

REVIEW

HIGHLIGHTS

- Anti-TNFa are the most studied drug for perianal Crohn's disease.
- Some studies conclude that women had a longer fistula closure time than men.
- Few data corroborate the difference between sexes in the treatment of fistulizing perianal Crohn's disease.
- Studies don't separate simple and complex fistula healing.

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Corresponding author: Leticia Rosevics. E-mail: leticia.rosevics@hc.ufpr.br



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Fistulizing perianal Crohn's disease: is the patient's sex a burden? A systematic review

Leticia **ROSEVICS**¹, Mariane Cristina **SAVIO**², Emilton **LIMA JÚNIOR**¹ and Odery **RAMOS JÚNIOR**¹

¹ Universidade Federal do Paraná, Curitiba, PR, Brasil. ² Pontifícia Universidade Católica do Paraná, Curitiba, PR, Brasil.

ABSTRACT – Background – Fistulizing perianal Crohn's disease poses a treatment challenge, and researchers postulate that this phenotype in young male patients could have a worst outcome. **Objective** – Thus, the aim of this study was to assess whether sex influences the response to treatment for these patients. **Methods** – This systematic review (PROSPERO CRD42022319629) was conducted in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses protocol. We selected articles published in English, Spanish, Portuguese, and Italian between 2010 and 2020 in the PubMed and Science Direct databases. According to the PICO acronym, prospective studies in patients older than 18 years with the objective of treating fistulizing perianal Crohn's disease were selected. Studies in pediatric populations, retrospective, without treatment objectives, and that included only rectovaginal fistulas or a single sex were excluded. Study quality was assessed using the Cochrane risk of bias tool and Newcastle–Ottawa scale. **Results** – Of the 1887 articles found, 33 were included. Most studies used anti-TNF drugs as treatment (n=11). Ten studies had subgroup analyses; of them, the two studies reporting sex differences used infliximab and adalimumab as treatment and showed that women had a longer fistula closure time than men. **Conclusion** – This systematic review showed that few data corroborate the difference between sexes in the treatment of fistulizing perianal Crohn's disease, possibly having a greater relationship with the phenotype. However, considering the lack of results, further studies with this objective and with standardization of fistulas and response assessment methods are needed.

Keywords – Crohn's disease; systematic review; perianal fistula; treatment.

INTRODUCTION

Crohn's disease (CD) is characterized by an inflammatory condition capable of affecting the entire gastrointestinal tract⁽¹⁾. It is subdivided into phenotypic profiles, among which fistulizing perianal disease occurs in up to 30% of patients, with marked impairment of quality of life^(2,3).

Several strategies are available for the treatment of fistulizing perianal CD, including surgical and drug interventions^(4,5). The use of biological drugs, including anti-TNF drugs as the first representatives, largely changed the natural history of the disease; these drugs have yielded higher and more sustained remission rates than did immunosuppressants^(4,5).

The literature has shown a worse prognosis and more difficult treatment of fistulizing perianal disease in young male patients^(4,6,7). With the development of new treatments, it is necessary to evaluate whether the change in the natural history of the disease has also influenced this paradigm⁽⁸⁾.

Thus, this systematic review aimed to evaluate whether sex influences the treatment outcomes of fistulizing perianal CD.

METHODS

This systematic review was registered in the PROSPERO database (CRD42022319629) and conducted in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses protocol. To elaborate the main question, we used the acronym PICO: Is sex a relevant factor in the treatment outcomes of patients with fistulizing perianal CD?

We included articles published during a 10-year period, from 2010 to 2020; with patients aged over 18 years; whose objective was the treatment of fistulizing perianal CD; published in English, Spanish, Italian, or Portuguese; and whose methodology involved prospective studies, clinical trials, cohort studies, or randomized studies. Articles found in secondary data sources and that met the inclusion criteria were also included for analysis. Meanwhile, studies in pediatric populations; without treatment evaluation objectives; involving only rectovaginal fistulas or a single sex; with a retrospective methodology; with a sub-analysis of the same group of

patients published previously; whose scope was fistulizing diseases, but with a small group of patients with CD, without analysis of this subgroup; and whose main objective was the treatment of CD, other than exclusively fistulizing perianal disease, but with a small subgroup of patients and no descriptive subgroup analysis of fistulizing perianal disease were excluded.

The research sources were the PubMed and Science Direct databases. The descriptors and Boolean operators used were as follows: "Crohn" OR "Crohn's disease" AND "fistula" OR "fistulae."

The article selection and analysis, including both data extraction and quality analysis, were performed by two independent reviewers (Rosevics L and Savio MC); in cases of disagreement between the reviewers, a third reviewer made the final decision (Ramos Júnior O).

The results were extracted in pre-defined tables, including the journal name, year, country of origin, objectives, main methodology, inclusion and exclusion criteria, therapy, results, and population characteristics, such as age, sex, time of disease, and disease phenotype, in addition to a column for specific results of the sex subgroup analysis.

The quality of the studies was assessed using pre-defined scales (Cochrane risk of bias tool for randomized clinical trials and Newcastle–Ottawa scale for cohort and case-control studies).

RESULTS

A total of 8950 articles were found, including 1464 from the PubMed database and 7486 from the Science Direct database. Considering the temporal and review exclusion filters, 1853 articles were obtained. Finally, 33 articles were included in the study, as shown in FIGURE 1.

One to five articles were published each year between 2010 and 2020, with only one article published in 2017 and five articles in 2019. Twenty-three studies had populations from European countries, two from the United States, two from Korea, one from Chile, and five from multiple countries, including Europe, the United States, Canada, and Israel.

The description of the included studies is presented in TABLE 1⁽⁹⁻⁴¹⁾.

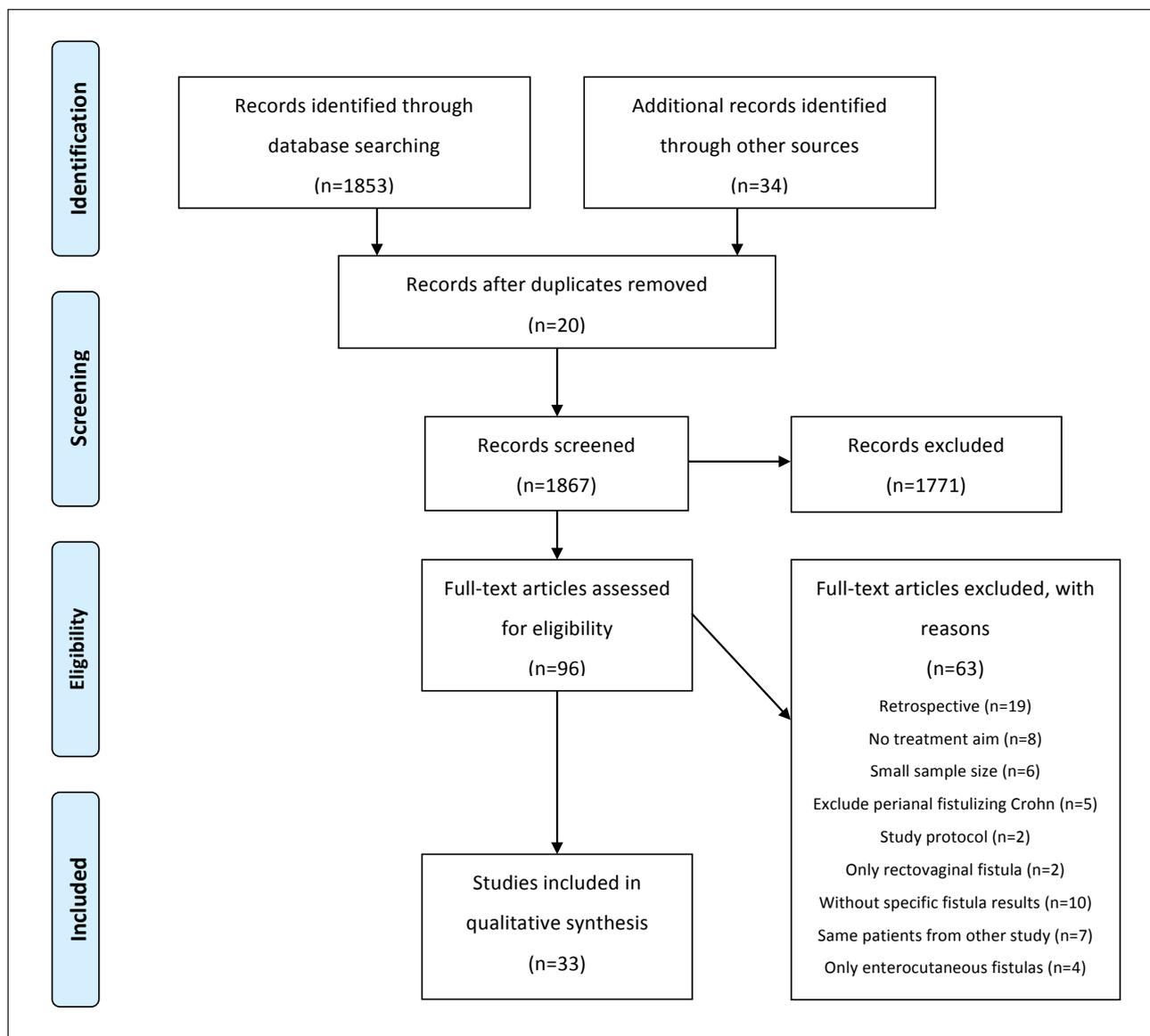


FIGURE 1. PRISMA article selection.

For the study treatments, seven studies investigated adalimumab; three, vedolizumab; one, ustekinumab; one, certolizumab; nine, stem cell therapy; three, infliximab and surgery; one, local infliximab; and one, each of the following treatments: fibrin glue, autologous hematopoietic stem cell transplantation, azathioprine, AST-120 (spherical carbon adsorbent), anal fistula plug (AFP)-seton removal alone with AFP insertion, autologous adipose tissue, autologous microfat and adipose-derived stromal vascular fraction, and Permacol™ collagen paste.

Seven studies considered the treatment response in patients with CD as their main study endpoint but included patients without fistulizing perianal disease

in their sample; the remaining studies had this population as their main focus.

The studies considered cicatrization as a total response to fistula development but also the absence or improvement of drainage as a positive response to treatments.

Regarding the study design, 10 studies were randomized studies, while the remaining studies were prospective and open cohort studies. The different statistical methods used were as follows: Fisher's exact test (n=10), chi-square test (n=8), Kaplan–Meier method (n=8), Mann–Whitney test (n=7), Wilcoxon test (n=6), logistic regression (n=5), Student's *t*-test (n=5), intention-to-treat analysis (n=5), OR assess-

TABLE 1. Included articles description.

Paper	Design	Treatment	Main objective	Population	Fistula (anatomy)	Location of disease	Duration of CD	Clinical endpoint	Gender prognostic factor
Erchari, 2010 ⁽⁹⁾	Cohort	Adalimumab	Determine if the use of MRI to initially assess complex fistulas, as well as guiding seton drainage, can improve the rate of durable fistula healing.	Female=6 Male=10 Total=16 Age (Mean±SD) =33.9±7.8	Number of fistulas at baseline: 1 fistula = 8 (50%) 2 fistulas = 4 (25%) 3 fistulas = 2 (12.5%) Type of fistulas: Simple = 7(44%) Complex = 9(56%)	L1 = 1 (6.25%) L2 = 9 (56.2%) L3 = 6 (37.5%)	-	4 weeks after commencing subcutaneous adalimumab treatment, 50% of patients had a complete response (CR). The CR rate after 24 and 48 weeks was 43.75%. Once CR was achieved, the recurrence rate was low and the effect of treatment was maintained in 87.5% of patients.	Not described
Grimaud, 2010 ⁽¹⁰⁾	Randomized	Fibrin glue	Efficacy and safety.	Fibrin group Female=23 Male=13 Total=36 Age=35 (27–41) Observational group Female=28 Male=13 Total=41 Age=36 (28–42)	Fibrin group Simple 20 (56) Complex 16 (44) Fistula duration (years) 1.4 (0.8–4.5) Observational group Simple 21 (51) Complex 20 (49) Fistula duration (years) 1.9 (1.1±.3)	Fibrin group L1=8 (22) L2=12 (33) L3=16 (44) Observational group L1=7 (17) L2=18 (44) L3=16 (39)	Fibrin group (years) 6.8 (3.6–14.2) Observational group 6.6 (3.1–11.1)	At week 8, clinical remission was observed in 38% of the fibrin glue group compared with 16% in the observation group, demonstrating a significant benefit of the fibrin glue (OR, 3.2; 95%CI: 1.1–9.8, <i>P</i> <.04). At week 4, clinical remission was observed in 35% in the fibrin glue group compared with 19% in the observation group (OR, 2.3; 95% CI: 0.8 – 6.9, respectively, <i>P</i> <0.12).	Not described
Schreiber, 2010 ⁽¹¹⁾	Randomized	Certolizumab	Post hoc analyses performed to examine the fistula closure effects of certolizumab pegol and to determine whether fistula closure observed at week 6 is maintained through to week 26.	Certolizumabe Female=14 Male=14 Total=28 Age=37.3±9.4 Placebo Female=10 Male=20 Total=30 Age=37.6±10.1	Certolizumabe Fistula type, n (%) Anal 27 (96) Other 1 (4) Placebo Fistula type, n (%) Anal 28 (93) Other 3 (10)	Certolizumabe L1=5 (18) L2=11 (39) L3=12 (43) Placebo L1=2 (7) L2=10 (33) L3=16 (53)	Certolizumabe 10.2±8.9 Placebo 7.8±5.9	In the certolizumab pegol group, 73% of patients maintained at least 50% fistula closure by week 26 and 67% maintained 100% closure by week 26.	Not described
Sciaudone, 2011 ⁽¹²⁾	Case-control	Infliximab and surgery.	Compare the outcomes of the management of perianal fistulas in Crohn disease between infliximab, surgery or a combination of surgery and infliximab.	Infliximab Female=7 Male=4 Total=11 Age=36.3 (19–63) Surgery Female=7 Male=3 Total=10 Age=33.1 (16–58) Infliximab + surgery Female=8 Male=6 Total=14 Age=35.3 (18–65)	All complex fistulas	Infliximab L1=2 L2=4 L3=5 Perianal Only 0 Surgery L1=2 L2=3 L3=5 Perianal Only 0 Infliximab+surgery L1=3 L2=4 L3=6 Perianal Only 1	Infliximab 8.8 (1–14) Surgery 7.9 (0.9–18) Infliximab + surgery 7.4 (0.8–21)	The time to healing of fistulas was significantly shorter among patients who received surgery and infliximab than among those who received surgery alone (<i>P</i> <0.05), and was close to statistically shorter among those who received both treatments than among those who received infliximab alone (<i>P</i> =0.06). Patients who received surgery and infliximab had a significantly longer mean time to relapse (<i>P</i> <0.05) than those who received infliximab or surgery alone.	Not described
Roumeguère, 2011 ⁽¹³⁾	Cohort	Infliximab, surgery and methotrexate.	Evaluate the short- and long-term efficacy of a combined schedule with infliximab, methotrexate, and sphincter-sparing surgery in patients with severe fistulizing anoperineal CD.	Female=26 Male=8 Total=34 Age=38.5 [23–68]	All complex anoperineal fistula (including nine with recto-vaginal fistulas, and 10 with anorectal stenosis).	L1=1 (3) L2=13 (38) L3=18 (53) Ano-perineal disease alone 2 (6)	7 (0–25) years	At week 14 the response rate was 85% with 74% complete responders. At 1 year, 50% were still responders; luminal CD worsening was the major cause of relapse. Median PDAI and MRI scores significantly decreased from baseline to week 50.	Not described
Alessandrini, 2011 ⁽¹⁴⁾	Cohort	Local infliximab.	Efficacy of surgical treatment combined with local perifistular infliximab injections in producing and maintaining closure of perianal fistulas associated with CD.	Female=4 Male=8 Total=12 Age=38 [18–52]	Transsphincteric =10 Intersphincteric =2	L1=2 L2=4 L3=6	10.8 (2–26) years	Eight patients continued treatment until all perianal fistulas were closed and setons were removed. Persistent closure was observed in 7 (87.5%, 95%CI: 47.4–99.6) of the eight patients 12 months after completion of treatment and in 5 (62.5%; 95%CI: 24.5–91.5) of eight at the end of follow-up (range: 19–43 months, median: 35 months).	Not described

Continuation →

Paper	Design	Treatment	Main objective	Population	Fistula (anatomy)	Location of disease	Duration of CD	Clinical endpoint	Gender prognostic factor
Clerici, 2011 ⁽¹⁵⁾	Cohort	Autologous haematopoietic stem cells transplantation (HSCT).	Effects of HSCT on the immune response of patients treated for moderate-severe Crohn's disease, refractory or intolerant to multiple drugs.	Six patients, fistulizing perianal: Female=2 Male=2 Total=4 Age=38,25 (28–45)	Not described, but includes rectovaginal fistula	L1=0 L2=2 L3=2	9 (3–22) years	Clinical exam, anal US and magnetic resonance (MRI) showed complete fistula closure in one case and stable perianal fistula tract, with no other complications, in three cases, even if pauci-symptomatic.	Not described
Lofberg, 2012 ⁽¹⁶⁾	Cohort	Adalimumab.	Clinical effectiveness, extraintestinal manifestation resolution, fistula healing, and safety in patients with moderate to severe CD, including those who had never responded to infliximab.	No prior Infliximab: Female=266 Male=212 Total=478 Prior Infliximab: Female=302 Male=165 Total=467	Multiples=60 Single=111 Total=171	No prior IFX Colonic=343 Ileal=341 Perianal=87 Rectum=90 Jejunum=28 Prior IFX Colonic=361 Ileal=320 Perianal=141 Rectum=100 Jejunum=19	No prior Infliximab 6.3 (0.4-45.4) years Prior Infliximab 9.1 (0.5-40.5) years	Complete fistula closure was observed in 19% of patients at week 4 and 26% at week 20. Fistula closure rates were numerically higher in the infliximab-naive group at weeks 4 and 20 (22% and 33%, respectively) than in the infliximab-experienced group (17% and 22%, respectively; <i>P</i> =0.369 at week 4, and <i>P</i> =0.275 at week 20). Similar rates of closure were seen in the primary nonresponse (15% at week 4, 19% at week 20) and the other reason for infliximab discontinuation groups (17% at week 4, 23% at week 20; <i>P</i> =0.840 at week 4, <i>P</i> =0.973 at week 20).	Gender difference was described only in relation to the pre-exposure group with Infliximab, most of them female, with fistulas and anal/perianal disease. No difference was described in relation to treatment by sex.
Cho, 2012 ⁽¹⁷⁾	Cohort	Adipose-derived stromal stem cell (ASCs)	Efficacy and safety of ASCs.	Female=6 Male=4 Total=10 Age=26.5±6.0	Transsphincteric = 5 (50%) Suprasphincteric= 4 (40%) Extrasphincteric = 1 (10%)	Not described	Not described	Three patients in group 1 (who were given were given 1 X 10 ⁷ cells/mL) showed partial closure with decreased drainage. Two patients in group 2, injected with 2 X 10 ⁷ ASCs/mL in proportion to fistula size, showed complete healing at week 8 after injection. Of the three patients in group 3, one showed complete healing.	Not described
Tonelli, 2012 ⁽¹⁸⁾	Cohort	Local Adalimumab	Effectiveness and safety of local Adalimumab injection.	Female=9 Male=3 Total=12 Age=43.5 [27–59]	Transsphincteric=7 Anovaginal=3 Complex=2	L1=2 L2=2 L3=8	13.8 (6–22) years	Nine had drainage stopped and three had improvement.	Not described
Lee, 2013 ⁽¹⁹⁾	Cohort	Adipose-derived stromal stem cell (ASCs).	Efficacy and safety of ASCs.	Modified per-protocol Female=11 Male=22 Total=33 Age=26.7±5.6 Modified Intention to treat Female=13 Male=30 Total=43 Age = 26.2 ± 5.4	Modified per-protocol Transsphincteric=42 Suprasphincteric=4 Extrasphincteric=5 Modified Intention to treat Transsphincteric=30 Suprasphincteric=5 Extrasphincteric=8	-	Modified per-protocol 0–12, n (%) 5 (15.2) 13–24, n (%) 5 (15.2) 25–36, n (%) 2 (6.1) 37–48, n (%) 3 (9.1) >49, n (%) 18 (54.5) Modified Intention to treat 0–12, n (%) 6 (14.0) 13–24, n (%) 5 (11.6) 25–36, n (%) 5 (11.6) 37–48, n (%) 4 (9.3) >49, n (%) 23 (53.5)	27 healed after the first injection. 1 of the 10 that had a 2nd application healed. 23 had sustained healing at 12 months.	No statistical significance was found between any of parameters and fistula healing (diameter or length of the fistula, fistula type according to Park's classification, patient gender, and duration of Crohn's disease)
Portilla, 2013 ⁽²⁰⁾	Cohort	Adipose-derived stromal stem cell (ASCs).	Safety and efficacy eASCs.	Female=13 Male=11 Total=24 Age=36.0 (9.0)	Extrasphincteric 1 (4.2 %) Intersphincteric 5 (20.8 %) Suprasphincteric 1 (4.2 %) Transsphincteric 17 (70.8 %)	-	-	69.2 % of the patients have had a reduction in the number of draining fistulas. 56.3 % of the patients achieved complete closure of the treated fistula achieved, and 30 % of the cases presenting complete closure of all existing fistula tracts.	Not described

Continuation →

Paper	Design	Treatment	Main objective	Population	Fistula (anatomy)	Location of disease	Duration of CD	Clinical endpoint	Gender prognostic factor
Schreiber, 2013 ⁽²¹⁾	Randomized	Adalimumab.	Compare clinical remission and response rates for patients with early versus late CD, and assess disease duration as a predictor of clinical remission with adalimumab treatment in patients with moderately to severely active CD in the placebo-controlled CHARM trial, and the follow-on open-label extension ADHERE trial.	Disease duration <2 years Female=59 Male=34 Total=93 Age=34.9 Disease duration 2–5 years Female=105 Male=43 Total=148 Age=34.3 Disease duration ≥5 years Female=318 Male=218 Total=536 Age=38.0	Not reported	Not reported	Not reported	At week 56, clinical remission rates were significantly greater for adalimumab-treated versus placebo-treated patients in all 3 duration subgroups (19% versus 43% for <2 years; <i>P</i> =0.024; 13% versus 30% for 2 to <5 years; <i>P</i> =0.028; 8% versus 28% for ≥5 years, <i>P</i> =0.001). Logistic regression identified shorter duration as a significant predictor for higher remission rate in adalimumab-treated patients.	Age, tobacco use, baseline immunosuppressant use, baseline steroid use, prior immunosuppressant use, prior steroid use, prior aminosalicylate use, and fistula at baseline were not significant factors at either time point.
Cosnes, 2013 ⁽²²⁾	Randomized	Azathioprina.	Compare the efficacy of early treatment (within 6 months after diagnosis) with azathioprine versus conventional management of patients at high risk for disabling disease.	Early azathioprine group Female=34 Male=31 Total=65 Age=25.6 (21.3–29.0) Conventional management Female=33 Male=34 Total=67 Age=24.7 (21.2–28.7)	Early azathioprine group Simple fistula=4 Complex fistula=0 Conventional management Simple fistula=5 Complex fistula=1	Early azathioprine group L1=16 L2=10 L3=60 Conventional management L1=20 L2=14 L3=33	Early azathioprine group 2.1 (0.9–3.6) years Conventional management 2.3 (1.4–3.9) years	Administration of azathioprine within 6 months of diagnosis of CD was no more effective than conventional management in increasing time of clinical remission.	Not significant between sex and fistulas
Dewint, 2014 ⁽²³⁾	Randomized	Adalimumab plus ciprofloxacin.	50% reduction in fistulas at week 12.	Ciprofloxacin Female=14 Male=20 Total=34 Age=25.6 (21.3–29.0) Placebo Female=19 Male=17 Total=36 Age=25.6 (21.3–29.0)	Ciprofloxacin 34.7 (11.0) Placebo 37.3 (12.4)	Not described	Ciprofloxacin 1.59 (1.02) Median (1–5) Placebo 1.56 (1.00) Median (1–6)	Clinical response was observed in 71% of patients treated with adalimumab plus ciprofloxacin and in 47% treated with adalimumab plus placebo.	Univariate analysis showed that outcome was not influenced by any of the patient characteristics.
Reinisch, 2014 ⁽²⁴⁾	Randomized	AST-120 (spherical carbon adsorbent).	Efficacy and safety of AST-120 in a Western population.	AST-120 Female=48 Male=74 Total=122 Age=37.5 (11.8) Placebo Female=62 Male=65 Total=127 Age=38.5 (11.5)	AST-120 1.6 (1.1) Number of fistulas - AST-120 group - 1.6 (1.1) - Placebo - 1.6 (1.0) Concomitant rectovaginal - AST-120 group - 2 (1.6) - Placebo - 4 (3.1)	AST-120 Jejunum=1 Ileum=56 Right or transverse colon=20 Left colon or sigmoid=25 Rectum=22 Placebo Jejunum=1 Ileum=63 Right or transverse colon=15 Left colon or sigmoid=22 Rectum=26	AST-120 12.1 (10.4) Placebo 11.0 (9.7)	The proportions of patients achieving the primary endpoint (50% reduction in the number of draining fistulae, at both weeks 4 and 8) were no different between treatment groups (13.9% versus 16.5%, <i>P</i> =0.6). No differences in fistula response were noted at week 4 (23.0% versus 25.2%, <i>P</i> =0.77) or week 8 (27.0 versus 34.6%, <i>P</i> =0.22). Serum C-reactive protein concentrations >0.6 mg/dL and Crohn's disease activity index scores >151 at baseline were associated with a reduced likelihood of treatment success.	No sex difference in univariate or multivariate analysis

Continuation →

Paper	Design	Treatment	Main objective	Population	Fistula (anatomy)	Location of disease	Duration of CD	Clinical endpoint	Gender prognostic factor
Molendijk, 2015 ⁽²⁵⁾	Randomized	Bone marrow derived mesenchymal stromal cells (MSCs).	Effects of local administration of bone marrow derived mesenchymal stromal cells (MSCs) in patients with CD from healthy donors in a double-blind, placebo-controlled study.	<p>Group 1 (injections of 1 X 10⁷) Female=1 Male=4 Total=5 Age=40.4 (4.6)</p> <p>Group 2 (injections of 3 X 10⁷) Female=1 Male=4 Total=5 Age=40.8 (1.7)</p> <p>Group 3 (injections of 9 X 10⁷) Female=4 Male=1 Total=5 Age=33.4 (5.2)</p> <p>Placebo Female=3 Male=3 Total=6 Age=37.3 (3.6)</p>	<p>Group 1 Simple=2 Complex=3</p> <p>Group 2 Simple=1 Complex=4</p> <p>Group 3 Simple=1 Complex=4</p> <p>Placebo Simple=2 Complex=4</p>	<p>Group 1 L1=1 L2=3 L3=1</p> <p>Group 2 L1=1 L2=2 L3=2</p> <p>Group 3 L1=2 L2=1 L3=2</p> <p>Placebo L1=1 L2=2 L3=2</p>	<p>Group 1 7.6 (1.1)</p> <p>Group 2 16.8 (4.0)</p> <p>Group 3 13.2 (4.1)</p> <p>Placebo 6.8 (2.9)</p>	<p>Healing at week 6 was observed in three patients in group 1 (60.0%), four patients in group 2 (80.0%), and one patient in group 3 (20.0%), vs one patient in the placebo group (16.7%) (<i>P</i>=0.08 for group 2 vs placebo). At week 12, healing was observed in two patients in group 1 (40.0%), four patients in group 2 (80.0%), and one patient in group 3 (20.0%), vs two patients in the placebo group (33.3%); these effects were maintained until week 24 and even increased to 4 (80.0%) in group 1. At week 6, 4 of nine individual fistulas had healed in group 1 (44.4%), 6 of 7 had healed in group 2 (85.7%), and 2 of 7 had healed in group 3 (28.6%) vs 2 of 9 (22.2%) in the placebo group (<i>P</i>=0.04 for group 2 vs placebo). At week twelve, 3 of 9 individual fistulas had healed in group 1 (33.3%), 6 of 7 had healed in group 2 (85.7%), 2 of 7 had healed in group 3 (28.6%), and 3 of 9 had healed in the placebo group (33.3%). These effects were stable through week 24 and even increased to 6 of 9 (66.7%) in group 1 (<i>P</i>=0.06 group 2 vs placebo, weeks 12 and 24).</p>	Not described
Khanna, 2015 ⁽²⁶⁾	Randomised	Adalimumab.	The mean proportion of patients in corticosteroid-free remission (HBI score ≤4) at month 12.	<p>Early combined Immunosuppression Female=627 Male=457 Total=1084 Age=44.1 (3.8)</p> <p>Conventional Management Female=511 Male=387 Total=898 Age=44.1 (2.7)</p>	<p>Early combined Immunosuppression 6.6%</p> <p>Conventional Management 8.2%</p>	<p>Early combined Immunosuppression L1=32.3% L2=24% L3=43.7%</p> <p>Conventional Management L1=36.7% L2=20.1% L3=43.2%</p>	<p>Early combined Immunosuppression 149.0 (40.0) months</p> <p>Conventional Management 158.1 (29.2) months</p>	<p>The 12 month practice-level remission rates were similar between the groups. The 24 month patient-level composite rate of major adverse outcomes defined as occurrence of surgery, hospital admission, or serious disease related complications was lower at ECI practices than at conventional management practices. There were no differences in serious drug-related adverse events.</p>	<p>Assignment to conventional management, younger age, perianal or fistulizing disease, high clinical disease activity, and corticosteroid therapy were associated with an increased risk of major adverse outcomes (complications, surgery or hospitalization). Male sex, no previous surgery, low disease activity or remission at baseline, and a shorter disease duration were independently associated with the presence of remission.</p>
Ciccocioppo, 2015 ⁽²⁷⁾	Cohort	Bone marrow derived mesenchymal stromal cells (MSCs).	Safety and efficacy of MSC.	<p>Female=3 Male=5 Total=8 Age=39.25 (22-66)</p>	<p>Complex fistula=7 Enterocutaneous=1</p>	Not described	Not described	<p>The probability of fistula relapse-free survival was 88% at 1 year, 50% at 2 years, and 37% during the following 4 years, and the cumulative probabilities of surgery and medical-free survival were 100% and 88% at 1 year, 75% and 25% at 2, 3, and 4 years, and 63% and 25% at 5 and 6 years, respectively. No adverse events were recorded.</p>	Not described
Haening, 2015 ⁽²⁸⁾	Cohort	Infliximab e cirurgia.	Efficacy of local surgery combined with infliximab on sustained fistula closure and to identify predictive factors for response after this combined treatment.	<p>Female=42 Male=39 Total=81 Age=31±13. 26.9</p>	<p>Complex fistula=71 Rectovaginal fistula=12</p>	<p>L1=6 L2=32 L3=42</p>	Not described	<p>Seton associated with anti-TNF was responsible for closing 75% of fistulas.</p>	<p>Bivariate analysis showed that female gender, complex fistula, rectovaginal fistula and anorectal stenosis are associated with a significantly longer time to complete closure. The time to closure was shorter for men than women and for simple compared with complex fistulae. A rectovaginal fistula required a longer interval to closure. After multivariate analysis only the presence of a rectovaginal fistula remained significant.</p>

Continuation →

Paper	Design	Treatment	Main objective	Population	Fistula (anatomy)	Location of disease	Duration of CD	Clinical endpoint	Gender prognostic factor
Panés, 2016 ⁽²⁹⁾	Randomised	Allogeneic adipose-derived mesenchymal stem cells (Cx601).	Safety and efficacy of Cx601.	Cx601 Female=47 Male=60 Total=107 Age=39.0 (13.1) Placebo Female=49 Male=56 Total=105 Age=37.6 (13.1)	All complex perianal fistulas, excluded rectovaginal fistulas.	Not described	Cx601 12.1 (10.0) Placebo 11.3 (8.9)	A significantly greater proportion of patients treated with Cx601 versus placebo achieved combined remission in the ITT ($P=0.024$) and modified ITT populations ($p=0.021$). 18 (17%) of 103 patients in the Cx601 group versus 30 (29%) of 103 in the placebo group experienced treatment-related adverse events, the most common of which were anal abscess and proctalgia.	Not described
Senéjoux, 2016 ⁽³⁰⁾	Randomised	Anal fistula plug [AFP] - seton removal alone [control group] with AFP insertion [AFP group].	Efficacy and safety of AFP.	AFP Group Female=36 Male=18 Total=54 Age=34 [26–41] Control group Female=32 Male=20 Total=52 Age=37 [26–43]	AFP Group Simple=39 Complex=15 Multiple tract on MRI=7 Anovaginal tract=0 Large ulceration at internal opening=2 Control group Simple=39 Complex=13 Multiple tract on MRI=6 Anovaginal tract=0 Large ulceration at internal opening=4	AFP Group Distal ileum=34 Proximal ileum, jejunum, Stomach=4 Colon=41 Rectum=20 Control group Distal ileum=33 Proximal ileum, jejunum, Stomach=3 Colon=37 Rectum=16	AFP Group 7 [3; 13] Control group 10 [3; 4]	Fistula closure at week 12 was achieved in 31.5% patients in the AFP group and in 23.1 % in the control group (relative risk [RR] 1.31; 95% confidence interval: 0.59–4.02; $P=0.19$). No interaction in treatment effect with complexity stratum was found; 33.3% of patients with complex fistula and 30.8% of patients with simple fistula closed the tracts after AFP, as compared with 15.4% and 25.6% in controls, respectively [RR of success = 2.17 in complex fistula vs RR = 1.20 in simple fistula; $P=0.45$]. Concerning safety, at Week 12, 17 patients developed at least one adverse event in the AFP group vs 8 in the controls [$P=0.07$].	Not described
Dietz, 2017 ⁽³¹⁾	Cohort	Autologous Mesenchymal Stem Cells.	Safety and feasibility.	Female=6 Male=6 Total=12 Age=35 (18–58)	Transesfincteriano=6 Interesfincteriano=3 Supraesfincteriano=1 Transsphincteric with puborectalis/levator plate extensions=2	–	Mean 6.5 Median 5	10 clinical responses. Radiographic criteria for response were demonstrated in 10 of 12 patients (83%).	Not described
Panaccione, 2018 ⁽³²⁾	Randomized	Adalimumab.	Efficacy and safety of adalimumab in failed patients at 96 weeks or 3 years.	Female=202 Male=108 Total=310 Age=38.3 [11.9]	–	Ileum=224 Colon=209 Rectum=43 Other=72 Presence of fistula=43	10.2 [0.6–46.7]	The rate of fistula remission among patients who presented with draining fistulae at GAIN baseline was 50.0% [21/42] at week 8 of ADHERE and increased to 70.0% [21/30] at week 48, and it remained at remained around 60% until week 96.	Not described
Feagan, 2018 ⁽³³⁾	Randomized	Vedolizumab.	Exploratory analyses of the GEMINI 2 maintenance intent-to-treat (ITT) population to evaluate the potential efficacy of vedolizumab for the treatment of fistulizing CD.	Patients with draining fistula at baseline Vedolizumab/placebo Female=10 Male=8 Total=18 Age=35.8±11.0 Vedolizumab/Vedolizumab Female=19 Male=20 Total=39 Age=32.6±9.5	Patients with draining fistula at baseline Vedolizumab/placebo 1=13 2=4 ≥3=1 Vedolizumab/Vedolizumab 1=30 2=6 ≥3=3	Patients with draining fistula at baseline Vedolizumab/placebo L1=2 L2=7 L3=9 Vedolizumab/Vedolizumab L1=3 L2=11 L3=25	Patients with draining fistula at baseline Vedolizumab/placebo 10.8±9.9 Vedolizumab/Vedolizumab 9.1±7.8	At entry into the maintenance period, 153 [33%] patients had a history of fistulizing disease and 57 [12%] patients had ≥1 active draining fistula. By week 14, 28% of VDZ/VDZ-treated patients compared with 11% of VDZ/PBO-treated patients (95% confidence interval [CI], –11.4 to 43.9) achieved fistula closure. Corresponding rates at Week 52 were 31% and 11% (absolute risk reduction [ARR]: 19.7%; 95%CI, –8.9 to 46.2). Similarly, VDZ/VDZ-treated patients had faster time to fistula closure and were more likely to have fistula closure at Week 52 [33% vs 11%; HR: 2.54; 95%CI, 0.54–11.96]. By week 14, 28% of patients with draining fistulae treated with VDZ/VDZ had fistula closure compared with 11% treated with VDZ/PBO (absolute risk reduction [ARR]: 17.1%; 95%CI, –11.4 to 43.9). Similar results were observed in the subpopulation of patients with only perianal fistulae [VDZ/VDZ, 34%; VDZ/PBO, 15%] and across vedolizumab dose groups [Q8W: 29.4%, n=17; Q4W: 27.3%, n=22]. Corresponding values at Week 52 were 31% [n=12] for VDZ/VDZ and 11% [n=2] [ARR: 19.7%; 95%CI, –8.9 to 46.2]. Patients who continued treatment with vedolizumab were more likely to have fistula closure by Week 52 than those who received placebo [HR: 2.54; 95%CI, 0.54–11.96].	No other covariates were significantly associated with fistula closure.

Continuation →

Paper	Design	Treatment	Main objective	Population	Fistula (anatomy)	Location of disease	Duration of CD	Clinical endpoint	Gender prognostic factor
Wainstein, 2018 ⁽³⁴⁾	Cohort	Adipose-Mesenchymal Stem Cells.	Describe long-term outcomes of patients with perineal Crohn's disease who received combined treatment with ASCs, platelet-rich plasma and endorectal advancement flaps.	Female=7 Male=2 Total=9 Age=38.6 (23-57)	All complex fistula	L1=1 L2=1 L3=6	7.4 (4-15)	10/11 (91%) fistulas were completely healed and 1/11 (9%) was partially healed.	Not described
Dige, 2019 ⁽³⁵⁾	Cohort	Autologous Adipose Tissue.	Complete fistula healing after 6 months.	Female=15 Male=6 Total=21	Transsphincteric (n=13) Anovaginal (n=7) High intersphincteric (n=1).	-	-	12 (57%) patients had complete fistula healing on clinical examination 6 months after 1 (n=9), 2 (n=2) or 3 (n=1) injections with adipose tissue.	Not described
Serrero, 2019 ⁽³⁶⁾	Cohort	Autologous Microfat and Adipose-Derived Stromal Vascular Fraction.	Fechamento das fístulas.	Female=4 Male=6 Total=10 Age=36 (19-63)	Intersphincteric=1 Trans sphincteric=8 Extrasphincteric=1	-	8 (2-38)	Seventy percent of patients had a clinical response at week 12, and 80% at week 48; 20% and 60% of patients achieved combined remission at weeks 12 and 48, respectively. In addition, 13 of 17 treated external openings showed complete re-epithelialization or an absence of drainage at week 48. Two patients showed complete occlusion of fistula tracts on magnetic resonance imaging at week 48.	Not described
Brunner, 2019 ⁽³⁷⁾	Cohort	Permacol™ collagen paste.	Assess the use of Permacol™ collagen paste.	Female=9 Male=3 Total=12 Age=33 [17-78]	Trans sphincteric=10 Retovaginal=2	-	-	The healing rate in all patients was 57% at 6 months and 63% at 12 months. One patient reported a worsening of fecal incontinence at 12 months; two patients had adverse events requiring fistula drainage. Patient characteristics, healing, incontinence, and adverse events did not differ significantly between patients with and without Crohn's disease.	Not described
Löwenberg, 2019 ⁽³⁸⁾	Cohort	Vedolizumab.	Ability of vedolizumab to induce endoscopic and histologic remission in patients with Crohn's disease.	Female=77 Male=33 Total=110 Fistula=9 Age=36 (28-46)	Not described	L1=26 L2=32 L3=50	9 (5-16)	3 of 9 patients closed the fistulas.	Not described
Herreros, 2019 ⁽³⁹⁾	Cohort	Autologous Mesenchymal Stem Cells.	To report experience in a compassionate use program for complex perianal fistula.	Female=21 Male=24 Total=45 Age=45 (29-69)	18 Crohn's-associated fistula-in-ano.	-	-	100% showed healing or improvement/ partial response, starting in a mean time of 5.3 weeks (range: 2-12 weeks). Healing was found in 10/18 (55.5%) cases. Most of them were cured in a meantime of 6.5 months (range: 0.5-24 months).	Not described
Biemans, 2020 ⁽⁴⁰⁾	Cohort	Ustekinumab.	Corticosteroid-free clinical remission.	Female=133 Male=88 Total=221 Age=38.2 [29.3-52.2]	Not described	L1=68 L2=76 L3=77 Perianal disease=37	12.3 [7.5-19.3]	35.7% resolved fistulas within 24 weeks.	Significant subgroups: BMI, upper gastrointestinal involvement, perianal fistula, anti-integrin exposure, moderate to severe activity.
Chapuis-Biron, 2020 ⁽⁴¹⁾	Cohort	Vedolizumab.	No draining fistula at clinical examination and no anal ulcers for primary lesions at 6 months without medical or surgical treatment for perianal Crohn's disease.	Female = 69 Male = 33 Total = 102 Age = 38.9 (10.8) [21-63]	Primary = 23 secondary lesions (fistulas, rectovaginal fistulas and abscesses) = 96 Tertiary = 17	L1 = 11 (10.8) L2 = 34 (33.3) L3 = 57 (55.9) L4 = 17 (16.7)	14.6 (7) [2-36]	Vedolizumab success in 23/102 patients with active perianal disease, dos com seton 9/61.	Factors associated with success were the number of prior biologic agents (≥3, odds ratio, OR: 0.13, 95%CI) and no antibiotics at initiation (OR: 4.12, 95%CI).

CR: complete response; MRI: magnetic resonance; US: ultrasound; CD: Crohn's disease; HSCT: Autologous haematopoietic stem cells transplantation; ASCs: Adipose-derived stromal stem cell; VZV: Vedolizumab; MSCs: mesenchymal stromal cells; AFP: anal fistula plug.

ment (n=4), Kruskal–Wallis test (n=2), Friedman test (n=1), modified per-protocol analysis (n=3), multivariate analysis (n=3), Pearson's correlation test (n=2), log-rank test (n=2), Cox regression (n=2), Hodges–Lehmann method with rank sum test (n=1), Stuart–Maxwell test (n=1), Mantel–Haenszel test (n=1), RR assessment (n=1), univariate and multivariate Cox regression (n=1), Cochran–Mantel–Haenszel test (n=1), Hochberg's testing (n=1), Wald's asymptotic method (n=1), hybrid non-response imputation (n=1), post hoc exploratory subgroup analysis (n=1), Cox proportional hazard model, Wilcoxon–Mann–Whitney test (n=1), independent *t*-test (n=1), and Wilcoxon rank sum test (n=1).

Eleven studies did not describe the phenotypic location of CD; in the remaining studies, there was a minimal prevalence of the ileocolonic pattern. However, some studies did not use the Montreal classification and listed the patients according to the intestinal segments of involvement, making it impossible to categorize them.

Eleven studies did not describe the anatomy of fistulas; 12 included only complex fistulas; and 10 included patients with both simple and complex fistulas.

Of the 33 studies evaluated in this systematic review, 10 performed subgroup evaluations; in the remaining studies, it was possible to infer that sex possibly had no influence or that the group was too small to make comparisons. A total of eight studies reported that there was no change in the outcome associated with sex, in which the following treatments were used: adalimumab (n=1), azathioprine (n=1), stem cell therapy (n=1), adalimumab plus ciprofloxacin (n=1), AST-120 (spherical carbon adsorbent) (n=1), vedolizumab (n=2), and ustekinumab (n=1)^(19,21–24,33,40,41). Only two studies, which used anti-TNF α drugs as their treatment, had different results regarding sex^(26,28).

The quality of the studies is described in FIGURE 2 and TABLE 2.

DISCUSSION

Patients with fistulizing perianal CD are considered as having a more severe disease profile. In the pre-biological therapy era, a worse disease prognosis has been reported in young patients owing to the risk

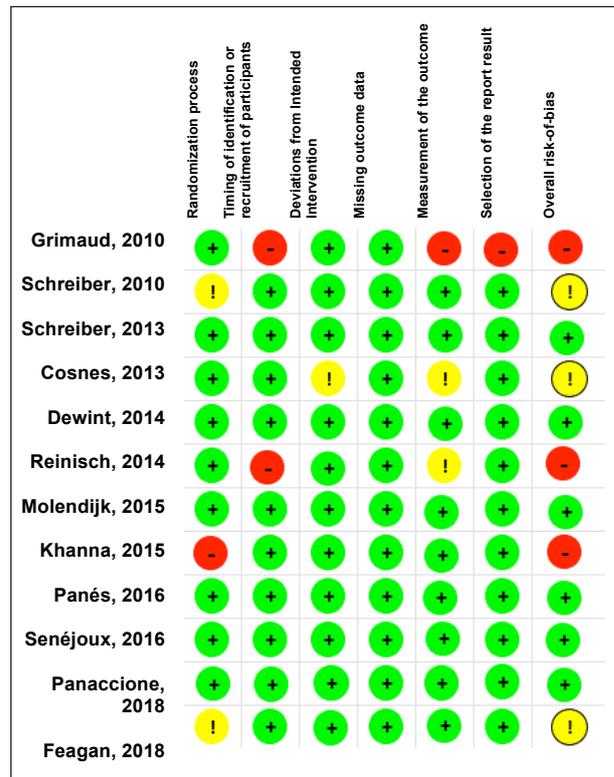


FIGURE 2. Randomized studies quality (Cochrane risk of bias).

of malnutrition and higher incidence of surgery⁽⁴²⁾. Further, a higher prevalence of fistulizing perianal disease has been observed in men, even though the mortality and disability rates were higher in women with CD^(43–45). More recent studies still show that perianal fistulae are more prevalent in young men with ileal disease, while complex fistulas with genital involvement are more difficult to manage and therefore must be evaluated separately in women^(46,47).

Systematic reviews have been conducted in the last decade to evaluate the sex difference in patients with CD; however, concerns regarding the treatment of fistulizing perianal disease have not been raised owing to the scarcity of data and disagreement in the literature^(48–50).

Haening et al., who investigated infliximab and surgery as the treatment for fistulizing perianal CD, demonstrated that female sex, complex fistulas, rectovaginal fistulas, and anorectal stenosis were associated with a longer time to complete fistula closure in their bivariate analysis. Further, the time to fistula closure was shorter in men than in women and for simple fistulas than for complex fistulas. However, in their multivariate analysis, the presence of rectova-

TABLE 2. Other studies quality (Newcastle-Ottawa quality assessment scale).

Paper	Selection	Comparability	Outcome	Total
Erchari, 2010	3	0	3	6
Sciaudone, 2011	2	2	3	7
Roumeguère, 2011	4	2	3	9
Alessandrini, 2011	3	0	3	6
Clerici, 2011	3	0	3	6
Lofberg, 2012	4	2	3	9
Cho, 2012	3	0	3	6
Tonelli, 2012	3	0	3	6
Lee, 2013	3	0	3	6
Portilla, 2013	3	0	3	6
Ciccocioppo, 2015	3	0	3	6
Haening, 2015	3	0	3	6
Dietz, 2017	3	0	3	6
Wainstein, 2018	3	0	3	6
Dige, 2019	3	0	3	6
Serrero, 2019	3	0	3	6
Brunner, 2019	3	2	3	8
Löwenberg, 2019	3	0	3	6
Herreros, 2019	3	0	3	6
Biemans, 2020	3	0	3	6
Chapuis-Biron, 2020	4	2	3	9

ginal fistulas remained significantly associated with a longer time to fistula closure⁽²⁸⁾. These data corroborate the literature, in which female genital fistulas require a different management strategy and are not always recorded; therefore, such data should be individualized to this type of complex fistulas⁽⁴⁶⁾. In clinical practice, it is established that patients with fistulizing perianal disease need biological therapy for their control and cicatrization. In systematic reviews and meta-analyses, surgical treatment of fistulas with exploration and placement of a seton before starting biological therapy has been reported to be necessary to avoid abscesses and complications with immunosuppressive therapy^(4,5,51,52).

The second anti-TNF α drug approved for use in patients with fistulizing perianal CD was adalimumab. In 2015, Khanna reported that young men with perianal disease and higher disease activity index would have more complications, surgeries, and hospitalizations. Meanwhile, male patients with no previous surgeries, shorter disease durations, and lower disease activity indices would independently have a higher risk of remission. However, the study data are

generalized to the sample population and not exclusively to patients with fistulizing perianal disease⁽²⁶⁾.

In 2014, a global consensus on the classification, diagnosis, and multidisciplinary treatment of perianal fistulizing CD was prepared, which established that adalimumab and infliximab are moderately effective in inducing and maintaining the closure of fistulas and that the association with thiopurines yields a better response than does that with monotherapy⁽⁵³⁾, but with a lower degree of evidence. In a study aimed at evaluating the recurrence of fistulas, it was observed that the suspension of anti-TNF drugs (infliximab and adalimumab), colonic location, and stenosing phenotype were independent risk factors for relapse⁽⁵⁴⁾. Another important factor in the healing of perianal fistulas is the presence of associated proctitis, leading to higher rates of proctectomy and refractory fistulas⁽⁵³⁾.

Regarding treatment and sex, it was observed that there is a longer time for the beginning of immunosuppressant prescription in women than in men, which was found to be a risk factor for complications⁽⁵⁵⁻⁵⁷⁾. With the launch of infliximab as the first

immunobiological drug under the anti-TNF drug class in 1998, the natural history of CD began to change; patients with a worse prognosis who received more hospitalizations and surgeries could achieve a deep and sustained remission⁽⁵⁸⁻⁶⁰⁾. Studies have also observed that women have more adverse events with the use of anti-TNF drugs; this is one of the causes of the interruptions in the use of infliximab and of greater maintenance of adalimumab in male patients^(57,61). There are several factors that can influence these findings, ranging from risks related to drug choice to the possibility of pregnancy, as in the case of methotrexate or at the beginning of anti-TNF drug use, as well as hormonal changes and differences in pharmacokinetics and body composition^(56,57,61).

Other medications, such as ustekinumab and vedolizumab, have yielded positive outcomes in the treatment of fistulizing perianal CD, which is an important fact considering the possibility of lack or loss of secondary response to the use of anti-TNF drugs^(4,52,62-64); however, this showed no difference between sexes in our review. Other surgical treatments, such as the use of fibrin glue, AFP, and autologous adipose-derived stem cells, have shown good results and may be considered⁽⁶⁾. However, no guideline has established the therapeutic choices associated with sex, but rather those with the phenotype of the disease; this demonstrates that this is a preponderant factor in the treatment of the disease and that sex possibly does not influence the outcomes of current treatments with superior effects to what was previously reported^(4,5,51-53).

The limitations of this study are the impossibility of performing a meta-analysis, given the heterogeneity of the studies, especially in terms of the different therapies used. Further, many studies excluded patients with fistulizing perianal disease, which decreased the number of studies with this scope.

Another limitation is the evaluation of simple and complex fistulas together, considering that each fistula presents a different prognosis.

Considering the advances in the treatment of CD in recent decades, it is important to evaluate the sex paradigm. Most studies discussing specific treatments for fistulas were conducted on fistulas already refractory to the usual therapy. Our study demonstrates that there are no substantial data supporting a worse prognosis of patients with fistulizing perianal CD according to sex in relation to the current treatments available. However, it is necessary to conduct prospective studies with this objective, including similar patients with similar fistula characteristics, to confirm this proposition. It is also important that studies uniformly evaluate variables that influence cicatrization and fistula development, such as the luminal activity of CD during treatment, BMI, corticotherapy, and use of the Perianal Disease Activity Index, as part of the outcome objectives.

Authors' contribution

Rosevics L conception and design of the study, acquisition of data, analysis and interpretation of data, drafting the article and revising it critically for important intellectual content, final approval of the version to be submitted. Savio MC acquisition of data. Lima Júnior E conception and design of the study. Ramos Júnior O conception and design of the study, revising critically the article for important intellectual content, final approval of the version to be submitted.

Orcid

Leticia Rosevics: 0000-0001-7307-1895.
Mariane Cristina Savio: 0000-0002-7901-6093.
Emilton Lima Júnior: 0000-0002-6887-9387.
Odery Ramos Júnior: 0000-0002-9730-6860.

Rosevics L, Savio MC, Lima Júnior E, Ramos Júnior O. Doença de Crohn perianal fistulizante: o gênero do paciente é relevante? Uma revisão sistemática. *Arq gastroenterol.* 2023;60(4):490-524.

RESUMO – Contexto – A doença de Crohn perianal fistulizante representa um desafio de tratamento, e postula-se que esse fenótipo em pacientes jovens do sexo masculino poderia ter um pior resultado. **Objetivo** – O objetivo deste estudo foi avaliar se o sexo influencia a resposta ao tratamento desses pacientes. **Métodos** – Esta revisão sistemática (PROSPERO CRD42022319629) foi conduzida de acordo com o protocolo *Preferred Reporting Items for Systematic Reviews and Meta-Analyses*. Foram selecionados artigos publicados em inglês, espanhol, português e italiano entre 2010 e 2020 nas bases de dados PubMed e Science Direct. De acordo com o acrônimo PICO, foram selecionados estudos prospectivos em pacientes maiores de 18 anos com objetivo de tratamento da doença de Crohn perianal fistulizante. Foram excluídos estudos em populações pediátricas, retrospectivos, sem objetivos de tratamento e que incluíssem apenas fistulas retovaginais ou um único sexo. A qualidade dos estudos foi avaliada usando a ferramenta de risco de viés Cochrane e a escala Newcastle-Ottawa. **Resultados** – Dos 1.887 artigos encontrados, 33 foram incluídos. A maioria dos estudos utilizou medicamentos anti-TNF como tratamento (n=11). Dez estudos tiveram análises de subgrupos; deles, os dois estudos que relataram diferenças entre os sexos usaram infliximabe e adalimumabe como tratamento e mostraram que as mulheres tiveram um tempo de fechamento da fistula maior que os homens. **Conclusão** – Esta revisão sistemática mostrou que poucos dados corroboram a diferença entre os sexos no tratamento da doença de Crohn perianal fistulizante, possivelmente tendo maior relação com o fenótipo. Porém, dada à falta de resultados, são necessários mais estudos com esse objetivo e com padronização das fistulas e métodos de avaliação da resposta.

Palavras-chave – Doença de Crohn; revisão sistemática; fistula perianal; tratamento

SUPPLEMENT

SELECTION: ABSTRACT READING

Title	Journal	Year
Autologous nonmyeloablative hematopoietic stem cell transplantation in patients with severe anti-TNF refractory Crohn disease: long-term follow-up	Blood	2010
Certolizumab Pegol in Patients With Moderate to Severe Crohn's Disease and Secondary Failure to Infliximab	Clinical Gastroenterology and Hepatology	2010
Chirurgia delle complicazioni anorettali della malattia di Crohn	EMC - Tecniche Chirurgiche Addominale	2010
Cirugía de las complicaciones anorrectales de la enfermedad de Crohn	EMC - Técnicas Quirúrgicas - Aparato Digestivo	2010
Combined treatment with adalimumab and surgery in a patient with steroid-dependent Crohn's disease complicated by perianal disease	Digestive and Liver Disease Supplements	2010
Efficacy and safety of certolizumab pegol induction therapy in an unselected Crohn's disease population: results of the FACTS survey	Inflamm Bowel Dis.	2010
Efficacy of synthetic glue treatment of high cryptoglandular fistula-in-ano	Gastroentérologie Clinique et Biologique	2010
Evaluation of adalimumab therapy in multidisciplinary strategy for perianal Crohn's disease patients with infliximab failure	J Crohns Colitis	2010
Fibrin glue is effective healing perianal fistulas in patients with Crohn's disease	Gastroenterology	2010
Fistulizing perianal Crohn's disease: contrast-enhanced magnetic resonance imaging assessment at 1 year on maintenance anti-TNF-alpha therapy	Inflamm Bowel Dis.	2010
Increased fatigability of external anal sphincter in inflammatory bowel disease: significance in fecal urgency and incontinence	Journal of Crohn's and Colitis	2010
Interleukin-15 and Its Soluble Receptor Mediate the Response to Infliximab in Patients With Crohn's Disease	Gastroenterology	2010

Continuation →

Title	Journal	Year
Long-term outcome of loose seton for complex anal fistula: a two-centre study of patients with and without Crohn's disease	Colorectal Dis.	2010
Long-term remission with adalimumab in steroid-dependent Crohn's disease patients with multiple drug intolerances	Digestive and Liver Disease Supplements	2010
Low-Dose Maintenance Therapy With Infliximab Prevents Postsurgical Recurrence of Crohn's Disease	Clinical Gastroenterology and Hepatology	2010
Mucosal Healing Predicts Sustained Clinical Remission in Patients With Early-Stage Crohn's Disease	Clinical – Alimentary Tract	2010
Outcomes of anal fistula surgery in patients with inflammatory bowel disease	The American Journal of Surgery	2010
Prevention of post-surgical recurrence with adalimumab in a patient with complicated Crohn's disease	Digestive and Liver Disease Supplements	2010
Randomised clinical trial: certolizumab pegol for fistulas in Crohn's disease - subgroup results from a placebo-controlled study	Aliment Pharmacol Ther.	2010
Steroid-free remission and closure of recto-vaginal fistula using adalimumab in a Crohn's disease patient naïve to anti-tumour necrosis factor alpha antibodies	Digestive and Liver Disease Supplements	2010
Surgery for intestinal Crohn's disease recurrence	Surgery	2010
The CHOICE trial: adalimumab demonstrates safety, fistula healing, improved quality of life and increased work productivity in patients with Crohn's disease who failed prior infliximab therapy	Aliment Pharmacol Ther.	2010
Tract length predicts successful closure with anal fistula plug in cryptoglandular fistulas	Dis Colon Rectum	2010
Treatment of anal fistulas by partial rectal wall advancement flap or mucosal advancement flap: A prospective randomized study	International Journal of Surgery	2010
Treatment of complex perianal fistulas in Crohn disease: infliximab, surgery or combined approach	Can J Surg.	2010
Treatment of fistula-in-ano with the Surgisis® AFPTM anal fistula plug	Gastroentérologie Clinique et Biologique	2010
A Crohn's Disease Patient Who Does Not Respond to Infliximab: What Is Next?	Clinical Gastroenterology and Hepatology	2011
A hospital-based study of clinical and genetic features of Crohn's disease	Journal of the Formosan Medical Association	2011
Adalimumab as second line anti-tumour necrosis factor alpha therapy for Crohn's disease: A single centre experience	Journal of Crohn's and Colitis	2011
Adalimumab is effective in long-term real life clinical practice in both luminal and perianal Crohn's disease. The Madrid experience	Gastroenterol Hepatol.	2011
Adenocarcinomas associated with perianal fistulae in Crohn's disease have a rectal, not an anal, immunophenotype	Pathology	2011
Certolizumab Pegol for Active Crohn's Disease: A Placebo-Controlled, Randomized Trial	Clinical Gastroenterology and Hepatology	2011
Combined approach with infliximab, surgery, and methotrexate in severe fistulizing anoperineal Crohn's disease: results from a prospective study	Inflamm Bowel Dis.	2011
Complex anal fistulas: plug or flap?	ANZ J Surg.	2011
Do Not Assume Symptoms Indicate Failure of Anti-Tumor Necrosis Factor Therapy in Crohn's Disease	Clinical Gastroenterology and Hepatology	2011
Efficacy and safety of adalimumab in Canadian patients with moderate to severe Crohn's disease: results of the Adalimumab in Canadian Subjects with Moderate to Severe Crohn's Disease (ACCESS) trial	Can J Gastroenterol.	2011

Continuation →

Title	Journal	Year
Efficacy and safety of certolizumab pegol in an unselected crohn's disease population: 26-week data of the FACTS II survey	Inflamm Bowel Dis.	2011
Efficacy of adalimumab in patients with Crohn's disease and failure to infliximab therapy: a clinical series	Rev Esp Enferm Dig	2011
Factors affecting the postoperative recurrence of Crohn's disease. New controversies with one centre's experience	Cirugía Española (English Edition)	2011
Immunomodulatory effects of unselected haematopoietic stem cells autotransplantation in refractory Crohn's disease	Digestive and Liver Disease	2011
Increases in body mass index during infliximab therapy in patients with Crohn's disease: An open label prospective study	Cytokine	2011
Local injection of infliximab in severe fistulating perianal Crohn's disease: an open uncontrolled study	Tech Coloproctol.	2011
Perineal reconstruction after rectal and anal disease using the local fascio-cutaneous-infragluteal flap: A new and reliable technique	Surgery	2011
Prediction of disease complication occurrence in Crohn's disease using phenotype and genotype parameters at diagnosis	Journal of Crohn's and Colitis	2011
Risk-benefit analysis of adalimumab versus traditional non-biologic therapies for patients with Crohn's disease	Inflamm Bowel Dis.	2011
Surgical repair and biological therapy for fecal incontinence in Crohn's disease involving both sphincter defects and complex fistulas	Journal of Crohn's and Colitis	2011
The C-reactive protein-to-prealbumin ratio predicts fistula closure	The American Journal of Surgery	2011
Twenty-year experience with surgical management of recto-urinary fistulas by posterior sagittal transrectal approach (York-Mason)	Surgery	2011
A Fistula Plug in the treatment of high anal fistulas--initial results from a German multicenter-study	Ger Med Sci.	2012
Activated thrombin activatable fibrinolysis inhibitor (TAFIa) is associated with inflammatory markers in inflammatory bowel diseases: TAFIa level in patients with IBD	Journal of Crohn's and Colitis	2012
Adalimumab for the prevention and/or treatment of post-operative recurrence of Crohn's disease: A prospective, two-year, single center, pilot study	Journal of Crohn's and Colitis	2012
Adalimumab Induces and Maintains Mucosal Healing in Patients With Crohn's Disease: Data From the EXTEND Trial	Gastroenterology	2012
Argentum-quarz solution in the treatment of anorectal fistulas: Is it possible a conservative approach?	Medical Hypotheses	2012
ASCA IgG and CBir antibodies are associated with the development of Crohn's disease and fistulae following ileal pouch-anal anastomosis	Dig Dis Sci.	2012
Autologous adipose tissue-derived stem cells for the treatment of Crohn's fistula: a phase I clinical study	Cell Transplant.	2012
Changing Crohn's disease management: Need for new goals and indices to prevent disability and improve quality of life	Journal of Crohn's and Colitis	2012
Corticosteroids and immunosuppressive therapy influence the result of QuantiFERON TB Gold testing in inflammatory bowel disease patients	Journal of Crohn's and Colitis	2012
Effectiveness and safety of local adalimumab injection in patients with fistulizing perianal Crohn's disease: a pilot study	Dis Colon Rectum	2012
Efficacy, tolerability, and predictors of response to infliximab therapy for Crohn's disease: A large single centre experience	Journal of Crohn's and Colitis	2012
Factors associated with the loss of response to infliximab in patients with Crohn's disease	Cytokine	2012

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Title	Journal	Year
Fibrin glue as the cell-delivery vehicle for mesenchymal stromal cells in regenerative medicine	Cytotherapy	2012
Genital fistulas in female Crohn's disease patients: Clinical characteristics and response to therapy	Journal of Crohn's and Colitis	2012
Initiating Azathioprine for Crohn's Disease	Clinical Gastroenterology and Hepatology	2012
Intensification of infliximab therapy in Crohn's disease: Efficacy and safety	Journal of Crohn's and Colitis	2012
Ligation of intersphincteric fistula tract compared with advancement flap for complex anorectal fistulas requiring initial seton drainage	Am J Surg.	2012
Maintenance of Remission Among Patients With Crohn's Disease on Antimetabolite Therapy After Infliximab Therapy Is Stopped	Gastroenterology	2012
Neuroimmune interactions in patients with inflammatory bowel diseases: Disease activity and clinical behavior based on Substance P serum levels	Journal of Crohn's and Colitis	2012
Patients with Crohn's disease experience reduced general health and vitality in the chronic stage: Ten-year results from the IBSEN study	Journal of Crohn's and Colitis	2012
Patología inflamatoria de recto y ano	Medicine - Programa de Formación Médica Continuada Acreditado	2012
Perianal Crohn's Disease - A Gastroenterologist's Perspective	Seminars in Colon and Rectal Surgery	2012
Perianal Crohn's Disease - A Surgical Perspective	Seminars in Colon and Rectal Surgery	2012
Phase I Clinical Trial of Smad7 Knockdown Using Antisense Oligonucleotide in Patients With Active Crohn's Disease	Molecular Therapy	2012
Physician perspectives on unresolved issues in the use of conventional therapy in Crohn's disease: Results from an international survey and discussion programme	Journal of Crohn's and Colitis	2012
Surgical Outcomes in Inflammatory Bowel Disease Patients and the Potential Impact of Biologic Therapies	Seminars in Colon and Rectal Surgery	2012
The Role of Genetics in the Surgical Management of Inflammatory Bowel Disease	Seminars in Colon and Rectal Surgery	2012
The usefulness of factor XIII levels in Crohn's disease	Journal of Crohn's and Colitis	2012
Thiopurine treatment in inflammatory bowel disease: Response predictors, safety, and withdrawal in follow-up	Journal of Crohn's and Colitis	2012
Traitement des fistules recto-vaginales de la maladie de Crohn par lambeau d'avancement vaginal	Gynécologie Obstétrique & Fertilité	2012
"In vitro" azathioprine-induced changes in peripheral T cell apoptosis and IFN- γ production associate with drug response in patients with Crohn's Disease	Journal of Crohn's and Colitis	2013
A role for tumor necrosis factor and bacterial antigens in the pathogenesis of Crohn's disease-associated fistulae	Inflamm Bowel Dis.	2013
A UK retrospective observational study of clinical outcomes and healthcare resource utilisation of infliximab treatment in Crohn's disease	Aliment Pharmacol Ther.	2013
Adalimumab and Infliximab Are Equally Effective for Crohn's Disease in Patients Not Previously Treated With Anti-Tumor Necrosis Factor- α Agents	Clinical Gastroenterology and Hepatology	2013
Adalimumab dose escalation and dose de-escalation success rate and predictors in a large national cohort of Crohn's patients	Journal of Crohn's and Colitis	2013
Adalimumab improves patient-reported outcomes and reduces indirect costs in patients with moderate to severe Crohn's disease: Results from the CARE trial	Journal of Crohn's and Colitis	2013
Adalimumab maintains remission of Crohn's disease after up to 4 years of treatment: data from CHARM and ADHERE	Aliment Pharmacol Ther.	2013

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Title	Journal	Year
Addition of an Immunomodulator to Infliximab Therapy Eliminates Antidrug Antibodies in Serum and Restores Clinical Response of Patients With Inflammatory Bowel Disease	Clinical Gastroenterology and Hepatology	2013
Assessment of microbiota and peptidoglycan in perianal fistulas	Diagnostic Microbiology and Infectious Disease	2013
Autologous adipose tissue-derived stem cells treatment demonstrated favorable and sustainable therapeutic effect for Crohn's fistula	Stem Cells.	2013
CD4+CD161+ T lymphocytes infiltrate Crohn's disease-associated perianal fistulas and are reduced by anti-TNF- α local therapy	Int Arch Allergy Immunol.	2013
Comparing medical treatments for Crohn's disease	J Comp Eff Res.	2013
Does Morbid Obesity Change Outcomes after Laparoscopic Surgery for Inflammatory Bowel Disease? Review of 626 Consecutive Cases	Journal of the American College of Surgeons	2013
Early Administration of Azathioprine vs Conventional Management of Crohn's Disease: A Randomized Controlled Trial	Gastroenterology	2013
Early Azathioprine Therapy Is No More Effective Than Placebo for Newly Diagnosed Crohn's Disease	Gastroenterology	2013
Efficacy and safety of interferon-gamma-targeted therapy in Crohn's disease: A systematic review and meta-analysis of randomized controlled trials	Clinics and Research in Hepatology and Gastroenterology	2013
Endothelial function and cardiovascular risk in active inflammatory bowel diseases	Journal of Crohn's and Colitis	2013
Establishing an Inflammatory Bowel Disease Practice in an Accountable World	Clinical Gastroenterology and Hepatology	2013
Expanded allogeneic adipose-derived stem cells (eASCs) for the treatment of complex perianal fistula in Crohn's disease: results from a multicenter phase I/IIa clinical trial	Int J Colorectal Dis.	2013
Four-week parenteral nutrition using a third generation lipid emulsion (SMOFlipid) – A double-blind, randomised, multicentre study in adults	Clinical Nutrition	2013
Health care costs of complex perianal fistula in Crohn's disease	Dig Dis Sci.	2013
Long-term Outcome of Patients With Crohn's Disease Who Respond to Azathioprine	Clinical Gastroenterology and Hepatology	2013
Long-term Outcome of Perianal Fistulizing Crohn's Disease Treated With Infliximab	Clinical Gastroenterology and Hepatology	2013
Outcome of Intestinal Transplants for Patients With Crohn's Disease	Transplantation Proceedings	2013
Seguimiento de los pacientes con enfermedad inflamatoria intestinal	Gastroenterología y Hepatología	2013
Subgroup analysis of the placebo-controlled CHARM trial: Increased remission rates through 3years for adalimumab-treated patients with early Crohn's disease	Journal of Crohn's and Colitis	2013
Surgical management of Crohn's disease	Langenbecks Arch Surg.	2013
Surgical repair of rectovaginal fistulas in patients with Crohn's disease	European Journal of Obstetrics & Gynecology and Reproductive Biology	2013
Tacrolimus salvage in anti-tumor necrosis factor antibody treatment-refractory Crohn's disease	Inflamm Bowel Dis.	2013
Tissue adhesives: cyanoacrylate glue and fibrin sealant	Gastrointestinal Endoscopy	2013
Tissue factor exposing microparticles in inflammatory bowel disease	Journal of Crohn's and Colitis	2013
Traitement des fistules rectovaginales/réservoir-vaginales par graciloplastie–Expérience monocentrique	Journal de Chirurgie Viscérale	2013

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Title	Journal	Year
Tratamiento de las fístulas de ano complejas de causa criptoglandular. ¿Aún se requiere un cirujano con experiencia?	Cirugía Española	2013
Treatment of Complex Cryptoglandular Anal Fistulas. Does it Still Require an Experienced Surgeon?	Cirugía Española (English Edition)	2013
Treatment of fistula-in-ano using a porcine small intestinal submucosa anal fistula plug	Tech Coloproctol.	2013
Treatment of recurrent rectovaginal/pouch-vaginal fistulas by gracilis muscle transposition – a single center experience	Journal of Visceral Surgery	2013
A Phase 2 Study of Tofacitinib, an Oral Janus Kinase Inhibitor, in Patients With Crohn's Disease	Clinical Gastroenterology and Hepatology	2014
Adalimumab combined with ciprofloxacin is superior to adalimumab monotherapy in perianal fistula closure in Crohn's disease: a randomised, double-blind, placebo controlled trial (ADAFI)	Gut	2014
Adalimumab for Crohn's disease: Long-term sustained benefit in a population-based cohort of 438 patients	Journal of Crohn's and Colitis	2014
Assessment of LIFT (ligation of the intersphincteric fistula tract) technique in patients with perianal transsphincteric fistulas	Journal of Coloproctology	2014
AST-120 (spherical carbon adsorbent) in the treatment of perianal fistulae in mild-to-moderate Crohn's disease: FFAST-1, a phase 3, multicenter, placebo-controlled study	Inflamm Bowel Dis.	2014
Chronic intestinal failure after Crohn disease: when to perform transplantation	JAMA Surg.	2014
Comparison between infliximab and adalimumab in the treatment of perianal fistulas in Crohn's disease	Journal of Coloproctology	2014
Crohn's disease outcome in patients under azathioprine: A tertiary referral center experience	Journal of Crohn's and Colitis	2014
Crohn's disease outpatients treated with adalimumab have an earlier secondary loss of response and requirement for dose escalation compared to infliximab: A real life cohort study	Journal of Crohn's and Colitis	2014
Crohn's disease patients in primary gastroenterology centres	European Journal of Internal Medicine	2014
Data from an Italian Group for the study of inflammatory bowel disease (IG-IBD) study on a large prospective multicenter cohort	Journal of Crohn's and Colitis	2014
Disappointing durable remission rates in complex Crohn's disease fistula	Inflamm Bowel Dis.	2014
Distinctive histopathologic phenotype in resection specimens from patients with Crohn's disease receiving anti-TNF- α therapy	Human Pathology	2014
Early-onset inflammatory bowel disease and common variable immunodeficiency-like disease caused by IL-21 deficiency	Journal of Allergy and Clinical Immunology	2014
Effectiveness and safety of infliximab and adalimumab for ambulatory Crohn's disease patients in primary gastroenterology centres	European Journal of Internal Medicine	2014
Hospitalisation, surgical and medical recurrence rates in inflammatory bowel disease 2003–2011—A Danish population-based cohort study	Journal of Crohn's and Colitis	2014
Incidence and clinical course of Crohn's disease during the first year — Results from the IBD Cohort of the Uppsala Region (ICURE) of Sweden 2005–2009	Journal of Crohn's and Colitis	2014
Increased Risk of Malignancy With Adalimumab Combination Therapy, Compared With Monotherapy, for Crohn's Disease	Gastroenterology	2014
Individualised therapy is more cost-effective than dose intensification in patients with Crohn's disease who lose response to anti-TNF treatment: a randomised, controlled trial	Gut	2014

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Title	Journal	Year
La patología benigna de ano y recto con RM 3.0T. 2.a Parte: patología inflamatoria ano-rectal. Anatomía postquirúrgica y complicaciones postratamiento	Radiología	2014
Management of inflammatory bowel disease in France: A nationwide survey among private gastroenterologists	Digestive and Liver Disease	2014
New tools and approaches for improved management of inflammatory bowel diseases	Journal of Crohn's and Colitis	2014
Once versus three times daily dosing of oral budesonide for active Crohn's disease: A double-blind, double-dummy, randomised trial	Journal of Crohn's and Colitis	2014
Outcomes after operations for anal fistula: results of a prospective, multicenter, regional study	Dis Colon Rectum	2014
Patient-Reported Outcomes as Primary End Points in Clinical Trials of Inflammatory Bowel Disease	Clinical Gastroenterology and Hepatology	2014
Perianal complete remission with combined therapy (seton placement and anti-TNF agents) in Crohn's disease: a Brazilian multicenter observational study	Arq Gastroenterol.	2014
Perianal fistulas in patients with inflammatory bowel disease	Seminars in Colon and Rectal Surgery	2014
Phenotypic concordance in familial inflammatory bowel disease (IBD). Results of a nationwide IBD Spanish database	Journal of Crohn's and Colitis	2014
Role of TNFRSF1B polymorphisms in the response of Crohn's disease patients to infliximab	Human Immunology	2014
SMAD3 gene variant is a risk factor for recurrent surgery in patients with Crohn's disease	Journal of Crohn's and Colitis	2014
Surgical management of rectovaginal fistula	Seminars in Colon and Rectal Surgery	2014
T-cell activation Rho GTPase-activating protein expression varies with inflammation location and severity in Crohn's disease	Journal of Surgical Research	2014
The Gonzalez hernia revisited: Use of the ischioanal fat pad to aid in the repair of rectovaginal and rectourethral fistulae	Journal of Pediatric Surgery	2014
The impact of preoperative steroid use on short-term outcomes following surgery for inflammatory bowel disease	Journal of Crohn's and Colitis	2014
The lectin pathway of the complement system is downregulated in Crohn's disease patients who respond to anti-TNF- α therapy	Journal of Crohn's and Colitis	2014
The LIFT procedure	Seminars in Colon and Rectal Surgery	2014
TNFSF15 is an independent predictor for the development of Crohn's disease-related complications in Koreans	Journal of Crohn's and Colitis	2014
Treatment of complex perianal fistulas with seton and infliximab in adolescents with Crohn's disease	Journal of Crohn's and Colitis	2014
Use of biologics in inflammatory bowel disease: Statements of the Italian Group for Inflammatory Bowel Disease	Digestive and Liver Disease	2014
Allogeneic Bone Marrow-Derived Mesenchymal Stromal Cells Promote Healing of Refractory Perianal Fistulas in Patients With Crohn's Disease	Gastroenterology	2015
CARD15 gene overexpression reduces effect of etanercept, infliximab, and adalimumab on cytokine secretion from PMA activated U937 cells	European Journal of Pharmacology	2015
Clinical Features of Tuberculous Versus Crohn's Anal Fistulas, in Korea	J Crohns Colitis	2015
Crohn's disease management after intestinal resection: a randomised trial	The Lancet	2015
Diagnostic and Prognostic Microbial Biomarkers in Inflammatory Bowel Diseases	Gastroenterology	2015

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Title	Journal	Year
Early combined immunosuppression for the management of Crohn's disease (REACT): a cluster randomised controlled trial	The Lancet	2015
Easy clip to treat anal fistula tracts: a word of caution	Int J Colorectal Dis.	2015
Effectiveness of adalimumab in perianal fistulas in crohn's disease patients naive to anti-TNF therapy	J Clin Gastroenterol.	2015
Efficacy of combined anti-TNF-alpha and surgical therapy in perianal and enterocutaneous fistulizing Crohn's disease - clinical observations from a tertiary Eastern European center	Scand J Gastroenterol.	2015
Evaluation of the concordance between biological markers and clinical activity in inflammatory bowel disease	Medicina Clínica (English Edition)	2015
Identification of Patients With Variants in TPMT and Dose Reduction Reduces Hematologic Events During Thiopurine Treatment of Inflammatory Bowel Disease	Gastroenterology	2015
Intravenous Versus Subcutaneous Anti-TNF-Alpha Agents for Crohn's Disease: A Comparison of Effectiveness and Safety	J Manag Care Spec Pharm	2015
Lateral internal sphincterotomy for surgically recurrent chronic anal fissure	The American Journal of Surgery	2015
Levels of drug and antidrug antibodies are associated with outcome of interventions after loss of response to infliximab or adalimumab	Clin Gastroenterol Hepatol.	2015
Long-term Artificial Urinary Sphincter Outcomes Following a Prior Rectourethral Fistula Repair	Urology	2015
Long-Term Follow-Up of Crohn Disease Fistulas After Local Injections of Bone Marrow-Derived Mesenchymal Stem Cells	Mayo Clinic Proceedings	2015
Long-Term Outcome of Patients With Crohn's Disease Who Discontinued Infliximab Therapy Upon Clinical Remission	Clinical Gastroenterology and Hepatology	2015
Mesenchymal stromal cells and chronic inflammatory bowel disease	Immunology Letters	2015
Multimodal treatment of perianal fistulas in Crohn's disease: seton versus anti-TNF versus advancement plasty (PISA): study protocol for a randomized controlled trial	Trials	2015
Normalización a largo plazo de la calidad de vida de los pacientes con enfermedad de Crohn con terapia de mantenimiento con adalimumab	Enfermedad Inflamatoria Intestinal al Día	2015
Novel treatment for recalcitrant rectovaginal fistulas: fat injection	Int Urogynecol J	2015
Outcomes of Bowel Resection in Patients with Crohn's Disease	Am Surg.	2015
Prospective multicenter study of a synthetic bioabsorbable anal fistula plug to treat cryptoglandular transsphincteric anal fistulas	Dis Colon Rectum	2015
Race and fistulizing perianal Crohn's disease	J Clin Gastroenterol	2015
Role of HLA typing on Crohn's disease pathogenesis	Annals of Medicine and Surgery	2015
The results of seton drainage combined with anti-TNF α therapy for anal fistula in Crohn's disease	Colorectal Dis.	2015
Tripterygium wilfordii Hook. f. versus azathioprine for prevention of postoperative recurrence in patients with Crohn's disease: A randomized clinical trial	Digestive and Liver Disease	2015
Use of Endoscopic Ultrasound to Guide Adalimumab Treatment in Perianal Crohn's Disease Results in Faster Fistula Healing	Inflamm Bowel Dis.	2015
A retrospective comparison of infliximab versus adalimumab as induction and maintenance therapy for Crohn disease	Intern Med J.	2016
Advanced age impacts surgical characteristics and postoperative course in patients with Crohn's disease	International Journal of Surgery	2016

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Title	Journal	Year
Allogeneic adipose-derived stem cells for the treatment of perianal fistula in Crohn's disease: a pilot clinical trial	Colorectal Dis.	2016
Can Red Cell Distribution Width Be Used as a Marker of Crohn's Disease Activity?	GE Portuguese Journal of Gastroenterology	2016
Combined Medical and Surgical Approach Improves Healing of Septic Perianal Crohn's Disease	Journal of the American College of Surgeons	2016
Conditions of prescription of anti-TNF agents in newly treated patients with inflammatory bowel disease in France (2011–2013)	Digestive and Liver Disease	2016
Cumulative Length of Bowel Resection in a Population-Based Cohort of Patients With Crohn's Disease	Clinical Gastroenterology and Hepatology	2016
Defunctioning Ileostomy is not Associated with Reduced Leakage in Proctocolectomy and Ileal Pouch Anastomosis Surgeries for IBD	J Crohns Colitis	2016
Early Course of Inflammatory Bowel Disease in a Population-Based Inception Cohort Study From 8 Countries in Asia and Australia	Gastroenterology	2016
Effectiveness of anti-TNF α drugs in patients with Crohn's disease who do not achieve remission with their first anti-TNF α agent	Digestive and Liver Disease	2016
Expanded allogeneic adipose-derived mesenchymal stem cells (Cx601) for complex perianal fistulas in Crohn's disease: a phase 3 randomised, double-blind controlled trial	The Lancet	2016
Expanded allogeneic adipose-derived mesenchymal stem cells (Cx601) for complex perianal fistulas in Crohn's disease: a phase 3 randomised, double-blind controlled trial	Lancet	2016
Fistula Plug in Fistulising Ano-Perineal Crohn's Disease: a Randomised Controlled Trial	J Crohns Colitis	2016
Increased Postoperative Mortality and Complications Among Elderly Patients With Inflammatory Bowel Diseases: An Analysis of the National Surgical Quality Improvement Program Cohort	Clinical Gastroenterology and Hepatology	2016
Infliximab Reduces Endoscopic, but Not Clinical, Recurrence of Crohn's Disease After Ileocolonic Resection	Gastroenterology	2016
Infliximab Reduces Endoscopic, but Not Clinical, Recurrence of Crohn's Disease After Ileocolonic Resection	Gastroenterology	2016
Laparoscopy improves clinical outcome of gastrointestinal fistula caused by Crohn's disease	Journal of Surgical Research	2016
Long-term Outcomes of Thalidomide Therapy for Adults With Refractory Crohn's Disease	Clinical Gastroenterology and Hepatology	2016
NOD2 gene variant is a risk factor for postoperative complications in patients with Crohn's disease: A genetic association study	Surgery	2016
Outcome after a dose "de-intensification" strategy with anti-TNF drugs in patients with Crohn's disease	Gastroenterología y Hepatología (English Edition)	2016
Patients with perianal Crohn's disease have poor disease outcomes after primary bowel resection	J Gastroenterol Hepatol.	2016
Perianal Crohn's Disease is Associated with Distal Colonic Disease, Stricturing Disease Behavior, IBD-Associated Serologies and Genetic Variation in the JAK-STAT Pathway	Inflamm Bowel Dis.	2016
Plastic reconstructive surgery techniques using VRAM or gracilis flaps in order to successfully treat complex urogenital fistulas	Journal of Plastic, Reconstructive & Aesthetic Surgery	2016
Post-operative recurrence of Crohn's disease: A prospective study at 5 years	Digestive and Liver Disease	2016
Protocolo de diagnóstico y tratamiento de las complicaciones perianales de la enfermedad de Crohn	Medicine - Programa de Formación Médica Continuada Acreditado	2016

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Title	Journal	Year
Surgical Management of Fistula-in-ano Among Patients With Crohn's Disease: Analysis of Outcomes After Fistulotomy or Seton Placement-Single-Center Experience	Scand J Surg.	2016
The proposed use of radiofrequency ablation for the treatment of fistula-in-ano	Medical Hypotheses	2016
Tratamiento endoscópico mediante inyección tópica de infliximab en estenosis inflamatorias en la enfermedad de Crohn	Enfermedad Inflamatoria Intestinal al Día	2016
Ustekinumab for the Treatment of Refractory Crohn's Disease: The Spanish Experience in a Large Multicentre Open-label Cohort	Inflamm Bowel Dis.	2016
Efficacy and Safety of MEDI2070, an Antibody Against Interleukin 23, in Patients With Moderate to Severe Crohn's Disease: A Phase 2 ^o Study	Gastroenterology	2017
Alternativas quirúrgicas en el manejo de la fistula rectovaginal: experiencia de 25 años	Revista Chilena de Cirugía	2017
An open prospective study evaluating efficacy and safety of a new medical device for rectal application of activated carbon in the treatment of chronic, uncomplicated perianal fistulas	Int J Colorectal Dis.	2017
Association of Induction Infliximab Levels With Clinical Response in Perianal Crohn's Disease	J Crohns Colitis	2017
Autologous adipose tissue-derived stem cells for the treatment of complex perianal fistulas not associated with Crohn's disease: a phase II clinical trial for safety and efficacy	Tech Coloproctol.	2017
Autologous Mesenchymal Stem Cells, Applied in a Bioabsorbable Matrix, for Treatment of Perianal Fistulas in Patients With Crohn's Disease	Gastroenterology	2017
Comparison of Health Care Utilization and Costs Between Patients with Perianal Fistulizing Crohn's Disease Treated with Biologics with or Without Previous Seton Placement	Inflamm Bowel Dis.	2017
Cross-sectional evaluation of transmural healing in patients with Crohn's disease on maintenance treatment with anti-TNF alpha agents	Digestive and Liver Disease	2017
Deoti surgical flap and sphincteroplasty for treatment of severe perineal deformity	Journal of Coloproctology	2017
Effect of tight control management on Crohn's disease (CALM): a multicentre, randomised, controlled phase 3 trial	The Lancet	2017
Efficacy of exclusive enteral nutrition in complicated Crohn's disease	Scand J Gastroenterol.	2017
Evolution after switching to bio1ilar infliximab in inflammatory bowel disease patients in clinical remission	Gastroenterología y Hepatología (English Edition)	2017
Factibility and Security Study of the PICS-AF™ Plug for the Treatment of Cryptoglandular Anal Fistula	Cirugía Española (English Edition),	2017
Immunomodulatory effects of M2000 (β-D-Mannuronic acid) on TNF-α, IL-17 and FOXP3 gene expression in patients with inflammatory bowel disease	International Immunopharmacology	2017
Improved Long-term Outcomes of Patients With Inflammatory Bowel Disease Receiving Proactive Compared With Reactive Monitoring of Serum Concentrations of Infliximab	Clinical Gastroenterology and Hepatology	2017
Induction therapy with the selective interleukin-23 inhibitor risankizumab in patients with moderate-to-severe Crohn's disease: a randomised, double-blind, placebo-controlled phase 2 study	The Lancet	2017
Is Stem Cell Therapy Ready for Prime Time in Treatment of Inflammatory Bowel Diseases?	Gastroenterology	2017
Lower skeletal muscle attenuation and high visceral fat index are associated with complicated disease in patients with Crohn's disease: An exploratory study	Clinical Nutrition ESPEN	2017
Medical versus surgical management of penetrating Crohn's disease: the current situation and future perspectives	Expert Rev Gastroenterol Hepatol.	2017

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Title	Journal	Year
Patrones de recurrencia/persistencia en la operación de LIFT para la fístula anal de origen criptoglandular. Estudio observacional a largo plazo	Cirugía Española	2017
Patterns of Recurrence/Persistence of Cryptoglandular Anal Fistula After the LIFT Procedure. Long-Term Observational Study	Cirugía Española (English Edition),	2017
Predictive factors for recurrence of high transsphincteric anal fistula after placement of seton	Journal of Surgical Research	2017
Thalidomide is a therapeutic agent that is effective in inducing and maintaining endoscopic remission in adult CD patients	Clinics and Research in Hepatology and Gastroenterology	2017
The changes in resting anal pressure after performing full-thickness rectal advancement flaps	The American Journal of Surgery	2017
The Impact of Ethnicity and Country of Birth on Inflammatory Bowel Disease Phenotype: a Prospective Cohort Study	J Crohns Colitis	2017
The surgical management of inflammatory bowel disease	Current Problems in Surgery	2017
Transanal opening of intersphincteric space (TROPIS) - A new procedure to treat high complex anal fistula	International Journal of Surgery	2017
Treatment of perianal Crohn's disease	Seminars in Pediatric Surgery	2017
What happens after a failed LIFT for anal fistula?	The American Journal of Surgery	2017
Anti-TNF therapy for genital fistulas in female patients with Crohn's disease: a nationwide study from the Groupe d'Etude Thérapeutique des Affections Inflammatoires du tube Digestif (GETAID)	Aliment Pharmacol Ther.	2018
Anti-tumour necrosis factor- α antibodies and B cell homeostasis in human inflammatory bowel diseases	International Immunopharmacology	2018
Clinical and Pharmacokinetic Factors Associated With Adalimumab-Induced Mucosal Healing in Patients With Crohn's Disease	Clinical Gastroenterology and Hepatology	2018
Clinical Benefit of Long-Term Adalimumab Treatment in Patients With Crohn's Disease Following Loss of Response or Intolerance to Infliximab: 96-Week Efficacy Data From GAIN/ADHERE Trials	J Crohns Colitis	2018
Concentrations Does Not Increase Clinical, Endoscopic, and Corticosteroid-Free Remission in Patients With Active Luminal Crohn's Disease	Gastroenterology	2018
Crohn's disease treatment practices in France in 1999–2013: A prospective survey in non-academic hospitals	Clinics and Research in Hepatology and Gastroenterology	2018
Efficacy of autologous fat graft injection in the treatment of anovaginal fistulas	Tech Coloproctol.	2018
Efficacy of Ustekinumab for Inducing Endoscopic Healing in Patients With Crohn's Disease	Gastroenterology	2018
Efficacy of Vedolizumab in Fistulising Crohn's Disease: Exploratory Analyses of Data from GEMINI 2	J Crohns Colitis	2018
Functional outcomes in patients submitted to restorative proctocolectomy with ileal pouch anal anastomosis in a single tertiary center	Journal of Coloproctology	2018
High ligation of the anal fistula tract by lateral approach: A prospective cohort study on a modification of the ligation of the intersphincteric fistula tract (LIFT) technique	International Journal of Surgery	2018
High Risk of Anal and Rectal Cancer in Patients With Anal and/or Perianal Crohn's Disease	Clinical Gastroenterology and Hepatology	2018
Incidence and Treatment of Patients Diagnosed With Inflammatory Bowel Diseases at 60 Years or Older in Sweden	Gastroenterology	2018
Long-term Efficacy and Safety of Stem Cell Therapy (Cx601) for Complex Perianal Fistulas in Patients With Crohn's Disease	Gastroenterology	2018
Long-term Outcome of Early Combined Immunosuppression Versus Conventional Management in Newly Diagnosed Crohn's Disease	J Crohns Colitis	2018

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Title	Journal	Year
Long-term outcomes of (Gore) fistula plug versus ligation of intersphincteric fistula tract for anal fistula	Journal of Coloproctology	2018
Major Abdominal and Perianal Surgery in Crohn's Disease: Long-term Follow-up of Australian Patients With Crohn's Disease	Dis Colon Rectum	2018
Outcomes 7 Years After Infliximab Withdrawal for Patients With Crohn's Disease in Sustained Remission	Clinical Gastroenterology and Hepatology	2018
Patients with perianal Crohn's fistulas experience delays in accessing anti-TNF therapy due to slow recognition, diagnosis and integration of specialist services: lessons learned from three referral centres	Colorectal Dis.	2018
Racial disparities in surgical outcomes of patients with Inflammatory Bowel Disease	The American Journal of Surgery	2018
Randomized clinical trial comparing a small intestinal submucosa anal fistula plug to advancement flap for the repair of complex anal fistulas	International Journal of Surgery Open	2018
Recursos empleados en el tratamiento de la enfermedad de Crohn perianal y sus resultados en una serie de vida real	Gastroenterología y Hepatología	2018
Resources used in the treatment of perianal Crohn's disease and the results in a real-life cohort	Gastroenterología y Hepatología (English Edition)	2018
Risankizumab in patients with moderate to severe Crohn's disease: an open-label extension study	The Lancet Gastroenterology & Hepatology	2018
Risk factors for postoperative complications in Crohn disease: analysis of 173 patients	Journal of Coloproctology	2018
Surgical Repair of Rectovaginal Fistula Using the Modified Martius Procedure: A Step-by-Step Guide	Journal of Minimally Invasive Gynecology	2018
The efficacy of infliximab combined with surgical treatment of fistulizing perianal Crohn's disease: Comparative analysis according to fistula subtypes	Asian Journal of Surgery	2018
The Place of Transanal Endoscopic Surgery in the Treatment of Rectourethral Fistula	Urology	2018
The role of the intestinal microbiota in the pathogenesis and treatment of inflammatory bowel diseases	Seminars in Colon and Rectal Surgery	2018
Tratamiento de la fistula anal mediante clip con el dispositivo OTSC®: resultados a corto plazo	Cirugía Española	2018
Treatment of Fistula-in-ano With OTSC® Proctology Clip Device: Short-term Results	Cirugía Española (English Edition)	2018
A Distinct Gut Microbiota Exists Within Crohn's Disease-Related Perianal Fistulae	Journal of Surgical Research	2019
A novel surgical predictive model for Chinese Crohn's disease patients	Medicine (Baltimore).	2019
Autologous haematopoietic stem cell transplantation in refractory Crohn's disease: Experience in our centre	Gastroenterología y Hepatología (English Edition)	2019
Cx601 (darvadstrocel) for the treatment of perianal fistulizing Crohn's disease	Expert Opin Biol Ther.	2019
Distinct Gut Microbiota Exists Within Crohn's Disease-Related Perianal Fistulae	J Surg Res.	2019
Early Initiation of Tumor Necrosis Factor Antagonist-Based Therapy for Patients With Crohn's Disease Reduces Costs Compared With Late Initiation	Clinical Gastroenterology and Hepatology	2019
Early Results of a Phase I Trial Using an Adipose-Derived Mesenchymal Stem Cell-Coated Fistula Plug for the Treatment of Transsphincteric Cryptoglandular Fistulas	Dis Colon Rectum	2019
Effects of Ustekinumab on Histologic Disease Activity in Patients With Crohn's Disease	Gastroenterology	2019
Efficacy and safety of bio1ilar CT-P13 compared with originator infliximab in patients with active Crohn's disease: an international, randomised, double-blind, phase 3 non-inferiority study	The Lancet	2019

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Title	Journal	Year
Efficacy of Injection of Freshly Collected Autologous Adipose Tissue Into Perianal Fistulas in Patients With Crohn's Disease	Gastroenterology	2019
Endorectal Advancement Flaps for Perianal Fistulae in Crohn's Disease: Careful Patient Selection Leads to Optimal Outcomes	J Gastrointest Surg.	2019
Endoscopic, Radiologic, and Histologic Healing With Vedolizumab in Patients With Active Crohn's Disease	Gastroenterology	2019
Epidemiological features and disease-related concerns of a large cohort of Italian patients with active Crohn's disease	Digestive and Liver Disease	2019
Gracilis muscle transposition for treatment of recurrent anovaginal, rectovaginal, rectourethral, and pouch-vaginal fistulas in patients with inflammatory bowel disease	Tech Coloproctol.	2019
Hyperbaric oxygen therapy for the treatment of perianal fistulas in Crohn's disease (HOT-TOPIC): study protocol of a prospective interventional cohort study with one-year follow-up	Undersea Hyperb Med.	2019
Laser fistula surgery [Filac]: When and how?	Seminars in Colon and Rectal Surgery	2019
Late-onset Crohn's disease: a comparison of disease behaviour and therapy with younger adult patients: the Italian Group for the Study of Inflammatory Bowel Disease 'AGED' study	Eur J Gastroenterol Hepatol.	2019
Long-term Safety and Efficacy of Local Microinjection Combining Autologous Microfat and Adipose-Derived Stromal Vascular Fraction for the Treatment of Refractory Perianal Fistula in Crohn's Disease	Gastroenterology	2019
New innovations in anal fistula surgery	Seminars in Colon and Rectal Surgery	2019
Outcomes of Patients With Inflammatory Bowel Diseases Switched From Maintenance Therapy With a Biologic to Remicade	Clin Gastroenterol Hepatol.	2019
Permacol™ collagen paste for cryptoglandular and Crohn's anal fistula	Tech Coloproctol.	2019
Perspectives of the International Society for Cell & Gene Therapy Gastrointestinal Scientific Committee on the Intravenous Use of Mesenchymal Stromal Cells in Inflammatory Bowel Disease (PeMeGi)	Cytherapy	2019
Plasma free amino acid profile in quiescent Inflammatory Bowel Disease patients orally administered with Mastiha (Pistacia lentiscus): a randomised clinical trial	Phytomedicine	2019
Previous colonic resection is a risk factor for surgical relapse in Crohn's disease	Digestive and Liver Disease	2019
Safety and Efficacy of Combination Treatment With Calcineurin Inhibitors and Vedolizumab in Patients With Refractory Inflammatory Bowel Disease	Clinical Gastroenterology and Hepatology	2019
Sphincter-sparing surgery for complex anal fistulas: radiofrequency thermocoagulation of the tract is of no help	Colorectal Dis.	2019
Trasplante de precursores hematopoyéticos en enfermedad de Crohn refractaria: experiencia en nuestro centro	Gastroenterología y Hepatología	2019
Vedolizumab Induces Endoscopic and Histologic Remission in Patients With Crohn's Disease	Gastroenterology	2019
Video-assisted anal fistula treatment (VAAFT): A decade experience	Seminars in Colon and Rectal Surgery	2019
Challenges in Crohn's disease: Complex perianal Crohn's disease	Seminars in Colon and Rectal Surgery	2020
Comparative study between intersphincteric ligation of perianal fistula versus conventional fistulotomy with or without seton in the treatment of perianal fistula: A prospective randomized controlled trial	Annals of Medicine and Surgery	2020
Complete Endoscopic Healing Associated With Better Outcomes Than Partial Endoscopic Healing in Patients With Crohn's Disease	Clinical Gastroenterology and Hepatology	2020
Deep Remission at 1 Year Prevents Progression of Early Crohn's Disease	Gastroenterology	2020

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Title	Journal	Year
Fistulizing Crohn's disease	Current Problems in Surgery	2020
Gammadelta T cells as a predictor of surgical relapse of Crohn's disease	Clinics and Research in Hepatology and Gastroenterology	2020
High-throughput sequencing provides insights into oral microbiota dysbiosis in association with inflammatory bowel disease	Genomics	2020
Implementation of infliximab standardized doses after pharmacokinetic modelization in a cohort of patients with Crohn's disease	Digestive and Liver Disease	2020
Inflammatory bowel disease symptoms at the time of anal fistula lead to the diagnosis of Crohn's disease	Clinics and Research in Hepatology and Gastroenterology	2020
Long-term Evaluation of Allogeneic Bone Marrow-derived Mesenchymal Stromal Cell Therapy for Crohn's Disease Perianal Fistulas	J Crohns Colitis	2020
NATURAL HISTORY OF PERIANAL CROHN'S DISEASE: LONG-TERM FOLLOW-UP OF A POPULATION-BASED COHORT	Clinical Gastroenterology and Hepatology	2020
Optimization of azathioprine dose in combined treatment with anti-TNF-alpha in inflammatory bowel disease	Gastroenterología y Hepatología	2020
Prediction of treatment failure during infliximab induction therapy in inflammatory bowel disease patients based on pharmacokinetic and pharmacodynamic modeling	European Journal of Pharmaceutical Sciences	2020
Tacrolimus induces short-term but not long-term clinical response in inflammatory bowel disease	Aliment Pharmacol Ther.	2020
Ustekinumab en enfermedad de Crohn: efectividad y seguridad en práctica clínica	Gastroenterología y Hepatología	2020
Ustekinumab for Crohn's Disease: Results of the ICC Registry, a Nationwide Prospective Observational Cohort Study	J Crohns Colitis	2020
Ustekinumab in Crohn's disease: Effectiveness and safety in clinical practice	Gastroenterología y Hepatología (English Edition),	2020
Variation Among Patients With Crohn's Disease in Benefit vs Risk Preferences and Remission Time Equivalents	Clinical Gastroenterology and Hepatology	2020
Vedolizumab for perianal Crohn's disease: a multicentre cohort study in 151 patients	Aliment Pharmacol Ther.	2020
OTHERS		
Adalimumab combined with ciprofloxacin is superior to adalimumab monotherapy in perianal fistula closure in Crohn's disease: a randomised, double-blind, placebo controlled trial (ADAFI)	Gut	2014
Fistula healing in pivotal studies of ustekinumab in Crohn's disease	Gastroenterology	2017
Expanded allogeneic adiposederived mesenchymal stem cells (Cx601) for complex perianal fistulas in Crohn's disease: a phase 3 randomised, double-blind controlled trial	Lancet	2016
Allogeneic bone marrow-derived mesenchymal stromal stem cells promote healing of refractory perianal fistulas in patients with Crohn's disease	Gastroenterology	2015
Vedolizumab for the treatment of fistulizing Crohn's disease: an exploratory analysis of data from GEMINI 2	Gastroenterology	2015
Lofberg R, Louis E, Reinisch W, Robinson AM, Kron M, Camez A, et al. Adalimumab produces clinical remission and reduces extraintestinal manifestations in Crohn's disease: results from CARE.	Inflamm Bowel Dis	2011

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SELECTION: FULL ARTICLE READING

Title	Journal	Year
Autologous nonmyeloablative hematopoietic stem cell transplantation in patients with severe anti-TNF refractory Crohn disease: long-term follow-up	Blood	2010
Certolizumab Pegol in Patients With Moderate to Severe Crohn's Disease and Secondary Failure to Infliximab	Clinical Gastroenterology and Hepatology	2010
Efficacy and safety of certolizumab pegol induction therapy in an unselected Crohn's disease population: results of the FACTS survey	Inflamm Bowel Dis.	2010
Efficacy of synthetic glue treatment of high cryptoglandular fistula-in-ano	Gastroentérologie Clinique et Biologique	2010
Evaluation of adalimumab therapy in multidisciplinary strategy for perianal Crohn's disease patients with infliximab failure	J Crohns Colitis	2010
Fibrin glue is effective healing perianal fistulas in patients with Crohn's disease	Gastroenterology	2010
Fistulizing perianal Crohn's disease: contrast-enhanced magnetic resonance imaging assessment at 1 year on maintenance anti-TNF-alpha therapy	Inflamm Bowel Dis.	2010
Interleukin-15 and Its Soluble Receptor Mediate the Response to Infliximab in Patients With Crohn's Disease	Gastroenterology	2010
Low-Dose Maintenance Therapy With Infliximab Prevents Postsurgical Recurrence of Crohn's Disease	Clinical Gastroenterology and Hepatology	2010
Randomised clinical trial: certolizumab pegol for fistulas in Crohn's disease - subgroup results from a placebo-controlled study	Aliment Pharmacol Ther.	2010
The CHOICE trial: adalimumab demonstrates safety, fistula healing, improved quality of life and increased work productivity in patients with Crohn's disease who failed prior infliximab therapy	Aliment Pharmacol Ther.	2010
Tract length predicts successful closure with anal fistula plug in cryptoglandular fistulas	Dis Colon Rectum	2010
Treatment of anal fistulas by partial rectal wall advancement flap or mucosal advancement flap: A prospective randomized study	International Journal of Surgery	2010
Treatment of complex perianal fistulas in Crohn disease: infliximab, surgery or combined approach	Can J Surg.	2010
Treatment of fistula-in-ano with the Surgisis® AFPTM anal fistula plug	Gastroentérologie Clinique et Biologique	2010
Adalimumab as second line anti-tumour necrosis factor alpha therapy for Crohn's disease: A single centre experience	Journal of Crohn's and Colitis	2011
Adalimumab is effective in long-term real life clinical practice in both luminal and perianal Crohn's disease. The Madrid experience	Gastroenterol Hepatol.	2011
Certolizumab Pegol for Active Crohn's Disease: A Placebo-Controlled, Randomized Trial	Clinical Gastroenterology and Hepatology	2011
Combined approach with infliximab, surgery, and methotrexate in severe fistulizing anoperineal Crohn's disease: results from a prospective study	Inflamm Bowel Dis.	2011
Efficacy and safety of adalimumab in Canadian patients with moderate to severe Crohn's disease: results of the Adalimumab in Canadian Subjects with ModErate to Severe Crohn's Disease (ACCESS) trial	Can J Gastroenterol.	2011
Efficacy and safety of certolizumab pegol in an unselected crohn's disease population: 26-week data of the FACTS II survey	Inflamm Bowel Dis.	2011
Efficacy of adalimumab in patients with Crohn's disease and failure to infliximab therapy: a clinical series	Rev Esp Enferm Dig	2011

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Title	Journal	Year
Immunomodulatory effects of unselected haematopoietic stem cells autotransplantation in refractory Crohn's disease	Digestive and Liver Disease	2011
Increases in body mass index during infliximab therapy in patients with Crohn's disease: An open label prospective study	Cytokine	2011
Local injection of infliximab in severe fistulating perianal Crohn's disease: an open uncontrolled study	Tech Coloproctol.	2011
Prediction of disease complication occurrence in Crohn's disease using phenotype and genotype parameters at diagnosis	Journal of Crohn's and Colitis	2011
Surgical repair and biological therapy for fecal incontinence in Crohn's disease involving both sphincter defects and complex fistulas	Journal of Crohn's and Colitis	2011
The C-reactive protein-to-prealbumin ratio predicts fistula closure	The American Journal of Surgery	2011
A Fistula Plug in the treatment of high anal fistulas--initial results from a German multicenter-study	Ger Med Sci.	2012
Adalimumab for the prevention and/or treatment of post-operative recurrence of Crohn's disease: A prospective, two-year, single center, pilot study	Journal of Crohn's and Colitis	2012
Adalimumab Induces and Maintains Mucosal Healing in Patients With Crohn's Disease: Data From the EXTEND Trial	Gastroenterology	2012
Autologous adipose tissue-derived stem cells for the treatment of Crohn's fistula: a phase I clinical study	Cell Transplant.	2012
Effectiveness and safety of local adalimumab injection in patients with fistulizing perianal Crohn's disease: a pilot study	Dis Colon Rectum	2012
Efficacy, tolerability, and predictors of response to infliximab therapy for Crohn's disease: A large single centre experience	Journal of Crohn's and Colitis	2012
Factors associated with the loss of response to infliximab in patients with Crohn's disease	Cytokine	2012
Genital fistulas in female Crohn's disease patients: Clinical characteristics and response to therapy	Journal of Crohn's and Colitis	2012
Intensification of infliximab therapy in Crohn's disease: Efficacy and safety	Journal of Crohn's and Colitis	2012
Ligation of intersphincteric fistula tract compared with advancement flap for complex anorectal fistulas requiring initial seton drainage	Am J Surg.	2012
Phase I Clinical Trial of Smad7 Knockdown Using Antisense Oligonucleotide in Patients With Active Crohn's Disease	Molecular Therapy	2012
Traitement des fistules recto-vaginales de la maladie de Crohn par lambeau d'avancement vaginal	Gynécologie Obstétrique & Fertilité	2012
Adalimumab improves patient-reported outcomes and reduces indirect costs in patients with moderate to severe Crohn's disease: Results from the CARE trial	Journal of Crohn's and Colitis	2013
Adalimumab maintains remission of Crohn's disease after up to 4 years of treatment: data from CHARM and ADHERE	Aliment Pharmacol Ther.	2013
Autologous adipose tissue-derived stem cells treatment demonstrated favorable and sustainable therapeutic effect for Crohn's fistula	Stem Cells.	2013
Early Administration of Azathioprine vs Conventional Management of Crohn's Disease: A Randomized Controlled Trial	Gastroenterology	2013
Early Azathioprine Therapy Is No More Effective Than Placebo for Newly Diagnosed Crohn's Disease	Gastroenterology	2013
Expanded allogeneic adipose-derived stem cells (eASCs) for the treatment of complex perianal fistula in Crohn's disease: results from a multicenter phase I/IIa clinical trial	Int J Colorectal Dis.	2013

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Title	Journal	Year
Long-term Outcome of Patients With Crohn's Disease Who Respond to Azathioprine	Clinical Gastroenterology and Hepatology	2013
Subgroup analysis of the placebo-controlled CHARM trial: Increased remission rates through 3 years for adalimumab-treated patients with early Crohn's disease	Journal of Crohn's and Colitis	2013
Traitement des fistules rectovaginales/réservoir-vaginales par graciloplastie—Expérience monocentrique	Journal de Chirurgie Viscérale	2013
Treatment of fistula-in-ano using a porcine small intestinal submucosa anal fistula plug	Tech Coloproctol.	2013
Treatment of recurrent rectovaginal/pouch-vaginal fistulas by gracilis muscle transposition – a single center experience	Journal of Visceral Surgery	2013
A Phase 2 Study of Tofacitinib, an Oral Janus Kinase Inhibitor, in Patients With Crohn's Disease	Clinical Gastroenterology and Hepatology	2014
Adalimumab combined with ciprofloxacin is superior to adalimumab monotherapy in perianal fistula closure in Crohn's disease: a randomised, double-blind, placebo controlled trial (ADAFI)	Gut	2014
Adalimumab for Crohn's disease: Long-term sustained benefit in a population-based cohort of 438 patients	Journal of Crohn's and Colitis	2014
Assessment of LIFT (ligation of the intersphincteric fistula tract) technique in patients with perianal transsphincteric fistulas	Journal of Coloproctology	2014
AST-120 (spherical carbon adsorbent) in the treatment of perianal fistulae in mild-to-moderate Crohn's disease: FFAST-1, a phase 3, multicenter, placebo-controlled study	Inflamm Bowel Dis.	2014
Crohn's disease outcome in patients under azathioprine: A tertiary referral center experience	Journal of Crohn's and Colitis	2014
Effectiveness and safety of infliximab and adalimumab for ambulatory Crohn's disease patients in primary gastroenterology centres	European Journal of Internal Medicine	2014
Early post-operative endoscopic recurrence in Crohn's disease patients: data from an Italian Group for the study of inflammatory bowel disease (IG-IBD) study on a large prospective multicenter cohort	Journal of Crohn's and Colitis	2014
Disappointing durable remission rates in complex Crohn's disease fistula	Inflamm Bowel Dis.	2014
Effectiveness and safety of infliximab and adalimumab for ambulatory Crohn's disease patients in primary gastroenterology centres	European Journal of Internal Medicine	2014
Incidence and clinical course of Crohn's disease during the first year — Results from the IBD Cohort of the Uppsala Region (ICURE) of Sweden 2005–2009	Journal of Crohn's and Colitis	2014
Individualised therapy is more cost-effective than dose intensification in patients with Crohn's disease who lose response to anti-TNF treatment: a randomised, controlled trial	Gut	2014
Management of inflammatory bowel disease in France: A nationwide survey among private gastroenterologists	Digestive and Liver Disease	2014
Once versus three times daily dosing of oral budesonide for active Crohn's disease: A double-blind, double-dummy, randomised trial	Journal of Crohn's and Colitis	2014
Outcomes after operations for anal fistula: results of a prospective, multicenter, regional study	Dis Colon Rectum	2014
Role of TNFRSF1B polymorphisms in the response of Crohn's disease patients to infliximab	Human Immunology	2014
SMAD3 gene variant is a risk factor for recurrent surgery in patients with Crohn's disease	Journal of Crohn's and Colitis	2014

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Title	Journal	Year
TNFSF15 is an independent predictor for the development of Crohn's disease-related complications in Koreans	Journal of Crohn's and Colitis	2014
Allogeneic Bone Marrow-Derived Mesenchymal Stromal Cells Promote Healing of Refractory Perianal Fistulas in Patients With Crohn's Disease	Gastroenterology	2015
Crohn's disease management after intestinal resection: a randomised trial	The Lancet	2015
Early combined immunosuppression for the management of Crohn's disease (REACT): a cluster randomised controlled trial	The Lancet	2015
Long-Term Follow-Up of Crohn Disease Fistulas After Local Injections of Bone Marrow-Derived Mesenchymal Stem Cells	Mayo Clinic Proceedings	2015
Multimodal treatment of perianal fistulas in Crohn's disease: seton versus anti-TNF versus advancement plasty (PISA): study protocol for a randomized controlled trial	Trials	2015
Novel treatment for recalcitrant rectovaginal fistulas: fat injection	Int Urogynecol J	2015
Prospective multicenter study of a synthetic bioabsorbable anal fistula plug to treat cryptoglandular transsphincteric anal fistulas	Dis Colon Rectum	2015
Race and fistulizing perianal Crohn's disease	J Clin Gastroenterol	2015
The results of seton drainage combined with anti-TNF α therapy for anal fistula in Crohn's disease	Colorectal Dis.	2015
Tripterygium wilfordii Hook. f. versus azathioprine for prevention of postoperative recurrence in patients with Crohn's disease: A randomized clinical trial	Digestive and Liver Disease	2015
Use of Endoscopic Ultrasound to Guide Adalimumab Treatment in Perianal Crohn's Disease Results in Faster Fistula Healing	Inflamm Bowel Dis.	2015
Allogeneic adipose-derived stem cells for the treatment of perianal fistula in Crohn's disease: a pilot clinical trial	Colorectal Dis.	2016
Can Red Cell Distribution Width Be Used as a Marker of Crohn's Disease Activity?	GE Portuguese Journal of Gastroenterology	2016
Early Course of Inflammatory Bowel Disease in a Population-Based Inception Cohort Study From 8 Countries in Asia and Australia	Gastroenterology	2016
Effectiveness of anti-TNF α drugs in patients with Crohn's disease who do not achieve remission with their first anti-TNF α agent	Digestive and Liver Disease	2016
Expanded allogeneic adipose-derived mesenchymal stem cells (Cx601) for complex perianal fistulas in Crohn's disease: a phase 3 randomised, double-blind controlled trial	The Lancet	2016
Fistula Plug in Fistulising Ano-Perineal Crohn's Disease: a Randomised Controlled Trial	J Crohns Colitis	2016
Infliximab Reduces Endoscopic, but Not Clinical, Recurrence of Crohn's Disease After Ileocolonic Resection	Gastroenterology	2016
NOD2 gene variant is a risk factor for postoperative complications in patients with Crohn's disease: A genetic association study	Surgery	2016
Outcome after a dose "de-intensification" strategy with anti-TNF drugs in patients with Crohn's disease	Gastroenterología y Hepatología (English Edition)	2016
Patients with perianal Crohn's disease have poor disease outcomes after primary bowel resection	J Gastroenterol Hepatol.	2016
Perianal Crohn's Disease is Associated with Distal Colonic Disease, Strictureing Disease Behavior, IBD-Associated Serologies and Genetic Variation in the JAK-STAT Pathway	Inflamm Bowel Dis.	2016
Post-operative recurrence of Crohn's disease: A prospective study at 5 years	Digestive and Liver Disease	2016

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Title	Journal	Year
Ustekinumab for the Treatment of Refractory Crohn's Disease: The Spanish Experience in a Large Multicentre Open-label Cohort	Inflamm Bowel Dis.	2016
Efficacy and Safety of MEDI2070, an Antibody Against Interleukin 23, in Patients With Moderate to Severe Crohn's Disease: A Phase 2a Study	Gastroenterology	2017
An open prospective study evaluating efficacy and safety of a new medical device for rectal application of activated carbon in the treatment of chronic, uncomplicated perianal fistulas	Int J Colorectal Dis.	2017
Association of Induction Infliximab Levels With Clinical Response in Perianal Crohn's Disease	J Crohns Colitis	2017
Autologous Mesenchymal Stem Cells, Applied in a Bioabsorbable Matrix, for Treatment of Perianal Fistulas in Patients With Crohn's Disease	Gastroenterology	2017
Comparison of Health Care Utilization and Costs Between Patients with Perianal Fistulizing Crohn's Disease Treated with Biologics with or Without Previous Seton Placement	Inflamm Bowel Dis.	2017
Cross-sectional evaluation of transmural healing in patients with Crohn's disease on maintenance treatment with anti-TNF alpha agents	Digestive and Liver Disease	2017
Effect of tight control management on Crohn's disease (CALM): a multicentre, randomised, controlled phase 3 trial	The Lancet	2017
Efficacy of exclusive enteral nutrition in complicated Crohn's disease	Scand J Gastroenterol.	2017
Evolution after switching to bio1ilar infliximab in inflammatory bowel disease patients in clinical remission	Gastroenterología y Hepatología (English Edition)	2017
Factibility and Security Study of the PICS-AF™ Plug for the Treatment of Cryptoglandular Anal Fistula	Cirugía Española (English Edition),	2017
Immunomodulatory effects of M2000 (β-D-Mannuronic acid) on TNF-α, IL-17 and FOXP3 gene expression in patients with inflammatory bowel disease	International Immunopharmacology	2017
Induction therapy with the selective interleukin-23 inhibitor risankizumab in patients with moderate-to-severe Crohn's disease: a randomised, double-blind, placebo-controlled phase 2 study	The Lancet	2017
Patterns of Recurrence/Persistence of Cryptoglandular Anal Fistula After the LIFT Procedure. Long-Term Observational Study	Cirugía Española (English Edition),	2017
The Impact of Ethnicity and Country of Birth on Inflammatory Bowel Disease Phenotype: a Prospective Cohort Study	J Crohns Colitis	2017
Transanal opening of intersphincteric space (TROPIS) - A new procedure to treat high complex anal fistula	International Journal of Surgery	2017
Anti-TNF therapy for genital fistulas in female patients with Crohn's disease: a nationwide study from the Groupe d'Etude Thérapeutique des Affections Inflammatoires du tube Digestif (GETAID)	Aliment Pharmacol Ther.	2018
Clinical and Pharmacokinetic Factors Associated With Adalimumab-Induced Mucosal Healing in Patients With Crohn's Disease	Clinical Gastroenterology and Hepatology	2018
Clinical Benefit of Long-Term Adalimumab Treatment in Patients With Crohn's Disease Following Loss of Response or Intolerance to Infliximab: 96-Week Efficacy Data From GAIN/ADHERE Trials	J Crohns Colitis	2018
Concentrations Does Not Increase Clinical, Endoscopic, and Corticosteroid-Free Remission in Patients With Active Luminal Crohn's Disease	Gastroenterology	2018
Crohn's disease treatment practices in France in 1999–2013: A prospective survey in non-academic hospitals	Clinics and Research in Hepatology and Gastroenterology	2018
Efficacy of autologous fat graft injection in the treatment of anovaginal fistulas	Tech Coloproctol.	2018
Efficacy of Ustekinumab for Inducing Endoscopic Healing in Patients With Crohn's Disease	Gastroenterology	2018

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Title	Journal	Year
Efficacy of Vedolizumab in Fistulising Crohn's Disease: Exploratory Analyses of Data from GEMINI 2	J Crohns Colitis	2018
High ligation of the anal fistula tract by lateral approach: A prospective cohort study on a modification of the ligation of the intersphincteric fistula tract (LIFT) technique	International Journal of Surgery	2018
Incidence and Treatment of Patients Diagnosed With Inflammatory Bowel Diseases at 60 Years or Older in Sweden	Gastroenterology	2018
Long-term Efficacy and Safety of Stem Cell Therapy (Cx601) for Complex Perianal Fistulas in Patients With Crohn's Disease	Gastroenterology	2018
Long-term outcomes of (Gore) fistula plug versus ligation of intersphincteric fistula tract for anal fistula	Journal of Coloproctology	2018
Major Abdominal and Perianal Surgery in Crohn's Disease: Long-term Follow-up of Australian Patients With Crohn's Disease	Dis Colon Rectum	2018
Randomized clinical trial comparing a small intestinal submucosa anal fistula plug to advancement flap for the repair of complex anal fistulas	International Journal of Surgery Open	2018
Risankizumab in patients with moderate to severe Crohn's disease: an open-label extension study	The Lancet Gastroenterology & Hepatology	2018
Early Results of a Phase I Trial Using an Adipose-Derived Mesenchymal Stem Cell-Coated Fistula Plug for the Treatment of Transsphincteric Cryptoglandular Fistulas	Dis Colon Rectum	2019
Effects of Ustekinumab on Histologic Disease Activity in Patients With Crohn's Disease	Gastroenterology	2019
Efficacy and safety of bio1ilar CT-P13 compared with originator infliximab in patients with active Crohn's disease: an international, randomised, double-blind, phase 3 non-inferiority study	The Lancet	2019
Efficacy of Injection of Freshly Collected Autologous Adipose Tissue Into Perianal Fistulas in Patients With Crohn's Disease	Gastroenterology	2019
Endoscopic, Radiologic, and Histologic Healing With Vedolizumab in Patients With Active Crohn's Disease	Gastroenterology	2019
Hyperbaric oxygen therapy for the treatment of perianal fistulas in Crohn's disease (HOT-TOPIC): study protocol of a prospective interventional cohort study with one-year follow-up	Undersea Hyperb Med.	2019
Late-onset Crohn's disease: a comparison of disease behaviour and therapy with younger adult patients: the Italian Group for the Study of Inflammatory Bowel Disease 'AGED' study	Eur J Gastroenterol Hepatol.	2019
Long-term Safety and Efficacy of Local Microinjection Combining Autologous Microfat and Adipose-Derived Stromal Vascular Fraction for the Treatment of Refractory Perianal Fistula in Crohn's Disease	Gastroenterology	2019
Outcomes of Patients With Inflammatory Bowel Diseases Switched From Maintenance Therapy With a Bio1ilar to Remicade	Clin Gastroenterol Hepatol.	2019
Permacol™ collagen paste for cryptoglandular and Crohn's anal fistula	Tech Coloproctol.	2019
Previous colonic resection is a risk factor for surgical relapse in Crohn's disease	Digestive and Liver Disease	2019
Safety and Efficacy of Combination Treatment With Calcineurin Inhibitors and Vedolizumab in Patients With Refractory Inflammatory Bowel Disease	Clinical Gastroenterology and Hepatology	2019
Sphincter-sparing surgery for complex anal fistulas: radiofrequency thermocoagulation of the tract is of no help	Colorectal Dis.	2019
Vedolizumab Induces Endoscopic and Histologic Remission in Patients With Crohn's Disease	Gastroenterology	2019

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Title	Journal	Year
Comparative study between intersphincteric ligation of perianal fistula versus conventional fistulotomy with or without seton in the treatment of perianal fistula: A prospective randomized controlled trial	Annals of Medicine and Surgery	2020
Deep Remission at 1 Year Prevents Progression of Early Crohn's Disease	Gastroenterology	2020
Long-term Evaluation of Allogeneic Bone Marrow-derived Mesenchymal Stromal Cell Therapy for Crohn's Disease Perianal Fistulas	J Crohns Colitis	2020
NATURAL HISTORY OF PERIANAL CROHN'S DISEASE: LONG-TERM FOLLOW-UP OF A POPULATION-BASED COHORT	Clinical Gastroenterology and Hepatology	2020
Optimization of azathioprine dose in combined treatment with anti-TNF-alpha in inflammatory bowel disease	Gastroenterología y Hepatología	2020
Prediction of treatment failure during infliximab induction therapy in inflammatory bowel disease patients based on pharmacokinetic and pharmacodynamic modeling	European Journal of Pharmaceutical Sciences	2020
Tacrolimus induces short-term but not long-term clinical response in inflammatory bowel disease	Aliment Pharmacol Ther.	2020
Ustekinumab for Crohn's Disease: Results of the ICC Registry, a Nationwide Prospective Observational Cohort Study	J Crohns Colitis	2020
Ustekinumab in Crohn's disease: Effectiveness and safety in clinical practice	Gastroenterología y Hepatología (English Edition),	2020
Vedolizumab for perianal Crohn's disease: a multicentre cohort study in 151 patients	Aliment Pharmacol Ther.	2020

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