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Rectovaginal fistula in Crohn's disease: a low long-term success rate and a high definitive stoma risk

Laurine Tracanelli

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Année : 2020

**RECTOVAGINAL FISTULA IN CROHN'S DISEASE: A LOW LONG-TERM
SUCCESS RATE AND A HIGH DEFINITIVE STOMA RISK**

THÈSE
PRÉSENTÉE POUR L'OBTENTION DU TITRE DE DOCTEUR EN MÉDECINE

DIPLÔME D'ÉTAT

Laurine TRACANELLI

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**LES FISTULES RECTO-VAGINALES DANS LA MALADIE DE CROHN: UN
FAIBLE TAUX DE SUCCÈS A LONG TERME ET UN HAUT RISQUE DE STOMIE
DEFINITIVE**

TRENTE-DEUX PATIENTES SUIVIES PENDANT 11 ANS

RÉSUMÉ :

Objectifs – Evaluer les résultats de la prise en charge médico-chirurgicale des femmes ayant une fistule recto-vaginale (FRV) due à la Maladie de Crohn (MC) dans un centre de référence.

Etats des connaissances – La prise en charge des FRV dans la MC est un défi. Le traitement médical repose sur les biothérapies, les options chirurgicales sont nombreuses mais sans gold standard. Les études disponibles sont hétérogènes, rétrospectives avec des suivis courts.

Méthodes – Toutes les patientes ayant eu une chirurgie pour une FRV de MC entre 1996 et 2019 dans un centre tertiaire ont été incluses rétrospectivement. Les chirurgies réalisées étaient classées en 3 groupes : préliminaire, techniques de fermeture, ou de sauvetage. L'objectif primaire était d'évaluer la rémission de la FRV, définie par la combinaison de la fermeture de la fistule, l'absence de symptômes et de stomie, au moins 6 mois après la dernière chirurgie.

Résultats – Etaient incluses 32 patientes, le suivi moyen était de 11,3 ans (0-23,7) après la première chirurgie. Un total de 138 chirurgies ont été réalisées, 45 (33%) étaient préliminaires (drainage +/- insertion d'un séton, stomie de protection), 80 (58%) étaient des techniques de fermeture, 13 (9%) étaient des procédures de sauvetage (stomie définitive). La rémission de la FRV était atteinte chez 7/32 patientes (22%). Le taux de succès par procédure (techniques de fermeture seules) était de 9% (7/80). A la fin du suivi 13/32 (41%) patientes avaient une stomie. Le pourcentage de la durée du suivi passée sous biotherapies était de 90% pour les

patientes guéries versus 50% pour les autres ($p=0,11$). Seule la biothérapie était un facteur pronostic de succès des techniques de fermeture après analyse univariée ($p=0,007$).

Conclusion – Même dans un centre référent le taux de rémission des FRV dans la MC est faible à long terme et le risque de stomie est important. La combinaison avec les biotherapies est cruciale.

MOTS CLÉS : Maladie inflammatoire chronique des intestins ; Maladie de Crohn ; Maladie de Crohn périanale ; Fistule recto vaginale ; Fistule ano vaginale ; Fistule pouch vaginal ; Stomie définitive.

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**RECTOVAGINAL FISTULA IN CROHN'S DISEASE: A LOW LONG-TERM
SUCCESS RATE AND A HIGH DEFINITIVE STOMA RISK.
*THIRTY-TWO PATIENTS FOLLOWED-UP FOR 11 YEARS***

ABSTRACT :

Objectives - To assess results of medico-surgical support in women with rectovaginal fistula (RVF) due to Crohn's disease (CD) in a tertiary referral center.

Background data - Management of RVF in CD is challenging, recommended medical treatment is mostly based on biologics, but surgical support still relies on various techniques with no gold standard. Available studies are heterogeneous, retrospective ones, with short term follow-up.

Methods - We conducted a retrospective analysis of women undergoing surgery for CD RVF between 1996 and 2019 in a tertiary referral center. All surgeries were classified as: preliminary, closure techniques or salvage procedures. Primary outcome was fistula remission defined by the combination of fistula closure, absence of symptoms, and no stoma, at least 6 months since last procedure.

Results - Were included 32 patients, median follow-up was 11.3 years (0-23.7) after first surgery. A total of 138 procedures were performed, 45 (33%) preliminary (drainage +/- seton insertion, diverting stoma), 80 (58%) closure techniques, 13 (9%) salvage procedures leading to planned definitive stoma. RVF remission was obtained in 7/32 patients (22%). Global remission rate per procedure was 5% (5/138), 9% (7/80) after closure techniques. At the end of follow up a stoma was present in 13/32 patients (41%). Percentage of time under biologics was 90% for patients in remission, versus 50% for the others (p=0.11). Only biologics were prognostic factor for successful closure techniques (p=0.007) in univariate analysis.

Conclusion - RVF remission in CD was low at long term, patients endured a succession of interventions, and stoma rate was high. Combination of biologics was crucial.

KEYWORDS : Intestinal Bowel Disease, Crohn's Disease, Perianal Crohn's Disease, Rectovaginal fistula, Anovaginal fistula, Pouch vaginal fistula, définitive stoma.

ABBREVIATIONS

AGA : American Gastroenterological Association

Anti TNF α : Antibodies against tumor against necrosis factor alpha

APE : Abdominoperineal excision

CD : Crohn's disease

IBD : Inflammatory bowel Disease

IPAA : Ileal pouch anal anstomosis

MRI : Magnetic Resonance Imagery

PDAI : Perianal Disease Activity Index

RVF : Rectovaginal fistula

ARTICLE

RECTOVAGINAL FISTULA IN CROHN'S DISEASE: A LOW LONG-TERM SUCCESS RATE AND A HIGH DEFINITIVE STOMA RISK

INTRODUCTION

Crohn's disease (CD) phenotype is characterized as inflammatory, stricturing, or penetrating. Penetrating disease is defined by fistula formation. Prevalence of perianal fistula is approximately 25% in patient with CD after 20 years of evolution (1).

In CD, perianal fistulas can be classified as simple or complex according to the American Gastroenterological Association classification (AGA classification) (2). Compared to simple ones, complex fistulas are more difficult to treat, have decreased healing rates, and are associated with less successful outcomes(3).

Among complex fistulas, CD rectovaginal fistula (CDRVF) is an infrequent but devastating manifestation of CD, leading to significant morbidity and social embarrassment for affected women(4) (5). The multiple of surgical options and lack of consensus between experts speak to the complexity and short-comings encountered to correct the disease process surgically.

According to French (6) and other guidelines, CDRVF treatment is based on prolonged seton drainage and aggressive medical care (principally antibodies against tumor necrosis factor alpha (anti TNF α), often associated with immunosuppressives), with the intent to treat to target clinical and symptomatic remission of fistula and associated luminal lesions. Surgery is almost always necessary, either to ease clinical remission, and/or to relieve symptoms.

Surgical options are various, ranging from drainage and seton insertion to abdominoperineal excision (APE). These patients require a multidisciplinary team support (specialized nurses, gastroenterologists, proctologists, and colo-rectal surgeons).

CDRVF closure success rate widely varies in literature from 16% to 80% (7) - (9). As controlled studies are rare, often combine different types of fistula, or include patients without CD, factors influencing success rate are difficult to isolate. Furthermore duration of follow up is important as recurrence rate after repair of complex fistulas for CD is high and continuously increases over time (10) (11).

The aim of our study was to assess overall medico-surgical support results over a long period of time in women with CDRFV treated in a tertiary referral center.

METHODS:

Study design and population

We conducted a single-institution retrospective study of CD patients undergoing surgery for an ano- or recto- or pouch-vaginal fistula, whose data were prospectively collected between 1996 and 2019.

A review of electronic and paper health records was conducted to identify patients with a diagnosis of CDRVF operated on during this period in the colo-rectal surgical unit. CD diagnosis was based on clinical, endoscopic, radiologic and histological findings documented in the medical record. In one case the diagnosis of CD was established after the discovery of the CDRVF. Patients with inflammatory bowel disease (IBD) and ileal pouch anal anastomosis (IPAA) developing a pouch-vaginal fistula one year or longer after closure of ileostomy were considered to have de novo CD and included.

The study was conducted in accordance with the ethical principles stated in the Declaration of Helsinki and local regulations.

Date of inclusion was that of first surgery performed in our Unit.

Preoperative characteristics included age, body mass index (BMI), vaginal delivery history, smoking habits, medical management. Crohn's disease characteristics included location and behaviour according to the Montreal classification (L1: ileal, L2: colonic, L3: ileo-colonic, L4: upper gastro intestinal ; B1: inflammatory, B2: stricturing, B3: penetrating) (12), duration of CD at first surgery, history of ileocolonic resection related to CD. Disease activity at first surgery was based on clinical evaluation, and endoscopy when performed during the last 3 months. Presence of proctitis and anal stenosis were recorded according to the findings of rectal exam performed at first surgery.

Medical management was recorded for each procedure performed (biologics and immediate previous optimization of biologics, association with an immunosuppressive). As maintenance treatment is important to decrease recurrence rate after induction treatment of CD fistulas (13) (14) we calculated the ratio of number of years under biologics to total follow-up duration.

Age at CD RVF diagnosis and duration of RVF at first surgery were collected. Fistula characteristics were determined from the first operative records. RVF were classified as simple (single isolated ano-vaginal tract) or complex (high, associate with ano-rectal stricture or with perianal abscess, or with multiple external openings). Pouch-vaginal fistulas were considered apart. Prior repair attempts of RVF in another center were logged.

If Magnetic Resonance Imagery (MRI) was available at the end of follow-up, we recorded the conclusion of the report.

Symptoms associated with the CDRVF were recorded from the last consultation available in our Center.

In December 2019 a doctor team member (LT) individually interviewed all patients by phone, evaluating their symptoms and continence.

Surgical procedures

All procedures were performed by a single experienced colo-rectal surgeon (JLF). Type and number of any surgical procedure performed during follow-up were recorded. Surgical procedures were separated according to their clinical intent into 3 groups: i- preliminary procedures group which were performed in order to prepare to a subsequent closure intent procedures, for example drainage +/- loose setons insertion in case of abscess or extensive perianal disease, ii- closure intent procedures group aimed to obtain closure of the RVF and included either conservative techniques (sole seton removal, fistula plug, fibrin glue, Ovesco clip, internal opening suture, advancement flap), or major procedure (pouch refection, Martius intervention) ; iii- salvage procedures group (definitive stoma alone or with colonic resection or abdominoperineal excision (APE)). The presence of a derivation stoma was also recorded.

Outcomes

The primary outcome was CDRVF remission assessed during the last available consultation distant from last surgical procedure for at least 6 months and on phone interview. Furthermore no subsequent RVF surgery should have been performed after the final visit follow-up, and no stoma should be present since at least 6 months. Remission was defined as closure of vaginal wound at physical examination, cessation of drainage despite gentle finger compression according to Present criteria (15), and absence of any symptom (vaginal discharge, passage of feces, flatus or mucous through the vagina). Remission assessment was carried out by either our colorectal surgeon or an IBD specialist. Were also considered as success patients with occurrence of another perianal fistula without vaginal opening. All the other patients were considered as failures. We considered as failures patients with unhealed CDRVF at final follow-up visit, or with RVF symptoms at phone interview, or followed-up after last surgical procedure for less than 6 months combined with no phone contact, or stoma presence at the end of study.

Secondary outcomes included: absence of any fistula tract as described by the radiologist on MRI at least 6 months after the last procedure ; perineal symptoms scored according to the Perianal Disease Activity Index (PDAI) (16) ; anal incontinence in patients without stoma according to the Vaizey score (17). Also were searched predictive factors of success for procedures performed with closure intent.

Statistical analysis

Quantitative data were reported as median (range), and categorical data as number of patient (percentage of patient). Normally distributed quantitative data were analyzed with the Student *t* test. Univariate analysis regarding assessment of CDRVF remission prognostics factor was performed according to per procedure basis using a backward stepwise logistic regression model. For this per procedure analysis, all procedures in closure intent were considered. Results of this univariate analysis are shown as odds ratio (OR) (95% confidence interval) and with p value. A p-value less than 0.05 was considered as significant.

RESULTS:

Patients

Thirty-two patients with CDRVF were operated on in our Center during the 1996-2019 period. Patients characteristics are detailed in Table I.

At first surgery median age was 34 years (21-55), overall CD duration was 143.5 months (0-329) and CDRVF duration was 7 months (0-166.) Most of the patients had an extensive luminal disease as 20 patients (63%) had an ileocolonic location (L3). Twenty-four (75%) of the patients had a complex fistula, 3 (9%) had a simple ano-vaginal fistula, and 5 (16%) had a

pouch-vaginal fistula. Fifteen (47%) had proctitis, 10 (31%) had an ano-rectal stenosis at the first surgery and 5 more developed an ano-rectal stenosis during follow-up.

A total of 9 patients (28%) were referred in our department after one or more previous surgical attempts of RVF repair performed in another institution.

Follow up:

Three patients were lost for follow-up (followed-up for less than 6 months after the last procedure and no phone interview), and were considered as failures. Median follow-up from first surgery to the last visit in the Unit was 8.3 years (0-21.4). For phone-interviewed patients, median follow-up to the last contact with the patient (either during a visit, or by phone contact) was 11.3 years (0-23.7). Median follow-up after last surgery was 1.4 years (0-14.9) to the last consultation, and 3.5 years (0-14.9) considering phone interviews.

Procedures

A total of 138 procedures were performed for the 32 included patients, leading to a median number of 3 (0–13) procedures per patient.

As detailed in Table II, among the 138 surgical procedures, 36(26%) of the total number of procedures were preliminary, and dedicated to prepare patients to further surgery. Eighty (58%) were closure techniques, of those 76 (95%) were local conservative, mostly advancement flap (n=20) and fibrin glue injection (n=16). The advancement flaps were rectal (n=11), vaginal (n=7), and ileal (n=2) in 2 patients with IPAA. At the end of follow-up an ileo- or colo-stomy was still present in 13 patients (including 4 after an APE). During follow-up, 9 derivation stomas have been performed in 9 patients, followed by bowel continuity restoration in only 2 (22%).

Outcomes

Per patients

CDRVF remissions

Remission was achieved in 7 patients (22%) after a 11.3 years follow-up. Of those, one patient was considered to be in remission although a non vaginal fistula occurred after the remission of RVF. Two of these seven patients had had pouch refection of an already present IPAA. For the 4 patients with a MRI performed, no fistula was visible.

For the four patients interviewed by phone at the end of follow-up, individual PDAI symptoms score values were 0, 0, 0 and 5 (worse possible value 20) ; and anal incontinence scores were 0, 0, 2 and 7 (worse possible value 24), the value of 2 and 7 were reported by the two patients with an IPAA .

All, except one, patients with CD RVF in remission were on biologics maintenance therapy (one refusal). Median percentage of time (years) under biologics during the total follow up was 0.9 (0-1). Biologics always consisted in anti TNF α therapy.

CDRVF failures

Failure was noted in 25 patients (78%) at the end of follow-up. Included in the failure group, 13 patients had a definitive stoma and clinical closure of CDRVf was achieved in 7 as confirmed by MRI in 5 of them. Among the 12 other failure patients three MRI were performed, and one demonstrated no fistula despite presence of symptoms.

Eight patients were phone-interviewed. Six had a permanent stoma, their median PDAI score was 5.5 (0-9). For the two others, individual PDAI scores were 7 and 9, and anal incontinence scores 8 and 10.

The median percentage of time under biologics was 0.5 (0-1). The difference between success and failure patients was not significant with a $p=0.11$.

Per procedures

Global success rate of surgical procedure was 5% (7/138). Considering only the 80 procedures performed with intent to closure, success rate was 9% (Table III). Among the 76 conservative procedures performed with intent to closure 5 (7%) were successful: 2/9 seton removals, 2/11 internal opening sutures, 1/16 glue injections; all the flaps failed. Among the 4 major procedures performed with intent to treat, 2 were successful (2 of the 3 pouch reconstructions performed).

A derivation stoma was present during surgery in 2/7 (29%) of successful procedures and in 29/73 (40%) of failed procedures ($p=0.009$). A total of 31 of the 80 with intent to closure procedures were performed with a derivation stoma (38%), distributed in 27/76 (36%) of the conservative procedures, and in 4/4 of the major procedures.

Thirty two of the 80 with intent to closure procedures were associated with anti TNF α at surgery (39%), distributed in 6/7 (86%) of successful procedures, and 26/73 (36%) of failed procedures ($p=0.0057$).

Prognostics factors of successful procedures

Were analyzed as factors eventually associated with procedure in intent to closure performed for RVF : smoker status, BMI, proctitis at first surgery, stenosis at first surgery, conservative or major procedure, presence of a stoma at the date of closure techniques, medical management (anti TNF α , combination therapy (anti TNF α and immunosuppressive)) at the date of closure technique. After univariate analysis only anti TNF α at the time of surgery was significantly related to successful closure techniques ($p=0.007$), results are detailed in Table IV. Multivariate analysis was not performed as only one prognostic factor was isolated after univariate analysis

DISCUSSION:

Our study including 32 patients and evaluating a total of 138 surgeries during a median follow-up time of 11.3 years, and dedicated to patients with CD, is one of the most important in terms of numbers of inclusions and follow-up duration. Fistula remission criteria were very strict and well defined.

Current knowledge

The evaluation of CD R VF medical treatment was the subject of a meta-analysis by Andreani and al (18). All the selected studies included small number of patients (maximum 15 patients) and reported variable success rates (0 to 33%). Medical treatment presently relies essentially on biologics notably anti TNF α therapies which have been the most studied. In a post-hoc analysis of ACCENT II trial including 25 women with a R VF, an initial response of 64% was noted, maintained longer by the continuation of infliximab as compared to placebo (19). However, this improvement was by far more modest than noted for other perianal fistulas (3). If medical treatment alone is a possible solution for pauci symptomatic patients, it is often combined with local surgical treatment to close the fistula after initial abscesses drainage and seton insertion (20).

However, very few retrospective studies have described and assessed the overall management of patients with CD R VF (5) (8) (10). In addition, these available studies are heterogeneous, the patients numbers lower, the follow-up shorter and the definition of success very heterogeneous.

The results:

In the present study, the overall success remission rate is 22%. As for the number of successful interventions, which is only 5% (7/138). In this work we listed all the interventions performed (median 3 per patient) and there were not always closure interventions. Even

considering these closure techniques alone, success rate was only 9%. The rate of stoma observed at the end of follow-up was significant since it concerned 41% of patients.

Compared to the available literature:

This success rate is low as compared to the cure rates reported in the literature, ranging from 16 to 81% (4) (7) - (10) (21). In their study on RVF (all etiologies combined), Pinto and al (10) reported 78% of CD cured patients (with a 44% success rate per procedure), and Corte and al (8) 40% of effective procedures performed for CD RVF. But most of these studies are heterogeneous combining CD and non-CD patients, and RVF with or without perianal fistulas. Furthermore follow-up was short, respectively 20 and 33 months.

Success rate may be much lower when strict criteria are used. Our definition of success included a follow-up of more than 6 months after the last surgery, the absence of symptoms suggestive of a CDRVF and an expert clinical examination confirming its closure. Were also considered as failures CDRVF in remission when a stoma was present at the end of follow-up.

Our study included highly selected severe CDRVF patients referred from other centers, and our experience may not reflect the success rate obtained in less severe patients.

Follow-up duration after surgery may also interfere with success rate as the frequency of secondary failures increases with time. In CDRVF women, Pinto and al described a 56% higher recurrence rate compared to 33% for the post obstetric RVF group. In addition, their average follow-up was only 33 months. Löffler et al described 47% recurrence for RVF versus 19% for other perianal fistulas after 5 years of follow-up (11). As CD is a chronic pathology, with frequent recurrences over time, especially in the case of CD RVF, long-term follow-up is crucial to affirm the remission of these fistulas. This is one of the strengths of our study, which includes an overall follow-up of more than 11 years and a median follow-up after the last surgery of 3.5 years.

Three studies including only CD RVF are available in the era of biologics. Ruffollo and al (8), with a follow-up comparable to ours (109 months) reported a success rate of 81%. The difference with our result can be explained by the fact that patients who were lost for follow-up, had a permanent stoma, or died were excluded in this series, whereas they were included in the failure group in our work. El-Gazzaz (4) and Gaertner (9) reported a success rate of respectively 46% (average follow-up 44.6 months), and 53% (average follow-up 38.6 months). For El-Gazzaz, only patients who had a procedure with intent to close the fistula were included, and for Gaertner, patients with another perianal fistula were excluded. No patient was excluded from our study as long as she had a CD RVF.

Concerning surgical techniques, we have reported a low success rate of fistula obturation techniques (glue, plug). This is in agreement for glue in particular with a randomized controlled trial carried out in patients with CD perianal fistulas, showing the absence of effect for the subgroup with RVF (22). In our study, all the advancement flaps were failures, in the opposite with classically reported success rates which range from 30 to 80% (23), possibly due to the severity of our patient's illness.

Rarely used in our series, major procedures were effective 2 times out of 4. However, they included 3 IPAA pouch resections.

Procedures that do not expose to a risk of significant complication, nor to continence disorders in the event of failure, can be promoted as a first step even if their failure rate is high as demonstrated in our study. However, if these local first line techniques fail, their repetition appears to be ineffective. In fact, we recommend as Corte and al. to quickly consider a more aggressive procedure after failure of a first conservative surgery(8).

Specific intent of respective procedures:

We were able to separate procedures according to their indication: preliminary procedure, closure techniques, and definitive rescue gesture. The largest group was the closure

techniques, but we highlight a large number of preliminary surgeries, corresponding to drainage and insertion of a seton. This is the first study to show that management does not only involve so called “noble” surgical procedures, but also many preparatory surgeries. Patients should always be informed, as this is a source of repeated procedures. Indeed Kelly and al reported a median number of 3 changes of setons per patient in their series (24). It should be noted that during CDRVF these preliminary procedures often involve placement of a seton, which discomfort must be explained to the patients. In fact, 37% of patients treated for a perianal fistula still had a seton in place after an average follow-up of 37 months in the study by Faucheron and al (25). In addition, this procedure does not formerly protect against further perianal sepsis, since 21% of patients with a seton in place may develop a recurrent perianal sepsis (26).

Temporary / permanent stoma:

Protective stomas are usually thought to improve the outcome of perineal fistulas surgery, especially when perianal or luminal inflammation is severe. In our series we have not shown any benefit from derivation stoma, in accordance to conclusions from previous studies (10) (27). Although in our study we can only suggest that stoma offers no advantage when associated with minimally invasive procedures, this might not be the case for more aggressive surgery. In addition, the supposed temporary derivation stomas may not always be closed, as shown by the 22% closure rate and the 41% of patients with a stoma, either definitive or temporary in intent, at the end of follow-up in our study. In their meta-analysis Singh and al reported a closure rate of diversion stoma of only 17% in CD with refractory fistulizing perianal disease (28). Recently Hain and al (29) in their serie, reported a closure rate of diversion stoma of 43% for CDRVF. Mueller and al (30) reported a 54% rate of permanent stoma for CDRVF.

Deep clinical remission rates:

In this study among the 7 patients in remission, 4 who underwent MRI had no visible fistula. Although the nature of our study design did not allow us to combine MRI and clinical criteria, this is an encouraging result for the patients in remission. However MRI seems less sensible than for other perianal fistula.

CDRVF have a major impact on the quality of life of patients. El-Gazzaz et al (4) reported that scores of quality of life, moral state, and quality of sexual life were lower than those of the general population, and it should be noted that they noticed no difference between healed or not healed groups. For example, the percentage of patients with no sexual activity represented 67% (all groups combined) against 4% in the general population. The values obtained in our patients for the PDAI score allowed us to highlight the persistence of symptoms even if the RVF was in remission, and even if the patients had a stoma.

The outcomes targeted while treating CD perianal fistulas, and more specifically CDRVF, should not be limited to the fistula closure. St Marks' Hospital group(31) proposed a list of relevant criteria for patients and caregivers in perianal Crohn's disease, thus combining clinical criteria with time based criteria such as the need for subsequent surgery. Subjective factors such as well-being should also be considered.

Prognostic factors:

Association of anti TNF drugs with surgery has changed the prognosis of CD fistulas, in particular the risk of recurrence is reduced by maintenance treatment(13) (14). In our series, the treatment with anti TNF α was sometimes fragmented. Therefore we calculated a ratio of time spent on anti TNF α . Even if it was not strictly a maintenance treatment evaluation, this overall assessment of biologics coverage seems to have influenced the results in our serie as it was higher in patients in remission, but it was no significant (p: 0.11). After univariate analysis, presence of biologics (anti TNF α exclusively) was the only significant factor

associated with the success of a surgical procedure. A debate arises whether patients with peri anal CD would benefit from higher drug levels (32).

Limitations, strength of the study:

There are several limitations in our study. This was a retrospective and monocentric study, the number of participants remains relatively small. A negative point was also the lack of MRI in our study to assess CDRVF remission. The positive points are that it exposes new results aside the very few numbers of available studies on the subject, patients had longer follow-up, it reflects real life conditions as no patient was excluded, treatment was homogeneous and strict judgment criteria had been adopted.

CONCLUSION:

RVF is a rare but dreaded complication of CD that is exceedingly difficult to manage. Multiple interventions are necessary, and long follow-up is necessary to confirm remission. Even in an expert IBD center, the overall success rate was low. We underlined the importance of long-term treatment with anti TNF α and the disappointing result of minimally invasive techniques which do not seem to have any interest in being repeated, even when associated with a stoma. Given the complexity of the disease process and the significant variability in treatment outcomes, the patient should play an active role in treatment decisions and clear expectations should be emphasized by the clinician.

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Table I: characteristics of the 32 patients with a RVF operated on between 1996 and 2019 in a Tertiary Specialized Unit, at the date of first surgery.

	Study population N=32
Age (years)*	34 (21-55)
Age at Crohn's disease diagnosis (years) *	21 (9-47)
Age at RVF diagnosis (years) *	32 (20-51)
Crohn's disease duration at first surgery (months) *	143,5 (0-329)
RVF duration at first surgery (months) *	7 (0-166)
Smoker status	13 (41)
BMI*	22,06 (17,4-43,7)
Vaginal delivery history	12 (38)
Disease Location	
L1	3 (9)
L2	9 (28)
L3	20 (63)
<i>Including L4</i>	1 (3)
Disease Phenotype	
B1	22 (69)
B2	10 (31)
Fistula classification	
Single tract ano vaginal	3 (9)
Complex	24 (75)
Pouch vaginal	5 (16)
Anorectal stenosis	11 (34)
Prior RVF surgery	9 (28)
Prior digestive resection	
Ileo caecal resection	7 (22)
Colonic resection	15 (47)
<i>Including ileoanal pouch anastomosis</i>	5 (16)
Ileo colonic disease activity at first surgery	
Clinical activity	15 (47)
Endoscopic activity	21 (66)
<i>Including Proctitis</i>	15 (47)
Preoperative medical therapy at first surgery	
Antibiotherapy	13 (41)
Corticosteroids	10 (31)
Immunosuppressive	20 (63)
Biologics	7 (22)

Data presented as median* (range) or n (%)

Table II: Nature and relative frequency of the 138 surgical procedures performed in the 32 patients with Crohn RVF, expressed as n (%).

Closure techniques 80 (58)	Conservative procedures	
	Advancement	20 (14)
	Fibrin glue	16 (12)
	Internal opening suture	11 (8)
	Plug	11 (8)
	Seton removal	9 (6)
	Ovesco® clip	9 (6)
	Major procedures	
	Pouch refection	3 (2)
	Martius Intervention	1 (1)
Preliminary 36 (26)	Drainage + seton insertion	36 (26)
Salvage 13 (9)	Abdomino-perineal excision	4 (3)
	Permanent stoma	9 (6)
Divertion stoma 9 (7)		9 (6)
Total number of interventions		138

Table III: Repartition in success or failure groups of the 80 closure techniques undertaken in the 32 patients with RVF, and association with protective stoma and biologics.

	80 procedures	
N (%)	Success N=7 (9)	Failure N=73 (91)
Conservative procedures	5 (7)	71 (93)
Seton removal	2	7
Internal opening suture	2	9
Fibrin glue	1	15
Ovesco® clip	0	9
Plug	0	11
Rectal advancement flap	0	11
Vaginal advancement flap	0	7
Ileal advancement flap	0	2
Contemporary associated with		
Protective stoma	0	27 (37)
Biologics	4 (57)	25 (34)
Major procedures	2 (50)	2 (50)
Pouch refection	2	1
Martius intervention	0	1
Contemporary associated with		
Protective stoma	2 (29)	2 (3)
Biologics	2 (29)	1 (1)

Table IV: Univariate analysis of Success Prognostic Factors of the 80 closure techniques performed in intent to close RVF.

	Univariate Analysis	
	OR (95% CI)	P
BMI \geq 30	0.909 [0.712-1.153]	p=0.433
Major procedure	0.992 [0.868-1.133]	p=0.910
Procedure with stoma	0.970 [0.855-1.102]	p=0.65
Proctitis	1.040 [0.910-1.187]	p=0.57
Anorectal stenosis	1.002 [0.875-1.149]	p=0.975
Smoker	0.990 [0.866-1.133]	p=0.892
Biologics	1.182 [1.049 -1.333]	p=0.007
Combination therapy (biologics+immunosuppressive)	1.026 [0.717-1.467]	p=1.47

THÈSE SOUTENUE PAR : Laurine TRACANELLI

TITRE :

LES FISTULES RECTO-VAGINALES DANS LA MALADIE DE CROHN : UN FAIBLE TAUX DE SUCCÈS A LONG TERME ET UN HAUT RISQUE DE STOMIE DEFINITIVE

CONCLUSION :

La prise en charge des fistules recto-vaginales dans la maladie de Crohn (FRV de MC) est un défi. Le traitement médical repose sur les biothérapies, les options chirurgicales sont nombreuses mais sans gold standard. Les études disponibles sont hétérogènes, rétrospectives, avec des suivis courts. L'objectif de cette étude est d'évaluer les résultats de la prise en charge médico-chirurgicale des femmes ayant une FRV de MC dans un centre de référence.

Toutes les patientes ayant eu une chirurgie pour une FRV de MC entre 1996 et 2019 dans un centre tertiaire ont été incluses rétrospectivement. Les chirurgies réalisées étaient classées en 3 groupes : préliminaires, techniques de fermeture ou de sauvetage. L'objectif était d'évaluer la rémission de la FRV, définie par la combinaison de : fermeture de la fistule, absence de symptômes et de stomie, au moins 6 mois après la dernière chirurgie.

Étaient incluses 32 patientes, le suivi moyen était de 11,3 ans (0-23,7) après la première chirurgie. Un total de 138 chirurgies ont été réalisées, 36 (26%) étaient préliminaires (drainage +/- insertion d'un séton), 80 (58%) étaient des techniques de fermeture (colle, lambeaux...), 13 (9%) étaient des procédures de sauvetage (stomie définitive). La rémission de la FRV était atteinte chez 7/32 patientes (22%). Le taux de succès par procédure était de 5% (7/138). A la fin du suivi 13/32 (41%) patientes avaient une stomie. Le pourcentage de la durée du suivi passée sous biothérapies était de 90% pour les patientes guéries versus 50% pour les autres ($p=0,11$). Seule la biothérapie était un facteur pronostic de succès d'une procédure de fermeture après analyse univariée ($p=0,007$).

Même dans un centre référent le taux de rémission des FRV dans la MC est faible à long terme et le risque de stomie est important. La combinaison avec les biothérapies est cruciale.

VU ET PERMIS D'IMPRIMER

Grenoble, le : 24/03/2020

LE DOYEN



Pr. Patrice MORAND

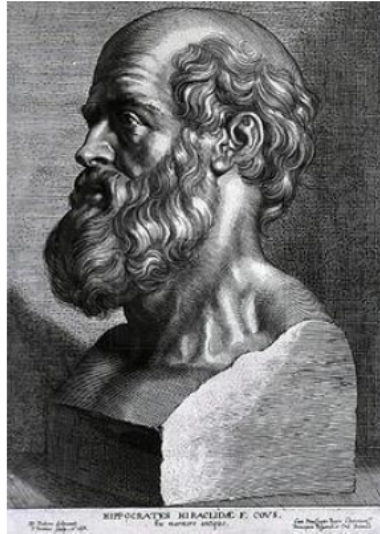
LE PRÉSIDENT DE LA THÈSE



Pr. Jean-Luc FAUCHERON

Le Doyen de l'UFR de Médecine

Pr. Patrice MORAND



SERMENT D'HIPPOCRATE

En présence des Maîtres de cette Faculté, de mes chers condisciples et devant l'effigie d'HIPPOCRATE,

Je promets et je jure d'être fidèle aux lois de l'honneur et de la probité dans l'exercice de la Médecine.

Je donnerai mes soins gratuitement à l'indigent et n'exigerai jamais un salaire au dessus de mon travail. Je ne participerai à aucun partage clandestin d'honoraires.

Admis dans l'intimité des maisons, mes yeux n'y verront pas ce qui s'y passe ; ma langue taira les secrets qui me seront confiés et mon état ne servira pas à corrompre les mœurs, ni à favoriser le crime.

Je ne permettrai pas que des considérations de religion, de nation, de race, de parti ou de classe sociale viennent s'interposer entre mon devoir et mon patient.

Je garderai le respect absolu de la vie humaine.

Même sous la menace, je n'admettrai pas de faire usage de mes connaissances médicales contre les lois de l'humanité.

Respectueux et reconnaissant envers mes Maîtres, je rendrai à leurs enfants l'instruction que j'ai reçue de leurs pères.

Que les hommes m'accordent leur estime si je suis fidèle à mes promesses.

Que je sois couvert d'opprobre et méprisé de mes confrères si j'y manque.