

Real-world Scottish experience of anti-TNF therapy and surgery in paediatric Crohn's disease 2016-2020 against the ECCO-ESPGHAN recommendations

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BACKGROUND/INTRODUCTION

- ECCO-ESPGHAN updated the guideline on the management of paediatric Crohn's disease (CD) in 2021.¹
- This promoted a move to early risk stratification and a 'top-down' (anti-TNF within 4 weeks of diagnosis) approach for patients who were deemed high-risk.
- High-risk was defined, based on Paris Classification at diagnosis, as extensive panenteric or severe disease, perianal disease, and stricturing and/or penetrating behaviour.

AIMS

We conducted a Scottish nationwide retrospective multi-centre cohort study in patients with paediatric Crohn's disease, diagnosed before introduction of the guidelines, to examine the need to escalate to anti-TNF therapy in high risk versus low risk patients and explore the impact the guidance has had on practice.

METHODS

We analysed a prospectively identified nationwide cohort of all new paediatric CD patients (<18 years) diagnosed in Scotland between 01/01/16 and 31/12/20. Data were retrospectively collected from electronic medical records on the use of anti-TNF therapy (infliximab or adalimumab) within 18 months of diagnosis. Paris location and behaviour at diagnosis were determined, allowing stratification into high-risk or low/medium-risk based on the ECCO-ESPGHAN guidelines. Data regarding surgical intervention was collected and defined as: Perianal (Seton suture or drainage of abscess) and/or bowel resection +/- stoma formation.

PATIENT CHARACTERISTICS

- 419 patients with Crohn's disease were included
 - 259/419 (61%) male; median age at diagnosis 13.2 yrs.
 - Median weight at diagnosis 42.2kg (zs -0.3, IQR: -1.32-0.6)
 - Median height at diagnosis 157.1cm (zs -0.03, IQR: -0.76-0.91)
- 225/419 (54%) were classified as high-risk and 194/419 (46%) as low/medium-risk
- High risk patient phenotypes:
 - B1 extensive disease or deep colonic ulcers: 167/419 (40%)
 - B1 fistulating perianal disease: 40/419 (10%)
 - B2 stricturing disease: 50/419 (12%)
 - B3 penetrating disease: 5/419 (1%)

Location	Total no. (%)	+ No upper GI disease	+ Upper GI disease	L4a	L4b	L4a+b
L1	62 (15)	38 (61)	24 (39)	11 (18)	7 (11)	6 (10)
L2	114 (27)	77 (68)	37 (32)	30 (26)	5 (4)	2 (2)
L3	198 (47)	77 (39)	121 (61)	80 (40)	20 (10)	21 (11)
Isolated L4	45 (10)					

Table 1: Paris classification disease phenotype

Behaviour	Total no. patients (%)
B1	368 (88)
B2	46 (11)
B3	3 (0.6)
B2B3	2 (0.4)
Perianal	40 (10)
- B1p	36 (9)
- B2p	4 (1)
- B3p	0 (0)

Table 2: Paris classification disease phenotype and behaviour

RESULTS ANTI-TNF

- High risk patients were more likely to commence anti-TNF within 18 months of diagnosis versus low-risk patients (171/225 (76%) vs 78/194 (40.2%) , <0.00001)
- 24% of high risk patients did not require anti-TNF during the time period

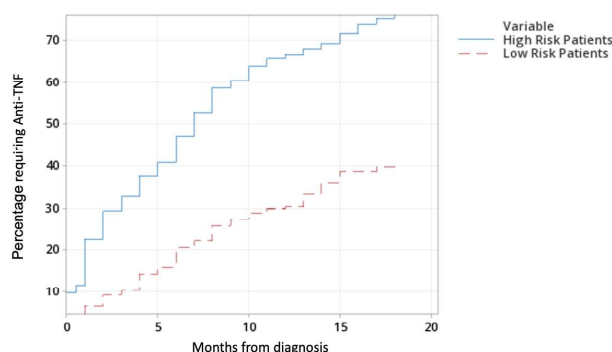


Figure 1: Cumulative Failure Plot (Kaplan-Meier Method) for high risk patients versus low risk patients need for anti-TNF escalation

- High risk patients requiring anti-TNF commenced this earlier post-diagnosis (p<0.014) (Figure 2)

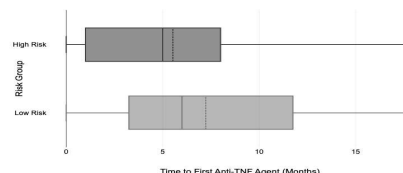


Figure 2: Time to first anti-TNF post diagnosis

SURGERY

- 43/419 (10.2%) patients required surgery within 18 months of diagnosis
- High risk patients were more likely to require surgery than low risk patients (37/225 vs 6/194: Fishers exact test <0.00001)
- Indications for surgery:
 - Perianal disease 22/43 (51%)
 - Intestinal resection 21/43 (49%)
 - Intestinal resection and stoma formation 3/43 (7%)
- There was no difference in time to surgery post diagnosis (p=0.503)

CONCLUSIONS

- The ECCO-ESPGHAN guidance seeks to shift practice towards "top-down" anti-TNF therapy in high-risk patients.
- Our real-world data supports this view by showing that high-risk patients, as defined in the guidance, are more likely to require biologics within 18 months and more likely to require surgery than low/medium-risk patients.
- The ECCO-ESPGHAN approach would however have led to unnecessary anti-TNF in 24% of our high-risk cohort within 18 months of diagnosis.
- The financial cost and risk:benefit profile of this group should be considered carefully both in clinical practice and future guidance.

References

1. van Rheenen PF, Aloï M, Assa A, et al. The Medical Management of Paediatric Crohn's Disease: an ECCO-ESPGHAN Guideline Update. *J Crohn's Colitis*. 2021;15(2):171-194. doi:10.1093/ecco-jcc/jjaa161