

Chapter 10.

General discussion and future perspectives.

Sigmoid vaginoplasty as reconstructive approach

Different surgical approaches to genital reassignment surgery exist and surgical indications for transgender women differ for centers around the world. In transgender women, penile inversion vaginoplasty is the most commonly performed surgical procedure for this goal.³ At the VU University Medical Center, transgender women are considered eligible for intestinal vaginoplasty in case of penoscrotal hypoplasia (penile length <7 cm) or as revision procedure when a previous vaginoplasty has failed. In patients with penile skin lengths between 7 and 12 cm, penile inversion vaginoplasty with additional (scrotal) FTGs is generally performed. In other centers, intestinal vaginoplasty is only considered as revision procedure. For patients with insufficient penile skin for penile inversion vaginoplasty, scrotal or non-genital (full-thickness) skin grafts are chosen as neovaginal lining. In literature, also non-grafted options have been reported as surgical option for revision procedures.⁴

Which surgical technique is most suited for which patient population may be subject of research for the near future for both vaginoplasty as primary procedure as well as revision vaginoplasty procedures. With increasing exchange of information between physicians involved in gender surgery in Europe (European Professional Association for Transgender Health (EPATH), European Society for Sexual Medicine (ESSM), European Network for the Investigation of Gender Incongruence (ENIGI)) and worldwide (World Professional Association for Transgender Health (WPATH)), opportunities arise for many forms of extensive scientific research regarding surgical results and patient-reported outcomes after gender reassignment surgery in transgender women in the future. Worldwide, surgeons from many different specialties perform gender reassignment surgery. This is reflected by the background diversity of scientific medical journals that report on vaginoplasty surgery outcomes in transgender women, e.g. urology, plastic and reconstructive surgery, gynaecology, sexology and psychology. A multidisciplinary approach to such research with international collaborative partners may benefit the transgender population globally. Before such research can be adequately performed, questionnaires regarding postoperative quality of life, satisfaction with surgery and sexual functioning have to be developed and validated specifically for the transgender population. Such a questionnaire should be simple, reliable, precise in wording, translatable in different languages, adequate for assessment of relevant outcome measures, including change of these over time.

The commonest used intestinal segments for intestinal vaginoplasty are the sigmoid and the ileum. Which of these provides the most satisfying result with the least surgical complications is debated. The choice for either of these is mainly based on the origin

and background of the surgeon.⁵ Generally, urologists tend to use an ileal graft more often, possibly due to their experience with surgical bladder reconstruction such as the Bricker bladder. Though in a Chinese study, focusing solely on laparoscopy-assisted intestinal vaginoplasty, slightly favorable surgical results have been shown in the ileal vaginoplasty group, in terms of operative time and intraoperative blood loss, no consensus has been reached which intestinal segment provides the best surgical and functional results.⁶ A thorough comparison between these grafts regarding surgical outcome, neovaginal bowel complications, patient-reported quality of life, sexual function, (excessive) lubrication and malodor has not been performed to date. At the VU University Medical Center, we aim to start a prospective, randomized clinical trial to study results of intestinal vaginoplasty with a sigmoid or ileum graft in transgender women in the near future.

Sigmoid tissue as neovaginal lining

Diversion colitis is a well-known complication after surgical colon diversion from the fecal stream. A chronic lack of luminal nutrients (SCFAs) may lead to nutritional deficiency of colonocytes and subsequently friability, atrophy and inflammation. We have coined the term 'diversion neovaginitis' for diversion colitis occurring in the sigmoid-derived neovagina. A standardized diagnostic and treatment protocol for patients with presumed diversion neovaginitis is lacking. This will be a focus point of future research of our department. It is likely that the presence of excessive neovaginal discharge and malodor will be important in the diagnostic process, because these symptoms are associated with endoscopic and histological signs of inflammation.^{1,2} However, besides diversion neovaginitis, neovaginal discharge and bleeding after sigmoid vaginoplasty can be due to other causes, such as bacterial overgrowth, sexually transmitted diseases (*Trichomonas vaginalis*, *Chlamydia trachomatis*, *Neisseria gonorrhoea*), hypergranulation, candidiasis, poor neovaginal hygiene, neovaginal cancer, polyps, neovaginal inflammatory bowel disease and rectoneovaginal or urethaneovaginal fistula. Thorough neovaginal examination, (sexual) history taking, endoscopic examination, biopsies, microbial swabs and MRI (in case of neovaginal fistulas) may aid to discriminate between these factors.

In patients who underwent rectal cancer resection with or without diversion ileostomy, significant microbial differences were noted between the diverted rectum and the control group.^{7,8} The severity of the diversion colitis was negatively correlated with *Bifidobacterium*. Patients who underwent sigmoid vaginoplasty at our institution, were yearly followed up with endoscopic, histologic and microbial examination of the

neovagina. We hypothesize that the combination of clinical, histopathological and endoscopic neovaginal characteristics with the microbial profiles, as determined by IS-pro, may lead to a simple diagnostic model discriminating patients with and patients without diversion neovaginitis. We intend to model our current dataset to delineate such a diagnostic algorithm.

Patients were previously invited yearly for endoscopic examination of the sigmoid neovagina and inventarisation of neovaginal complaints, as regular postoperative follow-up. In most sigmoid neovaginas, mild inflammation is observed, endoscopically and histologically.^{1,2} The clinical significance of this remains to be determined. In a case series of five transgender women who underwent sigmoid vaginoplasty at least 10 years before examination, endoscopic and histologic evaluation of the sigmoid-derived neovagina revealed predominantly mild inflammatory neovaginal changes.⁹ This has to be interpreted with caution, since the number of patients was low. The optimal follow-up schedule for patients who underwent sigmoid vaginoplasty has not been defined. Most likely, endoscopic examination as routine follow-up is necessary nor cost-effective, and only patients who experience symptoms of diversion neovaginitis, mucous discharge and malodor, are candidates for further follow-up. On the other hand, oncogenic changes may be triggered by persisting inflammation, as has been shown in colitis-associated cancer in patients with comorbid IBD.¹⁰ If patients with long-lasting diversion colitis or neovaginitis are at higher risk for colonic cancer is unknown.

Various treatment options are mentioned for diversion colitis in literature. Severe diversion colitis is traditionally treated by surgically restoring colonic continuity. This however, is undesirable after sigmoid vaginoplasty, since patients will lose their neovagina. Non-invasive, medical therapy seems the first treatment of choice for diversion neovaginitis. These comprise local irrigation with SCFAs, fibre, 5-aminosalicylic (5-ASA) acid or steroids. Historically, conflicting results have been reported regarding the beneficial effects of SCFAs on diversion colitis.¹¹⁻¹³ However, in more recent publications, butyrate enemas have been shown to improve endoscopic scores in patients with diversion colitis and cause concomitant upregulation of genes associated with mucosal repair.¹⁴ If regular neovaginal irrigation with SCFAs may prevent diversion neovaginitis is uncertain, however this appears to be an interesting approach, warranting future research. Questions which have to be addressed in such research are:

1. Does preventive neovaginal butyrate administration have a positive effect on patient-reported symptoms and endoscopic and histologic features?
2. Are all patients eligible for such a treatment?

3. What is the optimal administration form, composition, dosage and use frequency, bearing in mind patient comfort?
4. Is it cost-effective?
5. What is the relationship between symptomatic diversion neovaginitis and quality of life or sexual function?

The neovaginal microbiome is a microbial niche, which recently gained scientific interest.^{15,16} The surgically constructed neovagina is in some ways similar to, and in other ways different from the biological neovagina. While the anatomic location is similar and sexual intercourse is possible, its structure is inherently different.¹⁷ The neovaginal microbiome of the penile-inversion neovagina harbors some bacterial species that inhabit the native vagina as well. *Lactobacillus* species, native vaginal commensals, have been found to inhabit the neovagina frequently.¹³ Also, common pathogens of bacterial vaginosis may induce bacterial dysbiosis in the surgically constructed neovagina (chapter 8). Future research focusing on microbial differences and similarities between the penile-inverted neovagina, the intestinal neovagina, the native intestine and the penile skin, using molecular profiling techniques, is of great interest. Such microbial research may provide insight in various matters, e.g. which bacterial species or groups prefer which tissue or location to colonize, what are neovaginal commensals and where do they originate from, do commensals of the intestinal neovagina differ from those of the skin-lined neovagina, which rectal bacteria colonize the (neo)vagina and what is the influence of rectal bacteria on (neo)vaginal infections. Although the sigmoid is the segment of choice for intestinal vaginoplasty in our institution, if for some reason the sigmoid cannot be used safely during surgery (e.g. the vascular pedicle does not allow its' descent through the neovaginal tunnel), an ileal vaginoplasty is performed. The same follow-up protocol exists for these patients, with yearly clinical, endoscopic, histological and microbial evaluation. Diversion ileitis does not occur, but it would be interesting to see what the endoscopic and histological characteristics of the ileal neovagina are and how patients experience the neovaginal discharge. Also, a comparison of the ileal and the sigmoid neovaginal microbiome would be of scientific interest.

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