Surgical closure versus anti-TNF in the treatment of perianal fistulas in Crohn’s Disease (PISA-II): a comprehensive cohort design

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It is hypothesized that the surgical closure arm will result in an increased radiological fistula closure rate on MRI compared to the anti-TNF treatment arm (40 versus 15% respectively).

Ethical review	Not applicable
Status	Recruitment stopped
Health condition type	-
Study type	Interventional

Summary

ID

NL-OMON20965

Source
Nationaal Trial Register

Brief title
PISA-II

Health condition

Perianal Crohn's fistulas

Sponsors and support

Primary sponsor: Crohns and Colitis Foundation and ZonMw
Source(s) of monetary or material Support: Crohns and Colitis Foundation & ZonMW

Intervention

Outcome measures

Primary outcome

The primary outcome of this study is to the number of patients with radiologically closed perianal fistulas (on MRI) after 18 months. A radiologists blinded to treatment allocation will determine whether the fistula is completely fibrotic on MRI and/or will use a validated score, e.g. the van Assche score. The comparison between the anti-TNF and surgical closure arm will be assessed using Chi-square test.

Secondary outcome

The secondary outcomes parameters are clinical closure, defined as closure of the external opening without discharge of pus or faeces on palpation, number of patients undergoing surgical re-interventions and amount of re-interventions due to fistula related complications, fistula recurrence, defined as re-opening of the external opening after clinical closure, and quality of life as assessed by the PDAI.

Study description

Background summary

SUMMARY Rationale: Currently, the treatment of Crohn's patients with perianal fistulas predominantly exists of anti-TNF medication. However, its efficiency has never been directly compared to surgical closure of the perianal fistula. The primary objective of this study is to determine the optimal treatment for perianal Crohn’s fistulas by comparing two standard treatment strategies. Methods: In this multicenter comprehensive cohort design Crohn’s patients with a (re)active high perianal fistula will be allocated to anti-TNF for 1 year or surgical closure under a short course of anti-TNF (4 months). Patients with a distinct treatment preference will be treated accordingly, whereas only indifferent patients will be randomized in the usual way. The primary outcome parameter is the number of patients with a radiologically closed fistulas on MRI after 18 months. Secondary outcomes are clinical closure, re-interventions, recurrences and quality of life (QoL) based on Perianal Disease Activity Index (PDAI). Nature and extent of the burden and risks associated with participation, benefit and group relatedness: All patients will receive one of the two standard treatment approaches that are currently used for Crohn's fistulas. All effort has been performed to ensure most optimal treatment, according to best available evidence and current guidelines. Since there is no experimental study-arm, there are no additional risks associated with participation. During the study, the medical staff and trial nurses will monitor the necessity of surgical interventions and hospitalizations. At baseline and after 18 months all patients will undergo a MRI to score the fistula. Secondary outcome parameters will be assessed during visits to the outpatient clinic or telephone consultations at baseline and at intervals of 3 months for the duration of the study period. Every six months patients were asked to fill out the PDAI questionnaire with their physician. Based on the available literature, radiological

closure of fistulas is expected in 40% of patients in the surgical closure group compared to 15% in the anti-TNF group. The increase in closure rate from 15% to 40% is considered clinically relevant. Due to the combination of a preference and randomized cohort, the appropriate sample size to detect this 25% difference is flexible and is adjusted for a skewed distribution. The minimal sample size, in case of a 1:1 treatment allocation, needed to detect this difference with a Chi-square test equals 86 patients (alpha 0.05, and power 80%). The maximal allowed skewed distribution is set at 1:4, which will result in a maximal sample size of 116 patients.

Study objective

It is hypothesized that the surgical closure arm will result in an increased radiological fistula closure rate on MRI compared to the anti-TNF treatment arm (40 versus 15% respectively).

Study design

Patients visit the outpatient clinic regularly, as part of standard treatment. Additionally, patients will be contacted by telephone (CRF) every ± 3 months by a local investigator, trial nurse, or the Amsterdam UMC study coordinator to assess medication usage, complications, additional interventions, re-admissions, duration of hospital stay and visits to the outpatient clinic. Every 6 months, the patient will fill out the PDAI together with the gastroenterologist or surgeon at that time point. The PDAI is the gold standard for evaluating the severity of perianal disease. It includes five items: discharge, pain, restriction of sexual activity, type of perianal disease, and degree of induration.

Intervention

The following groups will be compared: Group I: Seton placement, followed by anti-TNF medication in combination with a immunomodulator after ± 2 weeks. The seton will be removed after ± 6 weeks. Continuation of anti-TNF medication for at least 1 year, after one year continuation is at the discretion of treating physician. Group II: Seton placement, followed by anti-TNF medication in combination with a immunomodulator after ± 2 weeks. After 8-12 weeks removal of seton and surgical closure (advancement plasty or ligation of the intersphincteric tract (LIFT) procedure). Anti-TNF in combination with a immunomodulator will be stopped after ± 4 months.

Contacts

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Eligibility criteria

Inclusion criteria

- ≥ 18 years - Active perianal fistula - High perianal fistula tract (intersphincteric, transsphincteric, suprasphincteric) located in the upper two-thirds of the external sphincter or puborectal muscle. - Fistula with one internal opening (based on MRI imaging). The number of external fistulas does not have to be taken into account. - Written informed consent

Exclusion criteria

- Proctitis (defined as any active mucosal inflammation or ulcer > 5mm in the rectum) - Anorectal stenosis (defined as the impossibility to introduce a proctoscope) - Submucosal fistulas & low intersphincteric fistulas (lower one-third of external sphincter) - Rectovaginal fistula - Multiple internal openings - Previous failure of anti-TNF treatment for perianal fistula - Patients with a stoma - Dementia or altered mental status that would prohibit the understanding and giving of informed consent

Study design

Design

Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Single blinded (masking used)
Control:	Active

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	01-09-2013
Enrollment:	116
Type:	Actual

IPD sharing statement

Plan to share IPD: Undecided

Ethics review

Not applicable
Application type: Not applicable

Study registrations

Followed up by the following (possibly more current) registration

ID: 48901
Bron: ToetsingOnline
Titel:

Other (possibly less up-to-date) registrations in this register

No registrations found.

In other registers

Register	ID
NTR-new	NL7625
CCMO	NL66176.018.18
OMON	NL-OMON48901

Study results