The impact of mismatch repair status on accuracy of clinical staging in upfront resected stage II/III rectal cancer in the Netherlands

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1 Background: Stage II/III rectal cancer

- Treatment decisions of rectal cancer depend on imaging-based clinical staging. Accurate staging is therefore of high importance.
- Colorectal tumours are often biologically stratified by mismatch repair status. ~3% of rectal cancer patients have deficient mismatch repair (dMMR) tumours.
- Accuracy levels in T- and N-staging have shown to be high, but the influence of MMR status has not yet been clarified in rectal cancer.
- dMMR tumours have increased immune infiltration compared to proficient mismatch repair (pMMR) tumours, which leads to overstaging in colon cancer.

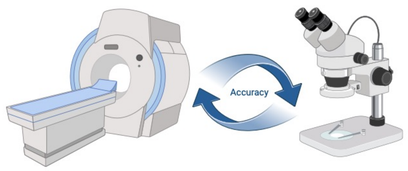
We aim to assess the real-world accuracy of clinical staging compared to pathological staging in dMMR versus pMMR rectal cancer patients.

2 Method: Real world data analysis

Patients with clinical stage II/III rectal cancer, diagnosed between 2015 and 2022 with known MMR status were selected from the Netherlands Cancer Registry.

Eligible patients were treated with upfront surgery (maximum interval of 3 months after diagnosis) (62.4%) or with short course radiotherapy (SCRT) (37.6%) followed directly by surgery.

Accuracy of clinical staging compared to pathological staging was analysed between dMMR and pMMR tumours using a Chi-square or Fisher's exact test.



3 Patient and tumour characteristics according to MMR status

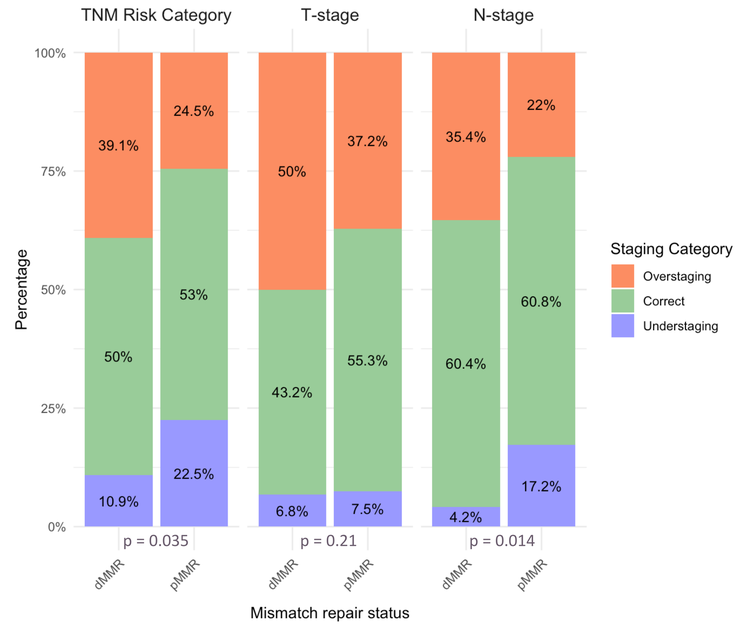
Although clinical TNM risk category is comparable, pathological TNM risk category is significantly lower in dMMR compared to pMMR patients. The number of patients treated with upfront surgery or SCRT was comparable between dMMR and pMMR patients (p=0.93).

	dMMR patients (N=50)	pMMR patients (N=2872)	P-value
Age			
Median (IQR)	59.5 (13.3)	63.0 (12.0)	0.06
Sex			
Male	24 (48.0%)	1814 (63.2%)	0.04
Female	26 (52.0%)	1058 (36.8%)	
Differentiation			
Good	2 (4.4%)	28 (1.0%)	0.007
Moderate	38 (84.4%)	2576 (93.2%)	
Poor	5 (11.1%)	161 (5.8%)	
Missing	5	107	
Histology			
Adenocarcinoma	40 (80.0%)	2747 (95.6%)	<0.001
Mucinous	7 (14.0%)	116 (4.0%)	
Signet ring cell	2 (4.0%)	8 (0.3%)	
Other	1 (2.0%)	1 (0.1%)	
Distance from anal verge (cm)			
0-5 cm	16 (36.4%)	1027 (37.1%)	0.017
5-10 cm	17 (38.6%)	1112 (40.2%)	
10-15 cm	11 (25.0%)	518 (18.7%)	
>15 cm	0 (0%)	111 (4.0%)	
Missing	6	104	
Clinical TNM risk category			
Low (cT1-3bN0/Nx)	20 (43.5%)	1287 (46.6%)	0.99
Intermediate (cT3c-dN0, cN1)	22 (47.8%)	1270 (46.0%)	
High (cT4, cN2)	4 (8.7%)	203 (7.4%)	
Unknown (cTxN0, cTxNx)	4	112	
Pathological TNM risk category			
Low (pT1-3bN0/Nx)	38 (76.0%)	1550 (54.0%)	0.02
Intermediate (pT3c-dN0, pN1)	5 (10.0%)	895 (31.2%)	
High (pT4, pN2)	7 (14.0%)	426 (14.8%)	
Unknown (pTxN0)	0	1	

CONCLUSION

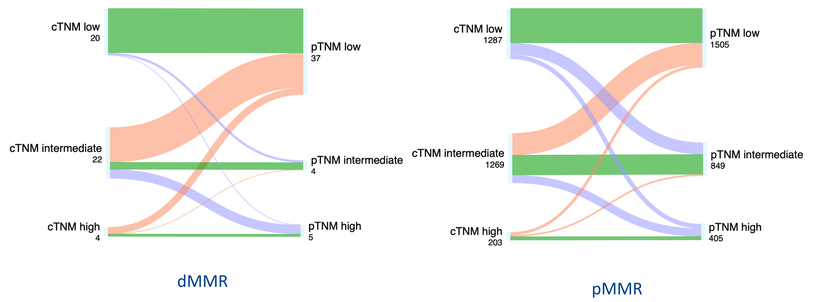
- In rectal cancer patients with upfront surgery or SCRT followed directly by surgery, dMMR tumours are more prone to clinical overstaging, while pMMR tumours are more likely understaged, primarily based on the N-stage.
- As the influence of MMR status on clinical staging may impact treatment decisions and prognosis estimation, future studies should lead to MMR-stratified staging criteria.

4 Accuracy of staging according to MMR status



dMMR tumours are more prone to overstaging of TNM risk category and N stage, while pMMR tumours are more likely understaged on N stage.

Comparing clinical versus pathological TNM risk category according to MMR status



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