failed infliximab plus either golimumab or adalimumab, and 26% (5/19) had also failed i.v. ciclosporine. At the start of ustekinumab, 12 of 19 patients (63.2%) had moderately or severely active disease and, in contrary, 36.8% (7/19) were in remission, but had intolerable side effects under TNF- or integrin-blocking treatment, which had to be stopped. In 4 patients ustekinumab was stopped due to refractory disease, in one at 3 months, in one at 6 months, and in two at 9 months. In another patient, therapy was stopped due to drowsiness at Week 4. Three patients underwent colectomy, 2 were received other studies medications. Including these 5 patients who dropped out, clinical remission was achieved in 68.4% (13/19) of patients at 12 months, whereas only 36.8% (7/19) of patients were in remission at the start of the study. The CAI at the start of the therapy in 19 patients ranged between 1 and 12, with a median of 7.5 points. In 14 patients who continued ustekinumab throughout 1 year, the median CAI at 12 months fell to 2 points (range 0–5.5). In 14 patients, we were able to perform colonoscopy at 1 year: MAYO endoscopy scores fell from a median of 2 points (range 1–3) and a mean of 2.3 points at start of the observation to a median of 1 point (range 0–3) and a mean of 1.3.

Conclusions: Ustekinumab is an effective short- and long-term medication in therapy-refractory or -intolerant ulcerative colitis. It is therefore likely, which large ongoing long-term trials will confirm our findings and ustekinumab will become a new therapeutic option for refractory UC.

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High incidence of hyperglycaemia in steroid treated hospitalised inflammatory bowel disease (IBD) patients and its risk factors identified by machine learning methods

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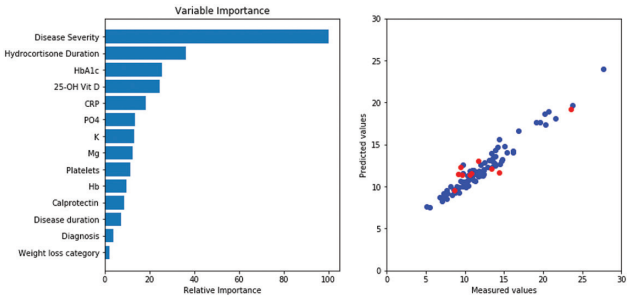
Background: Glucocorticoids (GC) have been first-line treatment for hospitalised IBD patients for over 60 years, despite the introduction of biologic therapy. IBD patients often have systemic inflammation complicated by malnutrition leading to metabolic stress. The frequency of and specific risk factors for hyperglycaemia in hospitalised IBD patients receiving GC are unknown.

Methods: In total, 93 consecutive IBD inpatients receiving intravenous hydrocortisone (IVH) for an acute flare had capillary blood glucose (CBG) monitoring automatically triggered by the electronic prescription. CBG, biomarkers, IBD severity scores (Harvey–Bradshaw, partial Mayo) and weight loss were prospectively recorded. Undiagnosed Diabetes Mellitus (DM) was defined as HbA1c >48 mmol/mol. Machine-learning (random forest regressor, RFR) was applied to the data to evaluate risk factors of hyperglycaemia.

Characteristic	Crohn's disease	Ulcerative colitis	IBDU	Combined
Total	54	32	7	93
Female	27 (50%)	18 (56%)	4 (57%)	49 (52%)
Age	41 (18–80)	46 (19–80)	51 (25–75)	44 (18–80)
Disease duration	8 (0–52)	5 (0–18)	1 (0–1)	6 (0–52)
HBI /partial Mayo	15 (6–31)	7 (3–9)	7 (3–9)	n/a
Admisison CRP	65 (<1–303)	86 (<1–440)	179 (114–300)	81 (<1–440)
Calprotectin	2652 (7–7049)	3266 (628–7091)	3692 (218–6000)	2915 (7–7091)
Pre-existing DM	6	1	1	8
Max CBG >11.0	27 (50%)	19 (59%)	5 (71%)	51 (55%)

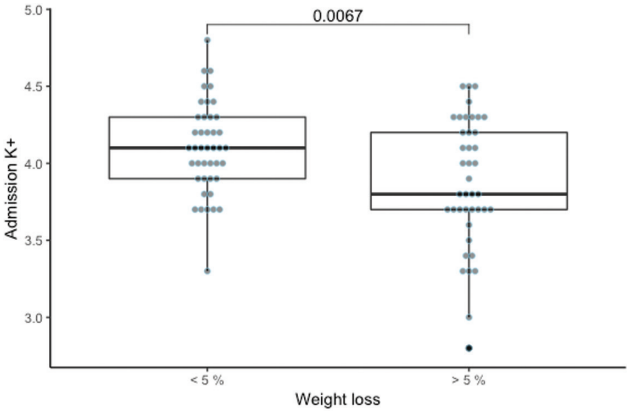
Characteristics of cohort and frequency of hyperglycaemia.

Results: Fifty-five per cent of hospitalised IVH-treated IBD patients met the WHO criteria of DM (CBG >11 mmol/l), while 22% and 8% had a CBG >14 mmol/l and >20 mmol/l, respectively. Only 8 patients had pre-existing DM, which was confirmed by admission HbA1c. RFR indicated disease severity score, duration of IVH, HbA1c and electrolyte imbalances (which affected 64%) were best predictors of hyperglycaemia.



Relative importance of input features of RFR model for prediction of CBG_max (left). Predictive value from RFR model vs. true value for training data set (blue) and test data set (red) (right).

Sixty-four per cent reported previous weight loss, which did not predict hyperglycaemia, although those with >5% weight loss had significantly lower admission serum potassium (p = 0.0067).



Admission serum potassium and preceding weight loss.

Conclusions: Our data demonstrate that hyperglycaemia is common in IVH-treated inpatients, therefore CBG monitoring should be routine practice. Predictive modelling (RFR) identifies more

severe disease activity, duration of IVH treatment and HbA1c as risk factors for hyperglycaemia. Preceding weight loss and electrolyte imbalance in the cohort demonstrate a tendency towards malnutrition-associated metabolic instability. The importance of IVH duration suggests hyperglycaemia risk may be physician modifiable. Alternative treatment strategies such as earlier introduction of biologics, rapid steroid taper and nutritional support could be used to minimise medication-associated metabolic instability in high-risk patients.

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TREM1, the first anti-TNF specific biomarker guiding therapeutic decision

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Background: With the expanding therapeutic armamentarium for inflammatory bowel diseases (IBD), biomarkers predicting efficacy are urgently needed. To predict outcome to anti-TNF therapy, we studied whole blood and mucosal expression of genes previously reported to predict outcome to anti-TNF therapy, and investigated whether the signature was specific for these agents.

Methods: We prospectively included 35 (discovery) and 19 (validation) consecutive IBD patients with active disease (both Crohn's disease and ulcerative colitis) initiating anti-TNF therapy, as well as 22 patients initiating ustekinumab and 51 patients initiating vedolizumab. Whole blood expression levels of OSM, TNF, TNFR2 and TREM1 (total and all individual transcripts separately) were measured prior to start of therapy using qPCR, and mucosal gene expression in inflamed biopsies using RNA-sequencing. Endoscopic remission was defined as an SES-CD ≤2 at Week 24 for Crohn's disease and a Mayo endoscopic sub-score ≤1 at Week 8–14 for ulcerative colitis.

Results: Baseline whole blood TREM1 expression was significantly down-regulated in future anti-TNF healers ($p < 0.001$, both discovery and validation cohort) (Figure).

Conclusions: We identified and validated low TREM-1 as a specific biomarker for anti-TNF-induced endoscopic remission. These results can aid in the selection of therapy in biological-naïve patients, but should be confirmed in a randomised trial prior to translation into daily clinical practice.

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Association of Infliximab trough levels and perianal disease activity in Crohn's disease

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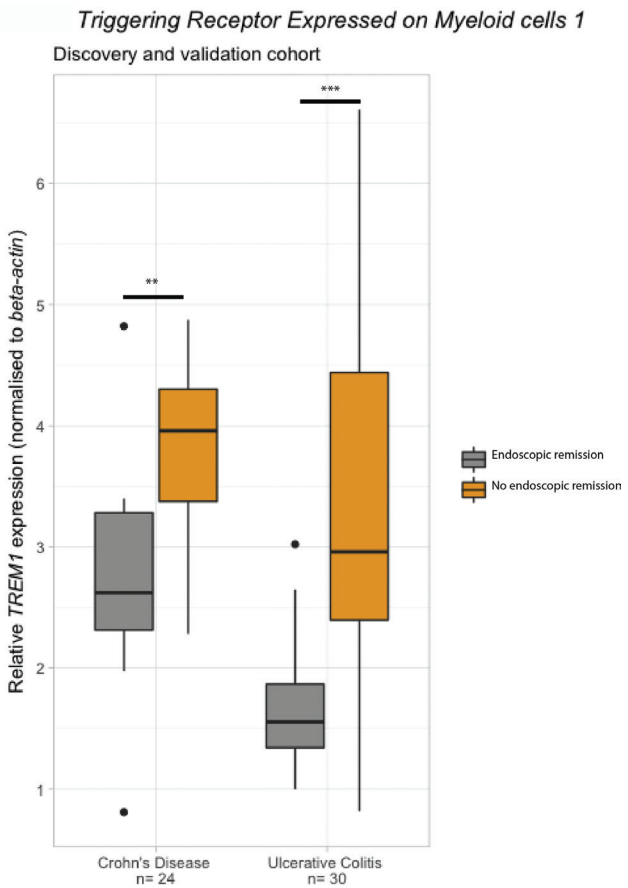

Baseline whole blood TREM1 expression in relation to endoscopic remission later on in both the discovery and validation cohort, visualised by diagnosis. ** $p < 0.005$, *** $p < 0.001$.

Receiver operator characteristic statistics showed an area under the curve (AUC) of 0.78 ($p = 0.001$), resulting in post-test probabilities of 77.1% and 90.0% for endoscopic remission and non-remission, respectively. A similar accuracy could be observed in mucosal TREM1 expression (AUC 0.77, $p = 0.003$), which outperformed the accuracy of serum TREM1 at the protein level (AUC 0.58, $p = 0.31$). Whole blood TREM1 expression did not significantly correlate with CRP (Spearman = −0.08, $p = 0.38$), faecal calprotectin (Spearman = −0.06, $p = 0.64$) or serum TNF (Sspearman = −0.15, $p = 0.63$). OSM, TNF, and TNFR2 were not differentially expressed in whole blood ($p = 0.09$, $p = 0.13$, $p = 0.24$, respectively), whereas they were at the mucosal level ($p = 0.007$, $p = 0.02$, $p = 0.008$, respectively). The whole blood TREM1 predictive signal was anti-TNF specific, as no changes in expression were seen in ustekinumab and vedolizumab treated patients, neither in whole blood ($p = 0.82$, $p = 0.53$, respectively), nor in tissue ($p = 0.24$, $p = 0.10$, respectively).

Background: Infliximab (IFX) has been proven to be efficacious in the treatment of perianal disease in patients with Crohn's disease (CD). Previous studies have shown a correlation between higher IFX trough levels and perianal fistula healing. We aimed to replicate these findings using a larger cohort of patients with Crohn's disease.

Methods: Retrospective cohort study including consecutive patients with Crohn's disease and perianal disease receiving treatment with infliximab between January 2016 and October 2018. Drug levels were compared between patients with active and inactive perianal disease. Active perianal disease was defined as an active draining fistula at physical examination and/or magnetic resonance imaging.