

Interposition of a biological mesh does not decrease the risk of rectovaginal fistula after excision of large rectovaginal endometriotic nodules: a pilot study of 209 patients

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Abstract

Background: Rectovaginal fistula is a major complication of surgery for deep endometriosis. Objective: To assess whether placement of a biological mesh (Permacol?) between the vaginal and rectal sutures reduces the rate of rectovaginal fistula, in patients with deep rectovaginal endometriosis. Study Design: Retrospective, comparative study enrolling patients with vaginal infiltration > 3cm diameter and rectal involvement in two centers. They benefited from complete excision of rectovaginal endometriotic nodules, with or without a biological mesh placed between the vaginal and rectal sutures. Rectovaginal fistula rate was compared between the two groups. Results: 209 patients were enrolled: 42 patients underwent interposition of biological mesh (cases) and 167 did not (controls). 92% of cases and 86.2% of controls had rectal infiltration greater than 3cm in diameter. Cases underwent rectal disc excision more frequently (64.3% vs. 49.1%) and had a lower distance between the rectal stapled line and the anal verge (4.4+/-1.4 cm vs. 6+/-2.9cm). Rectovaginal fistulae occurred in 4 cases (9.5%) and 12 controls (7.2%). Logistic regression analyses revealed no difference in the rate of rectovaginal fistula following the use of mesh (adj OR 0.61, 95%CI 0.2-2.3). A distance < 7cm between the rectal stapled line and the anal verge was found to be an independent risk factor for the development of rectovaginal fistulae (adj OR 16.4, 95%CI 1.8-147). Conclusions: Placement of a biological mesh between the vagina and rectal sutures has no impact on the rate of postoperative rectovaginal fistula formation following excision of deep infiltrating rectovaginal endometriosis.

Introduction

Rectovaginal fistula formation is a major complication following surgery for rectovaginal endometriosis, particularly when simultaneous excision of rectal and vaginal tissue is required for complete excision of disease¹. Although the vagina and rectum are always repaired separately, postoperative healing may lead to adhesions between the two suture lines due to their close proximity. This may result in formation of a fistula between the rectal lumen and the vagina, leading to passage of gas and faeces through the vagina.

Rectovaginal fistula is one of the most significant complications of surgery for deep endometriosis, and its prevalence varies considerably between published series²⁻⁴. Numerous factors have been reported to affect the risk of rectovaginal fistula formation. These include patient characteristics such as smoking status, disease characteristics such as nodule size and distance from the anal verge, and surgical factors such as the distance between rectal and vaginal sites of repair, vaginal suture calibre and the use of temporary diverting

stomas¹⁻⁴. In series reporting on patients undergoing excision of deeply infiltrating endometriosis involving any portion of the rectosigmoid, the rate of rectovaginal fistula formation is approximately 3%¹⁻⁴. In series specifically focusing on excision of low rectal deep endometriosis, rectovaginal fistula is more likely, and rates as high as 27% have been reported¹. Surgery for deep endometriosis, however, is a less common cause of fistulae overall than obstetric trauma and inflammatory bowel disease⁵.

To reduce the risk of rectovaginal fistula following excision of deep endometriosis, several techniques have been trialled. The main aim of these techniques is to interpose healthy tissue between the vaginal and rectal suture and staple lines, to create a degree of separation and therefore to reduce the likelihood of adhesion formation. Omentum is a well vascularised and highly lymphatic tissue, which is often used for this purpose. The technique of omentoplasty involves mobilisation of the omentum from the colon and placement between the rectum and vagina, whilst retaining its blood supply from the left gastroepiploic artery. Although frequently used in the repair of rectovaginal fistulae, the role of omentoplasty in the prevention of rectovaginal fistulae is not well established. Three randomized trials have reported on fistula rates following omentoplasty performed after colonic and rectal resections for pathologies including diverticular disease, inflammatory bowel disease and benign and malignant colorectal tumors, with conflicting results⁶⁻⁸. A single trial reporting on patients who underwent rectal resection revealed a similar incidence of circular staple line defects in patients who underwent omentoplasty, when compared to those who did not. The rate of clinically and radiologically detected leaks, however, was significantly lower⁸.

David Redwine proposed two techniques to separate the vaginal suture line and rectal anastomosis during healing to reduce the risk of rectovaginal fistula formation: 1. suturing adipose tissue from the rectovaginal septum over the rectal anastomotic line followed by: 2. reconstruction of the pouch of Douglas by suturing the anterior rectum, cephalad to the anastomotic line, to the posterior vaginal fascia, caudad to the vaginal sutures (unpublished data). This forces the rectal anastomotic line to lie within the rectovaginal septum and, hence, separate from the vaginal sutures. The sutures attaching the anterior rectum to the posterior vagina create a new pouch of Douglas. Although a small number of patients may have insufficient adipose tissue to accomplish the first stage of the procedure, Redwine postulated that almost all patients can be treated with the second procedure, as the rectal and vaginal tissues are pliable enough to accomplish this in most patients safely and with ease (unpublished data).

In patients with a low body mass index (BMI), the omentum and pelvic adipose tissues are thin, and their mobilisation and interposition may lead to tissue devascularization and delayed necrosis. In these circumstances, the interposition of other biological tissue (with FDA approval) might be suitable, with the goal of separation of the vaginal sutures and rectal anastomosis.

Permacol? (Medtronic, Minneapolis, MN, US) is an acellular porcine-derived collagen matrix graft cross-linked with hexamethylene diisocyanate. The cross-linking process supports fibroblast growth and provides resistance against collagenase enzymes. The inability of collagenase to digest the implant allows it to maintain its structural integrity; the mesh is, however, degraded over time^{9,10}. Permacol? has been successfully used to repair abdominal wall defects¹⁰, and rectovaginal fistulae where previous repair has failed, with a low recurrence rate¹¹.

These data underpin our hypothesis supporting the potential role of Permacol? in the prevention of rectovaginal fistulae following removal of large rectovaginal nodules requiring concomitant excision of both vaginal and rectal tissue, by interposition of the mesh between the vaginal suture and rectal stapled line.

The goal of our study was to assess whether or not the interposition of a biological mesh between vaginal and rectal staple and suture lines could prevent rectovaginal fistula in patients undergoing complete excision of large rectovaginal endometriotic nodules.

Material and methods

We performed a retrospective, comparative cohort study of patients who underwent surgery in 2 centers: at Rouen University Hospital, France between June 2009 and June 2018 and at the Endometriosis Center,

Clinique Tivoli-Ducos, Bordeaux, France between September 2018 and May 2019.

The inclusion criteria were: i) surgery for deep endometriosis involving both vagina and rectum; ii) extensive vaginal infiltration requiring the excision of a vaginal specimen measuring more than 3cm in diameter; iii) infiltration of the rectal muscularis propria, submucosa, deep mucosa or mucosa, requiring disc excision or segmental resection of the rectum; iv) consent to enrolment in the North-West Inter Regional Female Cohort for Patients with Endometriosis (CIRENDO) database.

The exclusion criteria were: i) treatment of rectal nodules by shaving, not requiring suturing; ii) infiltration of the vagina over an area of less than 3cm diameter.

Patients' baseline characteristics, intraoperative findings, surgical procedures and follow up were prospectively recorded in the CIRENDO database (NCT02294825) by a clinical research technician. All patients were asked to complete the following questionnaires: clinical history, Gastrointestinal Quality of Life Index (GIQLI)¹², the Knowles-Eccersley-Scott-Symptom questionnaire (KESS)¹³, and the Wexner score for faecal continence¹⁴. Prospective recording of data was approved by the French authority, Advisory Committee on Information Processing in Healthcare Research (CCTIRS).

The preoperative diagnosis and assessment of patients referred with deep endometriosis with bowel involvement included a gynecological examination and Magnetic Resonance Imaging (MRI) of the pelvis. When the presence of rectal endometriosis was confirmed by MRI, a transvaginal and/or endorectal ultrasound was performed to assess the degree of infiltration of the muscularis propria of the rectum. Computed tomography (CT)-based virtual colonoscopy was used to estimate the degree of rectal stenosis and to assess the presence and location of other gastrointestinal lesions (Fig 1).

Patients were examined by an experienced gynecologist. A requirement for bowel surgery was determined according to the presence of pelvic pain and/or gastrointestinal symptoms, despite adequate medical treatment, due to endometriosis infiltrating at least the rectal muscularis propria as demonstrated on the preoperative assessment described above. In a majority of cases, preoperative assessment provided a precise description of rectal endometriotic nodules (diameter and depth of nodules, and distance from the anal verge). Thus, the specific rectal surgical procedure was established preoperatively in the majority of cases, based on multiple factors including the features of the endometriotic nodules, and patient symptoms, age, and intention to conceive.

Rectal disc excision was reserved for nodules infiltrating to at least the deep muscularis propria and was carried out using transanal staplers. End-to-end staplers (EEA) were utilised for the removal of nodules measuring less than 3-4 cm in diameter (Video 1)¹⁵, while nodules measuring more than 4cm located in the mid/low rectum were removed by either double disc excision or using a semi-circular transanal stapler (Contour Transtar) and the Rouen technique (Video 2)¹⁵. Segmental resection was performed in patients presenting with multiple nodules in close proximity, or in patients with large rectal nodules measuring more than 4 cm in length and causing luminal stenosis of more than 30%. In patients with multiple nodules infiltrating the low/mid rectum and sigmoid colon, separated by more than 7cm of healthy rectosigmoid tissue, combined low disc excision and short segmental resection of the sigmoid colon was routinely performed¹⁶. To define the location of deep endometriotic nodules, we used the following thresholds: low rectum, up to 5 cm above the anal verge; mid rectum, 5 to 10 cm; upper rectum, 10 to 15 cm; sigmoid colon, greater than 15 cm¹⁷. Patients who underwent planned rectal disc excision or segmental rectal resection were informed about the risk of rectovaginal fistula, the preventive surgical techniques available and the surgical complexity of its repair, should it occur.

All procedures were completed laparoscopically. General surgeons with appropriate experience performed any rectal suturing required for disc excision and segmental rectal resection. Excision of vaginal lesions was performed either laparoscopically or via the vaginal route. When the vaginal route was utilized for excision of vaginal lesions, it was routinely followed by laparoscopy for the removal of rectal disease and associated pelvic and abdominal endometriosis. Vaginal lesions were excised with as narrow a margin as possible. Nerve sparing techniques were employed whenever technically feasible. In Rouen, from June 2009 to June

2018, omentoplasty was routinely attempted to separate vaginal sutures and the rectal anastomosis. From October 2016 onwards, the interposition of a 5cm x 5cm Permacol[®] mesh was introduced. The mesh was placed in the rectovaginal space, behind the vaginal sutures and in the front of the rectal anastomosis, and fixed in place with sutures at the origin of the uterosacral ligaments or at the torus uterinus (Fig 2, Video 1,2). A temporary diverting stoma was formed at the discretion of the surgeon in selected cases, particularly in patients who a) required extensive vaginal excision combined with a challenging vaginal repair, b) had a positive rectal staple line air leak test, or c) had rectal and vaginal staples and sutures in close contact at the completion of the surgery. All stomas were reversed 2 to 3 months postoperatively, after exclusion of a rectovaginal fistula or leak with a barium enema or CT scan.

At the end of all procedures, a questionnaire recording patient demographic and clinical information, and surgical procedures performed, was completed by the surgeon. Subsequently all data were recorded in the CIRENDO database. Postoperative complications were recorded using the Clavien-Dindo classification¹⁸.

Statistical analysis was performed using STATA 9.0 software (Stat Corporation, Lakeway Drive, TX). Patients who underwent insertion of biological mesh were compared to those who did not using either the Fischer exact test (qualitative variables) or the Kruskal Wallis test (continuous variables). Logistic regression analyses were used to identify independent risk factors for rectovaginal fistula formation and included factors of clinical interest, or those for which the relationship with development of fistula was shown to be <0.2 in univariate analysis. The study was approved by the Comité d’Ethique de la Recherche Non Interventionnelle, Rouen University Hospital (E2020-19, 7/4/2020). A P-value <0.05 was considered being statistically significant.

Results

We included a total of 209 patients with documented rectovaginal endometriosis. All patients had vaginal infiltration measuring greater than 3cm in diameter, and rectal infiltration invading to at least the muscularis propria. Of these, 42 patients underwent interposition of a 5x5cm Permacol[®] mesh between the vaginal sutures and rectal anastomosis, between October 2016 and October 2018. One hundred and sixty-seven patients or ‘controls’ did not undergo insertion of mesh. Patient baseline characteristics are presented in Table 1. The median value of the BMI in each group was relatively low: 21.8 kg/m² (95%CI 20.7-22.9) in the study group and 23.4 (95%CI 22.7-24) in controls (P=0.02). The majority of the patients were nulliparous, and more than half reported a history of subfertility. A wide range of pain and gastrointestinal symptoms were reported, with a majority of patients recording abnormal GIQLI scores. One in ten patients had evidence of hydronephrosis on preoperative imaging, and 20% of patients reported sub-acute obstructive bowel symptoms.

Table 2 presents our intraoperative findings. Infiltration of the rectum was present in all included patients, and numerous of them were found to have multiple additional endometriotic lesions involving the sigmoid, colon, appendix, caecum and ileum. Eight patients, presenting with rectal nodules measuring less than 1cm in diameter were also found to have larger nodules infiltrating the rectosigmoid junction and/or sigmoid colon, requiring en block segmental resection. Disc excision was performed in 108 patients, and segmental resection in 112. In 5.3% of patients, both procedures were performed simultaneously: this was required in patients presenting with multiple nodules within the rectum and sigmoid colon, where rectal disc excision was combined with short segmental sigmoid colon resection. On average, the disc excisions were closer to the anal verge than the segmental resections. Patients included in the study group had a lower overall distance of the rectal anastomosis from the anal verge, related to the increased use of the Rouen technique for removal of large nodules involving the low rectum. Consequently, temporary diverting stomas were required in a majority of patients, as the risk of rectovaginal fistula was considered to be high. Excision of deep endometriotic nodules infiltrating the parametria was recorded in 16.3% of patients, and excision of nodules involving the sacral nerve roots was recorded 11% of patients.

Sixteen patients (7.7%) developed a rectovaginal fistula: 4 in the study group (9.5%) and 12 in the control group (7.2%). Table 3 presents the results of the logistic regression analyses. As the distance of the rectal

anastomotic line from the anal verge (in cm) was not recorded in the CIRENDO database from 2009 onwards, and was therefore documented in only 187 patients (89.5% of the entire cohort), the logistic regression analysis included only these 187 patients who had full documentation on all of the following major risk factors: use of Permacol? mesh, distance of the anastomotic line from the anal verge, rectal surgery, excision of the parametria and formation of stoma. The analyses showed that the single independent predictive risk factor for development of rectovaginal fistula, after adjustment for the risk factors listed above, was the distance of the anastomotic line from the anal verge, as a distance of less than 7cm from the anal verge increased the risk of rectovaginal fistula by a factor of 16, independent of the use of Permacol? mesh.

Discussion

Our study investigated the potential benefit of the use of a biological mesh in the prevention of rectovaginal fistula, in patients undergoing excision of deep endometriosis with extensive infiltration of both rectum and vagina. Although biologically plausible, our study does not confirm our hypothesis: that the interposition of mesh between the rectal and vaginal suture and staple lines would be associated in a reduction in the risk of rectovaginal fistula. Rather, we report comparable rates of rectovaginal fistula rates between cases and controls regardless of the use of mesh. In addition, our study demonstrates that the risk of development of rectovaginal fistulae following extensive vaginal excision combined with excision of rectal endometriosis <7cm from the anal verge is far greater than pooled rates reported in patients undergoing excision of colorectal endometriosis of any location. On the basis of our results, we recommend that future attempts to prevent postoperative rectovaginal fistulae should focus on alternative techniques.

Our study has several weaknesses. Due to the lack of available evidence, we could not base our study's design on any previously reported literature. However, despite the lack of difference shown, our data is of value to surgeons managing patients with deep rectovaginal endometriosis. Another weakness is related to the long period of time over which our patient cohort underwent surgery. The studied surgeon's experience increased between 2009 and 2016, therefore patients included in the study group were operated on by a more experienced surgeon, as suggested by the lower overall duration of surgery in this group. This bias would also be expected to improve outcomes in patients included in the study group, and to have resulted in a change in fistula rate, with a lower rate observed in those patients undergoing interposition of mesh. This trend, however, was not observed, as fistula rates were similar between the two groups. Patients with deep endometriosis are usually referred to more experienced surgeons. A tendency towards more severe endometriosis, however, was likely present in the study group, as suggested by the higher number of patients with deep endometriosis involving parametria, sacral nerve roots or sciatic nerves, and higher rate of patients requiring more complex procedures including disc excision (the Rouen technique)¹⁵. Randomization minimises such differences between arms in a study, however the design of a future randomized trial and calculation of an appropriate sample size requires preliminary data, which our comparative retrospective study provides.

One may consider the heterogeneity of surgical procedures performed as another weakness of our study. This limitation, however, applies to the majority of studies reporting on surgery for endometriosis²⁻⁴, which is a heterogeneous disease with a multiple patient symptoms, differing in disease severity and lesion locations.

Our study has several strengths. To the best of our knowledge, this is one of the largest case series in the literature reporting on patients with rectovaginal endometriotic nodules causing deep infiltration of the rectal wall and extensive infiltration of the vagina over an area of greater than 3cm. Thus, we provide reliable information on symptoms, associated disease and lesion locations and expected complications in this selected population. We have demonstrated that the rate of rectovaginal fistula formation in patients undergoing excision of low rectal nodules less than 7 cm from the anal verge, with involvement of the vagina is, on average, 5 times higher than pooled rates reported in patients undergoing excision of colorectal endometriosis of any location without vaginal involvement^{2,3}. We have also shown that the interposition of a biological mesh has no role in the prevention of fistulae. Our data were rigorously and prospectively recorded by a dedicated clinical researcher. All procedures were performed by a surgeon with experience in the management of deep endometriosis¹⁹.

Various forms of mesh have been extensively used to treat prolapse of the uterus, bladder and rectum over the past 3 decades²⁰. Controversy over their use has arisen during the last 10 years, because of numerous reports of pain, vaginal erosions and infectious complications²¹. Biological meshes were previously considered to be safer, however a recent meta-analysis showed no benefit of biological over synthetic mesh in terms of infectious complications²². We cannot determine whether or not potential infectious complications influenced the rate of rectovaginal fistula formation in our patient cohort who underwent insertion of biological mesh. Fistula rates were similar between groups, inferring that the use of mesh had no impact on the probability of development of rectovaginal fistula. This finding is, however, unexpected, given our hypothesis that the interposition of mesh would separate the vaginal sutures and rectal anastomosis, creating favorable circumstance for tissue healing and prevention of fistula. Suggested hypotheses for fistula formation, despite the use of mesh, include migration of mesh in the immediate postoperative period, or development of rectovaginal fistula lateral to the mesh itself. It has been reported that surgical site infections are associated with a higher rate of recurrence of incisional herniae following repair with biological mesh. This is due to the observation that postoperative surgical site infections increase the secretion of collagenases and enhance enzyme activity, leading to mesh degradation²³. In our 4 cases of rectovaginal fistula after placement of mesh, the fistula occurred within a short timeframe following surgery without preceding evidence of surgical site infection. Regardless, our data suggest that the mechanism of formation of rectovaginal fistula is more complex than just close proximity of vaginal suture and rectal anastomotic lines.

Rectovaginal fistula is a significant postoperative complication of surgery for deep endometriosis. When a choice of bowel procedure is possible, bowel shaving rather than disc excision or colorectal resection is recommended given the lower associated rate of rectovaginal fistula formation². Such a procedure, however, is not always feasible when the rectal wall is deeply infiltrated, as was the case in the 209 patients included in our series. This information should be clearly communicated to patients prior to surgery, to facilitate informed decision making.

The use of biological mesh in the repair of complex rectovaginal fistula has been previously reported in the literature with conflicting results. Gottgens et al performed biological mesh repair in 12 patients with rectovaginal fistula, using a transperineal or transvaginal approach, and reported success in 8 patients (66%)¹¹. They proposed placement of a biological mesh as a first line management option for rectovaginal fistula. Conversely, Mege et al reported disappointing outcomes, with a success rate of 20% in a series of 10 patients with rectovaginal fistula²⁴. It should be noted, however, that their population presented with less favourable baseline characteristics, such as recurrent fistula in 90% of their cohort. In this cohort, patients had undergone up to 8 previous surgical repairs. Conclusions reported in patients undergoing complex fistula repair cannot be extrapolated to patients without a fistula, in whom the goal of mesh placement is fistula prevention. Our results suggest that the placement of a biological mesh is ineffective in the prevention of rectovaginal fistulae.

The reported rate of rectovaginal fistula following excision of low rectal nodules in our study may be perceived as high, bringing the external validity of our results into dispute. However, our results are concordant with those reported by others in papers with similar inclusion criteria. Belghiti et al (2014) reported their experience in 212 patients who underwent surgical treatment of colorectal endometriosis. Forty-four patients underwent partial colectomy combined with low colorectal excision and anastomosis <7 cm from the anal margin¹. Formation of a stoma was performed in 75% of these patients, and 8 rectovaginal fistulae were recorded (18.2%). The authors emphasized that patients with a temporary diverting stoma had a lower rate of fistula (15%) than those without a stoma (27%), and concluded that *“the location of the colorectal anastomosis and the association of partial colectomy are risk factors for rectovaginal fistula. Future studies should focus on effective ways to separate the vaginal suture line from the rectal staple/suture line, which is the determinant factor for rectovaginal fistula”*. Although their data are comparable to ours, we add to their statement by concluding that biological meshes are not an effective tool for the prevention of rectovaginal fistulae despite the separation of the vaginal suture line from the anastomotic line in the early postoperative period.

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Conflict of interests: Prof. Roman reports personal fees from Plasma Surgical Inc., ETHICON, Olympus and Nordic Pharma for his involvement in workshops. Other authors report no conflict of interest.

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Authors' roles:

Horace Roman and Jean Jacques Tuech designed the trial, performed the surgery, and wrote the first draft of the manuscript. Haitham Khalil, Valerie Bridoux and Clotilde Hennetier performed the surgery. Sophia Braund, Jennifer Pontre and Clemence Klaczynski performed data collection. All the authors contributed to the final manuscript.

Details of ethical approval:

All patients signed an informed consent before enrollement in CIRENDO database and the study was approved by the Committe d'Ethique de la Recherche Non Interventionnelle, Rouen University Hospital (E2020-19, 7/4/2020).

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Tables and figures:

Table 1. Patient characteristics.

Table 2. Intraoperative findings and surgical procedures.

Table 3. Independent factors related to the probability of bowel fistula (logistic regression analysis including N=187 patients with documented height of rectal stapled line (89.5% of 209 patients). Fig 1. Deep endometriosis infiltrating the vagina and rectum in a patient included in the study (a: T2 MRI sagittal view; b: T2 MRI axial view; c: computed tomography-based virtual colonoscopy sagittal view; d: 6.5 cm-diameter rectal disc removed by the Rouen technique and 3 cm-diameter vaginal patch). Fig 2. Interposition of Permacol? mesh between vaginal and rectal sutures, covered via omentoplasty. Video 1. Interposition of Permacol? mesh in a patient with deep rectovaginal endometriosis infiltrating the low rectum, vagina, right parametrium and right sacral nerve roots. The rectal nodule was removed via disc excision using the EEA transanal stapler. Video 2. Interposition of Permacol? mesh in a patient with deep rectovaginal endometriosis infiltrating the low rectum, vagina, both parametria, right sacral nerve roots and bladder. The rectal nodule was removed via disc excision using the Rouen technique.

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