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Review Article

The Relapse Rate of Inflammatory Bowel Disease (IBD) in Patients Who Discontinue Anti-TNF Therapy: A Systematic Review and Meta-Analysis

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Abstract

Background: Inflammatory bowel disease (IBD) patients who cease anti-tumor necrosis factor (TNF) therapy are at risk of relapse, which is a matter of concern for the medical community. This study aimed to determine the relapse rate of IBD in patients who cease anti- TNF therapy.

Methods: A systematic search of international databases (Medline, Web of Sciences, Scopus, and EMBASE) was conducted until Mar 9th, 2022. The random effects model was used to calculate the IBD relapse rate, accompanied by a 95% confidence interval.

Results: The IBD relapse rate in patients who discontinued anti-TNF therapy was 44%. The pooled IBD-UC and IBD-CD relapse rate in patients who stopped anti-TNF therapy were 43% and 46%, respectively. The studies using infliximab (IFX) showed a pooled IBD relapse rate of 45%, and the IBD relapse rate in the IFX/ADA (Adalimumab) group was 42%. The IBD relapse rate for papers with treatment durations of less than or equal to 12 months was 51%, while for articles with treatment durations of more than 12 months, it was 30%.

Conclusion: This study emphasizes the need for careful evaluation and monitoring of IBD patients who cease anti-TNF therapy, as well as further investigation of alternative treatments for those who exhibit intolerance or inadequate response to anti-TNF therapy.

Keywords: Inflammatory bowel diseases; Treatment discontinuation; Relapse; Tumor necrosis factor; Anti-TNF

Introduction

Inflammatory bowel disease (IBD) is a significant global public health concern (1). The burden of IBD is expected to worsen due to its early onset and the increase in global life expectancy (1).

Immunomodulatory (IM) and anti-tumor necrosis factor (anti-TNF) agents have been identified as crucial pharmaceuticals for the treatment of IBD (2). For the medical treatment of moderate to severe IBD, anti-TNF medications such as infliximab (IFX) and adalimumab (ADA) (MABs) are advised (3). The utilization of MABs is increasingly becoming prevalent in Asia as a novel approach for managing IBD (4). However, there are concerns about the long-term use of anti-TNF therapy, including serious potential adverse effects such as immunogenicity, opportunistic infections, melanoma (5). These factors may motivate doctors and patients to discontinue the drugs when deep remission has been reached (6). Anti-TNF therapy cessation is a difficult decision in clinical practice because biologics withdrawal may lead to relapse of disease activity with unfavorable effects on patients' quality of life, ability to work and possible hospitalization, which also results in higher costs (7). Until recently, a wide range of relapse rates from 19 to 41% after the first year of discontinuation was reported (7). In Canada, patients with Crohn's disease (CD) had a relapse risk of 43% within a year after discontinuing anti-TNF treatment (8).

Due to the importance of stopping the drug in patient with IBD, this study aimed to analyze the relapse rate in individuals with IBD who stop taking anti-TNF therapy and help healthcare practitioners make informed decisions about treating IBD patients who discontinue this therapy. Additionally, the study may contribute to developing treatment protocols for IBD patients who cease anti-TNF therapy, potentially improving the quality of care and clinical outcomes for these patients.

Materials and Methods

The present systematic review and meta-analysis was performed according to the PRISMA statement (9). The study protocol has been registered in PROSPERO with the code CRD42023394510.

Eligibility criteria

The study was designed using the PEO framework. In the current study, the population (P) consisted of IBP patients, the exposure (E) was stopping anti-TNF therapy, and the outcome (O) was IBD relapse. The systematic review and meta-analysis employed specific eligibility criteria, which included the reporting of IBD relapse in patients who ceased anti-TNF treatment, and studies with full-text articles. The analysis was conducted solely on studies that were written in the English languages as well as studies that were conducted on only two types of drugs, ADA and IFX. This meta-analysis excluded studies involving letters to the editor, poster presentations, and systematic reviews.

Search strategy and screening

Electronic literature searches in English international databases using Medline (accessible from PubMed), Scopus, Web of Science (WOS), and Embase (Elsevier) were carried out until Mar 9, 2022, to assess the IBD relapse in patients who stop taking anti-TNF. In this study, the search was conducted using the keywords "inflammatory bowel disease," "withdrawal", "anti-TNF therapy" and "relapse," along with corresponding MESH phrases. All database search results were entered into the Endnote software. After eliminating the duplicate cases, articles were screened based on their titles, abstracts, and complete texts while taking inclusion and exclusion criteria into account.

Data extraction

Authors, years, sample size, country, study population, IBD type, anti-TNF type, IBD relapse, treatment duration, time to relapse (week), follow-up duration (day), criteria for stopping anti-TNF therapy, predictors of IBD relapse, definition of relapse, and NOS score were all extracted from each study.

Risk of bias

The Newcastle-Ottawa Quality Assessment Scale (NOS) checklists were employed to evaluate the

risk of bias (10). The present checklist involved the evaluation of three distinct elements, namely comparability, outcome, and selection. The questionnaire in question has a scoring system that ranges from one star, which represents the lowest possible score, to nine stars, which represents the highest possible score. According to the source, a score range spanning from 0 to 4 is deemed to be indicative of low quality, while a range of 5 to 7 is considered to be indicative of moderate quality. Scores exceeding 7 are classified as high quality (11).

Statistical analysis

The Metaprop command was used to calculate the pooled estimate of relapse in individuals with IBD. Given the statistical significance of the heterogeneity test ($P<0.05$), rate estimates with a 95% confidence interval were derived using random-effects models.

Assessing heterogeneity

The Cochrane Q and I^2 tests, along with the Galbraith plot, were employed to examine the heterogeneity and variance among the studies that were chosen for the meta-analysis. The Cochrane criteria and the I^2 index were utilized to categorize the level of heterogeneity into four distinct groups: 0% to 40% (potentially insignificant), 30% to 60% (possibly indicating moderate heterogeneity), 50% to 90% (potentially indicating substantial heterogeneity), and lastly, 75% and above (indicating considerable heterogeneity) (12).

Publication bias

The Egger's test was employed to evaluate the presence of publication bias. A *P*-value of less than 0.05 in Egger's test suggests the presence of publication bias (13). Moreover, the DOI plot and LFK index can be used to assess the potential impact of publication bias. The Doi plot replaces the conventional scatter (funnel) plot of precision versus effect with a folded normal quantile (Z-score) versus effect plot. The studies form the limbs of this plot, if there is asymmetry there will be unequal deviation of both limbs of the plot from the mid-point or more studies making up one limb compared to the other. In the absence of asymmetry, it would be expected that a perpendicular line to the X-axis from the tip of the Doi plot would divide the plot into two regions with similar areas. The LFK index quantifies the difference between these two regions in terms of their respective areas under the plot and the difference in the number of studies included in each limb. The closer the value of the LFK index to zero, the more symmetrical the Doi plot. LFK index values outside the interval between -1 and +1 are deemed consistent with asymmetry (i.e. publication bias).

Subgroup analyses

A subgroup analysis was performed to identify the origin of heterogeneity, utilizing variables such as IBD type, anti-TNF type, duration of follow-up, and treatment duration. The chi-squared test of group differences with test statistic, Q_b, and *P*-value was used to determine if there is a significant difference between the subgroups in the categorical variable.

Sensitive analysis or Leave-one-out meta-analysis

The leave-one-out meta-analysis methodology involves conducting numerous meta-analyses, whereby one study is systematically excluded from each analysis. Exaggerated effect sizes are a frequent occurrence in research studies, potentially leading to distortions of the overall findings. The utilization of leave-one-out meta-analysis is advantageous in examining the impact of individual studies on the comprehensive effect-size estimation and in recognizing studies that hold significant influence.

Meta-regression

The meta-regression was employed to account for the influence of the publication year of the article.

Results

Search results

In the initial search, 6866 articles from the databases and 45 entries from additional sources were retrieved. Following the elimination of duplicates and a thorough examination of the title, abstract, and complete text of the articles, a total of 19 articles were retained (Fig. 1). Table 1 reports the characteristics of each study that was included in the present systematic review and meta-analysis.

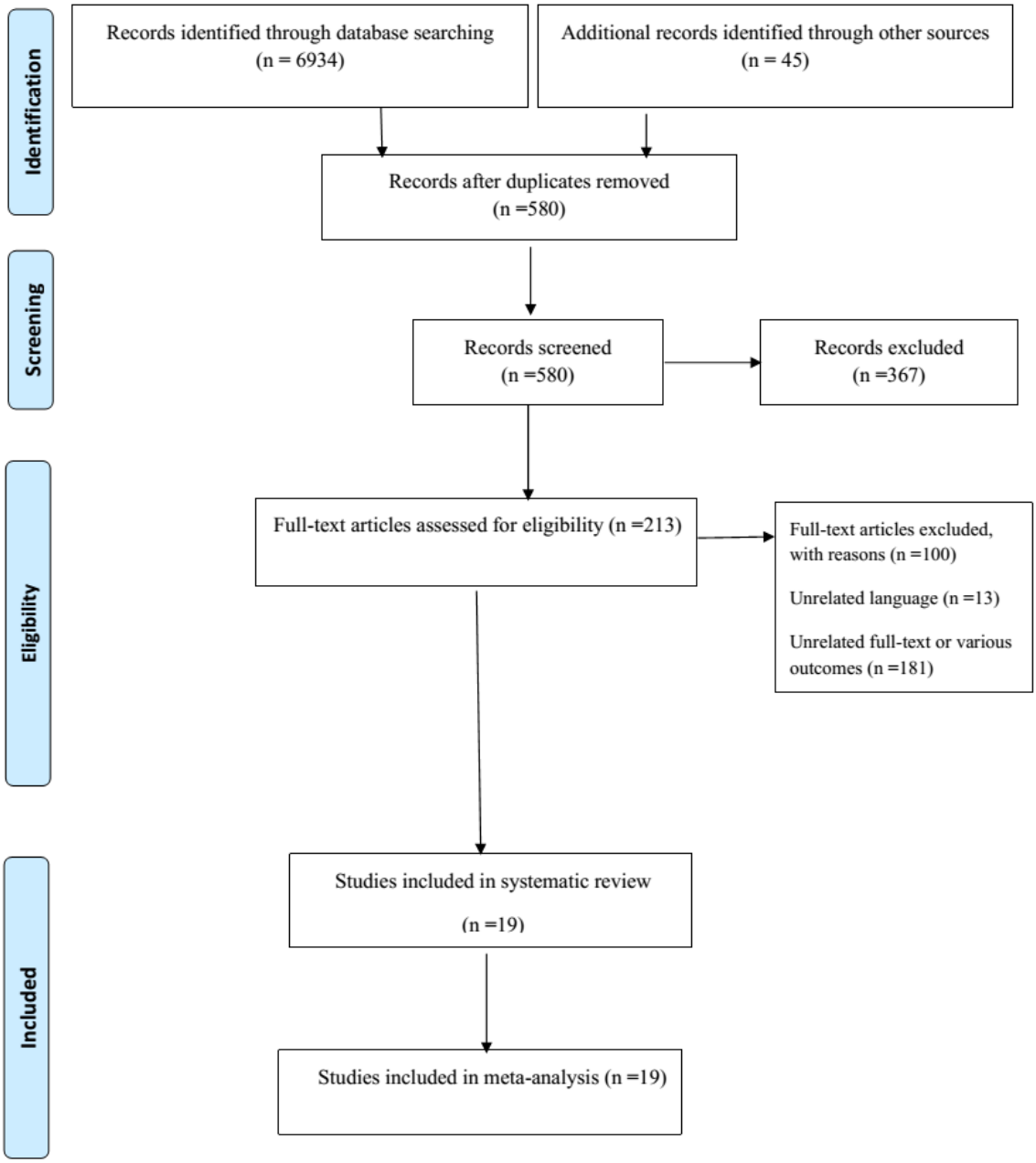

Fig. 1: Flow diagram of the literature search and study selection

Table 1: The characteristics of included studies (N = 19)

Authors (Ref)	*Year*	*Country*	*IBD type*	*Type of anti-TNF*	*IBD Relapse (n)*	*Treatment duration (month)*
Brooks A (14)	2015	United Kingdom	CD	IFX/ADA	10	23
Dart R (15)	2013	United Kingdom	CD	IFX/ADA	3	25
Song J (16)	2021	Korea	CD/UC	IFX/ADA	69	12
Waugh A (8)	2022	Canada	CD	IFX	25	12
Molander P (17)	2023	Finland	CD/UC/UN	IFX/ADA	17	27
Sahu P (18)	2020	India	CD/UC/UN	IFX/ADA	15	12
Bots S (5)	2019	Netherlands	NR	IFX/ADA	56	26.5
Chauvin A (19)	2014	France	CD	IFX	66	12
Lu C (20)	2012	Canada	CD	IFX	8	8.5
Wynands J (21)	2008	France	CD	IFX	8	12
Louis E (22)	2012	France and Belgium	CD	IFX	52	12
Crombé V (23)	2010	France	CD	IFX	4	16
Guidi L (24)	2008	Italy	CD	IFX	1	28
Domenech (25)	2005	German	CD	IFX	11	12
Bortlik M (26)	2015	Czech Re-public	CD/UC	IFX/ADA	41	NR
Steenholdt C (27)	2012	Denmark	CD/UC	IFX	46	NR
Dai C (28)	2013	China	CD/UC	IFX	38	12
Farkas K (29)	2013	Hungary	UC	IFX	24	12
Molander P (30)	2016	Hungary	CD	IFX /ADA	54	12

Table 1: (Continued). The characteristics of included studies (N = 19)

Authors (Ref)	*Time to relapse (week)*	*Follow-up duration (day)*	*Reason of stopping anti-TNF therapy*	*Definition of relapse*	*NOS score*
Brooks A (14)	32.5	512	Clinical and/or endoscopic/MR/SBM/ SB WCE/LB WCE remission	recurrent symptoms of CD requiring medical or surgical therapy	7
Dart R (15)	NR	365	Clinical and/or endoscopic remission	NR	7
Song J (16)	NR	1703	clinician's decision and patient's preference	Crohn's Disease Activity Index >220 or new-onset fistula in CD or Mayo score ≥6 and endoscopic sub score ≥2 in UC, requirement for hospitalization/ surgery associated with IBD progression, or re-initiation of steroids or biologics	6
Waugh A (8)	NR	1496	Clinical remission>6 months	Symptoms of disease activity and a therapeutic intervention with medications, or hospitalization with complications related to active CD	6
Molander P (17)	NR	395	NR	NR	6
Sahu P (18)	21.7	NR	NR	increase of 3 or more points of SCCAI with sigmoidoscopic evidence of active disease in UC patients and increased CDAI above 250 points or between 150 points and 250 points with a 70-point increase from baseline over 2 consecutive weeks in CD patients	7
Bots S (5)	NR	1410	NR	requirement for (re)treatment with IBD medication (i.e., corticosteroids, immunosuppressive, biologicals or experimental medication), dose increase of IBD medication in follow-up period or IBD-related surgical interventions	6
Chauvin A (19)	106	1413	Clinical and biological remission	HBI> 4 points or need to introduce any specific c	6

Table 1: Continued….

				treatment for CD	
Lu C (20)	52	NR	Clinical remission >6 months	CDAI >220 points and administration of medications for CD or hospitalization with complications related to active CD	6
Wynands J (21)	17.3	NR	Clinical remission at 12 months	HBI ≥5 points or an increase in the HBI ≥3 points	6
Louis E (22)	65.6	840	Clinical remission >12 months	DAI above 250 points or between 150 points and 250 points with a 70-point	6
Crombé V (23)	NR	3750	clinical remission	NR	6
Guidi L (24)	77.6	582	clinical remission	NR	6
Domenech (25)	37.7	365	Clinical remission at 12 months	Need for changes in medical therapy, need for a new course of IFX, or surgery	6
Bortlik M (26)	44	912	clinical remission endoscopic remission, regardless of their duration	confirmed by endoscopy and/or another imaging procedure (abdominal ultrasound, CT/MR heterography) with or without laboratory (CRP or FC) or new onset of perianal disease (abscess or fistula) leading to a change in medical therapy or to surgery.	6
Steenholdt C (27)	92.5	868	reating physicians' global assessment of the patient, indicating that he or she was in stable IFX-induced steroid-free remission	retreatment with a biologic, systemic steroid or surgery	6
Dai C (28)	22.5	365	Clinical and/or endoscopic remission	CD: CDAI >150 points and an increase of 100 points in CDAI UC: partial Mayo score >3 points	7
Farkas K (29)	32	365	Clinical remission at 12 months	NR	6
Molander P (30)	48	365	Clinical remission at 12 months	an increase of >100 points in CDAI to at least a CDAI of 150 points.	6

Quality assessment or risk of bias

The present meta-analysis involved an assessment of the quality of the studies utilizing the NOS scale, with the results displayed in Table 1. The range of NOS was observed to be between 6 and 7.

The overall of IBD relapse

The meta-analysis included 19 publications with 19 records. Overall, 1272 patients who stopped receiving anti-TNF therapy made up the sample size for all articles. After combining these investigations, the overall of IBD relapse in subjects who discontinued anti-TNF therapy was found to be 44% (95% CI: 34%-54%, *P*=0.000, I^2 = 90.97%). The studies' relapse range exhibited considerable variation, ranging from 12% to 73%. The study conducted by Brooks J. reported the lowest IBD relapse of 12% (95% CI 6%–20%) (19) while the research conducted by Wynands j et al. reported the highest IBD relapse rate of 73% (95% CI 39%-94%) (27) (Fig. 2 and Table 1).

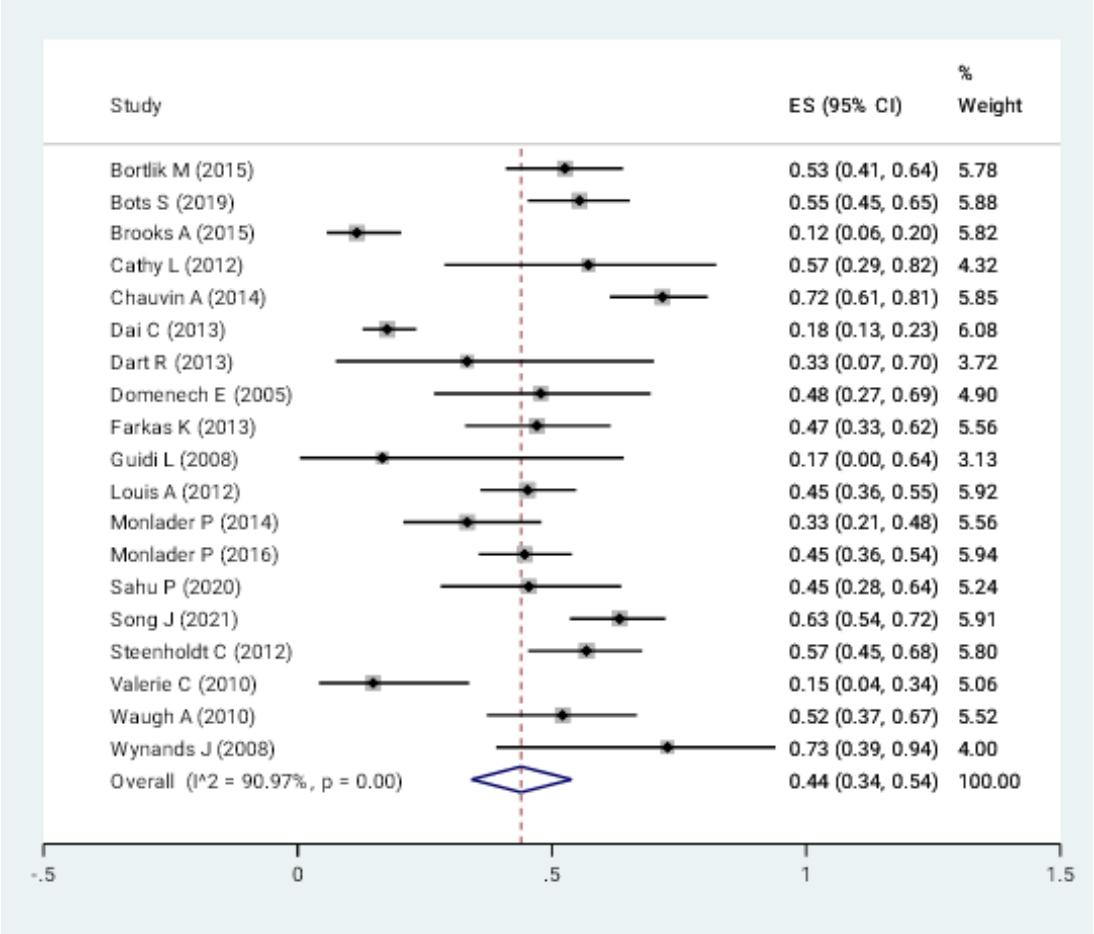

Fig. 2: Pooled IBD relapse in patients who discontinue anti-TNF therapy

The IBD-UC relapse

Six articles with 1272 patients were conducted on the topic of ulcerative colitis (UC) as a type of IBD. After combining these investigations, the pooled IBD-UC relapse in patients who discontinued anti-TNF therapy was found to be 43% (95% CI: 25%-60%, *P*=0.000, I^2 = 88.19%) (Fig. 3). The IBD-UC relapse in the IFX therapy group was found to be 23% (95% CI: 2%-44%; *P*=0.000, I^2 = 80.19%), while in the IFX/ADA group, it was observed to be 53% (95% CI: 37%-70%; *P*=0.000, I^2 = 73.86%).

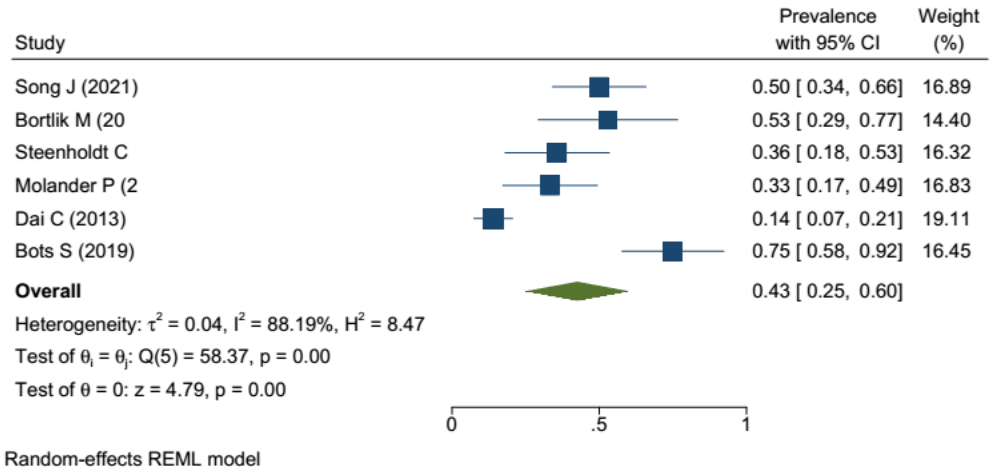

Fig 3: Pooled IBD-UC relapse in patients who discontinued anti-TNF therapy

The IBD-CD relapse

Among the studies, 1272 patients have been conducted on the topic of CD. After merging these studies, the pooled IBD-CD relapse in patients who discontinued anti-TNF therapy was found to be 46% (95% CI: 37%-56%, *P*=0.000, I^2=87.83%) (Fig. 4). IBD-DC relapse in therapy groups was similar.

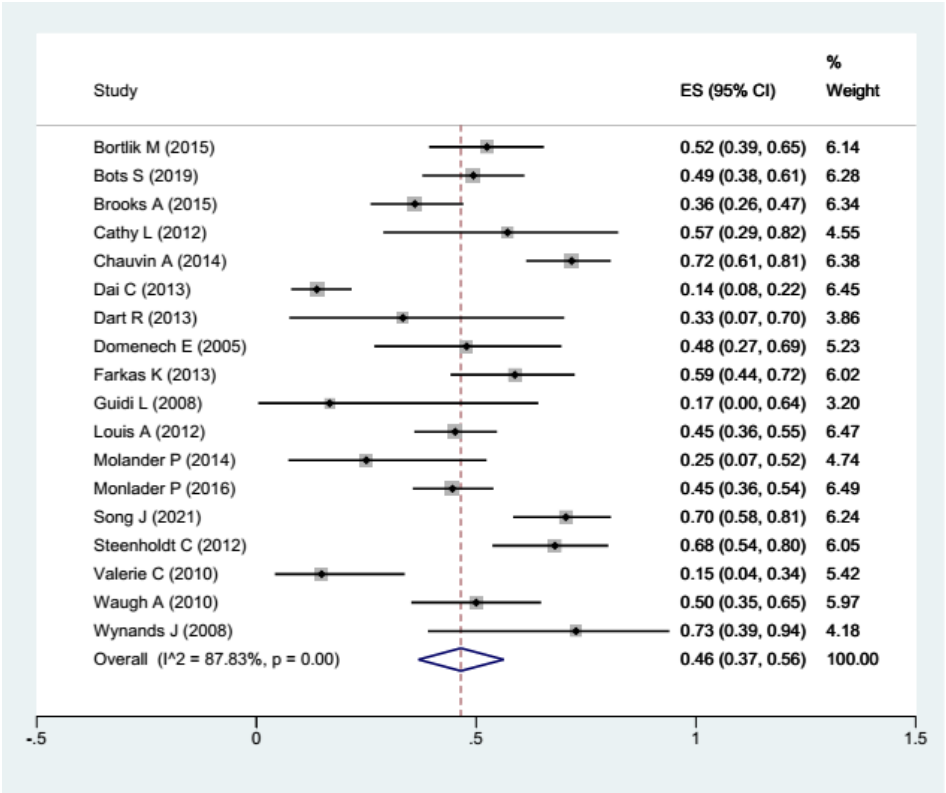

Fig. 4: Pooled IBD-CD relapse in patients who discontinued anti-TNF therapy

Heterogeneity

The statistical analysis using the Cochrane Q test indicated a statistically significant difference between the results of the studies (Z=10.21, *P*=0.000). The study exhibited a significant level of heterogeneity as per the I^2 test results (I^2=90.51%, *P*=0.000). Moreover, in the Galbraith plot, some studies were outside the confidence interval, which indicated heterogeneity between the studies (Fig. 5).

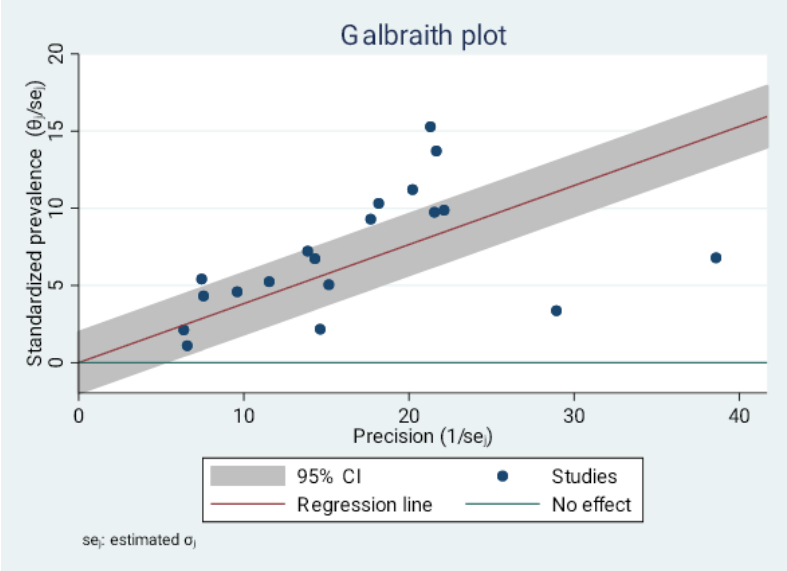

Fig. 5: Galbraith plot

Publication bias

The study's Egger's test findings indicated the absence of publication bias (Egger's test: β = 3.44, *P*= 0.092, 95% CI: -0.63 to 7.51). The result of the DOI plot and LFK index show there is no publication bias (LFK index=0.65) (Fig. 6).

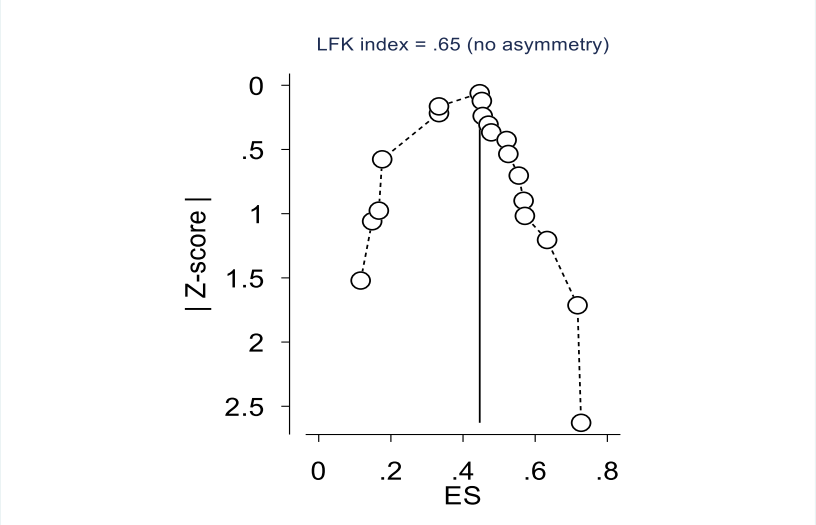

Fig. 6: The DOI plot and LFK index

Subgroup analysis

Subgroup analysis based on the type of anti-TNF therapy

The present meta-analysis investigated the efficacy of two anti-TNF therapies, namely IFX) and a combination of IFX and ADA (IFX/ADA), for the treatment of IBD. The pooled IBD relapse rate in studies utilizing IFX was 45% (95% CI: 31-60%, I^2: 91.88%). The IBD relapse rate observed in the IFX/ADA group was 42% (95% CI: 29-56%, I^2: 90.56%). The relapse of IBD in patients who cease anti-TNF was found to be greater in the IFX group compared to the IFX/ADA group (Table 2). However, the difference was not statistically significant (Q_b=0.08, *P*=0.777).

Subgroup analysis based on the study population

In the present meta-analysis, the IBD relapse in the adult group (P=45%, 95% CI: 34%-55%, I^2=91.38%) was higher (no statistically significant, Q_b=0.2.38, *P* =0.120) than the children group (P=29%, 95% CI: 15%-45%, I^2 = 90.56%) (Table2).

Subgroup analysis based on the follow-up time

The present study conducted a meta-analysis to investigate the IBD relapse in articles with varying follow-up times. The IBD relapse was 36% (95% CI: 23%-51%, I2 :87.33%) in articles with a follow-up time of less than or equal to 365 d, while it was 45% (95% CI: 32%-59%, I2 :91.96%) in articles with a follow-up time of more than 365 d. There was a higher (no statistically significant) relapse in patients who discontinued anti-TNF therapy during a follow-up period exceeding 365 d (Q_b=2.87, *P*=0.239) (Table3).

Subgroup analysis based on the treatment time

In this meta-analysis, the IBD relapse rate for papers with treatment durations of less than or equal to 12 months was 51% (95% CI: 36%-66%, I2:92.80%), while for articles with treatment durations of more than 12 months, it was 30% (95% CI: 10%-54%, I2:90.99%). The IBD relapse among patients who cease anti-TNF therapy was found to be greater (no statistically significant) when the duration of treatment was less than or equal to 12 months (Q_b=2.16, *P*=0.338), as indicated in Table2.

Table2: The overall and subgroup pooled IBD relapse among patients who discontinued anti TNF therapy (n = 19 articles)

Variables	*No. of study (sample size)*	*No. of IBD relapse*	*Pooled rate (95% CI)*	*Heterogeneity assessment*	
				I^2 (%)	*P*-value
Overall	19 (1272)	548	44 (36-53)	90.51	0.000
Type of anti-TNF therapy					
IFX	11 (684)	283	45 (31-60)	90.82	0.000
IFX/ADA	8 (588)	265	42 (29-56)	90.07	0.000
Study population					
Adults	17 (1234)	536	45 (34-55)	89.78	0.000
Children	2 (38)	12	29 (15-45)	93.23	0.000
Followup time					
≤365 d	6 (471)	147	36 (23-51)	87.33	0.000
> 365 d	10 (743)	370	45 (32-59)	91.96	0.000
Treatment time					
≤12 month	10 (718)	318	51 (36-66)	92.80	0.000
>12 month	5 (253)	87	30 (10-54)	90.99	0.000

Sensitive analysis or Leave-one-out meta-analysis

Table 3 and Fig. 2 of the appendix display the results of the leave-one-out meta-analysis. Through the exclusion of each of the 21 studies from the meta-analysis, the combined rate of the remaining studies experienced a negligible shift from approximately 42% to 46%, signifying an absence of alteration in the overall pooled estimation. The findings indicate a notable level of precision in the overall results of the present investigation.

Table3: Sensitivity analysis for the IBD relapse among patients who discontinued anti-TNF therapy (n = 19 articles)

Omitted study	*Rate*	*95% CI*
Brooks A (2015)	0.463	0.388-0.537
Dart R (2013)	0.451	0.369-0.532
Song J (2021)	0.435	0.355-0.515
Waugh A (2010)	0.441	0.359-0.523
Molander P (2014)	0.451	0.369-0.532
Sahu P (2020)	0.445	0.362-0.527
Bots S (2019)	0.439	0.358-0.521
Chauvin A (2014)	0.430	0.353-0.506
Caviglia R (2017)	0.432	0.354-0.510
Lu C (2012)	0.439	0.357-0.520
Wynands J (2008)	0.435	0.356-0.513
Louis A (2012)	0.445	0.362-0.527
Valerie C (2010)	0.461	0.384-0.537
Guidi L (2008)	0.453	0.374-0.532
Domenech E (2005)	0.443	0.362-0.525
Bortlik M (2015)	0.440	0.358-0.522
Steenholdt C (2012)	0.441	0.359-0.523
Dai C (2013)	0.460	0.383-0.537
Farkas K (2013)	0.444	0.361-0.526
Molander P (2016)	0.445	0.362-0.527
Molander P (2014)	0.451	0.369-0.532
Overall, by all study	0.44	0.34-0.54

Meta-regression

The meta-regression analysis revealed that the variable of years of publication (β = 0.007, 95% CI: -0.014 to 0.029, P=0.492) did not account for the observed heterogeneity in the present study.

Discussion

Achieving remission may not necessarily guarantee a successful withdrawal from medication. In order to enhance the risk stratification of relapse following de-escalation, it may be imperative to assess both the present and prior therapeutic interventions. This study is an update systematic review and meta-analysis that scrutinized 19 studies to examine the IBD relapse in patients who discontinued anti- TNF therapy less than half of patients experienced relapse after discontinuing anti- TNF therapy. The relapse rate was higher in patient's CD compared to those with UC. Additionally, patients who discontinued IFX had a higher risk of relapse compared to those receiving a combination of IFX and ADA. The length of treatment duration also exerted an influence, as patients who underwent treatment for a duration of 12 months or less exhibited a higher susceptibility to recurrence. While the differences between the groups may not have been statistically significant, there could still be medically significant differences. Statistical significance is just

one aspect of evaluating the results, and it is essential to interpret the clinical relevance of the findings in conjunction with statistical analysis.

There was a relapse rate of 44% among individuals with IBD who discontinued anti-TNF therapy. In a comprehensive review and meta-analysis, 27 relevant documents and studies were examined. The findings of this investigation revealed that patients with IBD who discontinued anti-TNF therapy saw a relapse rate of 44% (31). The results of our investigation align with the findings reported in Gisber's study (31). Nevertheless, our study's inclusion criteria encompassed only research that were published between the timeframe of 2000 to 2022. Additionally, we eliminated poster presentations and abstracts from our analysis. The relapse rate among patients diagnosed with IBD who discontinued anti-TNF therapy was found to be 55% (5). Chauvin et al reported a relapse rate of 72% among patients with IBD who discontinued anti-TNF therapy (19). The variation observed in relapse rates may be attributed to the various illness characteristics of individual patients and the dynamic nature of IBD, which is a relevant aspect to consider.

The current study revealed that the IBD relapse in CD was higher than in UC. Consistent with the results of our study, the relapse rate was 44% and 38%, among CD and UC, respectively (31). The relapse in CD patients was found to be 33% (15). The rate of relapse in CD was 43% in a study (8).

The higher rate of relapse in CD than in UC is caused by a number of factors. One reason is that CD affects any portion of the digestive tract, whereas UC only affects the colon and rectum. Consequently, the treatment of CD may pose greater challenges, and the likelihood of exacerbations or complications may be heightened. Furthermore, CD is frequently linked to heightened inflammation and harm to the gastrointestinal tract in comparison to UC. This can result in intestinal scarring and constriction, impeding the passage of food and elevating the likelihood of complications such as bowel obstructions (37).

An additional variable to consider pertains to the variations in the microbiome composition among people diagnosed with CD and UC. Variations exist in the structure and function of the intestinal microbiota among patients diagnosed with CD and UC, which could potentially account for the dissimilarities in the severity of symptoms and relapse rates observed in these two disorders (32). The pathogenesis and progression of IBD, comprising CD and UC, are influenced by genetic factors. Several genetic variations have been linked to a heightened susceptibility to IBD. This could potentially account for variations in disease severity and recurrence rates observed between CD and UC. The etiology and pathogenesis of IBD may be influenced by various environmental factors, including dietary habits and stress levels. However, the precise mechanisms underlying these associations remain incompletely elucidated (33).

The current study found that the relapse rate was higher in the IFX group compared to the IFX/ADA group. Bot's study reported a higher IBD relapse rate in the IFX/ADA groups as compared to the present study (5). The IBD relapse rate among groups treated with IFX/ADA was 36%, which was lower than current study (14). The IBD relapse in IFX groups was estimated to be 72%, which exceeded the current study (19). The IBD relapse among patients who take IFX and found it to be 42% (34).

One possible explanation for this difference is that the combination therapy of IFX and ADA may be more effective in mitigating inflammation in the gastrointestinal tract compared to IFX alone (35). The use of combination therapy (IFX/ADA) resulted in elevated rates of clinical remission in CD when compared to IFX monotherapy (36). Another explanation may be attributed to differences in the pharmacokinetic profiles of the two drugs. IFX has a comparatively brief half-life. In contrast, ADA has a prolonged half-life and may offer a more sustained anti-inflammatory effect (37).

The current study showed that the IBD relapse rate was higher in those treated for a shorter du-

ration compared to those treated for a longer duration. IBD is a persistent disease that necessitates continuous supervision to sustain remission and prevent relapse. Shorted treatment durations may not afford adequate time for the complete suppression of inflammation in the gastrointestinal tract by medications, thereby increasing the likelihood of relapse. Longer treatment durations may provide a greater opportunity for mitigation of inflammation, thereby potentially reducing the likelihood of relapse (38). Longer treatment periods with anti-TNF drugs were linked to a decreased likelihood of relapse. Treatment should be sustained for a minimum of two years in patients with moderate to severe UC (39).

The findings of our research emphasize the significance of careful monitoring and follow-up assistance for these individuals to prevent a relapse of the condition. Furthermore, the previously mentioned research emphasizes the need for further investigation into alternative therapies for persons with IBD who experience intolerance or insufficient response to anti-TNF medication. The discovery of effective alternative medicines holds promise in reducing the probability of illness relapse and improving patient outcomes.

The present study exhibits certain limitations. The relapse could not be classified, and subgroup analysis could not be performed due to inadequate reporting in most studies and the limited availability of studies in certain classifications. One of the study's strongest points is its extensive subgroup analysis. Taking into account variables including the kind of IBD, the particular anti-TNF medication utilized, and the features of the study group can lead to a more nuanced explanation of the findings. The sensitivity analysis that is included in the study is another asset. This kind of study enables researchers to evaluate the validity of their conclusions by examining the effects of various hypotheses or modifications in the data. It strengthens the validity and dependability of the study's findings. These advantages add to the study's overall caliber and reliability while offering insightful information on the connection between IBD, anti-TNF medication, and pertinent variables.

Conclusion

The careful consideration should be exercised when determining the appropriate timing and approach for terminating anti-TNF therapy in this specific group of patients. Furthermore, it is imperative to meticulously observe these individuals and investigate alternate therapeutic approaches in order to prevent recurrence. Further investigation is necessary to determine the variables that predict relapse and the most efficacious strategies for managing individuals who discontinue anti-TNF treatment.

Journalism Ethics considerations

Ethical issues (Including plagiarism, informed consent, misconduct, data fabrication and/or falsification, double publication and/or submission, redundancy, etc.) have been completely observed by the authors.

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Conflict of interest

The authors declare that there is no conflict of interests.

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