

Diffusion-weighted magnetic resonance imaging as an early predictive marker of chemoradiotherapy response in squamous cell carcinoma of the anus: an individual patient data meta-analysis

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INTRODUCTION

Patients with squamous cell carcinoma of the anus (SCCA) are at risk of locoregional recurrence after chemoradiotherapy (CRT). An early prognostic marker of treatment response would enable timely individualisation of treatment for patients with SCCA. Diffusion-weighted (DW) magnetic resonance imaging (MRI) features, such as apparent diffusion coefficient (ADC), may be prognostic.

AIMS

Using an individual patient data meta-analysis, we aimed to investigate in a larger cohort whether ADC based histogram parameters from paired DW-MRI at baseline and during CRT correlate with relapse in patients with SCCA.

MATERIAL AND METHODS

We included 3 prospective trials, run between 2013 to 2017, in patients receiving radical CRT for SCCA who had paired DW-MRI at baseline and during week 2 of treatment (1-3). Individual patient and treatment data, tumour and involved nodes >2 cm volumes, and ADC parameters (ADCmax, ADCmean, ADCmin, skewness, kurtosis, and standard deviation) were combined into one dataset (one-stage meta-analysis). The association between ADC parameters with relapse was analyzed using logistic regression. Deriving the area under the curve (AUC), each parameters ability to predict relapse was assessed. We investigated the effect of a change <20% in ADCmean between the two scans.

RESULTS

Table 1: Patient and tumour characteristics

	UK ART (n=23)	Norway (n=39)	Australia (n=20)	Combined (n=82)
Age (years)	53.2	59.0	58.5	59.0
Sex				
Male	8.7%	25.6%	15.0%	18.3%
Female	91.3%	74.4%	85.0%	81.7%
T stage				
T1	-	2.6%	5.0%	2.4%
T2	60.9%	51.3%	50.0%	53.7%
T3	13.0%	15.4%	25.0%	17.1%
T4	26.1%	30.8%	20.0%	26.8%
N stage				
N0	47.8%	38.5%	30.0%	39.0%
N1-N3	52.2%	61.5%	70.0%	61.0%
M stage				
M0	100%	97.4%	100%	98.8%
M1	-	2.6%	-	1.2%
GTV Volume (cm3)				
Median	13.6	14.6	no data	14.1

From 82 patients, 90 targets (primary tumours and lymph nodes >2cm) were analysed in the meta-analysis.

Among all patients, 13.4% (n=11) relapsed locally and 19.5% (n=16) had any relapse.

Patients with a change in ADCmean <20% between scans had a higher local relapse rate (18.0%) than patients with change in ADCmean ≥20% (9.3%).

No ADC based histogram parameter at baseline, during treatment week two or as percentage change between scans was associated with local or any relapse (p>0.05 for all).

Figure 1: Waterfall plot percentage change in ADCmean for local relapse

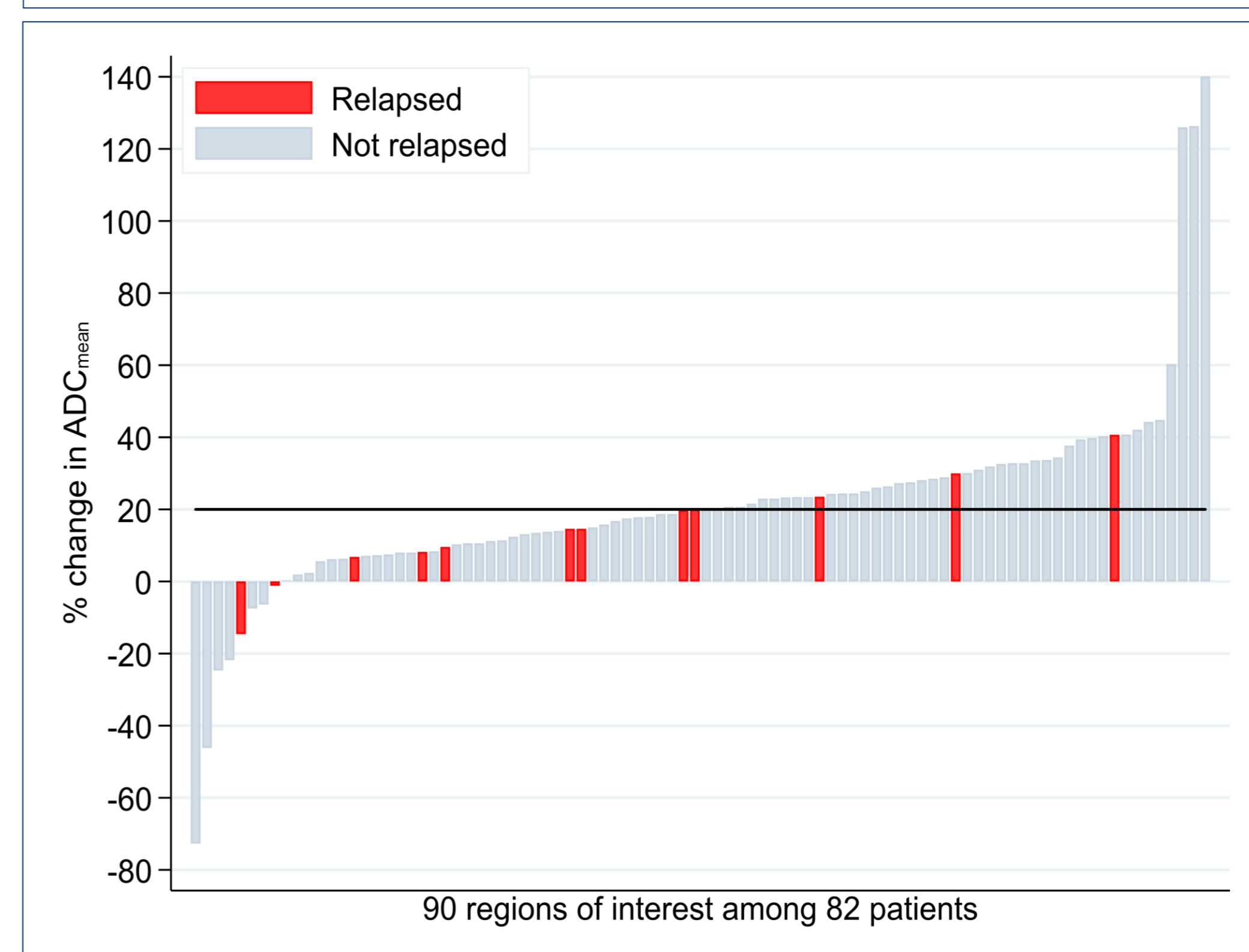


Table 3: Local relapse

ADC parameter	Baseline		Week 2 of CRT		Percentage change	
	OR (95% CI)	AUC (95% CI)	OR (95% CI)	AUC (95% CI)	OR (95% CI)	AUC (95% CI)
Mean	1.00 (0.99, 1.00)	0.603 (0.440, 0.765)	1.00 (0.99, 1.00)	0.702 (0.553, 0.851)	0.99 (0.96, 1.01)	0.591 (0.402, 0.779)
SD	1.00 (0.99, 1.01)	0.562 (0.386, 0.737)	1.00 (0.99, 1.01)	0.570 (0.412, 0.728)	1.00 (0.97, 1.02)	0.574 (0.413, 0.735)
Min	1.00 (1.00, 1.00)	0.604 (0.444, 0.763)	1.00 (1.00, 1.00)	0.690 (0.493, 0.887)	1.00 (1.00, 1.00)	0.532 (0.264, 0.799)
Max	1.00 (1.00, 1.00)	0.612 (0.417, 0.807)	1.00 (1.00, 1.00)	0.629 (0.442, 0.815)	0.99 (0.95, 1.03)	0.571 (0.390, 0.751)
Skewness	0.42 (0.16, 1.09)	0.679 (0.512, 0.846)	0.63 (0.25, 1.61)	0.592 (0.404, 0.781)	1.00 (1.00, 1.00)	0.589 (0.412, 0.766)
Kurtosis	0.77 (0.48, 1.24)	0.579 (0.417, 0.740)	1.08 (0.74, 1.56)	0.564 (0.404, 0.725)	1.00 (1.00, 1.01)	0.677 (0.507, 0.847)

Table 4: Any relapse

ADC parameter	Baseline		Week 2 of CRT		Percentage change	
	OR (95% CI)	AUC (95% CI)	OR (95% CI)	AUC (95% CI)	OR (95% CI)	AUC (95% CI)
Mean	1.00 (0.99, 1.00)	0.563 (0.420, 0.705)	1.00 (1.00, 1.00)	0.655 (0.527, 0.784)	1.00 (0.98, 1.02)	0.495 (0.333, 0.656)
SD	1.00 (1.00, 1.01)	0.527 (0.356, 0.699)	1.00 (1.00, 1.01)	0.524 (0.351, 0.698)	1.00 (0.98, 1.01)	0.511 (0.347, 0.675)
Min	1.00 (1.00, 1.00)	0.590 (0.431, 0.750)	1.00 (1.00, 1.00)	0.595 (0.450, 0.740)	1.00 (1.00, 1.00)	0.549 (0.370, 0.728)
Max	1.00 (1.00, 1.00)	0.554 (0.408, 0.699)	1.00 (1.00, 1.00)	0.526 (0.356, 0.697)	1.02 (0.98, 1.06)	0.601 (0.459, 0.744)
Skewness	0.49 (0.22, 1.08)	0.652 (0.508, 0.796)	0.80 (0.37, 1.73)	0.550 (0.394, 0.705)	1.00 (1.00, 1.00)	0.562 (0.418, 0.705)
Kurtosis	0.74 (0.50, 1.10)	0.613 (0.460, 0.765)	1.01 (0.73, 1.40)	0.541 (0.394, 0.689)	1.00 (1.00, 1.01)	0.546 (0.398, 0.694)

CONCLUSION

No definite parameters from paired DW-MRI at baseline or during week two of CRT were identified as useful biomarker in SCCA in this meta-analysis, however there was a trend towards higher local relapse rate in those with a change in ADCmean <20%. Further research should investigate different MRI sequences and parameters, different imaging modalities and the combination of multiple radiological and translational biomarkers to optimize individualized treatment.

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