Risk Factors for Non-adherence to Self-injectable Biologic Therapy in Inflammatory Bowel Disease: A Validation Cohort Study

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INTRODUCTION

- In inflammatory bowel disease (IBD), including Crohn's disease (CD) and ulcerative colitis (UC), we have shown that certain risk factors increase the risk of non-adherence to self-injectable biologic therapy and poorer outcomes
- These previously identified risk factors include narcotic use, psychiatric diagnosis, prior biologic medication use, and smoking

AIMS

- Verify risk factors for non-adherence to self-injectable biologic medication and heath outcomes associated with non-adherence in IBD patients in a multi-cohort study

METHODS

- This was a retrospective study to evaluate patients treated at the University of Maryland Medical Center and Vanderbilt University Medical Center prescribed self-injectable biologic therapy (adalimumab, certolizumab, golimumab, or ustekinumab)
- Eligible patients had at least 3 prescription claims through the respective center's specialty pharmacy with at least one year of follow up
- Data collected:
  - Demographic data: diagnosis, history of perianal or fistulizing disease, medication history, smoking status, psychiatric diagnoses (depression, anxiety, bipolar, schizophrenia), use of narcotics concurrently
  - Medication possession ratio (MPR),was defined as the sum of days' supply for all prescription claims divided by the total number of days elapsed during the study period
    - Medication non-adherence was defined as MPR <0.86
  - Health outcomes (hospitalizations, emergency room (ER) visits, steroid prescriptions)
- Statistical analysis included multivariable logistic regression to identify variables associated with non-adherence and Cox regression to assess the association between non-adherence and health outcomes
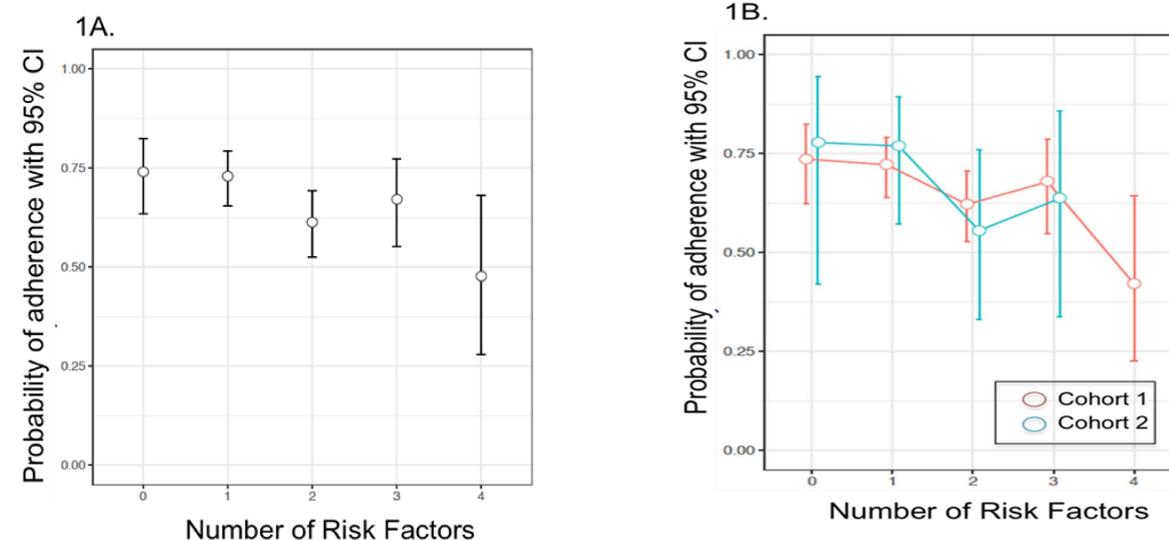
RESULTS

- 460 pts (343 CD, 67 UC) and 82 patients (71 CD, 11 UC) were identified from the original cohort (cohort 1) and validation cohort (cohort 2)
- Patient characteristics (Table 1) and adherence (68% and 70%) in cohorts were similar
- Medicaid insurance status and CD diagnosis were significantly associated with non-adherence
- As the number of previously described risk factors for non-adherence increased, the risk of non-adherence increased significantly when evaluated together (Figure 1A) or separately (Figure 1B)
  - Adherence (MPR > 0.86) was 74% and 73% in patients with 0 to 1 risk factors, decreasing to 61%, 67%, and 48% respectively in those with 2, 3, or 4 risk factors (p<0.05)

Table 1. Characteristics of patients with IBD on a self-injectable biologic medication in Cohort 1 and 2.

	Cohort 1 (n=460)	Cohort 2 (n=82)
Age (median (IQ range))	37 (30, 48)	25 (27, 44)
Crohn's disease (n,%)	393 (85%)	71 (86%)
Female (n,%)	283 (62%)	46 (56%)
Caucasian (n,%)	423 (92%)	69 (84%)
Insurance		
Commercial (n,%)	349 (74%)	60 (73%)
Medicare (n,%)	97 (21%)	5 (6%)
Medicaid (n,%)	20 (4%)	17 (21%)
Psychiatric History (n,%)	229 (50%)	39 (51%)
Current Smoker (n,%)	76 (17%)	8 (10%)
Current Narcotic use (n,%)	104 (32%)	27 (33%)
Prior Biologic Use (n,%)	271 (59%)	51 (62%)
Perianal Disease History (n,%)	150 (38%) n=393	29 (41%) n=71
Fistulizing Disease History (n,%)	212 (54%) n=393	28 (39%) n=71

Figure 1. The probability of adherence decreases as risk factors (prior biologic use, narcotic use, psychiatric history, and smoking) increase in the entire cohort (Figure 1A) (p<0.05) and in each cohort separately (Figure 1B).

RESULTS

- In unadjusted Cox regression models, non-adherent pts had increased rate ratio of hospitalization (HR 1.5 [1.1, 2.0]), p<0.05 and ER visits (HR 1.4 [1.1, 1.96]), p<0.05
- In the adjusted model, increased hospitalization rates remained significant (HR 1.5 [1.1, 2.0]), p<0.05 (Table 2)

Table 2. Association of non-adherence with health outcomes (Adjusted for age, gender, race, disease status)

Outcome	Rate Ratio	Confidence Interval
ER Visits	1.329	(0.949-1.85)
Hospitalizations*	1.473	(1.074-2.01)
Prednisone prescription	1.025	(0.712-1.48)

CONCLUSIONS

- In patients with IBD on self-injectable biologic medication, several previously described cumulative risk factors for non-adherence (narcotic use, psychiatric diagnosis history, prior biologic medication use, and smoking) were validated and remained significant
- Non-adherence to self-injectable medications increased the risk of hospitalization in our IBD population
- Patients with 2 or more risk factors for non adherence require intensified gastroenterology follow up

FUTURE DIRECTIONS

- In future studies we aim to corroborate these findings with additional IBD centers and confirm populations at risk of non-adherence
- Additionally, we plan to broaden validation study across diverse medical centers