



# Treatment Failure and Clinical Response Differences in Fixed-Dose vs Weight-Adjusted Anti-TNF Therapy in Obese Patients with Ulcerative Colitis

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## Introduction

Obesity is a risk factor for increased disease activity and complications in IBD [1–4]:

- Earlier time to loss of response
- Increased need for dose escalation
- Increased risk of biologic treatment failure
- Risk of surgery/hospitalization

Pharmacokinetic studies evaluating anti-TNFs in patients with ankylosing spondylitis have shown obesity is associated with [5]:

- Increased clearance and lower drug concentrations
- Decreased clinical response

Direct comparisons of clinical outcomes between fixed-dose and weight-adjusted anti-TNF dosing in UC are lacking.

**Aim:** Compare rates of treatment failure and clinical response of fixed-dose adalimumab (ADA) vs weight-based infliximab (IFX) in obese patients with UC.

**Hypothesis:** We hypothesized that obese patients would have higher rates of treatment failure and inferior clinical response with fixed-dose ADA vs weight-based IFX.

## Methods

Single-center, retrospective study with study period 01/2015–12/2020.

Inclusion criteria:

- Adult patients with UC
- BMI  $\geq 30$  kg/m<sup>2</sup> at time of biologic initiation
- New start of ADA or IFX during study period

Clinical measures of disease activity pre- and post-treatment (0–3 scale):

- Endoscopic Mayo score
- Histologic disease severity
- Physician Global Assessment (PGA) score

**Primary outcome:** Rate of treatment failure, defined by lack of clinical response, need for colectomy, or change in biologic therapy

**Secondary outcome:** Change in clinical measures of disease activity as above

## Results

Table 1: Characteristic data prior to anti-TNF initiation

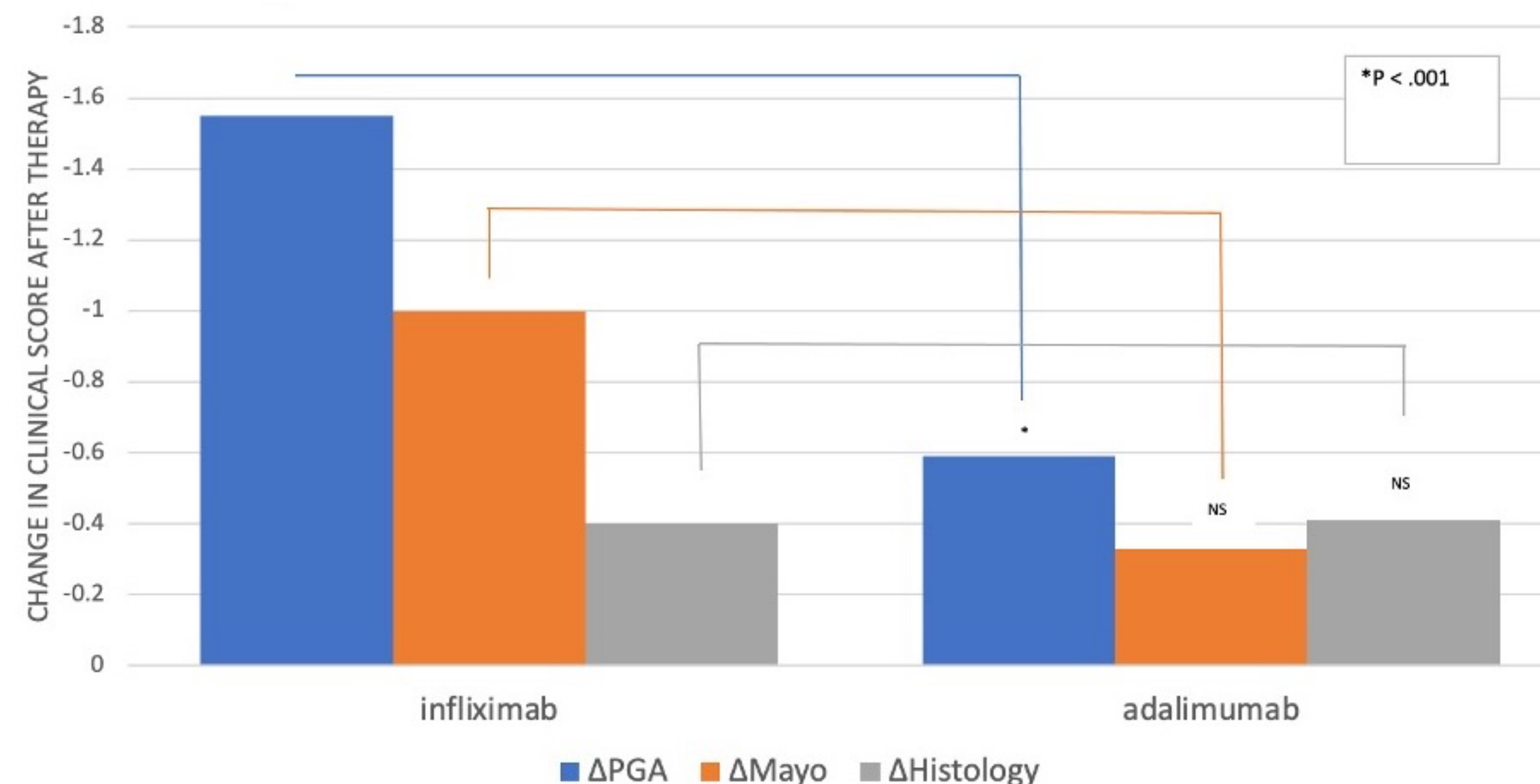
	IFX (n=38)	ADA (n=51)	p-value
Gender [male]: n (%)	18 (47%)	30 (59%)	0.284
Age: median	42.8	48.9	0.054
BMI: median	35.0	34.7	0.71
Race [Caucasian]: n (%)	34 (89%)	49 (96%)	0.138
Hypertension: n (%)	7 (18%)	20 (39%)	0.035
Hyperlipidemia: n (%)	6 (16%)	16 (31%)	0.092
Type 2 diabetes mellitus: n (%)	3 (8%)	8 (16%)	0.269
Prior IBD-related surgery: n (%)	1 (3%)	0 (0%)	0.244
Prior anti-TNF therapy: n (%)	20 (53%)	8 (16%)	<0.001
Hospitalization within last 6 mo: n (%)	21 (55%)	10 (20%)	<0.001
Current corticosteroid use: n (%)	30 (79%)	35 (69%)	0.278
Inpatient initiation: n (%)	16 (42%)	0 (0%)	<0.001
CRP: median	4.9	1	0.003
ESR: median	39	12	0.008
Fecal calprotectin: median	1250	322.8	0.035
Hemoglobin: median	11.7	13.4	0.002
Mayo score: median	2.68	2.24	0.001
Histologic severity: median	2.4	1.95	0.005
PGA score: median	2.2	1.95	0.124

Table 2: Primary and secondary outcomes

	IFX (n=38)	ADA (n=51)	p-value
Treatment failure: n (%)	13 (34%)	27 (53%)	0.079
Drug level $\geq$ threshold: n (%)	14/26 (54%)	10/30 (33%)	0.122

**Multivariate logistic regression analysis:** ADA associated with greater risk of treatment failure compared to IFX (OR 3.02 (95% CI 1.09-8.37), p=0.0337)

Figure 1: IFX vs ADA on Clinical Outcome Measures



## Conclusions

In obese patients with UC, fixed-dose adalimumab, compared to weight-adjusted infliximab anti-TNF therapy:

- Associated with inferior clinical outcomes (i.e., physician global assessment score)
- May be associated with increased with an increased risk of treatment failure

Differences may be attributed to the pharmacokinetics of increased drug clearance seen with greater body mass or fat content

Obese patients with UC may benefit from preferential use of weight-adjusted infliximab over fixed-dose adalimumab

Future prospective studies, including a control population of normal weight, are needed to further evaluate the impact of increased BMI on anti-TNF drug levels and clinical outcomes in patients with IBD.

## References

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## Disclosures

The authors have no relevant financial interests or relationships to disclose.