Vaginoplasty for Gender Dysphoria and Mayer-Rokitansky-Küster-Hauser Syndrome: A Systematic Review and Meta-analysis

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Abstract

BACKGROUND: About 8,800-34,200 Gender Dysphoria (GD)- and 39,000-650,800 Mayer-Rokitansky-Küster-Hauser (MRKH)-patients undergo vaginoplasty annually. Various procedures are available, but comparisons are lacking. OBJECTIVES: To highlight information gaps, weaknesses and strengths of vaginoplasty techniques, to aid well-informed decision making by patients and healthcare professionals. SEARCH STRATEGY: A systematic search in Medline, EMBASE, Web of Science and Scopus until October 6, 2022, by PICO method and PROSPERO registration. SELECTION CRITERIA: Original retrospective studies on complete neovaginal creation in adult GD- and MRKH-patients and discussing anatomy, Quality of Life (QoL), satisfaction, sexual function, complications or complaints. DATA COLLECTION AND ANALYSIS: The 95% confidence intervals were calculated with DerSimonian and Laird random-effects. Methodological quality and potential bias were assessed. MAIN RESULTS: In total, 35 GD- and 16 MRKH-studies were eligible. Vagina length was 11.6 and 9.5 cm, respectively. In GD-patients, Hemorrhage (6%), prolapse (1%), gastrointestinal complications (1%), revisions (26%), pain (6%), regret (1%), fecal- (11%) and urinary issues (17%) were reported. Necrosis, stenosis, dyspareunia and revisions decreased, while duration increased with higher graft quantity. Intestinal-vaginoplasty reported 100% sensation. MRKH-patients reported more necrosis (17%) [McIndoe] and average satisfaction with sexual function (91%) and vaginal discharge (32%). They were more sexually active (86%) and had 100% anatomical satisfaction. Only Intestinal-vaginoplasty reported overall dissatisfaction. CONCLUSIONS: For GD- and MRKH-patients, multiple safe vaginoplasty techniques demonstrated acceptable outcomes, with significantly improved QoL and self-image. However, standardized validation tools are needed for well-informed decision-making. Direct technique comparisons per patient-cohort and exploration of tissue-engineering methods are critical for future surgical advancements.

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DATA COLLECTION AND ANALYSIS: The 95% confidence intervals were calculated with DerSimonian and Laird random-effects. Methodological quality and potential bias were assessed.

MAIN RESULTS: In total, 35 GD- and 16 MRKH-studies were eligible. Vagina length was 11.6 and 9.5 cm, respectively.

In GD-patients, Hemorrhage (6%), prolapse (1%), gastrointestinal complications (1%), revisions (26%), pain (6%), regret (1%), fecal- (11%) and urinary issues (17%) were reported. Necrosis, stenosis, dyspareunia and revisions decreased, while duration increased with higher graft quantity. Intestinal-vaginoplasty reported 100% sensation.

MRKH-patients reported more necrosis (17%) [McIndoe] and average satisfaction with sexual function (91%) and vaginal discharge (32%). They were more sexually active (86%) and had 100% anatomical satisfaction. Only Intestinal-vaginoplasty reported overall dissatisfaction.

CONCLUSIONS: For GD- and MRKH-patients, multiple safe vaginoplasty techniques demonstrated acceptable outcomes, with significantly improved QoL and self-image. However, standardized validation tools are needed for well-informed decision-making. Direct technique comparisons per patient-cohort and exploration of tissue-engineering methods are critical for future surgical advancements.

KEYWORDS: Gender Dysphoria / Mayer-Rokitansky-Küster-Hauser / vaginoplasty / outcomes / complications

FUNDING
None.
Introduction

Vaginoplasty - General

When a vagina is absent or malformed by a congenital or acquired disease, various treatment options exist. Vaginoplasty should create a vagina with normal anatomy and function, and prevent scars, stenosis or contracture. Non-surgical methods (like dilation and traction) are often successful and avoid surgery-related risks, but lead to prolapse, shorter neovaginas, low satisfaction, long-term agony and mental/emotional stress. Many prefer surgery, as non-surgical approaches take 2-24 months and successive surgical corrections are common for (improved) sexual activity and severe defect restoration with extra-vaginal tissue. A growing annual 48,000-685,000 surgeries are performed. Based on 3,904,727,342 female and 3,970,238,390 male inhabitants in 2021, this results in 39,047-650,788 MRKH-surgeries and 8,822-34,226 GD-surgeries for 10-25% surgical vaginoplasty treatment. by over 20 methods, each with specific (dis)advantages and without golden standard. Vaginoplasty techniques are generally specified as cavity dissection with specific donor graft.

Vaginoplasty – Gender Dysphoria

Individuals with Gender Dysphoria (GD) express an inconsistency between their gender and sex. Documented prevalence greatly vary with geographical location between 1:2,900-45,000 genotypical males. Penile-inversion- and Penoscrotal-surgery are Male-to-Female (MtF-)specific methods, but local skin volume is not always sufficient due to hypoplasia. Alternatively, skin, bowel, amnion, oral mucosa or decellularized tissue is applied. Surgeons prefer Penoscrotal-vaginoplasty, but without consensus on the ideal technique. Complication- and outcome-reports are sparse and reviews compare at best two techniques and lack meta-analyses. Initially, male pronounces were applied and surgery aimed for genitalia removal without new partner awareness of previous sex, but today female identity is recognized, with emphasis on aesthetics and functionality. The neovagina requires to be hairless, moist and minimally 11 cm deep and 3 cm wide, with labia minora, majora and a sensate clitoris.

Vaginoplasty – Mayer-Rokitansky-Kuster-Hauser

Mayer-Rokitansky-Kuster-Hauser (MRKH) Syndrome presents as congenital aplasia of uterus and upper two-thirds of the vagina, with prevalence estimated as 1:1,500-10,000 genotypical females. Davydov-, McIndoe-, Vecchietti- and Wharton-Sheares-George-surgery are MRKH-specific methods and apply stretching, spontaneous epithelization by local vaginal epithelial cells, split-thickness skin or female peritoneum grafts for partial neovagina creation. Few reviews compare complications or outcomes and none compare surgical techniques. Initially, vaginoplasty outcome was assessed by anatomy, sexual activity and satisfaction of patient or partner. Today, sexual function and satisfaction are assessed by extensive patient-centered questionnaires.

Objective

We evaluated peri- and post-operative outcomes of nine vaginoplasty techniques for anatomy, complications, complaints, satisfaction, sexual function and Quality of Life with MRKH- and GD-indication. We hope that by highlighting weaknesses and strengths, this will aid well-educated decision making by patients and healthcare professionals. By revealing current information gaps, focal points for future research can be determined.

Methods
Protocol and guidance

This review was conducted in accordance to Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) guidelines\textsuperscript{30} and registered (May 19, 2021) in PROSPERO (CRD42021249785).

Eligibility criteria

Inclusion criteria: (i) original paper on surgical, complete neovagina creation; (ii) English; (iii) peer reviewed publication; (iv) discuss anatomy with complications, complaints, satisfaction, sexual functioning or Quality of Life; (v) ? 6 months Follow Up; (vi) ? 10 MRKH- or MtF-patients of (vii) ? 18 years during surgery.

Exclusion criteria: (i) unspecified technique, vaginoplasty as non-primary (or combined with other) treatment; (ii) merged results of patient types and/or control group; (iii) or merged vaginoplasty technique results.

Search strategy

A strategic, bibliography search in Medline, EMBASE, Web of Science and Scopus was performed by a medical information specialist (R.d.V.), on publications up to October 6, 2022 (Figure S1). The PICO-search (with MeSH and closely related terms), looked for Transgender persons and MRKH-patients (P articipants), Sex reassignment surgery and vaginoplasty (I ntervention), and neovagina combined with anatomy, complications, complaints, satisfaction, sexual function or Quality of Life (O utcome). The reference ‘snowballing’ method and a Google Scholar search on initial 200 hits were performed (J.S.). A Mendeley 1.19.4 database was formed after duplicate removal.

Study selection

Two researchers (J.S. and F.G.) screened titles and abstract for eligibility with EndNote 20.1 and assessed remaining articles independently for full content. Discrepancies were resolved with a third reviewer (J.H.).

Data extraction

Data from included studies were extracted according to a predefined standard. Neovagina depth and surgery duration were pooled per surgical technique. Quantity of reported complications and complaints were categorized as hemorrhage (transfusion and hematoma), gastrointestinal (rectal injury and recto-vaginal fistula), vaginal prolapse, tissue necrosis (of urethra, glans, clitoris and labia), (meatal or neovaginal) stenosis and revisions and excessive mucous production, (genital) pain, (vaginal) hair growth, fecal- and urinary issues with Clavien-Dindo classification.\textsuperscript{31,32} Patient-reported anatomical and aesthetic satisfaction, overall dissatisfaction and experienced regret were assessed. Sexual function included dyspareunia, experienced (erotic and orgasmic) sensation, sexual activity (sexually active patients) and satisfactory-graded sex life. Standardized questionnaires for aesthetics (Female Genital Self-Image Scale; FGSIS) and Quality of Life (QoL) were assessed but not included in the meta-analysis.

Risk of bias and quality of evidence

Methodological quality of included studies was assessed without filtering\textsuperscript{33,34} by the Newcastle Ottawa Scale (NOS).\textsuperscript{35} Potential bias was identified through the National Heart, Lung, and Blood Institute (NIH) Study Quality Assessment Tool for Observational Cohort and Cross-sectional Studies.\textsuperscript{11} Checklist at www.nhlbi.nih.gov/health-topics/study-quality-assessment-tools.
Data synthesis

By statistical analysis in Stata version 14.0 (StataCorp LLC, College Station, TX), surgery duration and anatomy were pooled by **metan**, with 95% confidence interval (CI) and DerSimonian and Laird random-effect size calculation.\(^\text{36}\) Complications, complaints, satisfaction and sexual function were pooled by **metaprop**, with 95% Wilson CI and DerSimonian and Laird random-effects,\(^\text{37}\) after variance stabilization by Freeman-Tukey double-arcsine-transformation and heterogeneity determination by I-square measures.\(^\text{38}\)

Results

Study selection and Characteristics

A total of 3954 articles (Figure 1) were identified and 51 included (Table i), of which 21 reported surgery duration (Figure S2), 29 vaginal depth (Figure 2), 44 surgical complications (Figure S3), 20 complaints (Figure S4), 33 satisfaction (Figure S5), 44 sexual function (Figure S6) and 9 QoL (Table ii). A high intercontinental diversity of patient-population and techniques was observed (Figure S7).

Risk of bias of included studies

A NOS quality assessment judged on: study group selection; group comparability; and ascertainment of exposure or outcome of interest (Figure S8). Articles rated as 34 (66.7%) high risk, 15 (29.4%) very high risk of bias and two (3.9%) high quality, based on bias likelihood and completeness of reporting (Figure S9). Bias according to the NIH tool (Figure S10) was rated as 1 (2.0%) bad, 9 (17.6%) poor, 21 (41.2%) fair and 20 (39.2%) good (Figure S11). MOOSE guidelines were followed.\(^\text{39}\)

Synthesis of results

**Gender Dysphoria**

Vaginoplasty outcomes of 3,310 MtF GD-patients were reported in 35 articles (Figure S7C). The majority discussed Penoscrotal- or Penile-inversion-vaginoplasty for reconstruction with local tissue, where inversed penile skin forms the neovaginal cavity and penile/scrotal skin the external genitalia. Other neovaginal lining approaches are Intestinal-, Skin flap-, Combined- or Peritoneal-intervention. Penoscrotal Gender Assignment Surgery (GAS) was covered most often (19 articles), with continuous attention since 1995 (Figure S7D). GAS duration (Figure S2) increased with required tissue quantity for reconstruction (from Penile-inversion-, to Penoscrotal- and to Combined-intervention). GAS resulted in ‘successful’ lengths of ?11 cm after Penoscrotal- and Intestinal-vaginoplasty and 11.57 cm (range 9.6-13.5 cm) total average length. Peritoneal-vaginoplasty for GAS is the most recent development.

**Mayer-Rokitansky-Kuster-Hauser**

Despite similar prevalence, surgical vaginoplasty of only 906 MRKH-patients was reported in 15 articles. These predominantly (43.93%) involved Davydov-surgery, for simplicity and good aesthetics.\(^\text{40}\) The oldest MRKH-publication dates from 2008 and Wharton-Sheares-George (2019) is the most recent technique. Only Intestinal-vaginoplasty created ‘successful’ lengths and 9.45 cm (range 8.1-10.8 cm) total average length was shorter than GAS-results.

Comparison

The oldest publication (1987) involved Penile-inversion-vaginoplasty and remained unpublished next until 2009, when vaginoplasty techniques and publications grew rapidly. GAS was significantly longer (274.75
Raised in both patient cohorts, Intestinal-vaginoplasty was most time consuming (Figure S2) and reported the longest neovaginas (Figure 2), because of abundantly available graft tissue. Intestinal-vaginoplasty is performed significantly less often on GD-patients (p<0.00001) based on one-tailed Z-score Calculation (Figure S7C). Vaginoplasty is performed open or vaginally, but Vecchietti-, Davydov- and Intestinal-vaginoplasty have laparoscopic alternatives to decrease complication rates. Complications were associated with length reduction and dilation prevents up to 4 cm depth loss in the first 10 post-operative days.

Surgical complications

Data on complications were retrieved from patient files. Wharton-Sheares-George- and Skin Flap-interventions reported no complications.

Gender Dysphoria

Hemorrhage was only reported after GAS (Figure S3A/B), with peri-operative estrogen continuation as associated risk factor. Hemorrhage (Clavien-Dindo classification II) was often non-severe and treated non-operatively by dressings, transfusion, cooling or adrenalin injection. Causes included hematoma, necrosis, infection, dilation injury, granulation or fistula and delayed wound healing.

Tissue necrosis was reported after Penile-inversion- and Penoscrotal-GAS and decreased with graft quantity (Figure S3C). Treatment (of Clavien-Dindo classification I – III) ranged from local wound care and surgical debridement to complete reconstruction for major necrosis, but labia majora disunion or graft loss was sporadically observed.

Vaginal prolapse was caused by inadequate vaginal canal dissection or non-adherence of skin grafts. This is prevented by sacropexy (fixation to sacrospinous ligament) or penoscrotal apex fixation to Denonvillier's fascia. Treatment (Clavien-Dindo classification IIIa, b) entailed neovaginal flap reinsertion (using fibrin glue) or revisions for mucosal prolapse (Figure S3E).

Stenosis is the most common complication reported after GAS, caused by contraction in the initial 3 post-operative months by dilation incompliance and inversely proportional to graft quantity (Figure S3G). Treatment (Clavien-Dindo classification IIIa, b) of introital/vaginal stenosis consists of self-dilation, pelvic floor physiotherapy and occasional revisions. Meatal stenosis can result from corpus spongiosum remains that obstruct urine flow by thickening during excitement and is treated by urethral dilation or meatotomy (with corpus spongiosum resection).

Gastrointestinal complications were caused by peri-operative rectal injury or vascular lesion after perineal dissection or by post-operative dilation injury, infection and retraction, abscess, hematoma or (rare) neovaginal malignancy (Figure S3I). This is avoided by meticulous dorsal preparation from perineal body to prostate along Denon Villiers fascia to the tips of seminal vesicals. Treatment (Clavien-Dindo classification IIIb) required temporary colostomy or graft interposition between rectum and vagina.

Revisions (with Clavien-Dindo classification IIIb) were required for introital/meatal stenosis, necrosis, prolapse, fistula, hematoma, infection/wound dehiscence, corpora tissue resection and mostly esthetical enhancement (of labia). These GAS-reported revisions were inversely proportional to graft quantity (Figure S3K). High revision rates were explained by full health-insurance coverage and post-operative transparency of options and were associated with decreased patient regret and dissatisfaction with (aesthetic or functional) surgery outcome.
Mayer-Rokitansky-Kuster-Hauser

Necrosis was reported often after McIndoe-surgery (Figure S3D) with sporadic graft loss and was associated with points of maximum tension (i.e., vaginal introitus) due to vascular spasm, restricted blood flow or altered blood supply after transverse lesion of the spinal cord.

Most prolapses were reported after Intestinal-vaginoplasty and were related to inadequate vaginal canal dissection or non-adherence of skin grafts (Figure S3F).

Stenosis after Peritoneal-vaginoplasty correlates to dilation incompliance and is avoided by a pedicled flap from rectosigmoid colon or four sutures at the introital, mucosa-peritoneum interface (Figure S3H).

Gastrointestinal complications were reported after Peritoneal-vaginoplasty (Figure S3J).

Complaints were rarely reported. Only Bouman et al. and Uncu et al. evaluated patient-reported outcomes by a short questionnaire and satisfaction scores, respectively. Excessive vaginal discharge (Clavien-Dindo classification I) was mostly reported during follow up or by secretion scent assessment by physicians (Figure S4A/B). Most studied grafts reported 0% vaginal hair and are praised for their non-hair bearing property like penile, scrotal and intestinal tissue. Complaint treatments were not discussed.

Gender Dysphoria

Excessive vaginal discharge was rarely reported, because mostly penile and/or penoscrotal skin is applied without inherent mucous producing tissue properties.

Vaginal hair growth was reported 5% by Gupta and Gupta after Combined-GAS and 26.3% by Gentile et al. through a patient satisfaction questionnaire.

Genital pain (Clavien-Dindo classification I) was reported after Penile-inversion- and Penoscrotal-GAS (Figure S4E), no treatment was mentioned. Buncamper et al. questioned patient satisfaction and Rossi Neto et al. studied clitoral and genital pain during follow up. Only Lawrence and Sigurjonsson et al. applied extensive self-made questionnaires to investigate satisfaction and pain, respectively.

Fecal issues (diarrhea, bowel complaints, incomplete emptying - Clavien-Dindo classification I) were assessed after Intestinal-GAS by Amsterdam Hyperactive Pelvic Floor Scale-Women (AHPFS-W) by Bouman et al. and after Penoscrotal-GAS by established questionnaires by Kuhn et al. and were left untreated (Figure S4F). These questionnaires also assessed urinary issues.

Urinary issues (urgency, stress incontinence, stream misdirection - Clavien-Dindo classification I-II) were reported during follow up after Penile-inversion-, Penoscrotal- and Combined-GAS (Figure S4E). Only Lawrence and Kuhn et al. used self-made and established questionnaires. Urinary issues were caused by small prostates, perineal dissection and urethral sphincter injury and often non-surgically resolved by medication or pelvic floor physiotherapy.

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Excessive vaginal discharge was predominantly reported after MRKH-vaginoplasty with mucus producing applied grafts. All McIndoe-patients experienced vaginal discharge with scent and Intestinal-vaginoplasty reported more discharge complaints amongst MRKH-patients. Vaginal discharge was often gradually decreasing and mainly present in the initial 3-6 post-operative months. Physicians often consider self-lubrication an advantage of Intestinal-vaginoplasty, but not all patients agree on this.

Vaginal hair growth was reported 42% during follow up by Hayashida et al. after McIndoe-surgery.
Satisfaction

Body self-image was often assessed with the General Health Survey (SF-36)\textsuperscript{62,63} and Female Genital Self-Image Satisfaction (FGSIS) questionnaire.\textsuperscript{16,17,25,47,64} Diverse evaluation tools assessed 2-point,\textsuperscript{14,43,65–67} 3-point,\textsuperscript{56,60} 5-point\textsuperscript{56,60} or 10-point satisfaction scales\textsuperscript{42,69} or surgeons’ view on aesthetics.\textsuperscript{70,71} Dissatisfaction was assessed with 2-point,\textsuperscript{58,65,72,73} 3-point\textsuperscript{17,25} or 5-point\textsuperscript{50,70,71} scales or by examiner’s rating of the vulva\textsuperscript{59} and the Short Questionnaire for Self-Evaluation of Vaginoplasty (SQSV) was applied most often.\textsuperscript{17,25}

Gender Dysphoria

Aesthetic satisfaction (Figure S5A) was high after Penoscrotal-, Intestinal- and Combined-GAS. Penile-inversion-, Penoscrotal- and Intestinal-GAS reported dissatisfaction (Figure S5E) and high anatomical satisfaction (Figure S5C), based on patient-reported outcome as yes/no\textsuperscript{14,50,58,60,66,74} or ‘deep enough for vaginal intercourse with a man’.\textsuperscript{17,25} Regret was solely investigated after GAS, absent in 2-point evaluations,\textsuperscript{65,66,69,74} sporadic and present after Penile-Inversion- and Penoscrotal-GAS (Figure S5G). Regret was associated with pain, vaginal hair and lower satisfaction and caused once by an unfulfilling new life. Another regretful patient (without mentioned cause) would undertake surgery again.

Mayer-Rokitansky-Kuster-Hauser

Aesthetic satisfaction (Figure S5B) was high after Intestinal- and Peritoneal-vaginoplasty. Full anatomical satisfaction was achieved for all MRKH-procedures (Figure S5D), based on assessment of patient-satisfaction\textsuperscript{72,73,75} or anatomical standard.\textsuperscript{41,64,76} Intestinal-vaginoplasty reported dissatisfaction (Figure S5F) and Peritoneal-Vaginoplasty reported full anatomical and overall satisfaction.

Sexual functionality

Intercourse initiation was at 6-8 months, at 70% epithelialization or when desired. Sexual activity varied gravely as 21-100\% at 1-132 post-operative months during assessment (Figure S6A/B). The definitions of sexual activity in the included articles varied as regular activity,\textsuperscript{58,73,74,77} any\textsuperscript{14,17,78–80,41,44,60,61,66,70,72,75} in the last month,\textsuperscript{47,62} vaginal intercourse\textsuperscript{43,45,81,82} with a man\textsuperscript{25} or married with sexual activity.\textsuperscript{83}

Sexual function was assessed most often with the Female Sexual Function Index (FSFI).\textsuperscript{16,17,76,78,80,81,84,47,64,72,73} Dyspareunia was also reported by 5-point,\textsuperscript{60} 4-point,\textsuperscript{59} 3-point\textsuperscript{68} and 2-point\textsuperscript{17,25,70,72,73} 3-point\textsuperscript{68,71,85} self-made questionnaires and present after all but the Wharton-Sheares-George-technique (Figure S6C/D).

Satisfaction with sexual function (overall, orgasmic function or vagina depth) amongst sexually active (or married\textsuperscript{76}) patients was also reported by diverse 10-point,\textsuperscript{69} 9-point,\textsuperscript{46,60} 3-point,\textsuperscript{58,71,85} and self-made questionnaires (Figures S6E/F). Sexual dysfunction associated with inadequate depth,\textsuperscript{45} lubrication issues, sexual discomfort, sporadic ejaculation and clitoral erection (after Penile-inversion-surgery)\textsuperscript{25} and excessive secretion, dyspareunia\textsuperscript{25,61,79} and vaginal stenosis.\textsuperscript{43}

Gender Dysphoria

Dyspareunia was inversely proportional to graft quantity. Intestinal-GAS reported full functional satisfaction\textsuperscript{16} and fullsensation\textsuperscript{16,17} (Figure S6G). Despite high sexual responsiveness, orgasmic capacity was postsurgically diminished in some to most GAS-patients.
Mayer-Rokitansky-Kuster-Hauser

Sexual activity was higher and initiated earlier after (Intestinal) MRKH-procedures than after (Intestinal-GAS. With Wharton-Sheares-George-surgery, satisfaction increased over time from 6-12 post-operative months. Orgasmic and erotic sensation were seldom reported (Figure S6H). Fertility was restored in three patients.

Quality of life

QoL was assessed in 9 articles (Table i) with Self-designed, Beck Depression Inventory (BDI), Short-Form-36 (SF-36), Fragen zur Lebenszufriedenheit (FLZ), Patient Health Questionnaire 4 (PHQ-4), Rosenberg Self-esteem Scale (RSES), Subjective Happiness Scale (SHS), Satisfaction With Life Scale (SWLS) and Cantril’s Ladder of Life Scale (CLL) questionnaires.

Gender Dysphoria

Intestinal-GAS reported 100% slight-to-extreme satisfaction with life, that ranged from struggling to thriving life. Penile-inversion-vaginoplasty reported normal QoL and partnered patients scored higher on vitality, social functioning and mental health. Skin flap-GAS reported minimal depression by decreased sexual satisfaction. Penoscrotal-vaginoplasty improved personality, lifestyle and self-esteem, body and femininity satisfaction and overall QoL with low post-operative depression and anxiety. Anatomical satisfaction and sensation correlated to increased and genital pain to decreased QoL-scores. Despite mostly positive QoL-outcomes, one study reported low general life satisfaction and unaltered aesthetic satisfaction compared to pre-operative results.

Mayer-Rokitansky-Kuster-Hauser

One QoL-study reported on MRKH-patients and showed 22.2% mild/moderate depression.

Comment

Gender Dysphoria

Penile-inversion- and Penoscrotal-vaginoplasty received major attention, which causes a bias. Penoscrotal-vaginoplasty is considered the best GAS-option, but reported high complaint-rates and overall dissatisfaction and relatively low sexual activity. Neovagina depth correlated with anatomical satisfaction. Graft quantity correlated with surgery duration and was inversely proportional to necrosis, stenosis, dyspareunia and revisions.

Mayer-Rokitansky-Kuster-Hauser

MRKH-articles were few and diverse, likely due to non-surgical alternatives. Peritoneal-vaginoplasty was the most performed technique. It reported high aesthetic-, anatomical- and functional-satisfaction but also dyspareunia, excessive discharge and ‘unsuccessful’ lengths. QoL-assessments were mostly lacking.
Discussion

Main findings

Non-surgical MRKH-treatment is likely still favored, as included article quantity was low despite higher prevalence. High intercontinental diversity showed no European or North-American MRKH-vaginoplasties, likely due to pre-adolescent surgeries that are less common in Asia by religion and tradition.\textsuperscript{101}

Intestinal-vaginoplasty was performed significantly less in GD-patients, likely due to preferred local tissue alternatives. GAS-vaginoplasty duration was longer, as complete vulva and neovagina opposed to partial vagina were formed, and increased with graft quantity.

Hemorrhage was only reported after GAS and originated from vascularized tissue (i.e., corpus spongiosum), likely due to estrogen continuation and higher surgery complexity.\textsuperscript{23} MRKH-vaginoplasty predominantly reported intercourse-related bleeding.\textsuperscript{62}

Tissue necrosis was associated with maximum tissue tension (i.e., introitus).

Prostate was often reported, affects 50\% of parous women\textsuperscript{55} and mostly vaginoplasty patients \textsuperscript{?}50 years. Pelvic floors are sex-specific,\textsuperscript{102} so long-term hormonal treatment might affect prolapase.\textsuperscript{55} In our center we occasionally treat transwomen for long-term prolapase (10-20 post-operative years).\textsuperscript{103} Prolapse is believed to increase with postoperative-time.\textsuperscript{42,104}

Stenosis was most common and hampered QoL through sexual dysfunction and dissatisfaction. Higher GAS-reports might relate to inherent skin properties that cause narrowing, incomplete corpus spongiosum resection or inclusion of meatal stenosis.

Gastrointestinal complications are rare and severe, especially perineal dissection and less invasive surgery make intra-operative observation of fistula hard.

Revisions were reported only and for all GAS-techniques and were inversely proportional to graft size (through stenosis, necrosis and dyspareunia) and likely related to dissatisfaction due to surgical complexity from anatomical dissimilarity. MRKH-patients showed higher overall and complete anatomical satisfaction, even for ‘unsuccessful’ lengths.

McIndoe-, Peritoneal- and Intestinal-surgery reported vaginal discharge, which is prevented in skin-based vaginoplasty-methods by inherent tissue differences. Genital pain hampered QoL-improvement after GAS and urinary issues hampered satisfaction and correlated to small prostates and pelvic floor dysfunction.

Penile-inversion- and Penoscrotal-GAS reported 1-4\% (sporadic or surgery-unrelated) regret. Many transgender-care opponents use regret as an argument. Strict WPATH-regulations should prevent regret and likely explain the presence of only GAS-investigated regret.

GD-patients were less sexually active. However, definition varied gravely between studies, from ‘any activity’ to ‘regular introital penetration with a man’. This presents a bias.

A large variety of evaluation was used. Complications, vaginal discharge and hair were derived from patient follow up reports. Self-made questionnaires were mostly used. Established questionnaires for fecal- and urinary-issues,\textsuperscript{51–54} overall dissatisfaction and aesthetic satisfaction were applied. The FSFI-questionnaire allowed reliable comparison of dyspareunia and satisfaction with sexual function.

Many established QoL forms are available and have been applied (SF-36, BDI, FLZ, PHQ-4, RSES, SHS, SWLS and CLL).
Strength and limitations

This is the first systematic review with meta-analysis on nine vaginoplasty techniques with MRKH- and GD-patients and a wide diversity of complications, satisfaction and function were assessed with Clavien-Dindo classification. The methodological quality, in line with PRISMA-guidelines, formed a strength. Diverse assessment scales for sexual function and coitus-centered, sexual activity assessment and uncorrected cohort variation, need to be considered for result reliability. These discrepancies invalidate quantitative comparison and emphasize need for standardized validation tools. More criticism was reported amongst GD-patients especially on aesthetics and penetration depth, where perhaps fertility restoration is more important for MRKH-patients. Most comprised studies had medium risk of bias and lacked control groups, blinding of assessors and cofounder assessment. Lastly, high cohort size diversity, variation in definitions, technique article quantity, (loss at) follow-up, recruitment and outcome assessment, are points of consideration.

Interpretation

It is impossible to identify one ideal vaginoplasty technique, due to lacking high-quality evidence and study heterogeneity. Tissue engineering alternatives were not included and could bring unexpected success, that should be further clarified in future research.

Conclusions

Vaginoplasty developments are rapidly evolving. However, MRKH-patients and transwomen have to face incomprehension, ignorance and internal challenges daily. Vaginoplasty forms a relatively safe and acceptable solution that improves their QoL and self-image. This meta-analysis showed weaknesses and strength of technique specific (patient-reported) outcomes, by inconsistencies, information gaps, lack of standardization and of comparative research with similar cohorts for well-informed decision-making. No ideal vaginoplasty method can be identified and a technique is still selected based on an expertise-based rather than an evidence-based decision. This, together with exploration of tissue-engineering, is critical for future surgical advancements. We sincerely hope that this review provides an overview of today’s options for well-educated decision, and formed a starting point for further background reading.

Supplementary data are available at BJOG online.

Contribution to authorship


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Disclosure of interest

None.
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Figure 1 - Flowchart search strategy.docx available at https://authorea.com/users/497321/articles/601594-vaginoplasty-for-gender-dysphoria-and-mayer-rokitansky-k%C3%BCster-hauser-syndrome-a-systematic-review-and-meta-analysis

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Figure 2 - Anatomical depth.docx available at https://authorea.com/users/497321/articles/601594-vaginoplasty-for-gender-dysphoria-and-mayer-rokitansky-k%C3%BCster-hauser-syndrome-a-systematic-review-and-meta-analysis

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Table i - Complications and outcomes.docx available at https://authorea.com/users/497321/articles/601594-vaginoplasty-for-gender-dysphoria-and-mayer-rokitansky-k%C3%BCster-hauser-syndrome-a-systematic-review-and-meta-analysis

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Table ii - Patient QoL assessment.docx available at https://authorea.com/users/497321/articles/601594-vaginoplasty-for-gender-dysphoria-and-mayer-rokitansky-k%C3%BCster-hauser-syndrome-a-systematic-review-and-meta-analysis