

Clinical predictors of response to anti-TNF α treatments in patients with Crohn's disease

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Background/Aims: Anti-tumor necrosis factor (anti-TNF) α agents are effective for the treatment of Crohn's disease(CD), demonstrating improvement in patients' quality of life, and reductions in surgeries and hospitalizations. Unfortunately about 10-30% of patients using anti-TNF agents, do not respond to the initial treatment(primary non-response, PNR). Even though, patients initially respond to anti-TNF, 23-46% of patients lose response over time(secondary loss of response, LOR). Using anti-TNF agents, is not always preferred, because they are expensive and strong immunosuppression which may induce tuberculosis, opportunistic infection, and malignancy. Still there were no clinical predictors of PNR or LOR in patients with CD on anti-TNF treatments. Therefore,our study aimed to identify clinical predictors of PNR and LOR in patients with CD with anti-TNF treatment. **Methods:** Study was designed to retrospective, longitudinal, observational cohort study. We reviewed 283 patients with CD on anti-TNF at Samsung Medical Center. The primary outcomes were to identify incidences and clinical predictors of PNR and LOR to anti-TNF treatments in patients with CD. **Results:** 212 patients with CD were included and divided into three groups: PNR,LOR and Responder. PNR occurred in 13 patients(6.1%). CRP level at initiation of anti-TNF was possible predictor of PNR, compared to non-PNR (LOR+Responder) group [CRP > 1mg/dl, OR=4.34, 95% CI,1.06-17.83, $p=0.042$]. During maintenance therapy, LOR occurred 14.0% at 1year, 24.1% at 2year, 38.0% at 3year and 54.4% at 5year, respectively. CRP level at initiation of anti-TNF was possible predictor of 1year LOR, compared to Responder group [CRP > 1mg/dl, OR=4.99,95 CI,1.72-14.43, $p=0.003$]. On the Cox hazard proportional model, CRP level at initiation of anti-TNF was possible predictor of LOR during maintenance therapy [CRP > 1mg/dl, HR=2.29,95 CI,1.40-3.74, $p=0.001$]. **Conclusions:** CRP level at initiation of anti-TNF might be clinical predictors for PNR or LOR to anti-TNF in patients with CD. Before starting anti-TNF therapy, this clinical predictor could guide early and proper therapeutic intervention in patients with CD.

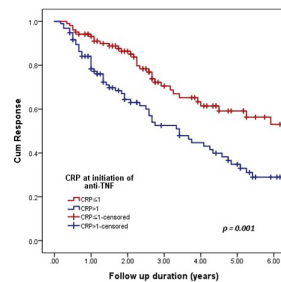


Figure 1. Clinical predictor of LOR during entire follow-up periods in Crohn's disease with anti-TNF treatment

		OR (95% CI)	p value
Age at initiation of anti-TNF	≤ 40yrs	0.91 (0.29-2.84)	0.876
	> 40yrs	1	
Gender	Male	1.50 (0.54-4.16)	0.436
	Female	1	
Disease duration	≤ 2yrs	0.84 (0.26-2.72)	0.776
	> 2yrs	1	
Montreal behavior	B1 (Inflammatory)	1	0.114
	B2+B3 (Complicating)	2.70 (0.79-9.27)	
Indication of anti-TNF	Luminal	1	0.248
	Fistulizing	2.31 (0.56-9.51)	
Types of anti-TNF	Infliximab	1	0.314
	Adalimumab	1.74 (0.59-5.11)	
Hemoglobin at initiation of anti-TNF (g/dl)	> 10	1	0.116
	≤ 10	2.58 (0.79-8.39)	
Albumin at initiation of anti-TNF (mg/dl)	> 3.5	1	0.976
	≤ 3.5	0.98 (0.32-2.99)	
CRP at initiation of anti-TNF (mg/dl)	> 1	4.99 (1.72-14.43)	0.003
	≤ 1	1	
BMI at initiation of anti-TNF (kg/m ²)	< 18.5	1.76 (0.68-4.58)	0.245
	≥ 18.5	1	

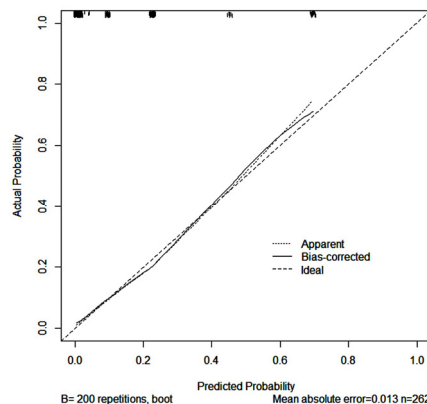
Clinical predictor of 1-year LOR in Crohn's disease with anti-TNF treatment

Predicting lymph node metastasis for endoscopic resection of SESCC

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Background/Aims: The aims of this study were to identify risk factors for lymph node metastasis and develop a reliable risk stratification system. **Methods:** Between May 2001 and December 2015, 262 patients who underwent endoscopic resection or surgery for superficial esophageal squamous cell carcinoma(SESICC) were enrolled. We evaluated possible predictive factors for lymph node metastasis: age, gender, tumor length, tumor area, circumferential spread, tumor location, gross appearance, depth of invasion, tumor differentiation, and lymphovascular invasion. **Results:** The incidence of lymph node metastasis was 14.5% (38/262). In multivariate analysis, tumor size (> 15 mm), depth of invasion (submucosal invasion), and lymphovascular invasion were significantly associated with lymph node metastasis. These factors were included in the risk stratification system and assigned scores; the total risk stratification system score was 0 to 6. The area under the receiver-operating characteristic curve for predicting lymph node metastasis was 0.869 (95% confidence interval, 0.813-0.926). The high-risk group (risk stratification system score ≥ 3) exhibited a significantly higher risk of lymph node metastasis than the low-risk group (score <3) (26.5% vs. 1.6%). There was no lymph node metastasis in patients with a risk stratification system of 0. The sensitivity, specificity, positive predictive value, negative predictive value, and accuracy of the risk stratification system were 94.7%, 55.4%, 26.5%, 98.4%, and 61.1%, respectively. **Conclusions:** We developed a risk stratification system that should facilitate the identification of patients with a high or low risk of lymph node metastasis. This may aid the precise selection of patients who can undergo endoscopic resection.



Variables	LN(-) (n=224) (n, %)	LN(+) (n=38) (n, %)	P
Age (years, median [range])	65.0 (55-83)	60.5 (42-75)	.069
Gender			.744
Male	208 (92.9)	35 (92.1)	
Female	16 (7.1)	3 (7.9)	
Tumor size			.001
≤ 15 mm	105 (46.9)	7 (18.4)	
> 15 mm	119 (53.1)	31 (81.6)	
Circumferential extension			.005
<1/4	53 (23.7)	2 (5.3)	
1/4-2/4	89 (39.7)	16 (42.1)	
2/4-3/4	57 (25.4)	9 (23.7)	
≥3/4	25 (11.2)	11 (28.9)	
Location within esophagus			.397
Upper third	15 (6.7)	4 (10.5)	
Middle third	69 (30.8)	8 (21.1)	
Lower third	140 (62.5)	26 (68.4)	
Tumor type on gross examination			.004
Flat	99 (44.2)	7 (18.4)	
Non-flat	125 (55.8)	31 (81.6)	
Depth of invasion			<.001
Mucosa	127 (56.7)	2 (5.3)	
Submucosa	97 (43.3)	36 (94.7)	
Tumor differentiation			<.001
Carcinoma in situ	23 (10.3)	0 (0.0)	
Well differentiated	79 (35.3)	4 (10.5)	
Moderately differentiated	106 (47.3)	29 (76.3)	
Poorly differentiated	14 (6.3)	5 (13.2)	
Lymphovascular invasion			<.001
Absence	208 (92.9)	19 (50.0)	
Presence	16 (7.1)	19 (50.0)	

LN(-), lymph node metastasis