriction").[9-11] Apparent diffusion coefficient (ADC) maps are derived from DWI to provide a quantitative metric for this random diffusion of water molecules. The Clermont score is a validated MRE activity score that incorporates the bowel wall ADC value alongside other morphological variables.[10,12] DWI has a reported sensitivity of 80%-100% to distinguish active inflammation from chronic, fibrotic disease, against a variety of reference standards.[13]

We aimed to establish the predictive ability of early DWI changes for longer-term therapeutic response and quality of life (QoL) after commencing biologic therapy for active, non-stricturing SBCD. We hypothesized that early changes in DWI parameters would predict RoR to biological therapy at 1 year, better than clinical predictors alone, including the inflammatory markers C-reactive protein (CRP) and faecal calprotectin (FC).

Methods

This was a pre-specified substudy of the MOTILITY trial (ISRCTN14481560), a prospective multicentre (13 UK hospitals), non-randomized, cohort study of patients aged 16 years or older with active, non-stricturing SBCD, commencing anti-TNFα or anti-IL-12/23 therapy. The primary outcome was the ability of changes in cine motility MRI (mMRI) between baseline and post-induction to predict 1 year RoR. A subset of patients consented to undergo additional DWI as part of MRE protocols and are reported here. The study was ethically approved [BLINDED].

Full trial inclusion and exclusion criteria, assessments, and procedures are reported in a publicly available protocol; [BLINDED]. In summary, patients commencing anti-TNFα or anti-IL-12/23 therapy for active SBCD documented by imaging or endoscopy within 90 days of recruitment underwent MRE and CRP at baseline and post-induction (12-30 weeks). FC was measured in a subset at the 2 time points. RoR at around 1 year (44-78 weeks) was judged, based on a combination of clinical, ileocolonoscopic (if available), and MRE morphological parameters, as detailed below.

MRE protocol and DWI-MRI imaging parameters

MRE was performed using standard MRI platforms (1.5 Tesla or greater) with DWI including a minimum of 600 s/mm^2 for the highest b value acquired. Higher b values were permitted if this was standard local practice. Conventional MRE sequences including single-shot fast spin echo (SSFSE; HASTE or equivalent) with and without fat suppression were acquired in coronal and axial planes. Intravenous contrast medium-enhanced sequences were permitted but not mandatory. Minimum sequence parameters are provided in the Supplementary Information S1.

MRI image retrieval and analysis

Images were uploaded onto a cloud-based viewing platform (Entrolytics, Motilent, United Kingdom) for analysis. Images were interpreted by 5 consultant radiologists with personal experience of >100 MRE studies and using MRE in their routine practice. Radiologists were blinded to all clinical information. They identified the most active segment of small bowel based on standard morphological features, such as bowel wall thickening and T2 signal, and derived the London disease activity index for each time point (baseline, post-induction, and around 1 year, if performed). The London disease activity index was calculated as 1.79 + (1.34 x mural thickness score) + (0.94 x mural T2 signal score).[14] Radiologists also placed an ROI within the bowel wall of the selected diseased segment on the ADC map (derived using a monoexponential model), excluding the bowel lumen and extra-enteric tissues, and recorded the ADC value. Thereafter, the modified Clermont score was calculated as follows: score = 1.646 * bowel thickness -1.321 * ADC + 5.613 * oedema + 8.306 * ulceration + 5.039.[10]

Patient-reported outcome measures

Patients completed the EQ-5D-5L QoL score, as well as 2 disease-specific patient-recorded outcome measures (PROMs): the Crohn's and Ulcerative Colitis Questionnaire 8 (CUCQ-8)[15,16] and IBD-Control 8[17] at baseline, post-induction, and around 1 year.

Definition of RoR

RoR was defined using ileocolonoscopy or MRE. Specifically, if baseline and 1 year ileocolonoscopy was available, change in Simple Endoscopic Score for Crohn's Disease (SES-CD) was used to define RoR. Response was defined as SES-CD reduction of ≥50% from baseline to 1 year. Remission was defined as SES-CD of 0 to 2.[1] If ileocolonoscopy was not performed at both time points, patients underwent a third MRE at around 1 year. RoR was defined using the London disease activity index. Response was defined as a ≥ 50% improvement in London score between baseline and 1 year, and remission was defined as a London score ≤4.1.[14]

Patients were automatically defined as non-responders to biologic therapy if, after their post-induction investigations,

they experienced any of: (1) surgery for small bowel disease; (2) loss of biological efficacy in the opinion of the treating physician; or (3) steroid rescue therapy for active luminal Crohn's disease confirmed by at least 1 objective test documenting active inflammation (including biochemical, imaging, or endoscopic indices).

Outcome measures

The primary outcome was the accuracy of DWI to predict RoR to biologic therapy at around 1 year, assessed using the sensitivity and specificity defined by (a) >10% increase in ADC and (b) >25% reduction in Clermont score, between baseline and weeks 12 to 30. These pre-specified thresholds were based on a previously published prospective multicentre study which found that a > 10% increase in ADC value and ≥25% improvement in Clermont score were predictive of corticosteroid-free remission at 1 year.[18]

Secondary outcomes were: (a) difference in prognostic accuracy and incremental prognostic value of change in ADC value and change in Clermont score between baseline and weeks 12 to 30 to (i) change in CRP and (ii) change in FC, for RoR to biologic therapy at 1 year; and (b), the difference in prognostic accuracy of change in Clermont score to predict improvement in QoL measures (EQ-5D-5L QoL score)[19], CUCQ-8[15,16] and IBD-Control 8[17] at 1 year, compared to (i) change in CRP and (ii) change in FC.

Statistical analysis

The sample size was based on 10 events per variable included in the logistic regression model. A priori, ADC, Clermont score CRP, and calprotectin were pre-identified for inclusion in the model meaning 80 patients (assuming an ROR rate of 50%) would be required. The COVID-19 pandemic prevented many patients from attending protocol-specified procedures, and statistical analysis plan was updated to simply the models to maintain adequate power based on the number of recruits.

Sensitivity and specificity was reported for each diagnostic parameter, ADC, Clermont score, CRP, and FC, with 95% confidence intervals (CIs), and McNemar's tests were used to compare sensitivity and specificity.

Separate multivariable logistic regression models were used to predict RoR to biologic therapy using change from baseline to 12 to 30 weeks in ADC and in Clermont score, in addition to change in CRP and baseline Montreal classification location. Due to a small sample size ($n = 9$), the incremental prognostic value of DWI parameters, in addition to change in FC, could not be assessed using multivariable models. Instead, we used separate univariable analysis to compare the prognostic value of DWI parameters to that of FC for RoR.

Separate univariable analysis was used to compare prognostic value of a change in ADC and in Clermont score to change in FC, in predicting RoR. Multivariable linear regression models were also constructed using the change in the relevant QoL score as the outcome variable, and change in Clermont score or change in CRP as explanatory variables. Models were compared using Akaike information criterion (AIC), with smaller AIC values indicating better model fit.

Statistical analyses were conducted according to a pre-specified statistical analysis plan. Analyses were performed using Stata/MP 18.0 (StataCorp LLC, Texas, USA) and statistical significance assigned at $P < 0.05$.

Results are reported according to TRIPOD (Transparent Reporting of a multivariable prediction model for Individual Prognosis Or Diagnosis) recommendations[20]: See the Supplementary Information S1 for the checklist.

Results

The flow of study participants is detailed in Figure 1. Twenty-five patients from 6 trial centres with active non-stricturing SBCD were eligible. Of those with DWI data, baseline and 12 to 30 weeks CRP was measured in 24 patients and FC in 9 patients. Table 1 details baseline characteristics of included participants.

Overall, 8 (32%) patients achieved RoR around 1 year. One of the 25 was deemed a non-responder based on predefined clinical criteria. No patient underwent both baseline and end-of-trial ileocolonoscopy for response assessment using SES-CD, and so the remaining 24 patients had RoR status defined using the MRE London index.

Accuracy of early changes in ADC and Clermont score for RoR at 1 year

The sensitivity and specificity of ADC and Clermont score at 12 to 30 weeks for RoR is shown in Table 2. Overall, a > 10% increase in ADC had just 37.5% [95% CI, 8.5, 75.5%] sensitivity and 41.2% [95% CI, 18.4, 67.1%] specificity. A > 25% reduction in the Clermont score had 37.5% [95% CI, 8.5, 75.5%] sensitivity and 64.7% [95% CI, 38.3, 85.8%] specificity. There was no significant difference in accuracy between the 2 measures ($P = 1.00$ and 0.13 for sensitivity and specificity, respectively).

Exploratory analyses

When comparing ADC and Clermont score to CRP where this was available ($n = 24$), the difference in sensitivity and specificity for RoR at 1 year was not statistically significant (Supplementary Information S1).

Incremental prognostic value of an early change in ADC value and Clermont score in addition to change in CRP for RoR at 1 year

Table 3 shows the incremental prognostic value of an early change in ADC value (between baseline and weeks 12 to 30) and of an early change in Clermont score as part of multivariable logistic regression models, to predict RoR at 1 year, in addition to early changes in CRP ($n = 24$). There was no significant incremental prognostic ability of ADC or Clermont score.

Prognostic value of an early change in ADC value and Clermont score versus changes in FC for RoR at 1 year

Table 4 shows that there was no prognostic value of either an early change in ADC value or Clermont score over FC ($n = 9$) for RoR at 1 year.

Prognostic accuracy of early changes in Clermont score versus changes in CRP and in FC on QoL outcomes at 1 year

Of the 25 patients, the total completing each of the EQ-5D-5L, CUCQ-8, and IBD-Control 8 QoL measures at baseline and at 1 year, in addition to having early CRP and FC

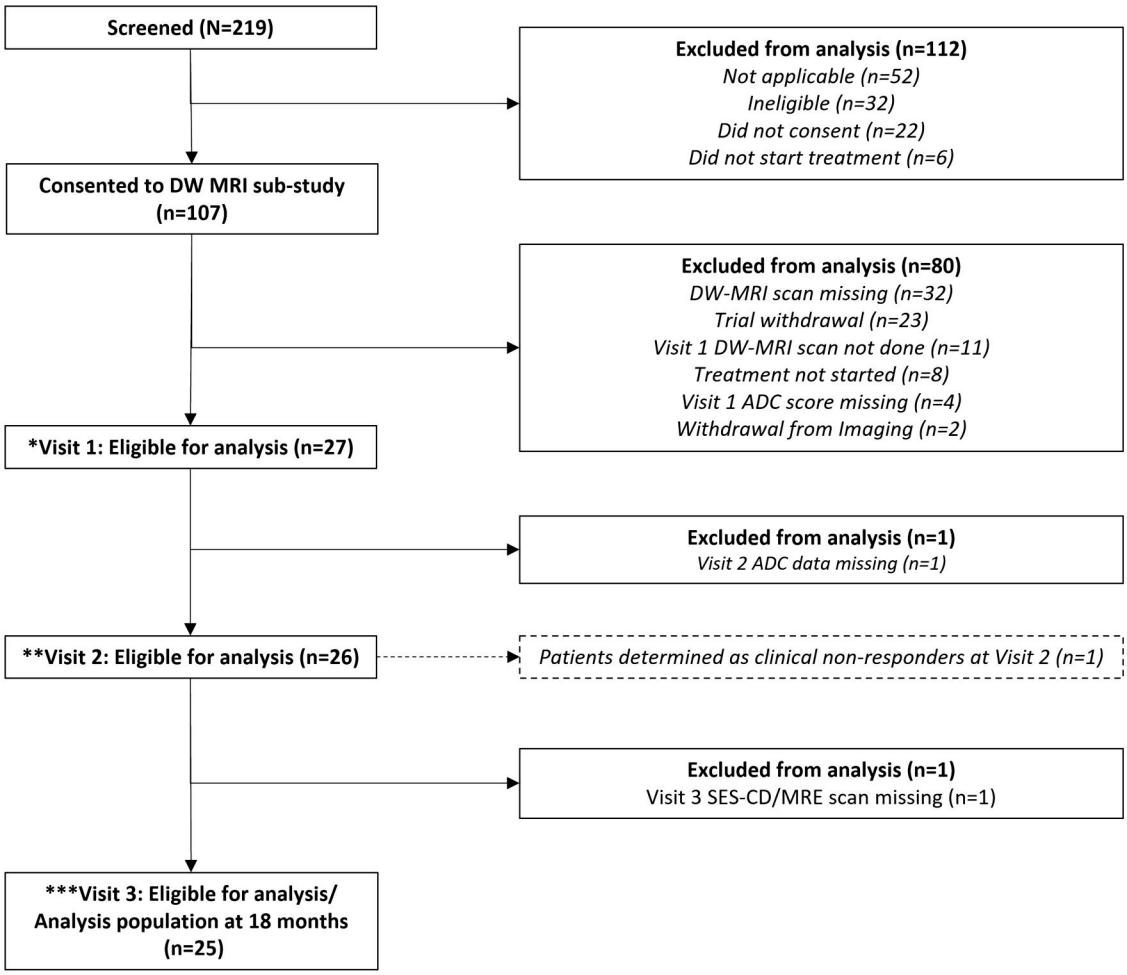

Figure 1. CONSORT diagram of the flow of study participants. *Visit 1 eligible: includes baseline SES-CD score or baseline MRE score, baseline ADC/Clermont score. **Visit 2 eligible: includes visit 2 ADC/Clermont score. ***Visit 3 eligible: includes visit 3 SES-CD score or visit 3 MRE score. ~Other reason (*n*=32): 32 patient's consent were later ineligible due to a substantial amendment and consent was no longer appropriate. Abbreviations: ADC = apparent diffusion co-efficient; DWI = diffusion-weighted magnetic resonance imaging; MRE = magnetic resonance enterography; SES-CD = Simple Endoscopic Score for Crohn's Disease.

measurements, are presented in Table 5. There was no significant prognostic value of early changes in Clermont score, CRP, or FC to predict improvement in QoL measures between baseline and 1 year. Tables 5 part (ii) show the prognostic accuracy and fit of the multivariable logistic regression models.

Discussion

In this multicentre, prospective cohort study of 25 active SBCD patients, early (post-induction) changes in DWI, namely ADC value and Clermont score, had poor sensitivity and specificity for predicting biologic therapeutic RoR at 1 year. Additionally, we found that changes in DWI parameters, CRP, or FC were not able to predict RoR reliably, or QoL improvement at 1 year. Incomplete recruitment and losses to follow up limited study power, and so our results should be treated as exploratory.

There is good evidence that DWI and associated scoring systems identify active disease in SBCD, when tested against a range of reference standards, including endoscopic and histopathological.[13,21,22] DWI is non-inferior to intravenous contrast-enhanced MRE sequences for detecting active disease and also increases diagnostic confidence when combined with intravenous contrast protocols.[23,24] A meta-analysis of 21 studies reported a strong negative correlation between ADC value and endoscopically confirmed small bowel inflammation (pooled coefficient of −0.8).[22] Furthermore, when used in conjunction with conventional morphological sequences, DWI may have utility in differentiating between active and chronic fibrotic SBCD, and therefore could be more responsive to treatment effects of biologic therapy and a better candidate predictor of treatment response.[25] Of note, there is some overlap between inflammation and fibrosis on DWI, limiting specificity.[13]

In contrast to detecting active SBCD, little indexed literature supports a potential prognostic role for DWI, including whether early change in DWI can indicate subsequent RoR. DWI parameters could potentially be employed at different time points if suitably prognostic: (i) pre-treatment to predict induction response or (ii) to predict longer-term response. We explored the latter.

Regarding whether DWI can predict induction response, Buisson et al.[26] proposed a mean ADC absolute cut off baseline value of <1.96 as predictive of remission at 12 weeks

(20/40 patients, AUC = 0.703 [0.535-0.872]). This was also maintained during multivariable analysis (OR = 4.87, 95% CI, 1.04-22.64) alongside the global MaRIA score >42.5.

Table 1. Baseline characteristics of the 25 study participants.

	DWI-MRI analysis population $N = 25$	
	Mean	**(sd)**
Age (years)	36.9	(11.7)
SES-CD score	3.0	(0.0)
MRE score	6.4	(1.9)
C-reactive protein	12.1	(13.2)
EQ-5D-5L	0.8	(0.2)
CUCQ-8	34.5	(22.2)
IBD-Control-8	9.1	(3.0)
Faecal calprotectin (μg/g)	225.1	(280.4)
	n	(%)
Gender		
Female	8	(32.0)
Male	17	(68.0)
Smoking status		
Non-smoker	19	(76.0)
Current smoker	2	(8.0)
Ex-smoker	2	(8.0)
Missing	2	(8.0)
Previous bowel surgery		
No surgery	17	(68.0)
Single surgery	3	(12.0)
Multiple surgeries	5	(20.0)
History of biological therapy		
No	21	(84.0)
Yes	4	(16.0)
Age at diagnosis (years)		
A1 (≤ 16)	2	(8.0)
A2 (17-40)	20	(80.0)
A3 (> 40)	3	(12.0)
Location		
L1 (ileal)	12	(48.0)
L2 (colonic)	0	(0)
L3 (ileocolonic)	13	(52.0)
Behaviour		
B1 (non-stricturing, non-penetration)	18	(72.0)
B2 (stricturing)	5	(20.0)
B3 (penetrating)	2	(8.0)
Perianal disease modifier (*P*)		
No	23	(92.0)
Yes	2	(8.0)

Abbreviations: CUCQ-8 = Crohn's and Ulcerative Colitis Questionnaire 8; MRE = magnetic resonance enterography; sd = standard deviation; SES-CD = Simple Endoscopic Score for Crohn's Disease.

However, this has not been validated or explored over longer time frames.

Exploratory studies have investigated the longer-term therapeutic prognostic value of DWI parameters but are predominantly single centre, retrospective studies. In a study of 24 patients, pretreatment Clermont score (but not ADC value) had moderate predictive value for endoscopic mucosal healing, albeit with varying intervals between baseline and post-treatment MRE, and varying intervals between post-treatment MRE and endoscopic assessment.[27] Another study of 70 patients demonstrated that the mean ADC value could stratify patients who would benefit from conservative medical therapy at up to 1 year. An optimal threshold of $>1.081 \times 10^{-3}$ mm^2 s^{-1} was suggested (negative predictive value of 90.2%).[28] In a prospective, 4-centre study addressing longer-term therapeutic response prediction using DWI, Messadeg et al. employed early MRE at 12 weeks in 46 ileocolonic CD patients commencing anti-TNFα therapy. They found that a > 10% increase in ADC value and ≥25% improvement in Clermont score predicted corticosteroid-free remission at 1 year (OR: 3.6 [95% CI, 1.6, 13.6], $P = 0.049$, and OR: 7.7 [95% CI, 1.7, 34.0], $P < 0.001$ respectively). A ≥ 25% decrease in the Clermont score had sensitivity of 65.4% (95% CI, 44.3, 82.8%) and specificity of 80.0% (95% CI, 61.4, 92.3%) for remission, versus the 37.5% (95% CI, 8.5, 75.5%) and 64.7% (95% CI, 38.3, 85.8%) that we found here.[18] This discrepancy could be due to our adopting of different, potentially more stringent, definitions of response and remission, a greater number of centres, and a longer interval between baseline and second MRI.

We assessed patients with active, non-stricturing disease. Some data from a study of 21 patients suggest that ADC may predict treatment failure at 1 year in stricturing CD.[29] The prognostic value of DWI in mixed phenotype active and stricturing SBCD remains unevaluated.

Our study has several limitations. The main limitation is that the number of patients ultimately analysed was smaller than planned, despite 107 patients originally consenting to this substudy. This was due to an elevated dropout rate due to the COVID-19 pandemic, for example, biologic treatment not started, non-completion of follow up at 3 time points, and varied QoL completion rates. However, our RoR rate of 32% was comparable to that reported in larger cohorts; 36%-40%.[2] Instead of developing multivariable logistic regression models as was originally intended, we used separate models to compare the predictive ability of each individual parameter. DWI protocols varied between centres (we only

Table 2. Sensitivity and specificity of (i) >10% increase in ADC score and (ii) >25% reduction in Clermont score between baseline and weeks 12-30 to predict response or remission (RoR) at 1 year.

	ADC				
12 months	**Response**	**No response**	**Total**	**Sensitivity (%) (95% CI)**	**Specificity (%) (95% CI)**
Response or remission	3	5	8	37.5 (8.5, 75.5)	41.2 (18.4, 67.1)
No response	10	7	17		
Total	13	12	25		
	Clermont score				
Response or remission	3	5	8	37.5 (8.5, 75.5)	64.7 (38.3, 85.8)
No response	6	11	17		
Total	9	16	25		
McNemar's test *P*-value				1.00	0.13

Abbreviation: ADC = apparent diffusion co-efficient.

Table 3. Incremental prognostic value of multivariable logistic regression models including an early change in ADC value (model 2) or in Clermont score (model 3) versus a binary model including an early change in CRP and Montreal classification alone.

	Factor variable	Odds ratio (95% CI)	*P*-value	AIC[b]
Univariable analysis	CRP	0.97 (0.91, 1.05)	0.48	34.0
	Location			31.4
	L1 (ileal)	Reference		
	L3 (ileocolonic)	5.00 (0.75, 33.2)	0.10	
	Age	1.00 (0.93, 1.07)	0.95	34.5
	ADC	1.00 (0.99, 1.00)	0.86	34.5
	Clermont score	1.00 (0.99, 1.00)	0.86	34.5
Multivariable model 1[a]	CRP	0.96 (0.89 , 1.03)	0.32	32.3
	Location			
	L1 (ileal)	Reference		
	L3 (ileocolonic)	6.15 (0.84, 45.14)	0.07	
Multivariable model 2[a]	**ADC**	**0.99 (0.99, 1.00)**	**0.44**	33.7
	CRP	0.96 (0.88, 1.03)	0.28	
	Location			
	L1 (ileal)	Reference		
	L3 (ileocolonic)	7.69 (0.92-64.11)	0.06	
Multivariable model 3[a]	**Clermont score**	**1 (0.99, 1.00)**	**0.44**	33.7
	CRP	0.96 (0.88, 1.03)	0.28	
	Location			
	L1 (ileal)	Reference		
	L3 (ileocolonic)	7.65 (0.92, 63.53)	0.05	

[a]Adjusted model using Montreal classification location L3 (ileocolonic).
[b]AIC (Akaike information criterion)—smaller values indicate better model fit.
Abbreviations: ADC = apparent diffusion co-efficient; CRP = C-reactive protein.

Table 4. Prognostic value based on binary logistic regression analysis of an early change in ADC value and Clermont score versus an early change in FC.

	N	Odds ratio (95% CI)[a]	*P*-value	AIC[b]
ADC	9	1 (0.99-1.00)	0.19	12.9
Clermont score	9	1 (0.99-1.00)	0.19	12.8
FC	9	1 (0.98-1.00)	0.32	13.3

[a]Unadjusted odds ratios obtained from separate univariable analysis.
[b]AIC (Akaike information criterion)—smaller values indicate better model fit.
Abbreviations: ADC = apparent diffusion co-efficient; FC = faecal calprotectin.

stipulated that the long b value acquisition be at least 600 s/mm2), and it is possible that different scanners were used at different time points in the same patient. However, we adopted this stance so that our data would be more reflective of real-world clinical practice. We did not measure interobserver variation, but all DWI interpretation was performed by experienced consultant MRE reporters, and agreement has previously been reported to be excellent.[18,30]

In summary, we found no prognostic value for early DWI changes after biological therapy, either alone or in combination with CRP for therapeutic RoR at 1 year. DWI parameters were also unable to predict improvements in QoL.

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Table 5. Difference in prognostic accuracy and multivariable model fit between early changes (baseline to weeks 12-30) in the Clermont score versus early changes in (i) CRP and (ii) FC to predict improvements from baseline to 1 year in each quality of life measure.

		Clermont score			CRP		
Quality of life measure	*N*	Clermont score (95% CI)	*P*-value	AIC[a]	CRP (95% CI)	*P*-value	AIC[a]
EQ-5D-5L[b]	17	−0.0007 (−0.003, 0.001)	0.46	−16.9	−0.004 (−0.016, 0.008)	0.52	−16.8
CUCQ-8[b]	22	0.034 (−0.16, 0.22)	0.71	190.1	−0.29 (−1.47, 0.88)	0.61	190.0
IBD-Control 8[b]	16	−0.0178 (−0.06, 0.019)	0.32	83.6	0.03 (−0.25, 0.31)	0.82	84.7
		Clermont score			FC		
Quality of life measure	*N*	Clermont score (95% CI)	*P*-value	AIC[a]	FC (95% CI)	*P*-value	AIC[a]
EQ-5D-5L[b]	10	0.0001 (−0.0004, 0.0006)	0.68	−31.9	7.62 (−0.0003, 0.0003)	0.95	−7.9
CUCQ-8[b]	10	0.001 (−0.02, 0.02)	0.92	84.1	0.00002 (−0.03, 0.03)	0.99	84.1
IBD-Control 8[b]	8	−0.001 (−0.007, 0.005)	0.68	45.4	−0.003 (−0.01, 0.004)	0.29	44.0

EQ-5D-5L quality of life score, Crohn's and Ulcerative Colitis Questionnaire 8 (CUCQ-8), and IBD-Control 8.
[a]AIC (Akaike information criterion)—smaller values indicate better model fit.
[b]Unadjusted model.
Abbreviation: CRP = C-reactive protein.

Supplementary material

Supplementary material is available at *BJR* online.

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Conflicts of interest

A.M. holds shares in Motilent (an image analysis technology company). S.A.T. is a consultant to AstraZeneca, has research grant support from Takeda and shareholder in Motilent. G.B. is an employee of and shareholder in Motilent, is a consultant for Alimentiv, and owns patent for P295276.US.02: system to characterize topology and morphology of fistulae from medical imaging data. H.L. receives speaking honoraria from Takeda Pharmaceuticals. D.T. has research funding from GSK for an oncology trial unrelated to the current work.

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