

## Chapter 1.

**General introduction.**

Absence of a functional vagina impairs the psychological well-being and quality of life of biological women, with congenital or acquired absence of a functional vagina, and transgender women. For these patients, it is essential to (re)create a vagina with satisfactory sexual function and appearance.<sup>1-4</sup> Sexual quality of life is regarded to be low in transgender women before gender reassignment surgery.<sup>5,6</sup>

Different surgical techniques have been described to create a neovagina. They vary in what type of graft is used for the surgical reconstruction. In non-transgender women with vaginal agenesis, the Vecchiotti procedure can be performed, in which a neovagina is created by traction of an intra-abdominally placed device on an olive-shaped bead placed in the vaginal dimple.<sup>7</sup> Because of the applied traction on the bead, it is pulled inward to gradually create a vagina. In transgender women, penile inversion vaginoplasty is the most commonly performed technique for vaginal construction.<sup>8</sup> During this procedure, a tunnel is dissected in the vesicorectal space to form the neovaginal cavity. Penile skin is dissected from the shaft and inverted in the neovaginal tunnel to serve as neovaginal lining. The urethra is shortened, the corpora cavernosa are removed and an orchiectomy is performed. From a part of the glans penis, on its dorsal neurovascular bundle, and prepuce, the neoclitoris and the labia minora are formed. Excessive scrotal skin is used to form the labia majora. Postoperative vaginal stenting and regular neovaginal dilatation is necessary.

However, penile inversion vaginoplasty is not an option for:

1. Patients who lack sufficient penile skin. This patient group comprises transgender women who developed penoscrotal hypoplasia due to previous treatment with puberty suppressing hormones and patients who previously underwent circumcision.
2. Patients who previously underwent vaginoplasty which failed to provide sufficient neovaginal depth.
3. Biological women with congenital, post-ablative or traumatic absence of a functional vagina.

For these patients, another surgical approach has to be determined. Alternatives like non-genital skin grafts, pedicled local (musculo)cutaneous flaps, peritoneum and pedicled intestinal segments can be used as neovaginal lining, each with its own advantages and disadvantages.<sup>8</sup> In intestinal vaginoplasty, an intestinal segment, most commonly a sigmoid or ileum conduit of 12-18 cm long, is isolated on its vascular pedicle and transferred to a dissected pouch between bladder and rectum to form the neovaginal lining.<sup>9,10</sup> In most institutions, sigmoid vaginoplasty is performed as open or

laparoscopy-assisted procedure. At the VU University Medical Center, sigmoid vaginoplasty is performed totally laparoscopic. Generally, a laparoscopic approach has the advantages of avoiding large incisions (with large scars and increased chance of incisional herniation), faster return to normal activity and decreasing blood loss, risk on surgical site infections, postoperative pain, discomfort and hospital stay.

Using intestine as neovaginal lining provides some proposed advantages when compared to other types of grafts, such as sufficient neovaginal depth and natural self-lubrication, which both may have a positive effect on sexual function. Also, it has little tendency to shrink, precluding the need for perpetual (self)dilatation. Its texture is somewhat similar to that of the biological vagina. Little is reported on patient-reported quality of life and sexual function after intestinal vaginoplasty in transgender women. Short-term disadvantages are the need for intestinal surgery and bowel anastomosis with concomitant risks. Reported long-term disadvantages comprise the risk of development of neovaginal diversion colitis ('diversion neovaginitis'), neovaginal inflammatory bowel disease, malignancy, excessive mucus production, introital stenosis and malodor. Adversaries of the sigmoid vaginoplasty technique argue that these complications are rare, but clinically significant, adverse events.

Diversion colitis is well-known to gastroenterologists and gastrointestinal surgeons. Diversion colitis is inflammation of the colon caused by a lack of luminal nutrients after surgical diversion of the fecal stream. It is traditionally observed after ileostomy or colostomy. An insufficient supply of luminal nutrients, especially short-chain fatty acids (SCFAs), a key energy source for colonocytes, appears to play a pivotal role.<sup>11,12</sup> SCFA shortage may lead to apoptosis of colonocytes and, subsequently, to an inflammatory response of the colonic mucosa and epithelial barrier disruption. Clinical manifestations may comprise mucous discharge, (abdominal) pain, tenesmus and bleeding, but most patients experience little to no symptoms. Endoscopic features comprise erythema, friability, granulation, decreased vascular pattern and edema of the colonic mucosa.<sup>13-16</sup> Diversion colitis of the sigmoid-derived neovagina, coined as diversion neovaginitis, may similarly occur after sigmoid vaginoplasty, since the colonic segment is surgically diverted from fecal nutrients. Although the risk on diversion neovaginitis is frequently reported in literature, little is known on its prevalence and characteristics.<sup>17-20</sup> Diagnosis of neovaginal disease and its subsequent treatment relies on a proper and adequate knowledge of clinical characteristics, course of disease and mucosal appearance in health and disease.

## Aims and outline of this thesis

This thesis addresses the following aims in two different parts.

1. Part 1 aims to provide insight in surgical and patient-reported outcomes of (laparoscopic) intestinal vaginoplasty performed as either primary or revision procedure.
2. The incidence or prevalence of neovaginal bowel diseases remains unclear. The sigmoid tissue in its original environment has a specific role in the digestive system. It functions in a symbiotic relationship with the microbial flora, which is in turn dependent on the fecal stream. Presently, we do not know what happens after transplantation of this graft tissue to the neovagina. Part 2 aims to assess clinical, histopathological, microbial and endoscopic features of the sigmoid-derived neovaginal mucosa in health and disease. The disease state 'diversion neovaginitis' and its clinical features are described.

### **Part 1. Sigmoid vaginoplasty**

In **Chapter 2**, patient reported functional and aesthetic outcomes of primary total laparoscopic sigmoid vaginoplasty in a series of 31 transgender women are evaluated by means of questionnaires. **Chapter 3** comprises a retrospective study in which the surgical outcomes of laparoscopic intestinal versus perineal full thickness skin graft revision vaginoplasty have been compared. In **Chapter 4**, an assessment is made of surgical and very long-term psychological outcomes of secondary intestinal vaginoplasty performed between 1970 and 2000 in transgender women.

### **Part 2. Diversion neovaginitis**

In **Chapter 5**, the endoscopic appearance of the sigmoid neovagina is described and compared to the remaining colon. Endoscopic signs of neovaginal inflammation were assessed. In **Chapter 6**, the morphological characteristics of biopsy specimens from the sigmoid neovagina were compared to those of the proctosigmoid using a descriptive item-score, comprising signs of chronic and active colonic inflammation. The effect of fecal diversion on the microbiome of the sigmoid-derived neovagina has been analyzed in **Chapter 7**. In **Chapter 8**, a case series of four transgender women with bacterial overgrowth of the neovagina and the effectiveness of subsequent treatment is described. In **Chapter 9**, a case report of a native female with refractory diversion neovaginitis of a sigmoid colon-derived neovagina is presented. Finally, results of all studies are discussed in the summary and general. General conclusions are drawn and future perspective on surgical, physiological and further research are provided.

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