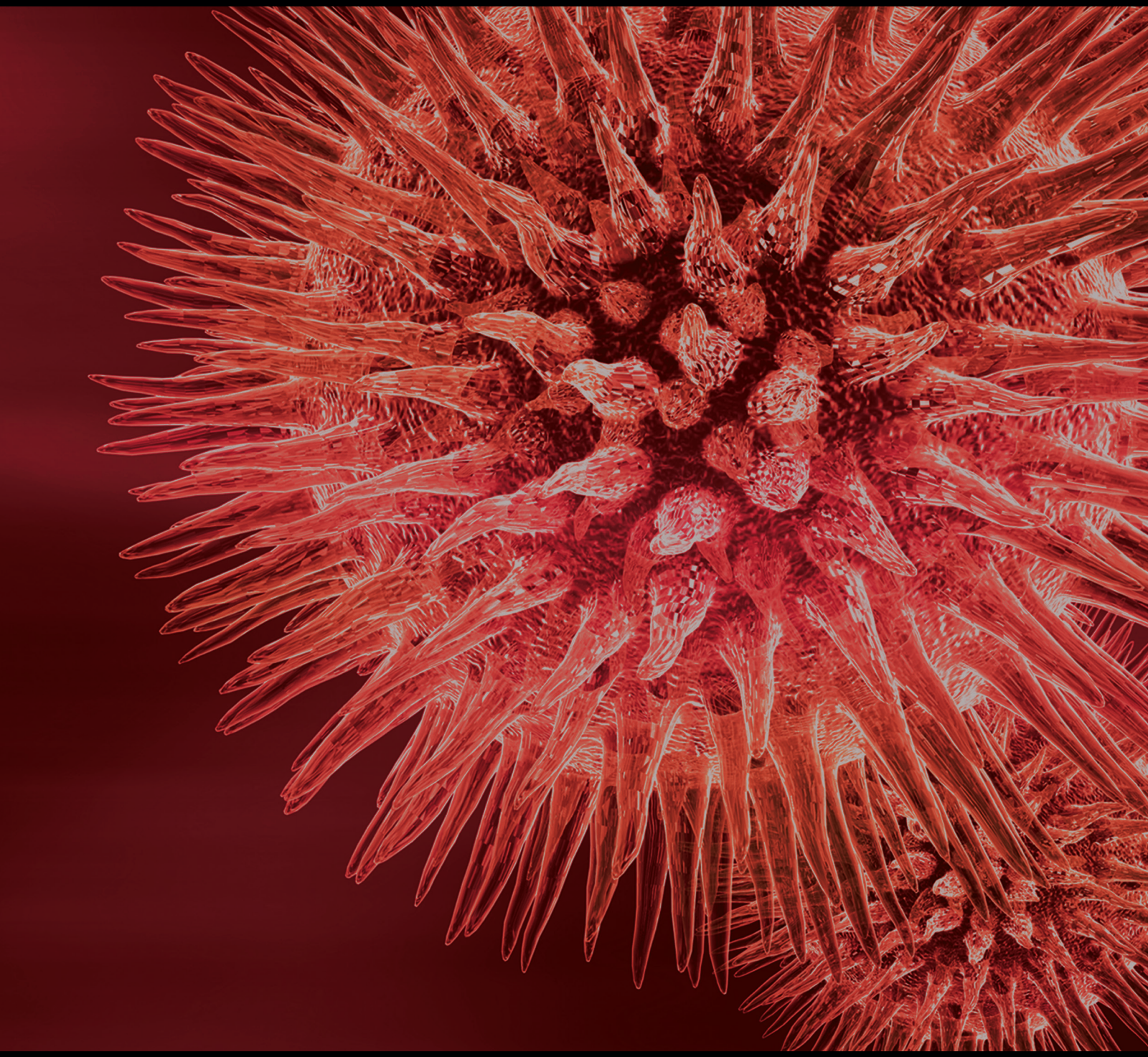
BioMed Research International

# Gender Affirmation Surgery

Lead Guest Editor: Gennaro Selvaggi
Guest Editors: Christopher J. Salgado, Stan Monstrey, and Miroslav Djordjevic



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*Editorial*

# Gender Affirmation Surgery

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Gender Affirmation Surgery (GAS) is a collection of surgical procedures performed in patients presenting with diagnosis of "Gender Dysphoria" (according to the Diagnostic Statistical Manual of Mental Disorders (DSM-V), published by the American Psychiatric Association [1] (2013)) or "Transsexualism" (according to the International Classification of Diseases (ICD-10), published by the World Health Organization [2, 3] (WHO, 1992; WHO, 2007)).

Gender Dysphoria (GD) and Transsexualism (T) are both referring to the "discomfort or distress caused by the discrepancy between a person's gender identity and that person's sex assigned at birth" [4, 5] (Fisk, 1974; Knudson, De Cuypere, and Bockting, 2010). Mental health professionals are in charge of making a diagnosis; however as surgeons operating on patients we need to agree with the diagnosis prior to our interventions.

The treatment for GD may consist of mental health therapy, cross-sex hormone therapy, and different forms of surgery. More specifically, GAS refers to the whole genital, facial, and body procedures required to create a body phenotype that best represents one's own identity. The requested body phenotype is not always representing a fully masculine or feminine aspect, and this may be representative of patient satisfaction of their desired goals in transition. Many individuals, in fact, might opt to undergo only some of the surgical procedures currently available, while others opt to receive the full collection of treatments. Those who are requesting only part of the collection of procedures, for example, transmen seeking mastectomy and not penile construction, might do so either because they represent a gender nonconforming identity or because they realize that the surgical technique(s) available will not fulfill their expectations.

Indeed, there are also individuals that, although having discrepancy between one's own gender and that assigned at birth, might experience only a minimum distress, or no distress at all, and therefore they might opt for other treatments (mental health therapy and/or hormonal therapy) but surgery, or no treatment at all.

To date, the majority of the academic centers worldwide are managing this condition according to the Standards of Care [6] as proposed by the World Professional Association of Transgender Health.

Gender Affirmation Surgery remains an area of superspecialization and is in constant development. Few surgical refinements have been published within the last few years, and follow-ups of long-term series of patients proceed slowly. Cooperation among centers represents a solution to standardize approaches and techniques and achieves a higher level of evidence. This cooperation is realized through reciprocal visiting and meetings, discussion during conferences, and live-surgery sessions in order to learn "the way he/she does it". At the same time, multicenter studies are to be promoted, in order to collect large series of cases that would add to the evidence of a given procedure. Finally,

standardized and validated methods of assessment need to be defined (Patient Reported Outcome Measures) [7, 8], in order to measure objectively, without bias, the outcomes of each treatment.

Lastly, the development of medical and surgical techniques must advance in parallel to ethical discussions on the permissibility of specific treatments, research protocols, or more innovative surgeries. In fact, the large variability of the transgender population (considering both one's experience of the gender identity and the relationship within one's sociocultural background) poses ethical questions that often go beyond medical ethics and extend to areas of sociopolitical sciences and human rights. In this issue, we highlight scientific advances made in the field of Gender Affirmation Surgery with an international collaborative approach that allows this issue to be both comprehensive and informative.

*Gennaro Selvaggi*
*Christopher J. Salgado*
*Stan Monstrey*
*Miroslav Djordevic*

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*Review Article*

# Gender Dysphoria: Bioethical Aspects of Medical Treatment

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Gender affirmation surgery remains one of the greatest challenges in transgender medicine. In recent years, there have been continuous discussions on bioethical aspects in the treatment of persons with gender dysphoria. Gender reassignment is a difficult process, including not only hormonal treatment with possible surgery but also social discrimination and stigma. There is a great variety between countries in specified tasks involved in gender reassignment, and a complex combination of medical treatment and legal paperwork is required in most cases. The most frequent bioethical questions in transgender medicine pertain to the optimal treatment of adolescents, sterilization as a requirement for legal recognition, role of fertility and parenthood, and regret after gender reassignment. We review the recent literature with respect to any new information on bioethical aspects related to medical treatment of people with gender dysphoria.

## 1. Introduction

Gender dysphoria (GD) represents a condition where a person's gender assigned at birth and the gender with which they identify themselves are incongruent. Hence, these individuals can be very uncomfortable with their biological sex, primary and secondary sex characteristics, and social gender roles and they experience various levels of distress. Presence of public figures who are openly transgender, their appearance in mainstream media, and political and social climate lead to more individuals coming out in the open as to their state. Prevalence rate cannot be correctly estimated considering that people are still hesitant to come forward to health centers. According to DSM-5, the prevalence of gender dysphoria is 0.005-0.014% for adult natal males and 0.002-0.003% for adult natal females [1].

In accordance with their wishes, individuals with this condition can choose the direction in which their transition will proceed. To take the edge off their state, one can choose to go through a social transition. The social transition includes using a different name, pronouns, transformation of physical appearance, use of suitable bathrooms, and taking social roles of the affirmed gender. A more radical approach is the medical transition that includes hormonal and surgical treatment. Medical treatment requires a team of experienced experts, and it usually includes mental health professionals, endocrinologists, and surgeons. Psychiatric assessment is the first step and is very complex because it is necessary to exclude other conditions that might mimic gender dysphoria. The next step is hormonal treatment, under the care of an endocrinologist, which is then followed by "a real-life trial." Some individuals decide to stop here, while others continue to gender-affirming surgery (GAS). The seventh edition of the Standards of Care of the World Professional Association of Transgender Health (WPATH) offers flexible guidelines for the treatment of people experiencing gender dysphoria and describes the criteria for surgical treatment [2]. Patients undergoing GAS of their choice are required to provide two recommendation letters from certified psychiatrists and a gender specialist, as well as a confirmation of having been on hormonal therapy prescribed by an endocrinologist for a period of a minimum of one year. Gender affirmation

surgery refers to all surgical procedures that a patient wishes to undergo in an attempt to become as similar as possible to the desired gender.

Treatment of gender dysphoria always raised numerous ethical issues, and with rapid acknowledgment and recent achievements, new complex issues in medical management have emerged. With unknown etiology and questionable definition (mental/medical illness, social construct, and variation of sex) who can decide, with 100% certainty, what treatment is in the best interest of a particular patient? The most prominent challenges and ethical questions pertain to the treatment of underage individuals, fertility after GAS, and possibility of regret after GAS. Main ethical principles are autonomy, beneficence, nonmaleficence, and informed consent. The individual must have autonomy of thought and intention when making decisions about medical treatment. This is an especially sensitive field in treatment of gender dysphoria, because sometimes the individual's desires, hopes, and expectations might not correlate with reality. Experts must be very straightforward regarding specific possibilities, risks, and benefits of medical treatment, especially considering that the last step in medical transition, GAS, is irreversible. Beneficence implies doing only good, only what is in the patient's best interest. However, some may consider that surgical alteration of healthy organs, in case of GAS, is not in line with this principle. Nonmaleficence must ensure that the treatment does not harm the individual in an emotional, social, or physical sense. Always keeping these principles in mind, WPATH Standards of Care and criteria for diagnosis might not be enough to be ascertain that we are doing the right thing. Although it may seem that an individual fulfills all these criteria on paper, sometimes we can observe their personal disadvantages, youth, impairment, or desperation. It seems that, even with the reassurance and recommendation from a mental health professional, ethical unease cannot be entirely erased because treatment guidelines have preceded the answers to vitally relevant questions [3, 4].

## 2. Transgender Youth

Children represent a small number of individuals with gender dysphoria and in only 10-20% of the children, gender dysphoria will continue to manifest in adolescence [5]. However, psychological therapy and support are highly recommended; while such services are now far more widely available, they are still insufficient to provide for complete wellbeing of these patients. Inadequate management of children with persistent gender dysphoria can lead to isolation, feeling of self-hatred, and suicidal ideas and attempts. Also, "passing through the wrong puberty" can have serious consequences for these individuals. Viable treatment options vary from fully reversible treatment, such as puberty-suppressing gonadotropin-releasing hormone analogues (GnRH) to partly reversible treatment, gonadal steroid treatment, as well as irreversible treatment, such as surgical removal of genitalia and reconstruction of new ones according to the desired gender. Surgery includes bilateral mastectomy with chest reconstruction, hysterectomy with oophorectomy followed by either metoidioplasty or phalloplasty for trans-male individuals, and bilateral orchiectomy with penectomy followed by vulvoplasty and vaginoplasty in trans-female individuals [6].

Pubertal suppression is implemented using GnRH analogues at Tanner 2 or 3 stage of puberty. Hypothalamus produces GnRH at low levels in prepubertal children. Levels become cyclical during puberty, leading to the production of luteinizing hormone (LH) and follicle stimulating hormone (FSH) by the anterior pituitary. LH and FSH stimulate ovaries and testicles to produce sex hormones, estrogen and testosterone, which are responsible for stimulating the growth of genitalia. Also, they lead to the development of breasts, voice deepening, menstrual cycle, and so forth, which transgender youth can find particularly tough to handle [7].

There are only a few reports related to the use of GnRH analogues in transgender youth. De Vries et al. were the first to introduce the concept and research on the use of puberty blockers for treatment of transgender youth. The main idea behind the suppression of endogenous puberty was to decrease distress by preventing the development of "noncongruent" secondary sexual characteristics. This would give young individuals more time to get accustomed to their situation and to better explore their gender. In the examined group, all of 70 eligible candidates showed improved mental health and general functioning. Authors concluded that the treatment was fully reversible, which was one of its main advantages [8]. Despite the positive outcomes in puberty suppression, many experts still have concerns and resist the implementation of this treatment in their regular practice. Viner et al. proposed that GnRH therapy can be physically damaging for teenagers and can lead to unfavorable psychological consequences [9]. Olson-Kennedy et al. also recognized these dilemmas, stating that available data on puberty suppression was limited and many questions remained unanswered [10]. One of the main reasons against this treatment is that going through puberty may help the individual to become congruent with their biological sex, meaning that their GD would not persist into adolescence. Results from Steensma et al. showed that majority of children developed homosexual orientation after completion of the GnRH treatment [11]. As for potential consequences, Hembree recently reported no long-term consequences in follow-up studies of GnRH treatment [12].

Finally, the decision about implementing GnRH treatment is very difficult and cannot be made without ethical dilemmas. Both opponents and advocates of pubertal suppression are guided by the same ethical principles, beneficence, nonmaleficence, and autonomy, but have different views on where these principles lead. A unique and clear overview is necessary, and, to this day, it has not yet been elaborated. Considering that GnRH treatment is relatively new and controversial, additional qualitative research and empirical studies are necessary for appropriate bioethical definitions.

Transgender persons require safe and effective hormonal support to develop the physical characteristics that affirm their gender identity. The main indications for the beginning of hormonal therapy are confirmed persistence of gender dysphoria and adequate mental capacity to give informed

consent and accept this partially irreversible treatment. According to the most recent Endocrine Society guidelines, most adolescents develop this capacity by the age of 16 [12]. Also, Hembree et al. recognized some compelling reasons to initiate sex hormonal therapy before 16, but there is little data published on the experiences with this treatment prior to 14 years of age [12]. The main goals of cross-sex hormonal therapy are suppression of endogenous sex hormone secretion, determined by the person's genetic/gonadal sex, and maintaining sex hormone levels within the normal range for the person's affirmed gender. This therapy harmonizes the external appearance with affirmed gender, leading to, in transgender men, male-sounding voice, different fat distribution, increase in muscle mass and, in transgender women, breast growth, decreased facial and body hair, more feminine fat redistribution, and decreased muscle mass [12].

Many studies demonstrated long-term safety and high efficiency of hormonal therapy in transgender adults. For trans-women, Asscheman et al. emphasized a warning to a side effect of particular concern, estrogen-induced hypercoagulability and subsequent venous thromboembolism. Hembree addressed some potential adverse physical effects of testosterone treatment, such as polycythemia vera and dyslipidemia, in transgender men. Generally, a majority of the authors concluded that this therapy was safe, with necessary follow-up for potential complications [12–14]. However, only a few studies looked into the impact of cross-sex hormonal therapy on transgender youth. Jarin et al. performed a retrospective study on 116 adolescents aged 14–25 years with gender dysphoria and have reported minimal impact of hormone treatment. In trans-men, the only findings were an increase in hemoglobin, hematocrit, and body mass index with lowering of high-density lipoprotein levels; in trans-women, only lower testosterone and alanine aminotransferase (ALT) were reported [15]. Olson-Kennedy et al., in their prospective study, found several statistically significant changes in mean values of physiological parameters over time but of no consequence to clinical safety concerns [16]. In both studies, the authors indicated that this cross-sex hormonal therapy is safe for transgender youth over a period of approximately two years. However, the strongest argument against cross-sex therapy lies in the lack of knowledge of its long-term effects, which means that more studies and follow-up information are necessary. One of the questions is a possibility for cross-sex hormonal therapy in individuals below 16 years of age. The authors of the latest guidelines of the Endocrine Society recognized this possibility but only on a "case by case" principle, meaning that age does not always accurately reflect one's readiness for medical interventions. Also, some experts noticed that a clear majority of children on GnRH therapy will decide to pursue cross-sex hormonal therapy. Only a few side effects of using GnRH were observed, such as decreased bone density [17].

Based on bioethical principles, children usually do not have the power to make legal decisions and actions at the initiation of cross-hormonal therapy. Nevertheless, their judgment and opinions should not be disregarded. Cross-sex therapy primarily helps individuals with GD to harmonize their external appearance with their experienced gender. In this case, proper education of the patient and pointing out advantages and shortcomings of such treatment are of crucial importance. Following the principle of beneficence, clinicians are always obliged to help the person and to follow the prescribed hormonal treatment, since there are no better options at this moment. Patients who are denied treatment can develop serious psychological consequences. Generally, the transgender population is at higher risk of self-harm and suicide [18]. A more individualized approach, as in the "case by case" system, will ensure that a right decision is made in accordance with the patient's maturity, age, and judgment.

Gender affirmation surgery is the last step in the medical transition. It is considered to be irreversible and is technically demanding to perform, even for experienced surgeons. According to WPATH Standards of Care, a criterion for eligibility for GAS is "reached legal age of maturity in a given country." Presumably, the threshold is 18 years of age in most countries [19]. The increasing usage of puberty blockers and pushing the limits for the start of the cross-sex hormone therapy lead to further problems and dilemmas. With these developments, it was only a matter of time before the issue of GAS in minors would arise. Viewpoints are different and vary between the beneficence principle embodied in the motto "doing nothing is doing harm" and the nonmaleficence variation of "the treatment plan that involves less extensive surgery or none at all," reported by Cohen-Kettenis and Holman, respectively [20, 21].

Changing the legislation for hormonal therapy without GAS increases the gap between the two medical procedures and postpones the desired outcome of the transition. During this interim period, someone living with atypical genitalia can easily be exposed in public and lose control over something that used to be very private [22]. Transgender community is more often targeted by bullying and has higher rates of suicide. Leaving these patients to wait for the final stage in their transition can have an impact on their social and psychological state. Goffman's theory of stigma postulates that the transitioning adolescents must prove their affirmed gender to others [23]. If others question the individual's gender identity, including the presence of gender-congruent genitals, he or she fails to manage the stigma and becomes "discredited." In addition, postponing romantic relationships and dating until the age of 18 can also lead to psychological struggles and challenges.

On the other hand, the main "technical" issue in case of children treated with puberty blockers lies in their undeveloped genitalia. Thus, the GAS will be more troublesome, especially in case of penile inversion vaginoplasty. Some authors reported autologous skin grafting from donor site or use of bowel segments as viable solutions for this issue [24, 25]. However, the main concern is the possibility of regret after the GAS. As already mentioned in Introduction, GD does not persist through adolescence in the vast majority of children. The results of GAS in transgender minors and their possible regret are a great cause of concern and a huge responsibility for medical professionals [26]. The dilemmas remain: is it better to suffer the consequences of GD or GAS? Are children or teenagers mature enough to make these

kinds of decisions? Further research and data are necessary to resolve these crucial dilemmas.

## 3. Fertility

Treatment of GD enables the individuals to continue their life in their affirmed gender. For some transgender individuals, this implies the same as for cisgender persons, marriage or/and children. Members of the transgender population have the same desire for offspring, for the same reasons as the cisgender population, and fertility presents one of the most delicate issues. Infertility in trans-women is caused by orchiectomy as a part of the GAS. Conversely, hysterectomy and oophorectomy eliminate the chance of pregnancy in trans-men. Cross-sex hormonal therapy also has an impact on fertility, but such treatment is not a definitive cause of infertility, due to the possibility of reversal. Three decades ago, Payer described that estrogen in trans-women leads to the reduction of testicular volume and has a strong suppressive effect on sperm motility and density [27]. Testosterone therapy for trans-men leads to reversible amenorrhea according to Van Den Broecke's study in 2001 [28]. Patients are usually at full reproductive age at the initiation of their transition and a clear majority of them express the desire for reproductive potential after transition [29, 30]. This is almost impossible, as irreversible transition means losing the option for having children. Dunne reviewed sterilization requirements for transgender people in Europe and found sterilization as the only possible option in 20 European countries; this means that any chance for biological offspring is lost with this transition [31]. This discrimination deeply undermines the fundamental bioethics law, and societies such as WPATH and the Endocrine Society advocate for counseling and detailed explanation of the consequences of treatment and viable options for fertility preservation. In addition, the possibility of sterility following the use of puberty blockers and cross-sex hormones gives rise to further controversy and ethical dilemmas, as do options of cryopreservation prior to the start of cross-sex hormonal therapy and uterus transplantation for trans-women.

As we have previously mentioned, puberty blockers are considered to be the reversible part of the transition, preventing secondary sex characteristics from developing. However, some authors confirmed that these blockers also have an impact on maturation of germ cells, which could be used for preservation of the biological fertility potential [32]. Individuals on puberty suppression therapy may show an interest in offspring but, at the same time, may not want to pass through the wrong puberty in the gender assigned at birth. Thus, their options for offspring are very limited, since prepubertal cryopreservation is still in the experimental stages [33]. There are other questions as well, including their maturity for making these kinds of decisions and the responsibility of their parents as legal guardians. In the literature, a few authors reported the desire of transgender people to have children and found that about half of both trans-men and trans-women wanted offspring after transition [29, 34].

Cryopreservation of embryos, oocytes, or ovarian tissue is a viable option for trans-men. Some authors recommend cryopreservation just before initiation of hormonal transition due to the possibility that cross-sex hormone therapy might cause amenorrhea or affect follicle growth. In cases where the hormonal transition has already started, they suggest an interruption of hormone treatment for minimum 3 months with a goal to revert any potential therapy-induced effects [35]. These could be very aggravating facts, since other doctors reported that majority of transgender individuals did not want to postpone their transition for these procedures. Interestingly, Wallace et al. noticed that transvaginal ultrasound examination, as a necessary part for cryopreservation of embryos and oocytes, is not always in accordance with individuals' male identity and can lead to distress [36].

Sperm cryopreservation, surgical sperm extraction, and testicular tissue cryopreservation could be offered as possibilities for preserving fertility in trans-women. The issues with hormonal therapy exist in this case, too. De Sutter et al. described additional distress, caused by masturbating in clinical settings or sperm banking as a reminder of their former gender [34].

In some countries, cryopreservation is not technically available to the transgender population and thus cannot be offered during the transition. Despite the fact that cryopreservation is a routine procedure in case of malignant diseases, it still remains a controversial topic in less economically developed countries.

In some countries, like USA, sterilization is not mandatory and trans-men can keep their ovaries and uterus for later pregnancy. They must discontinue cross-sex therapy in this period. Light et al. described transgender pregnancies and challenges that come with this phenomenon [37]. Conversely, pregnancy is still not an option for trans-women. There is hope on the horizon from the first successful uterus transplantation, performed by a gynecology team from Sweden [38]. This is a solution for all women suffering from absolute uterine infertility who want to carry their own children. This procedure brings a new insight for researchers, making the possibility for transplantation in trans-women realistic. The main problems could arise from the different anatomy of the male pelvis, as well as from immunosuppressive therapy.

Fertility, including all the related issues and dilemmas, should be discussed very profoundly and meticulously. Transgender population should be informed about all possibilities, advantages, and drawbacks before any treatment and each option should ultimately be the patient's decision.

## 4. Regret and Revision Surgery

There are various levels of regret after GAS. Definite regret happens when the patient wants to get back to their gender assigned at birth after the GAS is performed. They come to surgeons with the request for the restitution of congenital anatomical features. Regret manifests with a more or less pronounced expression of dissatisfaction and second thoughts about the GAS. After suicide, regret could be considered one of the worst possible complications.

Reasons for regret vary greatly. Inadequate social adaptation, comorbidity with certain psychiatric disorders, poor psychological and psychiatric evaluation, and dissatisfaction with aesthetic or functional outcome of GAS can lead to regret. Researchers have concluded that the presence of the following factors can be associated with a risk of regret: age above 30 years at first surgery, personality disorders, social instability, dissatisfaction with surgical results, and poor support from partner or family [39–41].

In 2016, we published a retrospective analysis of seven patients who underwent reversal surgery after regretting undergoing male-to-female GAS elsewhere [42]. Main reasons for regret in these cases were related to inadequate psychiatric assessment. First stages of transition like the "real-life experience" were mostly skipped, cross-sex hormonal therapy was not carried out properly, and letters of recommendation were written by psychiatrists who lacked experience. Also, main diagnostic criteria for gender dysphoria had been neglected. It is therefore important to avoid situations where inadequately trained or inexperienced psychologists or psychiatrists work with transgender patients without supervision or collaboration with more experienced colleagues. Satisfying postoperative results were achieved in all patients. Reversal surgery significantly enhanced their general well-being.

Each regret occurrence represents a major issue for every expert in the field of transgender medicine. Proper diagnosis and listening to and monitoring our patients are of crucial importance for avoiding these kinds of mistakes [43]. Every physician should be aware that not all individuals suffering from GD want or need all three elements of therapy.

## 5. Conclusion

All physicians included in gender dysphoria treatment are facing great bioethical challenges and dilemmas. A multidisciplinary approach is necessary, but it does not always guarantee a successful outcome. The most sensitive issues are the treatment of transgender youth, fertility and parenting in transgender individuals, and the risk of regret after the irreversible part of the treatment, the gender affirmation surgery. In order to avoid the complex issue of regret, proper preoperative evaluation by experienced professionals, psychologists, and psychiatrists is necessary. More research and studies are necessary to shed light on these issues.

## Conflicts of Interest

The authors declare that there are no conflicts of interest regarding the publication of this article.

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*Research Article*

# Sexuality after Male-to-Female Gender Affirmation Surgery

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Male-to-Female (MtF) gender affirmation surgery (GAS) comprises the creation of a functional and aesthetic perineogenital complex. This study aimed to evaluate the effect of GAS on sexuality. We retrospectively surveyed all 254 MtF transsexual patients who had undergone GAS with penile inversion vaginoplasty at the Department of Urology, University Hospital Essen, Germany, between 2004 and 2010. In total, we received 119 completed questionnaires after a median of 5.05 years since surgery. Of the study participants, 33.7% reported a heterosexual, 37.6% a lesbian, and 22.8% a bisexual orientation related to the self-perceived gender. Of those who had sexual intercourse, 55.8% rated their orgasms to be more intensive than before, with 20.8% who felt no difference. Most patients were satisfied with the sensitivity of the neoclitoris (73.9%) and with the depth of the neovaginal canal (67.1%). The self-estimated pleasure of sexual activity correlated significantly with neoclitoral sensitivity but not with neovaginal depth. There was a significant correlation between the ease with which patients were able to become sexually aroused and their ability to achieve orgasms. In conclusion, orgasms after surgery were experienced more intensely than before in the majority of women in our cohort and neoclitoral sensitivity seems to contribute to enjoyment of sexual activity to a greater extent than neovaginal depth.

## 1. Introduction

Male-to-female (MtF) gender affirmation surgery (GAS) comprises the resection of all clearly defining features of male genitalia. The aim is the formation of a perineogenital complex in appearance and function as feminine as possible [1] with a sensitive clitoris to enable orgasms. GAS should be performed by a surgeon with specialized competence in genital reconstructive techniques [2]. The aim is to "create a perineogenital complex as feminine in appearance and function as possible" [1]. There is a broad agreement that GAS has a positive impact on gender dysphoria [3–13]. The inversion of penile skin is used by most gender surgeons. While some trans∗ and gender nonconforming people do not require surgical therapy to express their preferred gender role and identity, others see GAS as a pivotal step to relieve their gender dysphoria [14]. GAS might reduce risk of stigmatization and discrimination in venues like swimming pools and health clubs or when dealing with authorities [2, 15]. Without doubt surgery has a positive effect on subjective wellbeing and sexual function [16–18].

Sexual orientation can change after GAS [19] but little is known about changes of orgasmic experience after GAS. Bartolucci et al. found a positive impact of cross gender hormone replacement therapy on sexual quality of life in transgender who had not undergone GAS yet [20]. However effects of GAS in this field remain unclear so far. This study aimed to evaluate the effect of GAS on sexuality and satisfaction with sexual life of MtF-transgender patients.

## 2. Material and Methods

*2.1. Participants.* Our study cohort comprised all 254 MtF patients who had undergone GAS with penile inversion vaginoplasty at the Department of Urology, University Hospital Essen, Germany, between 2004 and 2010, as has been

previously reported [6]. Transsexualism was diagnosed by two independent mental healthcare professionals competent to work with gender dysphoric adults in accordance with 10th version of the International Classification of Diseases (ICD-10). All patients were contacted by mail using their last known address and asked if they would be willing to answer the questionnaire. In cases of invalid addresses the local residents' registration offices were contacted in order to reconsign a new questionnaire. Patients who had not sent back the questionnaire could not be followed up due to previous anonymization.

*2.2. Statistics.* Statistical calculation was performed using Statistical Package for the Social Sciences (SPSS 21.0). Fisher's exact test and Chi Square were used to compare categorical and ordinal variables in independent samples. The Mann–Whitney U test was used to compare satisfaction scale distribution of two independent samples. This nonparametric test was used in preference to the t-test because the Shapiro–Wilk test indicated that distribution was not normal. Spearman's correlation analysis was performed.

## 3. Results

In total, 119 completed questionnaires were received, all of which were included in the evaluation (response rate 46.9%). Due to anonymization of the questionnaires, it was not possible to obtain information on patients' ages. However, the average age of a comparable cohort of patients at our department between 1995 and 2008 [21] was 36.7 years (16 to 68 years). Not all patients completed the questionnaire, so for some questions the total number of responses was not 119. The results are given in absolute numbers and percentage in relation to total participants or number of answers. After a median of 5.05 years (standard deviation: 1.6 years; range: 1 to 7 years) since surgery, 67 participants (56.3% of the total cohort) did not encounter sexual intercourse on a regular basis at the time of questioning (which depicts 67.7% of those who answered that question). Twenty of the 119 patients (16.8%) did not answer this question. Of those who answered the question nearly a quarter (n = 24; 24.2%) reported a mean frequency of one to three times per month, seven (7.1%) stated a frequency of one to three times per week, and one woman (1.0%) stated a frequency of over three times per week. Time since GAS did not correlate with the frequency of intercourse and the self-rated intensity of orgasms. There was neither an association of the extent to which women felt female themselves nor with the degree to which they felt considered as women with time since surgery.

In our cohort, 18 (15.1% of all participants) patients refused to answer regarding sexual attraction related to the self-perceived gender. Of those who answered (n = 101), slightly more of the patients (n = 38; 37.6%) indicated a sexual attraction towards women than towards men (n = 34; 33.7%). 23 women (22.8%) were attracted by both men and women and six (5.9%) neither by men nor by women (Figure 1). In total, 38 subjects (41.3%) were highly satisfied, 30 (32.6%) were satisfied, 18 (19.6%) were not satisfied, and six (6.5%) were highly unsatisfied with the sensitivity of the neoclitoris (Figure 2). This question was not answered by 27 individuals (22.7% of all participants). When asked how satisfied the women were with the depth of the neovaginal canal, 19 were very satisfied (20.9%), 42 (46.2%) were satisfied, 23 (25.3%) were unsatisfied, and seven (7.7%) were very unsatisfied, with 28 (23.5% of all participants) not answering the question (Figure 3). We asked our patients whether it was easy to get sexually aroused. In total 91 women responded to this question, and about a quarter (n = 28; 23.5% of all participants) declined to answer. Of these 91 women 22 (24.2%) stated that this was always easy; for 43 (47.3%) it was mostly easy; for 15 (16.5%) it was seldom easy; and for eleven women (12.1%) it was never easy to get sexually aroused. The modality as to how orgasms were achieved is shown in Figure 4(a) (absolute numbers of patients; n = 119) and Figure 4(b) (percentages expressed in relation to total answers; n = 126). The majority of participants achieved an orgasm with masturbation, followed by sexual intercourse and "other" not further specified sexual practices. 29 women (24.4% of all participants) did not answer that question.

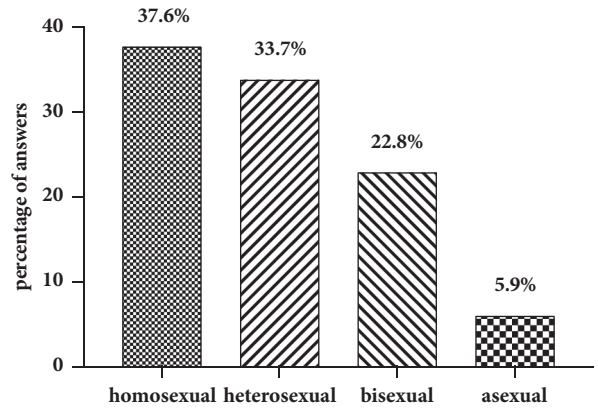


Figure 1: Sexual orientation related to the self-perceived gender.

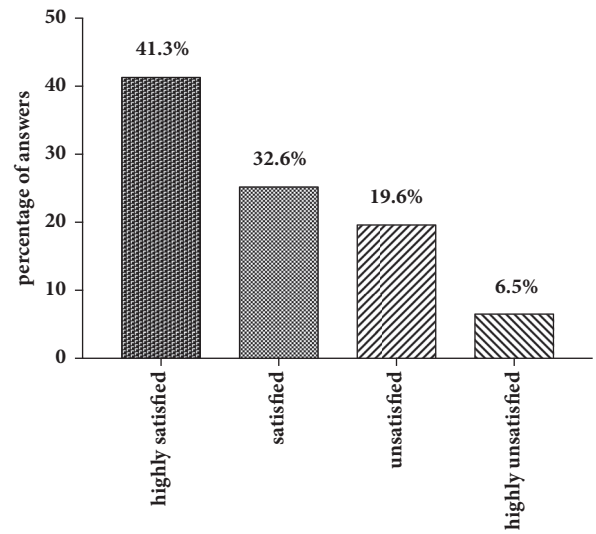


Figure 2: Satisfaction with neoclitoral sensitivity.

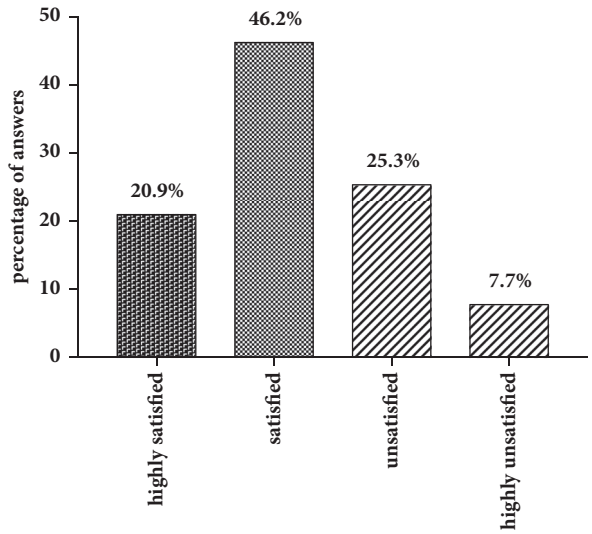


Figure 3: Satisfaction with neovaginal depth.

Of those who answered that question (n = 77), 43 women (55.8%) quoted that orgasms were more intense after GAS compared with those experienced before surgery, 18 (23.4%) women stated that it was less intense than before, and 16 (20.8%) felt no difference. Frequency of achieved orgasms changed in our cohort after GAS. Of all 119 patients 41 (34.5%) refused to answer that question. Of the residual 78 women 41 (52.6%) indicated that orgasms were achieved less frequently, 21 women (26.9%) reported more frequent orgasms, and for 16 women (20.5%), frequency did not change. In order to gather information on patients' general satisfaction with their sex lives, they were asked to place themselves on a Likert scale ranging from 0 ("very dissatisfied") to 10 ("very satisfied"). Nearly a quarter of participants either selected scores from 0 to 3 (n = 29; 24.4%), from 4 to 6 (n = 30; 25.2%), or from 7 to 10 (n = 29; 24.4%) or refused to answer (n = 31; 26.1%). Figure 5 shows a detailed illustration. We received feedback regarding pleasure of sexual activity from 88 women (73.9%). Of these respondents 31 (35.2%) stated that sexual activity was always pleasurable; 44 (50.0%) said it was sometimes pleasurable and 13 (14.8%) never felt pleasure with sexual activity. In our cohort, there was a significant correlation between the ease of getting sexually aroused and the ability to achieve an orgasm ($r_s = 0.616$, $p = 0.01$). The better the sexual arousal, the easier it was to achieve an orgasm. The correlation between arousal and sensitivity of the neoclitoris was less distinctive but still significant ($r_s = 0.506$, $p = 0.01$). The self-estimated pleasure of sexual activity was significantly correlated with the sensitivity of the neoclitoris ($r_s = 0.508$, $p = 0.01$) but not with the depth of the neovaginal canal ($r_s = 0.198$, $p = 0.079$); i.e., neoclitoral sensitivity seems to contribute to the enjoyment of sexual activity to a greater extent than the depth of the neovagina.

## 4. Discussion

Overall, subjective satisfaction rates can be expected to be 80% and higher after GAS [22]. Löwenberg reported a general satisfaction with the outcome of GAS to be even over 90% [10]. Studies often stress the emphasis on functional or aesthetic aspects after GAS [5–7, 23–25] or, at best, on sexual quality of life before GAS [20, 26]. To our best knowledge, this is the first study placing a particular focus on sexual life after MtF GAS.

In our study, sexual attraction was referred to the self-perceived sexual identity on the basis of self-identification. Accordingly, we used the term "heterosexual" or "homosexual" when participants reported on sexual attraction towards men (natal men as well as transmen) and women, respectively. Due to the existing stigmatization of homosexual and lesbian individuals in a heteronormative community or to patients' wish for social desirability, it is possible that reports on the prevalence of homosexuality (gay and lesbian) are underestimations. A representative study with over 14.000 men and women in Germany reported on a prevalence of 4% of men and 3% of women who self-identified as "gays". Another 9% of male and 20% of female heterosexual participants felt sexually attracted by the same sex without identifying themselves as gay [27]. International surveys found a prevalence of homosexuality in up to 3% with regional and age-dependent variations [28–32]. In our study, the percentage of homosexuality (gay and lesbian) related to self-perceived gender was much higher. This could be because the interviewees knew the interrogators well, had generally revealed their sexual orientation beforehand, and had no fear of societal stigmatization. There is also the possibility that the rate of homo- and bisexuality is, in fact, higher in transsexuals compared with nontranssexuals. [33] Lawrence found a change in predominant sexual attraction in 232 MtF transsexuals before and after genital reassignment [19]. In her study, 54% and 25% of participants reported a gynephile orientation before and after surgery, respectively. Androphilic orientation changed from 9% preoperatively to 34% postoperatively. Regarding asexuality, we followed the definition of Prause and Graham who found that asexuality is defined to be a lack of sexual interest or desire, rather than a lack of sexual experience [34]. In our cohort, in total 6% of the women self-identified as asexual. Bogaert reported on approximately 1% asexual individuals of a total sample size of over 18.000 (nontranssexual) British residents, with more women being asexual than men [35]. He found both biological and psychosocial factors contributing to the development of asexuality. Prause and Graham found significantly lower sexual arousability and lower sexual excitation in asexual individuals with a prevalence of 4% [34]. A reduced sensitivity of the neoclitoris could therefore be a prognostic factor for asexuality. Our results support this assumption. The sensitivity of the neoclitoris correlated with the ability of sexual arousal and achieving an orgasm, as well as with the self-estimated pleasure of sexual activity. In our cohort, satisfaction with the sensitivity of the neoclitoris was higher than with the depth of the neovaginal canal. This could be due to the time of questioning, which was a median of 5.05 years after GAS. While neoclitoral sensitivity is unlikely to diminish, it is more likely that the neovaginal canal shrinks over time. Of the subjects 6% reported a stenosis of the neovagina and 45% a loss of initial neovaginal depth [25]. The

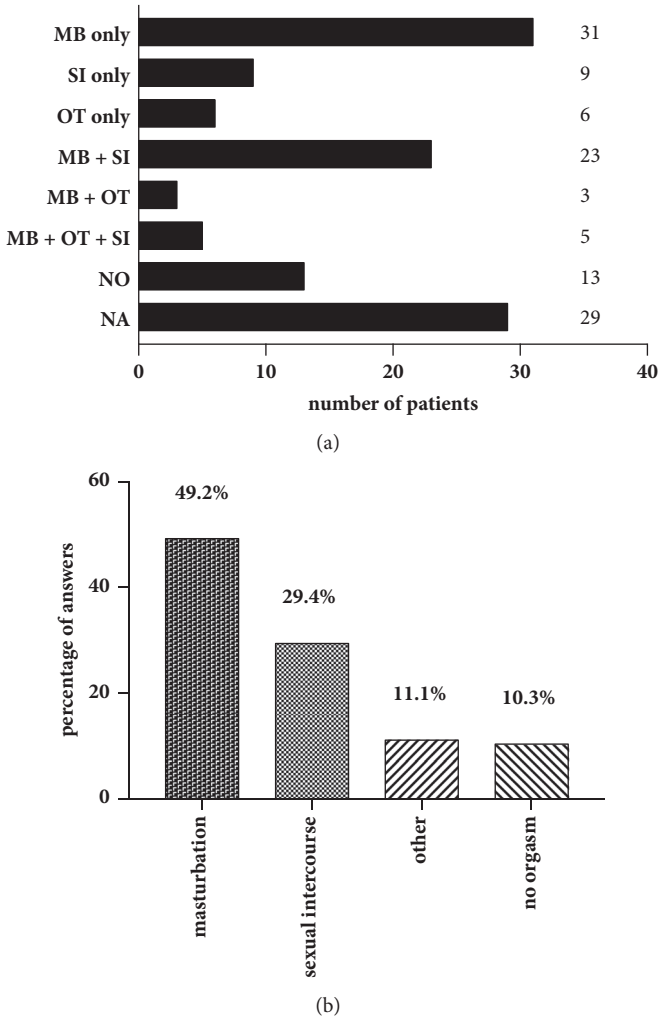


Figure 4: Modality as to how orgasms were achieved (multiple answers possible). (a) Absolute number of patients. MB = masturbation; SI = sexual intercourse; OT = other (not further specified); NO = no orgasm; NA = no answer. (b) Modality as percentage of answers.

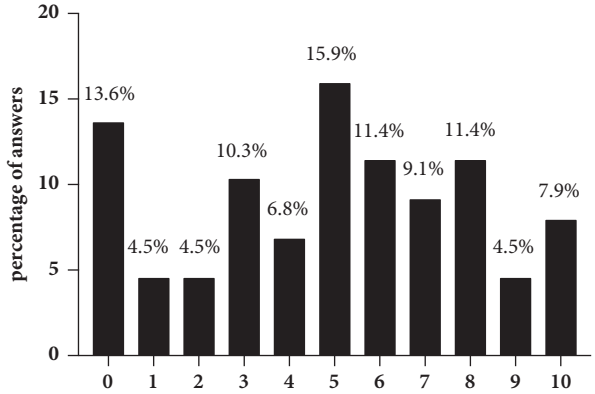


Figure 5: Patients' general satisfaction with their sex lives. Likert scale ranging from 0 ("very dissatisfied") to 10 ("very satisfied").

longer the period after GAS is, the more prevalent the stenosis of the neovaginal canal seems to be [36]. Ineffective dilatation of the neovaginal canal is obviously a key factor contributing to neovaginal stenosis. Over half of all patients (58%) do not use vaginal dilators appropriately, which is a major reason for this kind of long-term complication [36].

Postsurgical sexuality plays an important role in overall satisfaction and depends substantially on the functionality of the neovagina [5, 6]. Satisfaction with functionality ranges between 56% and 84% [7, 9, 10, 37, 38]. Previously, we reported a satisfaction rate with functionality, including satisfaction with depth and breadth of the neovagina and the satisfaction with penetration or intercourse, to be 72% ("very satisfied" and "satisfied") or 91% (including also "mostly satisfied") [6]. The self-reported enjoyment of sexual activity correlated significantly and to a greater extent with neoclitoral sensitivity than with neovaginal dimensions, which was not significant. Though genital dimensions were not surveyed in our study, penile size often exceeds the depth of the vaginal canal in natal women without causing problems with, or pain during, sexual intercourse. However in contrast to a skin derived vaginal canal of transgender women the

vagina of natal women is able to expand 2.5 to 3.5 cm in length when sexually stimulated [39]. Neoclitoral sensitivity is usually assessed by means simply of asking the women and can be biased by the patients' wish for social desirability. In this retrospective study we could not rule this out. However, we previously introduced a measurement tool to assess semiquantitatively the sensitivity with a customary brush and a tuning fork [40] which could be used for future studies on this topic. Though the rate of women, who were able to achieve an orgasm, was lower in the present study than in an earlier cohort from our department [9], our data aligns well with comparable studies of a similar size [11, 19, 41–43]. Interestingly, Dunn et al. found a similar rate of natal women who were unsure or not able to achieve an orgasm during intercourse (16%) or masturbation (14%) [44]. In total 55.8% of the women in our study rated their orgasms postoperatively as more intense than before surgery, one in five women (20.8%) felt no difference, and 23.4% reported less intense orgasms after surgery. These results are roughly in line with a study by Buncamper et al. [45]. Since it is very unlikely that handling of the neurovascular bundle during surgery will make the neoclitoris more sensitive than the glans penis was before, a possible explanation could be that postoperative patients were able to experience orgasm for the first time in a body that matched their perception. Furthermore, a decline in sexual desire after sex reassignment therapy (hormonal and surgical) could contribute to an altered orgasmic experience [46]. Interestingly, in their systematic review, Guillamon et al. reported on results of three longitudinal studies showing a transformation in the brain morphology of MtF after initiation of cross sex hormonal therapy towards a more female morphology [47]. Moreover, receiving hormonal treatment was one of the factors related to a better subjective perception of sexual quality of life [20]. Rolle et al. registered a cerebral modification after sex reassignment in fifteen MtF transsexual individuals towards a more female cognitive response [48]. It is unclear whether this could explain differences in subjective orgasm experience before and after GAS. Further prospective studies with a larger sample size are needed to validate this preliminary aspect.

## 5. Limitations

The study was limited by its retrospective character with a response rate below 50%. Suicide is a very unlikely reason for nonparticipation since the suicide rate after successful GAS is not higher than in the general population [49]. However, contacting trans-female patients for long-term follow-up is generally difficult [3, 37, 50–54] particularly in countries like Germany where there is no central registration. Another reason is that patients often move following successful surgery [5]. Response rates to surveys in retrospective research in this field are between 19% [54] and 79% [55]. With 49%, Löwenberg et al. achieved a similar response rate in a follow-up inquiry of a comparable cohort [10]. Another bias could be that the answers represent patients' wishes for social desirability, rather than the reality of their situation. However, this cannot be verified retrospectively.

## 6. Conclusion

To our best knowledge, this was the first study to survey sexuality after MtF GAS in a very detailed way. In the majority of women, orgasms after surgery were experienced more intense than before. In our cohort, neoclitoral sensitivity seems to contribute to enjoyment of sexual activity to a greater extent than the depth of the neovaginal canal.

## Conflicts of Interest

The authors declare that they have no potential conflicts of interest.

## Ethical Approval

All procedures performed were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards.

## Disclosure

Parts of the data were presented as an abstract at the 2nd Biennial Conference "Contemporary TransHealth in Europe: Focus on Challenges and Improvements" 2017 in Belgrade, Serbia.

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*Review Article*

# Primary Sigmoid Vaginoplasty in Transwomen: Technique and Outcomes

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*Background*. Many techniques have been described for reconstruction of the vaginal canal for oncologic, traumatic, and congenital indications. An increasing role exists for these procedures within the transgender community. Most often, inverted phallus skin is used to create the neovagina in transwomen. However, not all patients have sufficient tissue to achieve satisfactory depth and those that do must endure cumbersome postoperative dilation routines to prevent contracture. In selected patients, the sigmoid colon can be used to harvest ample tissue while avoiding the limitations of penile inversion techniques. *Methods*. Records were retrospectively reviewed for all transwomen undergoing primary sigmoid vaginoplasty with the University of Miami Gender Reassignment service between 2014 and 2017. *Results*. Average neovaginal depth was 13.9 +/− 2.0 centimeters in 12 patients. 67% were without complications, and all maintained tissue conducive to sexual activity. No incidences of bowel injury, anastomotic leak, sigmoid necrosis, prolapse, diversion neovaginitis, dyspareunia, or excessive secretions had occurred at last follow-up. *Conclusions*. Sigmoid vaginoplasty is a reliable technique for achieving a satisfactory vaginal depth that is sexually functional. Using a collaborative approach, it is now our standard of care to offer this surgery to transwomen with phallus length less than 11.4 centimeters.

## 1. Introduction

Gender affirming surgery is now an established part of the transition experience for transgender patients [1]. These procedures improve quality of life and allow them to participate in relationships that are psychologically and sexually fulfilling [2–5]. Many techniques are used in the creation of the neovaginal canal [1, 6, 7]. Though there is no single optimal technique, inversion vaginoplasty with penile-scrotal flaps is the preferred and most commonly practiced method among surgeons [7]. However, sufficient penile-scrotal skin is not always available because of limitations in either patient anatomy or patient expectations for vaginal depth. Additionally, it is becoming more common for younger patients to undergo hormonal blockade in anticipation of gender transition [8]. Though this forestalls the distressing aspects of going through puberty incongruent with one's gender, it may limit the amount of tissue for penile-scrotal based vaginoplasty. Patients who require revision of a failed primary vaginoplasty encounter a similar problem where sufficient tissue must be derived from elsewhere. Full-thickness skin grafts [9], local flaps, musculocutaneous flaps [10–12], peritoneum [13–15], and various segments of intestinal tissue have been previously described as alternative sources for vaginal reconstruction [16–19].

Intestinal vaginoplasty is a well-described modality for the treatment of congenital or acquired absence of the vagina [20]. In transgender patients, the technique is more often used as a revision procedure after primary failure or complications like vaginal stenosis [21]. Recent analysis of pooled data suggests that patients who undergo intestinal vaginoplasty experience complication and mortality rates

comparable with penile inversion vaginoplasty with several advantages [16]. Harvesting the intestinal segment provides for reliable achievement of adequate depth. There are less tendency for intestinal grafts to shrink and therefore less need for lifelong dilation. Additionally, the mucosa feels and appears more like vaginal mucosa with the added benefit of self-lubrication. Performing an elective bowel resection is often perceived as an unnecessary risk to the patient, but recent data suggests that there are fewer gastrointestinal complications in intestinal vaginoplasty than once thought [9, 16]. In this study we present a retrospective series of 12 consecutive patients who underwent primary sigmoid vaginoplasty between 2014 and 2017 at University of Miami Hospital.

## 2. Materials and Methods

A database was created retrospectively to document patients who underwent sigmoid colon vaginoplasty for primary creation of a neovagina between 2014 and 2017 at University at Miami Hospital. Baseline demographics, medical/surgical history, smoking status, complications, and postoperative vaginal depths were collected. Vaginal depth was measured with a dilator and reported in inches. Informed consent was obtained for all patients, including the use of intraoperative photography for publication. This project was granted IRB exempt status.

*2.1. Preoperative Evaluation.* A detailed physical history was taken with special attention to abdominal surgery. In our practice, colonoscopy is recommended for all patients over 40, unless personal or family history indicates otherwise. Elevated BMI was not a contraindication to the procedure. On the morning of surgery or the day before, venous US/Doppler of the upper and lower extremities was performed to rule out deep venous thrombus. Consistent with WPATH guidelines, we recommend that all patients stop estrogen supplementation 2–4 weeks before surgery, and all patients underwent a bowel preparation with GoLYTELY©, Braintree Laboratories, Braintree, MA.

*2.2. Surgical Procedure.* At our institution, laparoscopic sigmoid vaginoplasty is performed in conjunction with a colorectal surgeon, who harvests the pedicled sigmoid conduit for creation of the neovagina. A simultaneous abdominoperineal approach is utilized with the patient in lithotomy position. Perioperative antibiotics are delivered to prevent surgical site infection. An epidural may be placed intraoperatively to assist with postoperative pain.

The abdominal cavity is accessed through a periumbilical trocar. Pneumoperitoneum is obtained and after no contraindication to proceeding is found, additional trocars are placed. Attention is first directed to the sigmoid colon. Dissection begins lateral to medial along the white line of Toldt. The ureter is identified and retracted. Mobilization of the colon continues up to the splenic flexure using blunt and sharp dissection and the LigaSure device. After adequate mobilization, the colon is medialized. An area of distal sigmoid colon with the longest mesentery is selected to serve as the conduit. A window is created in the adjacent mesentery in order to transect the sigmoid with a linear stapler. The mesentery is further divided along the length of the pedicle while preserving the blood supply to the transected end (Figure 1). The periumbilical incision is extended by 2-3 centimeters. With a wound protector placed, the distal sigmoid is extracorporealized (Figure 2). Proximal to the distal end, a 12–15 cm sigmoidal segment is marked and transected with a linear stapler. Intraoperative injection of indocyanine green and SPY system may be used to confirm perfusion of the sigmoid conduit (Figure 3). The proximal end is prepared for anastomosis by placing the anvil of a circular stapler through the bowel and securing it with a purse string. Visual pulsation of the pedicle to the sigmoid conduit is verified and then returned to the abdominal cavity. The anastomosis is performed with use of an end-to-end circular stapling device. A leak test is performed with the anastomosis submerged in saline and air insufflated into the anus.

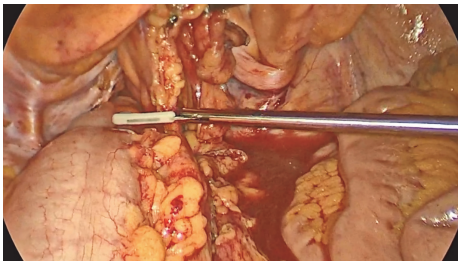

Figure 1: Distracted segment of sigmoid colon with linear staple dissecting it from mesentery at its most lateral extent.

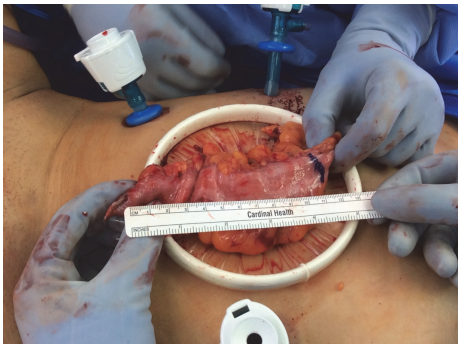


Figure 2: Sigmoid colon segment at the time of laparoscopic harvest.

The plastic surgeon begins the primary vaginoplasty and perineal dissection simultaneously. An ellipsoid incision is made with the scrotal raphe midline. Bilateral orchiectomies are performed. At this point they are transected and suture ligated with retraction into the external inguinal ring. The external ring is then closed with absorbable sutures to decrease the risk of an inguinal hernia. The penile skin flap is elevated off the neurovascular bundle and deep underlying corporal tissues. The neoclitoris is harvested from a portion of the glans penis and raised off Buck's fascia under loupe magnification, paying careful attention to harvest all dorsal penile nerves and the deep dorsal artery and veins from the

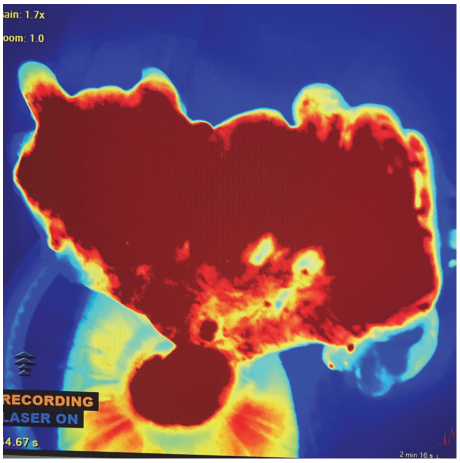


Figure 3: Intraoperative screen capture of extra-abdominal colon segment at the time of laparoscopic harvest using SPY system. Imaging demonstrates abundant perfusion on its pedicle.

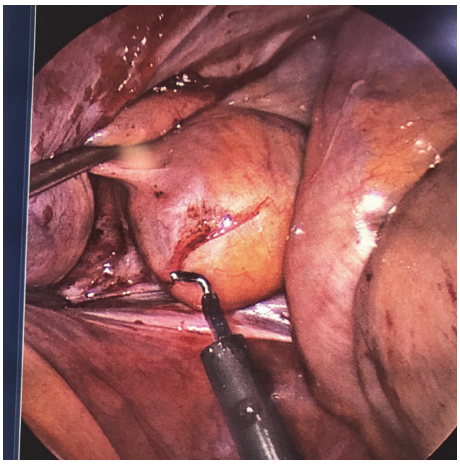

Figure 4: Caudal view of the pelvic cavity showing gentle pressure from the perineal dissection as the peritoneum is opened with electrocautery.

phallus. A Foley is then placed via the corpus spongiosum, which is then dissected from the corpora cavernosa bodies. The corpora cavernosa are further skeletonized proximally to the corporal crura and divided individually with careful suture ligation. The perineal dissection is carried out at the intended posterior fourchette following an inverted U skin design. The dissection is directed to the patient's right to avoid rectal injury. Skin flaps are raised along the inguinal crease for later creation of labia majora tissue. Intra-abdominally, the colorectal surgeon opens the peritoneum with electrocautery while the plastic surgeon unites the abdominal and perineal dissections with gentle traction and electrocautery (Figure 4). The sigmoid conduit is brought through the neovaginal space in an antegrade direction, exteriorized for several centimeters, and inset with minimal tension at the level of the penile stump. Adequate mobilization of the sigmoid is usually achieved by release from lateral attachments and thorough mesenteric dissection. If the segment cannot be transposed tension-free then ligation of the first 1-2 sigmoid arteries and release of accompanying mesentery can further mobilize the sigmoid conduit. The penile skin is then shortened to 1-2 inches to provide for normal appearing external genitalia. Following excision, the penile stump is sutured to the sigmoid conduit with interrupted absorbable sutures. The vascular supply with its mesentery prevents the intestinal segment from prolapsing and allows for a visual appearance like that of a cis-gender vaginal canal. Tissue rearrangement of the scrotal and inguinal skin is performed to contour the labia majora and the urethra is brought just cephalad to the introitus, spatulated, and sutured in place. A clitoroplasty is then performed with a triangular skin incision within the caudal portion of the native mons pubis skin for creation of a clitoral hood. An expander is then placed into the introitus and inflated minimally to avoid compressing the tissues. The final cosmesis of the external genitalia is the same as in penile inversion vaginoplasty (Figures 5(a) and 5(b)).

*2.3. Postoperative Care and Follow-Up.* Patients are admitted to the hospital for 5–7 days, and the condition of the neovagina is checked daily with clear visualization of the intestinal segment. The patient may ambulate after 48 hours of bed rest. If an epidural is used it is discontinued on postoperative days 4–6. The Foley is commonly left in place for ten days and removed in the office. The patient is instructed not to dilate until a follow-up visit and Foley catheter removal.

## 3. Results

12 consecutive patients underwent primary sigmoid colon vaginoplasty from 2014 to 2017. Our patient cohort was on average 47 +/− 15.4 years of age and had a BMI of 26.8 +/− 4.9, and all were white with the exception of one Hispanic patient. Each patient was on a cross-gender estrogen regimen. All patients had an average penis length on stretch of 4.01 +/− 0.76 inches or 10.2 +/− 1.9 centimeters. Overall, 67% (8/12) had no intraoperative or postoperative complications; 6 complications occurred, 4 of which were minor complications (2—ileus, 1—surgical site infection, and 1—intraoperative bladder laceration) and two were considered major complications (1—DVT and 1—suspected PE). There was one return to the operating room (8%) for a suspected intra-abdominal problem, which was negative upon diagnostic laparoscopy and for two patients who underwent secondary revision procedures (17%). Vaginal stenosis occurred in two cases (2 of 12 or 17%) at the neointroitus, which were managed with dilation procedures under anesthesia. A detailed account of complications and their management is available below.

*3.1. Complications and Hospitalization.* A minor bladder injury occurred in one patient. It was repaired intraoperatively through a pfannenstiel incision and the patient recovered without any sequelae. A Foley catheter was left in place for 3 weeks. The average length of stay was 12.5 +/− 9.5 days. This variance was mostly due to one outlier

(a) (b)

Figure 5: (a) Preoperative image of transwoman in lithotomy position. (b) Postoperative image of transwoman after 6 months. The external genitalia do not differ from traditional penile inversion techniques.

whose long hospital stay was due largely to an anomalous vascular pathology discussed below. Excluding this patient, length of stay was 9 +/− 2.1 days. Two patients developed postoperative ileus that resolved with dietary measures. The patient developed diffuse abdominal pain and leukocytosis on postoperative day 3 and was taken for a diagnostic laparoscopy, sigmoidoscopy, and vaginoscopy that was found to be negative for associated pathology. She received an abdominal washout with continued IV antibiotic treatment and was noted to have symptomatic resolution. One patient developed a deep venous thrombosis of the left external iliac that eventually required thrombolysis, placement of an IVC filter, and stenting for treatment of May-Thurner syndrome, which was discovered during her workup. This prolonged her hospital stay significantly (37 days) but did not compromise the success of her sigmoid vaginoplasty. Her past medical history was significant for a provoked DVT after surgery in the other leg. Her preoperative lower extremity ultrasound was negative for a deep vein thrombosis.

There was one mortality in this series. One patient died from a suspected pulmonary embolism nine days following surgery. A postmortem exam was not requested by the family. This patient had no past history of DVT/PE and discontinued estrogen therapy four weeks before surgery. She received subcutaneous heparin postoperatively for DVT prophylaxis. She could be considered high risk for DVT because she drove >10 hours the day before vaginoplasty and had breast augmentation 24 hours before discharge.

One patient developed a minor surgical site infection 3 weeks after surgery that responded to oral antibiotics. One patient developed mild, while another developed moderate, introital stenosis, 5 and 6 weeks, respectively, after surgery. They were both treated with dilation under anesthesia. Both recovered satisfactory vaginal circumference and continued with dilation regimens. There were no cases of diversion neovaginitis, vaginal prolapse, necrosis of the sigmoid conduit, or rectovaginal fistula in our series.

*3.2. Outcomes.* Average follow-up time was six months by either phone consultation or clinic visit depending on patient distance. The average neovaginal depth at last follow-up was 5.5 +/− 0.8 in. or 13.9 +/− 2.0 cm. 42% of patients reported vaginal intercourse after the procedure, and they all reported pleasurable sensation and satisfaction with their vaginal depth. All achieved vaginal depths conducive to penetrative sex. None of the patients experienced malodorous or excessive neovaginal secretions.

## 4. Discussion

Sigmoid vaginoplasty is a reliable, low morbidity procedure for achieving adequate vaginal depth in the transgender patient [16, 20]. It is our practice to have a careful, informed discussion about our patient's desires for penetrative sex, patient and partner anatomy, and expectations before considering sigmoid vaginoplasty. In our clinic, we tailor the planned vaginal depth to every individual rather than a preconceived ideal. We propose consideration of sigmoid vaginoplasty for patients with less than 4.5 inches or 11.4 centimeters of stretched penile length. This procedure involves releasing a segment of sigmoid colon from its mesentery on the distal sigmoid arteries. Most typically, it is inset in an isoperistaltic fashion and anastomosed with a single line of interrupted sutures to the penile-scrotal elements of the neovaginal canal. Other intestinal conduits have been described, such as the ileum [22–24] and cecum [25], which

may preserve the colon's stool reservoir. However, the cecum can be more difficult to inset tension-free given its position and more limited mesentery. Compared with the ileum, the sigmoid colon produces less copious secretions and better approximates vaginal circumference without additional surgical manipulation [6]. The advantages of this procedure over full-thickness skin grafting include reliable creation of vaginal depth, more natural appearing neovaginal mucosa that produces its own secretions, and lower rates of diffuse vaginal stenosis [9]. It is crucial that informed consent explains that the use of colon segments does not eliminate the need for postsurgical dilation. A regimen of dilation is advisable for the first 6–12 months after surgery. However, the goal of dilation is to prevent introital stenosis of the penile-scrotal flaps or penile-colon anastomosis. Long term, patients can usually anticipate less aggressive dilation regimes. Disadvantages include the need for abdominal surgery and bowel anastomosis. Alternatively, omental and peritoneal flaps have been proposed [13–15]. This preserves bowel continuity with the added benefit of reduced operative time and perhaps reduced hospital stays [14, 15]. Omental and peritoneal flaps, however useful, will always require surgical manipulation to tubularize the graft into a neovaginal canal, the healing of which cannot be predicted [15]. Results of peritoneal grafts in transwomen have not been published in peer-reviewed literature. On the other hand, studies have documented the use of the sigmoid for vaginoplasty in transwomen with high rates of sexual and aesthetic satisfaction for the patient [26].

Our retrospective series reports the surgical outcomes of 12 patients undergoing primary sigmoid colon vaginoplasty. The power of our series is limited by its small cohort size ($n = 12$) and by limited follow-up time (6 months). Many of our patients traveled a great distance for the procedure, making long-term clinical follow-up more difficult and burdensome for the patient. Nonetheless, compared to pooled data on this procedure, our technique accomplished reliable, sexually functional neovaginal canals with satisfactory vaginal depth [16]. Postoperative vaginal depth in our series was 5.5 +/− 0.8 inches or 13.9 +/− 2.0 centimeters compared with a range of 11.5–13.0 centimeters [16]. All of our sexually active patients reported sufficient depth for both sexual function and satisfaction. There were two instances of introital stenosis (17%) compared to an 8.6% stenosis rate reported in pooled data [16] and 14.6% in Bouman et al.'s recent series [27]. Both patients were successfully treated with dilation under anesthesia. In our experience, dilation regimens are usually sufficient to relieve this type of stenosis. When stenosis does occur, it normally does so within the first postoperative year [7, 16]. Our limited follow-up time may not have captured every complication or management thereof that may have occurred in this cohort. The rate of complications in our series was 33%, compared with 6.4% in pooled data [16] and 42% [27]. Like Bouman et al.'s recent study, we encountered few intraoperative or postoperative abdominal complications [27]. Clearly, the ability to carry out simultaneous intra-abdominal and perineal operations maximizes visualization and safe retraction of important structures, and this may contribute to lower rates of bowel injury.

Of note, there was one patient mortality in this series from a presumed pulmonary embolism and a deep vein thrombosis in another. The safety and thrombogenesis of hormonal supplementation in transwomen have been the subject of much inquiry [28–30]. WPATH SOC criteria require 12 continuous months of hormone therapy before genital surgery in male-to-female transgender patients [31]. Extensive evidence shows that hormone replacement with estrogen increases the risk for venous thrombosis and pulmonary embolism in cis-gendered women [32]. Some retrospective studies on transwomen demonstrate dramatically increased rates of VTE that approach 20% in those using synthetic estrogens like ethinyl estradiol, a formulation that is no longer recommended [33]. Other studies show no increased risk [29, 30]. Non-first pass route estrogens like transdermal estradiol and estradiol valerate carry lower inherent thrombogenic potential [30, 34]. Epidemiologic research has shown that transwomen may derive estrogen from nonmedical sources, supplement or self-dose prescribed estrogen, use higher risk formulations, and often face barriers to receiving regular follow-up with a health care provider [35]. These factors can lead to supraphysiologic estrogen levels that further increase VTE risk. For these reasons, we recommend discontinuing estrogen therapy 2–4 weeks prior to surgery with resumption only when the patient is ambulatory. Maintaining dialogue with the patient's care team can help monitor estrogen levels. However, there are no tests to monitor synthetic estrogens and no evidence that establishes a risk optimization protocol in transwomen [29, 30, 34]. Both of the aforementioned patients took oral estradiol, stopped estrogen therapy as recommended, and were treated with heparin DVT prophylaxis.

Other known risk factors like obesity were not a factor for these patients, but preoperative venous stasis is a possibility. Given the relative paucity of surgeons well versed in these techniques, many patients must travel long distances pre- and postoperatively. Additionally, there is a short period of bedrest after this procedure that prolongs immobility. The patient mortality in our series underwent breast augmentation on postoperative day 9, which may have further increased her risk. Both patients with thrombotic complications traveled long distances from other states preoperatively. Though there is no data that demonstrates preoperative venous studies are efficacious in reducing DVT or PE risk in transgender patients, we now perform these studies on all patients immediately before surgery. The patient that developed a DVT did so even after instituting this policy. However, given her aberrant venous pathology and past history of DVT, it is difficult to extrapolate her outcome to other patients. Future studies should evaluate estrogen regimens and safety protocols to limit thrombogenic potential in this population.

## 5. Conclusions

Sigmoid vaginoplasty is a reliable technique for achieving satisfactory vaginal depth that is both sexually functional and pleasing to the patient. The procedure is a collaborative undertaking that requires a skilled laparoscopic surgeon, transgender medicine team, and plastic surgeon to work with the patient to optimally achieve their goals. It is now our

standard of care to offer this surgery to our transfemale patients with phallus length of less than 4.5 inches or 11.4 centimeters.

## Disclosure

Ajani Nugent, M.D.; Joseph Kuhn, B.S.; Meghan Janette, B.S.; and Heidi Bahna, M.D., are contributing authors.

## Conflicts of Interest

The authors declare that there are no conflicts of interest regarding the publication of this article.

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*Research Article*

# En Bloc Surgical Dissection for Penile Transplantation for Trans-Men: A Cadaveric Study

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*Introduction*. The surgical techniques currently available for penile reconstruction for trans-men with gender dysphoria present with multiple drawbacks and often fail to meet patients' expectations. Literature reports three cases where penile transplantation has been performed for cis-men, with the last two cases being considered successful. *Aim*. To determine whether an en bloc surgical dissection can be performed in a male cadaver, in order to include structures necessary for penile transplantation (from a deceased donor male) to a recipient with female genitalia in gender affirmation surgery. *Method*. The study was conducted in the form of explorative dissections of the genital and pelvic regions of three male cadavers preserved in phenol-ethanol solution. *Results*. The first two dissections failed to explant adequately all the relevant structures. The third dissection, which was performed along the pubic arch and through the perineum, succeeded in explanting the relevant structures: it, in fact, allowed for identification and adequate transection of urethra, vessels, dorsal nerves, crura of corpora cavernosa, and bulb of corpus spongiosum, in en bloc explantation of male genitalia. *Conclusions*. It is possible to explant the penis and associated vessels, nerves, and urethra en bloc from a cadaver. This study suggests a surgical technique for en bloc explantation aiming for transplantation of the penis from a cadaveric donor male to a recipient with female genitalia.

## 1. Introduction

In gender affirmation surgery (GAS) trans-men patients chose which surgical technique or penis reconstruction best corresponds to their wishes. The choice is normally taken in accordance and following discussion with the surgeon and possibly the mental health professionals [1, 2]. However, for some of the patients the surgical techniques currently available (e.g., phalloplasty with radial forearm flap, thigh flap, and metoidioplasty) are not adequate. In addition, some patients will incur in complications that will result in poorly functioning genitalia, or simply the outcomes will not be satisfactory [3, 4]. All the options available today for penile reconstruction for trans-men, in fact, present with multiple drawbacks, with a relative lack of scientific data regarding complications and results [5, 6]; in addition, dissatisfaction and regret after SRS, though infrequent, are correlated with a poor surgical outcome [7]. Thus, there is a need to explore new surgical options for penile reconstruction for trans-men. Already in 2006, it was argued that transplantation could have advantages compared to the current available techniques [8]; if successful, in fact, a penile transplant has a chance of providing a cosmetic and functional result superior to that of a surgically constructed neophallus.

Recent literature reports three allogenic human penile transplantations [9] performed in cis-men: therefore, none of them was performed for GAS. The first one was performed in China in 2006 on a man after traumatic severance of

the penis, with the surgery reversed after two weeks due to a negative psychological reaction [10]. The second was performed in South Africa and reported in 2015, on a man who lost his penis in a failed ritual circumcision; results have been described as satisfactory, with the recipient reporting natural spontaneous erections and impregnating his partner [11, 12]. All three patients were able to void spontaneously through the urethra.

Following the first case of penile transplantation, authors in [8, 13] criticized the approach adopted in patient selection and possibly some aspects of the surgical technique used by the Chinese group. Nevertheless, penile transplantation was still believed to potentially offer the best outcomes in penile reconstruction [8].

With this vision in mind, recent research is investigating the anatomical structures and the feasibility of penile transplantation; so far, previous research has not focused specifically on penile explantation with the purpose of penile construction for trans-men.

This study aims to determine whether an en bloc surgical technique can be employed for penile transplantation from a cadaveric donor male to a recipient with female genitalia for trans-men GAS. Options for explantation of the penis and associated vessels, nerves, and urethra are investigated.

## 2. Materials and Methods

*2.1. Subjects.* Subjects of the study are three male cadavers preserved in a phenol-ethanol solution. They have been provided by the Department of Medical Biochemistry and Cell Biology at Sahlgrenska Academy, University of Gothenburg. Their ages were not provided, but all subjects were elderly at their deaths. The cadavers had been dissected for teaching purposes prior to the dissections in this study but had only been moderately dissected in the genital area. More specifically, the groin area was partially dissected to expose vessels; the abdomens had been opened to show internal organs; and the scrotums had been opened on one side and one spermatic cord was removed.

*2.2. Ethics for the Cadaver Dissection.* It is not within the purpose of this manuscript to discuss the ethics of penis transplantation. Ethical issues related to penis transplantation have been initially announced by Caplan et al. [14]

The subjects of this study are cadavers willingly donated to Karolinska Institutet for teaching and research purposes. No reservations or caveats regarding genital dissection or transsexual research were made by the donors.

The Department of Medical Biochemistry and Cell Biology at the Sahlgrenska Academy, University of Gothenburg, operates under a statutory right to conduct anatomical research on donated bodies. This is replacing and waiving a IRB approval specific for the present study.

The identity of the donors is protected and no identifying information whatsoever has been available to the researchers.

*2.3. Method.* The study was conducted in the form of explorative dissections on the genital and pelvic regions of the cadavers, which were placed in a dorsal recumbent position.

## 3. Results

*3.1. Dissection of the First Specimen.* On the first specimen, the dissection was begun by identifying the internal iliac vessels in the abdomen. Dissection of the perineal area was carried out in a manner similar to the approach used to reach the prostate during trans-perineal prostatectomy or to create a cavity during vaginoplasty for trans-women: the surgical dissection went through the perineum, above the rectum, and toward the prostate; then perineal structures as pudendal nerves and internal pudendal vessels were located.

While dissecting the groin areas, one of the external pudendal vessels on the left hand side could be identified and dissected with a patch from the femoral artery. Remaining external pudendal vessels could not be identified due to previous dissection of the cadaver for educational purposes.

The testicles and spermatic cords were removed from the scrotum. The next step was to dissect downwards from the abdomen to reach the groin area, in the plane between the urinary bladder and prostate ventrally and the colon and rectum dorsally, in order to be able to pull the pelvic structures (vessels, urinary bladder, and prostate, with the ureters transected) out through the perineum. Branches of the internal iliac arteries that appeared to be going to nongenital structures were transected.

To free the transplant, the dissection was continued above the penis down to the pubic symphysis. The suspensory ligament of the penis was transected, and the dissection continued along the pubic arch to free the penile bodies and the entire transplant.

The transplant unit was then removed and placed on the back table; next step was to separate the prostate and urinary bladder from the specimen without causing damage to the urethra, nerves, or vessels. At this point, it became visible that the dissection had only spared one iliac branch on each side, and as these spread diffusely in the bladder-prostate complex, it appeared more likely that they were the inferior vesical arteries than the internal pudendal arteries that were intended to be retrieved.

The section of the explant containing the penis and the section containing the bladder and prostate are connected by a cordlike structure described as the deep perineal pouch containing muscular structures, branches of the internal pudendal artery and vein, branches of the perineal nerves, and the membranous urethra. This section was dissected in an attempt to locate structures in order to free the prostate and bladder from the specimen. The urethra could be identified but not the internal pudendal vessels (Figure 1).

Thus, the first dissection failed in explanting the necessary structures intact from the male specimen.

*3.2. Dissection of the Second Specimen.* The second male specimen was dissected more proximally, without removal of the pelvic structures. It was attempted to explant the genitals and to identify the relevant vessels and nerves without abdominal dissection. The dissection was carried out down to the suspensory ligament of the penis, similarly to the first specimen. Differently from the first dissection, in the second specimen the corpora were transected. The inguinal

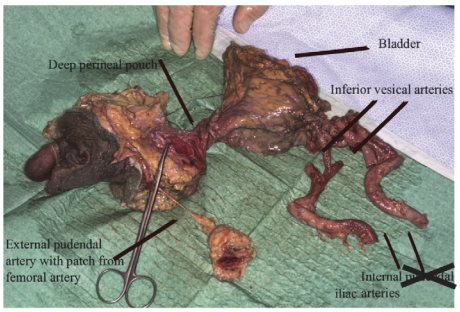


Figure 1: Explant from first specimen. The section containing the penis and the section containing the bladder and prostate are connected by a cordlike structure described as the deep perineal pouch. This is containing muscular structures, branches of the internal pudendal artery and vein, branches of the perineal nerves, and the membranous urethra. It is not possible to identify the internal pudendal vessels.

dissection was then conducted to free the penis from the perineum, as in the first dissection. However, upon back table dissection, it was visually determined that relevant vessels and the urethra had dimensions that were considered inadequate for transplantation onto female genitalia.

*3.3. Dissection of the Third Specimen.* For the dissection of the third male specimen, another approach for explantation was explored. First, external pudendal vessels were attempted to be identified, dissected, and followed to where they spread in the skin. On the right hand side, one external pudendal artery could be identified and dissected (superficial external pudendal artery); another transected vessel was identified below, likely to be the deep external pudendal artery. One external pudendal vein could also be identified, though it had been transected in the previous dissections.

On the left hand side, one external pudendal artery could be identified, passing below the femoral vein and into the skin.

The vessels were dissected and removed with a patch from the femoral artery.

Then, the spermatic cord on the left hand side was identified and cut above the point where the vessels crossed; the testicle was left in place, since it was determined it could just as well be removed at a later stage.

Next, the perineum was dissected. The crura of the corpora cavernosa were located. The bundle of vessels associated with the crura was assumed to contain the internal pudendal vessels.

The skin was incised similarly to the dissection of the first male. Dissection was continued above the penis, down to the pubic symphysis, with transection of the suspensory ligament, location of the dorsal penile vein, and dorsal nerves and continued dissection along the pubic arch (Figure 2).

The bulb of the corpus spongiosum was identified through locating the bladder and prostate in the abdomen. The deep perineal pouch could be identified between the bulb and the prostate and transected. Vessels, nerves, and soft tissue were transected. The explant was removed and dissected separately on the back table.

Figure 2: Identification of deep dorsal vein and dorsal nerves in the third specimen. Clockwise from the right in vessel loops: left crura of corpus cavernosum, left dorsal nerve, deep dorsal vein, right internal pudendal vessels, and right dorsal nerve.

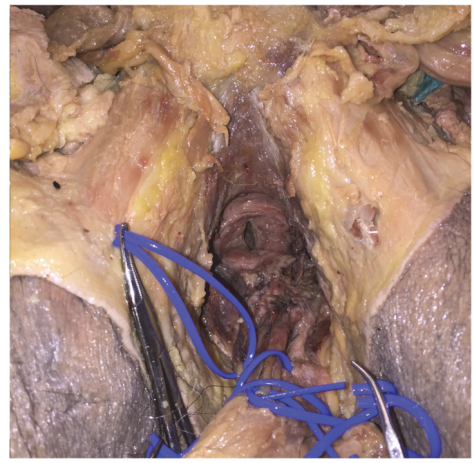

Figure 3: Transection of urethra, nerves, and vessels during explantation of genitals from the third specimen. Lumen of urethra entering prostate visible.

The dissection of the third male specimen thus succeeded in explanting the relevant structures en bloc, with a note that not all the external pudendal vessels could be identified due to the state of the cadaver (Figures 3 and 4).

## 4. Discussion

Through the dissections of the three male specimens, a method was developed to explant the male genitalia and associated structures en bloc.

The dissection of the first specimen was unsuccessful in preserving necessary vessels, due to difficulties in locating the internal pudendal vessels. The dissection of the second specimen failed in preserving adequate lengths of the necessary structures. Finally, in the third specimen, male genitalia were explanted by dissection along the pubic arch and through the perineum to locate the crura of the corpora cavernosa, which were freed from the bone, and the internal pudendal vessels, which were transected. The suspensory ligament of the penis, the dorsal penile nerves, and the deep dorsal vein were identified and transected just below the symphysis. The

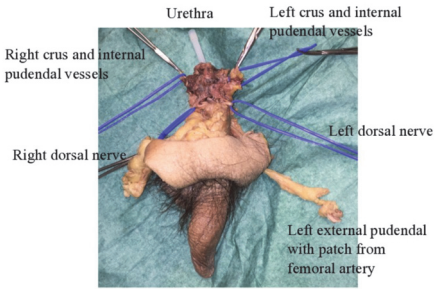


Figure 4: Explant from third specimen, showing penis; right and left dorsal nerves; right and left crus and internal pudendal vessels; left external pudendal artery with a patch from the femoral artery; and urethra (with needle cover inserted).

prostate and bulb of the corpus spongiosum were identified between and superior to the crura, and the deep perineal pouch containing the membranous urethra was transected. The external pudendal vessel which could be identified was followed from the femoral artery to where they branched in the inguinal skin, which was included in the transplant.

In the third specimen, the internal pudendal vessels were transected close to the crura of the corpora cavernosa. It was suggested that instead the abdomen could be dissected similarly to in the dissection of the first male specimen, and a greater length of the vessels was preserved, by following the branches of the internal iliac vessels and meeting the dissection of the perineum. This would ensure preservation of a length of vessel adequate to reach the recipient's vessels for anastomosis. Further, if the vessels are transected close to the crura, the posterior scrotal arteries (which branch further dorsally in the pelvis) will not be included in the explant, and vascularization to the skin of the explant is not entirely guaranteed. This means that abdominal dissection might be necessary to avoid necrosis of the skin.

It is possible that there are additional options for surgical technique of explantation which have yet to be attempted and which could come to light with future dissections. For example, it was suggested that the vasculature might be more accessible if the most ventral part of the pubic arch was sawed off. In addition, the question of whether the erectile tissue of the transplant and recipient could be aligned has not been investigated.

It should be noted that vascular anatomy is subject to individual variation. The internal pudendal vessels, for example, can have an aberrant course or have accessory vessels. In some cases, an accessory vessel may be solely responsible of the blood supply to the corpora cavernosa [15, 16]. Radiographic imaging of the vasculature of prospective recipients will likely be necessary.

*4.1. Previous Anatomical Studies.* In 2014, Tuffaha et al. conducted a cadaveric study of the perfusion territories of the arteries of the penis to find the cause behind skin necrosis following penile replantation and to find surgical options for penile transplantation to natal males. They concluded that the primary reason for skin necrosis after replantation is that the external pudendal arteries, which branch in the groin area and generally cannot be repaired after traumatic penile amputation, are responsible for supplying blood to the greater part of the penile shaft skin. It was suggested that the external pudendal system, which is easily identified, should be included in the case of proximal penile transplantation [15, 17].

In 2016, Tiftikcioglu et al. presented a cadaveric dissection study to investigate the anatomic feasibility of penile transplantation: seventeen male cadavers were dissected to reveal detailed anatomy of the dorsal neurovascular structures including dorsal arteries, superficial and deep dorsal veins, and dorsal nerves of the penis. They concluded that the level of harvest should be determined according to the extension of the defect, where a cis-male patient with a proximal penile defect will receive a partial shaft allograft, while a transgender patient will receive a total allograft [18]. More specifically for the latter, the penis must be harvested deep to its root at the hilum where the bulbar and ischiocavernosal muscles sit. The arterial dissection should continue retrograde until internal pudendal artery is reached so all the branches, dorsal, cavernosal, and bulbourethral arteries, can be included in the allograft. Internal pudendal artery should be divided at a point after it has given its rectal branches [18]. Dorsal nerve dissection should start at the penile root and proceed to perineum with care, on the same plane with the internal pudendal artery and vein. Nerve harvest does not need to proceed too far, as it will be coapted to the dorsal clitoral nerve [18]. In the trans-man recipient, female urethral length can be performed for anastomosis [18], as it is already commonly performed in association with other techniques for penis reconstruction as, for example, radial forearm flap [19].

*4.2. Knowledge from the Current Techniques for Penile Reconstruction in GAS.* The possible gold standard for phalloplasty for trans-men with gender dysphoria might be represented by free radial forearm flap [3]. With this technique, perfusion is ensured by microsurgical anastomosis of the radial artery end-to-side to the femoral artery and the cephalic vein to the saphena magna. Neural sensation is accomplished by connecting forearm cutaneous nerves to one dorsal nerve of the clitoris, leaving the other intact, and to one ilioinguinal nerve, allowing the neophallus to have both tactile and erogenous sensation. The clitoris is not removed, but deepithelialized, freed from its ligaments, and repositioned at the base of the penis, ensuring erogenous sensation and capability to achieve orgasm [3, 4, 20, 21].

In metoidioplasty, the clitoris is similarly freed from the clitoral ligaments, and the urethral plate was divided, in order to lengthen and straighten the constructed phallus. The clitoris retains its erogenous sensitivity in this manner [22].

In both phalloplasty for trans-men and metoidioplasty, the pars fixa of the neourethra is constructed by using the labia minora and eventually a buccal mucosa graft, while other flaps (e.g., tubularized radial forearm flap) are used for the reconstruction of the pars pendulans [4, 6]. Urinary complications (e.g., fistula, stenosis) following urethra reconstruction are high [3, 4, 6, 23].

*4.3. Remaining Questions.* There are a number of issues that need to be addressed before penile transplantation could become an option for GAS. First, it should be investigated to which extent the trans-male population is interested in penile transplantation and whether a potential recipient could psychologically accept a transplanted penis as their own. A pilot study with an initial assessment of this issue is confirming some interest from the trans-men recipient population [2]. Second, ethical issues are as follows: is the benefit (improved quality of life) versus risk (of life-time immunosuppression) ratio favorable? Is there an ethical issue in retrieving genital organs from donors who may have not consented specifically to this type of donation? How to justly allocate public resources, in both research and clinical care?

Additional necessary steps to consider are animal research, radiographic imaging of vascular anatomy and mapping of variant anatomies, and live explantation trials. Likely, further cadaveric research will be required as well. For example, it needs to be established which vessels are appropriate for anastomosis in the recipient, the femoral and epigastric vessels being the candidates closest at hand.

*4.4. Methodological Considerations.* Inductive reasoning from the available knowledge on anatomy and urogenital and transsexual surgery has been employed to construct a theory on how the transplant could achieve perfusion and sensation, but it will remain a theory until tested in a live setting. In addition, the very small number of specimens makes it impossible to draw empirical conclusions regarding the feasibility of the method.

The present study demonstrated the possibility to explant the penis and associated vessels, nerves, and urethra en bloc from a cadaver. We thus suggest a surgical technique for en bloc explantation aiming for transplantation of the penis from a cadaveric donor male to a recipient with female genitalia.

This, being a starting point for research into penile transplantation in trans-men GAS, will obviously need further research before becoming a clinical reality.

## Conflicts of Interest

The authors declare that they have no conflicts of interest.

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*Research Article*

# Hysterectomy with Bilateral Salpingo-Oophorectomy in Female-to-Male Gender Affirmation Surgery: Comparison of Two Methods

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*Introduction*. The optimal route for hysterectomy with bilateral salpingo-oophorectomy in female-to-male gender affirmation surgery is still under debate, due to the quite limited and inconsistent published data. The aim of this study is to present and compare the results of vaginal and laparoscopic hysterectomy as part of gender affirmation surgery in female-to-male transsexuals. *Materials and Methods*. Between 2012 and 2017, 124 female-to-male transsexuals, aged 18–43 years (mean age: 28.5), underwent hysterectomy with bilateral salpingo-oophorectomy, followed by colpocleisis and gender affirmation surgery. Transvaginal and laparoscopic hysterectomy were performed in 92 and 32 patients, respectively. Standard outcome measures (types and rates of complications, operative time, blood loss, and postoperative hospital stay) were used to compare the two groups of patients. *Results*. The mean follow-up was 41 months (ranged from 6 to 65 months). The duration of transvaginal approach was significantly shorter (51 minutes compared to 76 minutes, $p < 0.001$). The total complication rates (less than 3%), reoperation rates (0%), blood loss, and postoperative hospital stays (4.3 days compared to 4.5 days) showed no statistical difference. *Conclusions*. Both approaches are safe, with minimal complications. However, we prefer transvaginal hysterectomy due to its shorter operative time, cost-effectiveness, and simpler continuation with one-stage female-to-male gender affirmation surgery.

## 1. Introduction

The goal of female-to-male gender affirmation surgery is to remove all female attributes, accomplish male appearance of the entire body, and ultimately improve the quality of life. Several complex procedures are included: removal of female genitalia (hysterectomy with bilateral salpingo-oophorectomy and vaginectomy), chest masculinization (bilateral mastectomy), and genital reconstructive surgery (metoidioplasty or phalloplasty, urethral lengthening, and scrotoplasty with testicular implants). In many countries, hysterectomy with salpingo-oophorectomy is a condition for legal recognition of the male sex; in addition, all transsexuals consider it extremely important for their well-being. Therefore, it is usually the first surgical step in their transition, and it can be performed as an isolated procedure, or at the same time with mastectomy and/or sex reassignment surgery. Generally, hysterectomy with bilateral salpingo-oophorectomy should be performed as a safe, minimally invasive, and expeditious procedure, with a low risk of complications and fast postoperative recovery. This way, further reconstruction of new male genitalia should not be compromised [1–3].

Although all available hysterectomy procedures have been utilized and reported in transsexuals (abdominal, vaginal, laparoscopic, and robotic-assisted), there is no clear gold standard. Transvaginal hysterectomy, with its numerous advantages, has been our method of choice in female-to-male gender affirmation surgery for decades. We have recently introduced the laparoscopic approach as a possible alternative in selected cases. The aim of our study is to compare

transvaginal and laparoscopic hysterectomy with salpingo-oophorectomy as part of gender affirmation surgery, as well as the advantages and disadvantages of the two procedures.

## 2. Materials and Methods

Between January 2012 and March 2017, a total of 124 female transsexuals, aged 18–43 years (mean age: 28.5), underwent hysterectomy with bilateral salpingo-oophorectomy, followed by colpocleisis and gender affirmation surgery (metoidioplasty or total phalloplasty, urethral lengthening, and scrotoplasty). Bilateral mastectomy was performed at the same stage in 42 patients. Single-stage gender affirmation surgery is performed by a team of gynecology specialists and gender surgeons. The approach begins with hysterectomy and proceeds with metoidioplasty or total phalloplasty at the same stage. When bilateral mastectomy is planned, it is performed at the same time as transvaginal hysterectomy or, if laparoscopic hysterectomy is used, simultaneously with metoidioplasty. Indications for laparoscopic approach include patients' preference and nonobese persons. After complete preoperative gynecological evaluation, transvaginal and laparoscopic hysterectomy were performed in 92 and 32 patients, respectively.

All patients were required to fulfill requirements according to WPATH Standards of Care prior to surgery [4]. They had been receiving hormonal treatment for a mean period of 3 years (range: 18 months to 23 years). Testosterone treatment was discontinued two weeks before surgery in all patients.

Transvaginal hysterectomy was performed with bilateral oophorectomy, in a standard manner [5, 6]. After uterine vessels are identified on each side and clamped, uterine fundus is delivered posteriorly to identify, cut, and suture-ligate uteroovarian ligaments. Infundibulopelvic ligament is clamped and suture-tied, and adnexa are removed. Laparoscopic hysterectomy is performed using an optic camera and three trocars. After division of the uterus and cervix from the upper vagina, the uterus and both adnexa are removed [7]. Subsequent vaginectomy is performed by total removal of the vaginal mucosa (colpocleisis), with preservation of the part of the anterior vaginal wall near the urethra, which is used for urethral lengthening [1, 3]. Metoidioplasty and phalloplasty are performed as already described [8, 9]. The clitoris is maximally lengthened by division of all ligaments, dorsally, and straightened by dissection and division of the short urethral plate, ventrally. Phalloplasty is performed using musculocutaneous latissimus dorsi free flap. Neophallus is fixed in the pubic region, and microvascular anastomosis is performed with the blood vessels at the recipient site. In both procedures, urethral lengthening is performed using all available well-vascularized genital flaps combined with buccal mucosa grafts. Silicone testicular implants are inserted into the newly created scrotal pockets. Suprapubic urinary drainage is introduced and left indwelling for three weeks. In case of simultaneous chest masculinization, transareolar approach with reduction of the nipple-areola complex is preferred. In case of large breasts and poor skin elasticity, radical mastectomy is performed, with free grafting of the nipple-areola complex.

Table 1: Patients' characteristics in the two groups.

| Route of hysterectomy | Number of patients (%) | Mean age (years, range) | Parity |
|---|---|---|---|
| Transvaginal | 92 (74%) | 28 (18–36) | 2 (2%) |
| Laparoscopic | 32 (26%) | 32.5 (21–43) | 0 (0%) |
| Total | 124 (100%) | 28.5 (18–43) | 2 (1.6%) |

There are two patient groups, classified according to the type of hysterectomy with bilateral salpingo-oophorectomy (transvaginal and laparoscopic); the results are compared using standard outcome measures (types and rates of complications, operative time, blood loss, and postoperative hospital stay). Nonparametric Mann–Whitney $U$ test and Spearman's rank correlation are used for statistical analysis, with $p < 0.05$ presenting statistically significant result.

## 3. Results

Follow-up ranged from 6 months to 65 months (mean: 41 months). Two patients who underwent transvaginal hysterectomy had previous delivery, and both were uniparous. All other patients were nulliparous. None of the patients had significant gynecological complaints during the preoperative evaluation (Table 1).

Outcomes for the two groups are presented in Table 2. Transvaginal hysterectomy with bilateral salpingo-oophorectomy had shorter operative times (mean: 51 minutes) compared to laparoscopic approach (mean: 76 minutes), with the difference being statistically significant ($p < 0.05$). The type of hysterectomy procedure was probably the predictor of the total operative time for one-stage gender affirmation surgery. Mean duration of the total gender affirmation surgery was shorter in case of transvaginal approach than in the laparoscopic approach (Table 3). Postoperative hospital stay ranged from 3 to 8 days, depending on the type of sex reassignment surgery (metoidioplasty or total phalloplasty). Mean hospital stay in transvaginal and laparoscopic group was 4.3 and 4.5 days, respectively, and the difference was not statistically significant ($p = 0.897$). No correlation between operative time and postoperative hospital stay was observed for transvaginal ($p = 0.162$) or laparoscopic ($p = 0.677$) approach.

One patient that underwent transvaginal hysterectomy with bilateral oophorectomy received blood transfusion due to extreme bleeding caused by the previously undiagnosed Von Willebrand disease. However, it was not statistically different from 0 transfused patients in the laparoscopic group. Total rates of complications were quite similar in both groups, 1% for transvaginal and 3% for laparoscopic approach. Conversion of vaginal hysterectomy to laparotomy was necessary in one patient, to obtain bleeding control. In the laparoscopic group, pelvic hematoma was observed in one case and spontaneously resolved. None of the complications required reoperation. Consequently, there was no statistically

Table 2: Comparison of results of transvaginal and laparoscopic hysterectomy with bilateral salpingo-oophorectomy.

| Route of hysterectomy | Mean operative time (min) | Complications | Reoperation rate | Blood transfusion | Mean hospital stay |
|---|---|---|---|---|---|
| Transvaginal | 51 (46–72) | 1/92 (1%)* | 0/92 (0%) | 1/92 (1%) | 4 (3–6)[1]<br>6 (5–8)[2] |
| Laparoscopic | 76 (68–90) | 1/32 (3%)** | 0/32 (0%) | 0/32 (0%) | 4 (3–6)[1]<br>7 (6–8)[2] |
| $p$ | <0.05 | 0.386 | / | 0.375 | 0.897 |
| Total | 57.5 (46–90) | 2/124 (1.6%) | 0/124 (0%) | 1/124 (0.8%) | 4 (3–6)[1]<br>6 (5–8)[2] |

*Conversion of vaginal to abdominal approach. **Pelvic hematoma, spontaneously resolved. [1]Metoidioplasty with urethral lengthening. [2]Total phalloplasty with urethral lengthening.

Table 3: Duration of one-stage gender affirmation surgery in correlation with hysterectomy route.

| Mean operative times (min, range) | Metoidioplasty | Total phalloplasty |
|---|---|---|
| Transvaginal hysterectomy | 245 (215–325) | 435 (390–550) |
| Laparoscopic hysterectomy | 280 (240–375) | 475 (410–590) |

significant difference between groups, comparing both complication and reoperation rates.

## 4. Discussion

Hysterectomy and bilateral oophorectomy are very important parts of female-to-male gender affirmation surgery, in both the esthetic and psychological respect [10]. Although laparoscopic, robotic-assisted, and vaginal hysterectomy have similar outcomes in females with benign gynecological disease, the vaginal route is currently associated with greater benefits, such as shorter operative times, lower infection rates, vaginal dehiscence, and conversion to laparotomy, as well as lower costs [11–14].

In female-to-male transgender populations, several specific aspects must be considered when planning the removal of female genitalia, including effects of testosterone treatment and the patient's high esthetic expectations. Long-term testosterone administration is associated with increased risks of intraoperative and postoperative bleeding and thromboembolic events, as well as possible gynecologic malignancy [15, 16]. On the other hand, its effect on the endometrium is still debated. While some data suggest that testosterone induces proliferative activity of the endometrium and hypertrophic myometrial changes, others report opposite effects [17, 18]. Lower uterine weight, compared to females without gender dysphoria, has also been reported [19]. It is therefore important to stop testosterone administration two weeks prior to surgery, in order to avoid excessive intraoperative bleeding. Some authors prefer laparoscopic hysterectomy in transsexuals due to better visualization of tissues and control of hemorrhage [3, 19, 20]. Gomes da Costa et al. reported 1 out of 23 transgender patients (4.3%) with significant postoperative bleeding, who underwent second-look laparoscopy and hemostasis [20]. O'Hanlan et al.'s study includes 41 transsexuals who underwent laparoscopic hysterectomy; one included a conversion to open laparotomy for observation of a large retroperitoneal hematoma (2.4%), while two (4.9%) required reoperation due to excessive bleeding [19]. Ott et al. performed conversion from laparoscopy to laparotomy in 1 out of 32 patients (3.1%), and none of the patients required reoperation [3]. There was no need for conversion of laparoscopic approach to laparotomy in our 32 cases, and reoperation rate was 0%. It is noteworthy that all previous studies evaluated hysterectomy performed in female-to-male transsexuals as a single procedure, or with vaginectomy and/or mastectomy. On the other hand, our group of 124 female-to-male transsexuals underwent simultaneous sex reassignment surgery, thus having a potentially increased risk of bleeding and associated complications. However, only 1 out of 124 patients required a blood transfusion, due to a coagulation disorder.

In case of our one-stage gender affirmation surgery, increased operative time could put the patient at a higher risk. This is why we prefer the transvaginal approach, as a significantly shorter procedure compared to the laparoscopic approach. Moreover, laparoscopic hysterectomy with bilateral oophorectomy requires additional, time-consuming activities, such as repositioning the patient and removing the equipment, in order to continue with sex reassignment surgery.

We did not experience any injury of vaginal mucosa during the vaginal approach that would compromise vaginal flaps for subsequent urethral lengthening, as a complication reported by other authors [20]. Kaiser et al., in one of the largest studies on vaginal hysterectomy in 103 female-to-male transsexuals, reported a complication rate of 5.4%, with mean duration of surgery of 52 minutes [21]. In 1 of our 92 patients (1%), it was necessary to convert the initial vaginal hysterectomy to abdominal hysterectomy due to excessive bleeding and hematoma formation. There were no other complications.

The potential shortcoming of this study is the disproportion in the number of patients in two groups; however, they are statistically comparable. In our study, both vaginal and laparoscopic hysterectomy have been proven to be safe,

with minimal complication rates and without compromising simultaneous sex reassignment surgery (colpocleisis, urethral lengthening, metoidioplasty, and total phalloplasty). However, the laparoscopic approach is associated with a longer operative time and higher cost. It also requires three or four pelvic points of access in the abdominal wall, a visible trace of surgery, and a kind of stigma with potential psychological consequences in vulnerable patients. The scars in the anterior abdominal wall may also compromise abdominal phalloplasty, while possible injury of epigastric vessels with trocars may compromise microvascular anastomosis in total phalloplasty. These characteristics make transvaginal hysterectomy with bilateral salpingo-oophorectomy the optimal choice in transsexuals. The clear advantages of transvaginal approach are especially important in our setting of one-stage gender affirmation surgery, where a fast and the least invasive procedure, with minimal blood loss, is highly appreciated [5, 22]. Also, it is much easier and more comfortable to continue with sex reassignment surgery following transvaginal hysterectomy. Laparoscopic and robotic single-port access hysterectomy, less invasive than standard laparoscopy, may be a future alternative in transgender surgery, but current experiences are still quite limited [23, 24].

## 5. Conclusions

Comparisons of transvaginal and laparoscopic approach for hysterectomy with bilateral salpingo-oophorectomy remain relevant. Based on our experience, transvaginal approach as part of female-to-male gender affirmation surgery is safe, feasible, and valuable, bringing about numerous benefits. Laparoscopic hysterectomy presents a good alternative and could be recommended in selected cases.

## Conflicts of Interest

The authors declare that there are no conflicts of interest regarding the publication of this article.

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*Research Article*

# Gender Minority Stress and Depressive Symptoms in Transitioned Swiss Transpersons

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Compared to the general population, transpersons are exposed to higher levels of discrimination and violence. The stigmatization of transpersons can lead to physical and psychological problems. In particular, transindividuals exhibit a higher prevalence of depression compared to the cispopulation. The gender minority stress model (GMSM) provides a comprehensive theoretical basis to interpret these biopsychosocial interactions. Using the GMSM, this study aimed to identify associations between experience of stigmatization and the mental health of transitioned transpersons using correlational analyses and multiple regression models. In total, 143 transpersons were recruited. Multivariate analyses identified three variables (i.e., unemployment, nonaffirmation of gender identity, and internalized transphobia) to explain variance of depressive symptoms. Furthermore, a mediation of the proximal factors between distal factors and depressive symptoms was found. However, the moderating effect of resilience factors was not demonstrated. The results confirmed the importance of distal and proximal minority stressors for the mental health of transpersons. At the same time, the protective influence of resilience factors seemed to be surprisingly minor. In the treatment of transpersons, practitioners should not only focus on somatic aspects, but also consider the person's previous experiences of stigmatization.

## 1. Introduction

In recent years, there has been an increase in the number of studies reporting a growing transpopulation [1]. For practitioners, the rise of the visibility of transpersons is reflected in a higher demand for medical transition interventions such as gender affirming interventions (GAI) [2]. By reducing the gender dysphoria of transpeople, these medical procedures also contribute secondarily to improving their mental health and quality of life [3]. Even though the risk of developing psychiatric problems decreases after initiation of gender reassignment measures [4], depressive disorders [5] and suicidality [6] are especially discrepantly increased in the transpopulation in comparison to the cispopulation. Other studies have also found higher prevalence of substance use and abuse [7] as well as posttraumatic stress disorder [8].

On a daily basis, transpersons are subjected to stigmatization due to normative gender conceptions in society [9–12]. Experiences of exclusion can take place on structural (e.g., through institutional laws and practices), interpersonal (e.g.,

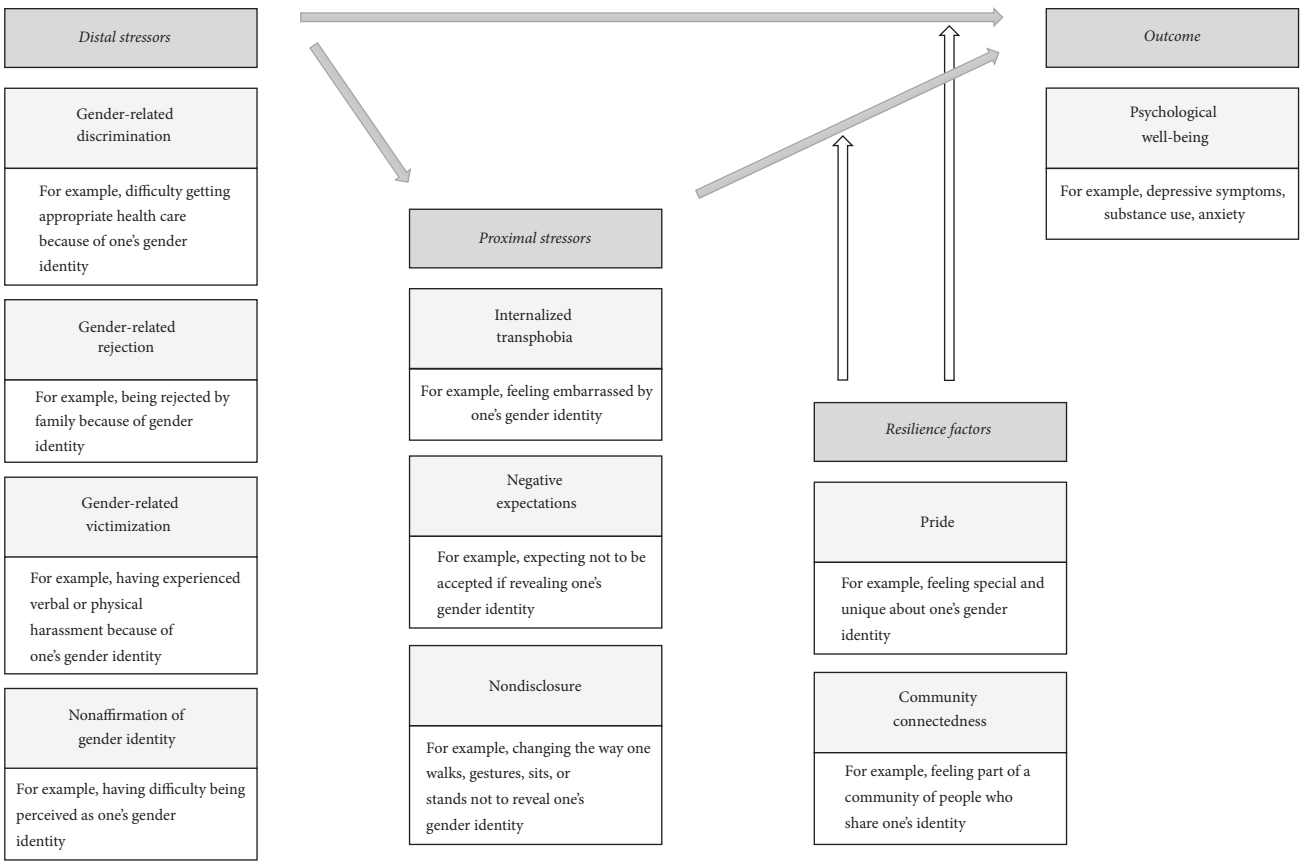


Figure 1: Gender minority stress model as proposed by Testa et al. [17] with distal stressors having a negative effect on psychological well-being, proximal stressors mediating their relationship, and resilience factors moderating the effect of distal and proximal stressors on psychological well-being. Grey arrows reflect a negative relationship to the outcome.

through victimization), or personal (e.g., through negative feelings towards one's identity) level [13]. Stigmatization is ubiquitous and can also be found in the healthcare sector. The treatment barriers and the discriminations on the part of the practitioner with which many transpersons are confronted provide examples of structural and interpersonal stigmatization within the various medical care systems [14]. The relationship between stigma, mental health, and the quality of life of transpersons also has clinical implications for those practitioners who care for this group before, during, and especially after medical transition [15]. Thus, there are situations where transpeople do want to undergo a specific GAI (e.g., genital operation and facial feminization), not mainly due to an existing intrinsic gender dysphoria, but primarily to avoid the extrinsic consequences of persistent stigmatization. Without knowledge of these relationships and interactions, there is hardly enough preoperative counselling and education on transpatients, which in turn is likely to affect the degree of satisfaction with the completed surgery.

The gender minority stress model (GMSM) integrates the findings of the higher prevalence of mental problems with the permanent stigmatization in transpersons [16]. The model is based on the premise that the experiences of stigmatization take the form of a specific, so-called minority stress, which in turn affects the state of health of the transperson concerned (Figure 1). Minority stressors are divided into two different types, distal stressors and proximal stressors. Distal stressors are stressors that are caused by an external source and proximal stressors refer to internal and subjective thoughts and processes within a transperson. However, transpersons are typically confronted with various forms of minority stressors, which can interact with each other. Thus, negative effects caused by minority stress are caused by both individual factors and their interactions. In addition to the description of minority stress effects, two resilience factors are considered within the GMSM. These act on a group-specific (not individual) level and can help to minimize the negative consequences of stigmatization.

In the past, several studies have examined the applicability of GMSM to the development of depressive symptoms in transpersons [5, 7, 8, 18–21]. Depending on the research's focus, different conclusions have been drawn. While studies examining the association between distal minority stressors and depressive symptoms have supported the validity of the GMSM [7, 8, 18–20, 22–26], results of studies focused on the relationship between depressive symptoms and proximal minority stress factors [5, 18, 21] or on the relationship between depressive symptoms and the resilience factors

[5, 19–21, 27–29] were less clear. However, it is difficult to compare results across different studies due to different factors. First, previous studies have not consistently standardized minority stressors and resilience factors and have not all used the same instruments, complicating comparisons of collected data between studies. Second, previous studies have neglected to assess if a moderated mediation is taking place by only focusing on partial aspects of GMSM. Moderated mediation is when proximal stressors mediate the relationship between distal stressors and mental health and resilience factors moderate the relationships between distal stressors and mental health and proximal stressors and mental health (see Figure 1). Thus, neglecting to assess all aspects of GMSM inhibits the ability to determine the validity of the overall model.

The aim of this study was to utilize the GMSM to explore the effects of stigmatization on the mental health of transitioned transpersons. In particular, the relevance of each individual factor (i.e., distal minority stress, proximal minority stress, and resilience) and the impact of their interactions were examined using a validated minority stress measurement tool. This holistic and methodologically founded approach overcomes previous research limitations and contributes to a better understanding of stigma-related processes and mental health outcomes. This study focused on transitioned transpersons, because pretransitioned transpersons and transpersons in medical transition are faced with other stressors related to the initiation or completion of the transition (e.g., hormonal side effects and complications with surgery), which do not meet the specific definition of minority stressors [16]. The exclusion of transpersons before and during medical transition in the study helped ensure that there would be no interaction between transition-related stressors and minority stressors. Furthermore, this study concentrated on depressive symptoms for the mental health outcome, as depressive disorders crucially contribute to the global burden of disease of transpersons [30].

In this study, we defined three hypotheses: firstly, there is a positive correlation between distal stressors and depressive symptoms and proximal stressors and depressive symptoms; inversely, there is a negative correlation between resilience factors and depressive symptoms; secondly, all minority stress factors contribute substantially to the explanation of depressive symptoms; thirdly, proximal stressors mediate the relationship between distal stressors and depressive symptoms; resilience factors moderate the relationships between distal and proximal stressors and depressive symptoms.

## 2. Methods

*2.1. Patients and Procedures.* The study was a multicentric collaboration of four Swiss hospitals specialized in treating transpersons: Basel and Zurich (psychiatric, endocrine, and surgical interventions), Bern (endocrine and surgical interventions), and Olten (psychiatric interventions). To maximize the number of potential participants, members of the transcommunity were recruited through Swiss transorganisations.

Transpersons were included in the study if they met the following criteria: German-speaking, at least 18 years of age, and self-identified as transitioned. For this study, patients were characterised as transitioned if they were not currently attending transspecific psychotherapy/counselling, have not taken hormone therapy for at least one year, or did not plan to have any surgical interventions within the next year. Transpersons were excluded if they were in the process of medical transition or transrelated counselling.

Transpersons treated in the four hospitals were recruited via postal notifications and asked to complete either the paper-pencil or online version of the questionnaire battery. Transpersons recruited by the transorganisations could only complete the questionnaire online. Participants gave informed consent before proceeding to fill out the questionnaires and data was anonymized. The Ethics Committee Northwest and Central Switzerland approved this procedure.

*2.2. Measures*

*2.2.1. Gender Minority Stress.* Gender minority stress was assessed by the validated *Gender Minority Stress and Resilience Measure* (GMSR), which includes four distal minority stress factors, three proximal minority stress factors, and two resilience factors [17]. The measure contains 58 items, with five to nine items per factor and each factor functioning as scale. For the distal factors "gender-related discrimination" ("I have experienced difficulty getting identity documents that match my gender identity"), "gender-related rejection," and "gender-related victimization," the categories "never," "yes, before age 18," "yes, after age 18," and "yes, in the past year" items are scored 0 for "never" and 1 for any other category. For the items of the factors "nonaffirmation of gender identity" ("I have to work hard for people to see my gender accurately"), "internalized transphobia" ("Because of my gender identity or expression, I feel like an outcast"), "negative expectations," "nondisclosure," "community connectedness" ("I feel connected to other people who share my gender identity"), and "pride" items responses ranged from "strongly disagree" to "strongly agree" with the corresponding score from 0 to 4. For the distal and proximal scales, a higher value signified higher stigmatization, and inversely, a higher value represented higher resilience.

As there was no German version of the questionnaire, the GMSR was translated into German and back to English (with the permission of the developer) to ensure the quality of the translation. The German translation was examined for readability and content. The obtained Cronbach alphas were comparable to the original paper [17] and ranged from acceptable ($\alpha = .71$ for "nondisclosure") to excellent ($\alpha = .93$ for "negative expectations"). However, this study resulted in an unacceptable $\alpha = .48$ for "gender-related discrimination," whereas the original paper obtained questionable $\alpha = .61$.

*2.2.2. Depressive Symptoms.* Depressive symptomatology was assessed by the *Allgemeine Depressionsskala* (ADS-K) [31], which is the German equivalent to the *Center of Epidemiologic Studies Depression Scale* (CES-D) [32]. The ADS-K consists of 15 items, which can be answered on a Likert scale ranging

from 0 to 3 with the corresponding answers "rarely or none of the days," "some or a little of the time," "occasionally or a moderate amount of time," or "most or all the time." The score of every item is summed to obtain one score representing the severity of depressive symptoms. Participants look one week back and self-report if they experienced symptoms associated with depression such as difficulty concentrating, feeling depressed, or having a restless sleep. A higher score indicates more depressive symptomatology. Previous analyses have demonstrated that the ADS-K had good to very good reliability and validity [31]. The Cronbach's alpha for this study was $\alpha = .94$.

*2.2.3. Sociodemographics.* The extensive sociodemographic survey was thematically divided into three sections: general, transspecific, and transition-specific. In the general section, participants self-reported their age, place of residence, current living arrangement, sexual orientation, relationship status, highest education, and current occupational situation. Experienced gender, gender assigned at birth, and preferred gender label were considered transspecific variables. Gender was added as a new variable and included experienced gender and gender assigned at birth. We defined a transfeminine person as an individual that identified as female but was assigned as a male at birth, a transmasculine person as an individual that identified as male but was assigned as a female at birth, and a gender nonbinary person as an individual that identified as between male and female gender or identified as having no gender, independently of their sex assigned at birth. Transition-specific variables assessed psychological/psychiatric evaluations as well as hormonal and surgical interventions.

*2.3. Statistical Analyses.* For the first hypothesis, bivariate Spearman correlational analyses between the ADS-K score and each gender minority stress factor were conducted [33]. Effect sizes were evaluated following Cohen's guidelines [34].

To test the second hypothesis, a multiple hierarchical regression was performed. Preliminary data analysis revealed a lack of homogeneity of variance and normality of the residues [35]. A Cox-box transformation was conducted in order to counteract the missing prerequisite for multiple linear regression [35]. Control variables for the linear model were selected if they significantly correlated with the ADS-K score and granted sufficient statistical power for the model. Categorical variables were dummy coded: for gender, transfeminine was chosen as the reference category, as the literature reports a higher vulnerability for depressive symptoms in this group [36]. Equivalently, unemployed was chosen as reference category for occupational status [37].

A moderated mediation analysis was conducted to check the last hypothesis [38]. To have sufficient power to conduct the analysis, gender minority stress and resilience factors were summed to obtain the combined variables' distal stress, proximal stress, and resilience. All statistical procedures were conducted using the software IBM SPSS Statistics for Windows [39] and the macro PROCESS [40].

## 3. Results

*3.1. Participant Characteristics.* Data from 143 people were analysed in this study. The age range of the participants was 18–75 years with a mean of 45.2 years (SD = 18.2 y). Most participants were transfeminine (52%) and labelled themselves as "transgender," "transsexual," or "transwoman." At the same time, 30% of the participants defined themselves as transmasculine and 18% as nonbinary. The nonbinary group described themselves as "agender," "genderfree," "neutrois," "genderfluid," "genderqueer," or "nonbinary-gender." When age was split up by gender, a bimodal age distribution became evident, where transfeminine persons (M = 51.5, SD = 17.1) were significantly older in comparison to transmasculine persons (M = 36.0, SD = 12.8; $F = 10.32$, $p < 0.01$). Nonbinary persons had a mean age of 42.2 years (SD = 24.4), which was between the mean ages of the other groups.

The relationship status between groups varied significantly. Participants with binary genders mainly stated that their relationship status was single (transfeminine: 53.9%/transmasculine: 42.5%) or in a relationship (transfeminine: 43.4%/transmasculine: 57.5%), but only 28% of the nonbinary persons were in a relationship and 44.0% stated to be single. In contrast, 28% of this group described themselves as being in an "other" form of relationship (e.g., open or polyamorous network).

In regard to employment status, most transfeminine persons were active on the labour market either employed (35.5%) or self-employed (19.7%). While 19.7% reported to be unemployed, 25.0% found themselves in another situation (e.g., studying, being retired, or getting disability pension). In the transmasculine group, 61.0% reported to be employed and 12.2% to be self-employed; only 7.3% were unemployed and 19.5% were facing another situation. Only 25.0% of nonbinary persons were employed and 16.7% reported to be self-employed. Unemployment in nonbinary persons was 20.8%, while 37.5% found themselves in another situation. More information on the participants' characteristics can be found in Jellestad et al. [15].

Depressive symptomatology varied among the different gender groups ($F = 5.98$, $p < 0.01$). Nonbinary persons exhibited a significantly higher ADS-K score (M = 18.04, SD = 10.17) compared to transfeminine (M = 10.76, SD = 7.80) and transmasculine (M = 12.59, SD = 10.16) persons.

Similarly, there were significant gender specific differences in the scales "gender-related discrimination," "nonaffirmation of gender identity," "internalized transphobia," and "pride" of the GMSR (Table 1).

*3.2. Correlational Analyses.* To check the first hypothesis, correlations between the ADS-K score and each gender minority stress and resilience factor were conducted (Table 2). Accordingly, each distal and proximal factor exhibited significant positive correlations between depressive symptoms and gender minority stress factors with medium to strong effects (ranging from $r = .30$ for gender-related victimization to $r = .52$ for nonaffirmation of gender identity). Resilience factors did not yield clear results. Even though the correlation

Table 1: Descriptive statistics of the gender minority stress scales divided by gender and ANOVA results.

| Scale | Transfeminine M (SD) | Transmasculine M (SD) | Nonbinary M (SD) | $F$ (df) | $p$ |
|---|---|---|---|---|---|
| Gender-related discrimination | 2.19 (1.77) | 3.14 (2.20) | 3.58 (2.55) | 5.48 (2, 137) | **0.005** |
| Gender-related rejection | 3.19 (2.57) | 3.67 (3.71) | 4.52 (3.42) | 1.69 (2, 133) | 0.188 |
| Gender-related victimization | 1.99 (2.42) | 2.69 (2.79) | 2.80 (2.93) | 1.44 (2, 139) | 0.241 |
| Nonaffirmation of gender identity | 6.69 (5.82) | 4.95 (5.97) | 14.68 (6.84) | 21.95 (2, 138) | **0.001** |
| Internalized transphobia | 6.34 (6.78) | 10.38 (8.85) | 7.88 (5.44) | 4.00 (2, 134) | **0.020** |
| Negative expectations | 12.75 (9.20) | 12.53 (7.84) | 16.22 (7.54) | 1.65 (2, 133) | 0.197 |
| Nondisclosure | 7.72 (4.61) | 8.37 (4.26) | 10.32 (5.17) | 2.72 (2, 136) | 0.070 |
| Pride | 17.15 (7.95) | 12.46 (6.89) | 16.44 (7.02) | 5.34 (2, 138) | **0.006** |
| Community connectedness | 11.50 (4.53) | 12.14 (3.15) | 11.68 (4.16) | .34 (2, 140) | 0.718 |

Table 2: Correlational analyses between the ADS-K score and different gender minority stress and resilience factors.

| GMSR factor | ADS-K | $p$ |
|---|---|---|
| Distal stress factors | | |
| Gender-related discrimination | .39 | <0.01 |
| Gender-related rejection | .43 | <0.01 |
| Gender-related victimization | .30 | <0.01 |
| Nonaffirmation of gender identity | .52 | <0.01 |
| Proximal stress factors | | |
| Internalized transphobia | .42 | <0.01 |
| Negative expectations | .47 | <0.01 |
| Nondisclosure | .32 | <0.01 |
| Resilience factors | | |
| Pride | −.13 | 0.14 |
| Community connectedness | −.22 | <0.01 |

between community connectedness and depressive symptoms revealed a small significant negative effect, pride and depressive symptoms did not have a significant correlation.

*3.3. Regression Analyses.* For the second hypothesis, a hierarchical multiple regression model was calculated with the normalized ADS-K score as a dependent variable. Since gender and occupational status significantly correlated with the ADS-K score, they were used as control variables. The variable highest education also correlated significantly with the ADS-K score, but issues concerning the power of the model led to rejecting that variable as control variable. In the first step, the control variables age, gender, and occupational status were inserted to the model. Model 1 explained 21% of the variance ($R^2 = .21$, $F = 4.62$, $p < 0.001$), with the variables nonbinary ($\beta = .21$, $p = 0.030$), self-employed ($\beta = -.33$, $p = 0.003$), and employed ($\beta = -.40$, $p = 0.002$) contributing individually to the explanation of variance. In the second step, distal factors were added to the model. Model 2 explained an additional 23% of the variance ($R^2 = .44$, $F = 7.97$, $p < 0.001$) with the variables self-employed ($\beta = -.23$, $p = 0.018$), age ($\beta = -.18$, $p = 0.027$), gender-related rejection ($\beta = .20$, $p = 0.042$), and nonaffirmation of gender identity ($\beta = .45$, $p < 0.001$) contributing individually to the explanation of variance. In the third step, proximal factors were added to the model. Model 3 additionally explained 6% of the variance ($R^2 = .50$, $F = 7.51$, $p < 0.001$) with the variables self-employed ($\beta = -.22$, $p = 0.025$), nonaffirmation of gender identity ($\beta = .31$, $p = 0.005$), and internalized transphobia ($\beta = .25$, $p = 0.005$) explaining variance individually. For the last step, resilience factors were added to the model. Model 4 could only explain an additional 1% of the variance ($R^2 = .51$, $F = 6.63$, $p < 0.001$) (Table 3).

*3.4. Mediation-Moderation Analysis.* Distal stress had a significant direct effect on depressive symptoms ($\beta = 3.78$, $p < 0.001$) and proximal stress had a significant indirect effect on depressive symptoms ($\beta = 2.47$, $p < 0.05$). The moderation of resilience did not yield significance (Figure 2).

## 4. Discussion

This study aimed to expand research on the health consequences of gender minority stigmatization in transpersons. For the first time, the relationships between gender minority stressors, resilience-promoting factors, and depressive symptoms in transpersons were examined simultaneously and in a comprehensive manner using the GMSM [16]. Thus, this

Table 3: Model 4 of the hierarchical linear regression with the dependent variable ADS-K (normalized).

| Scale | Unstandardized coefficient | | Standardized coefficient | $F$ | $R^2$ |
|---|---|---|---|---|---|
| | $b$ | SE | $\beta$ | | |
| Final model | | | | $6.63^{***}$ | .51 |
| Intercept | 12.62 | 3.78 | | | |
| Age | −.01 | .04 | −.01 | | |
| Transmasculine[a] | −1.25 | 1.73 | −.06 | | |
| Nonbinary[a] | .61 | 2.02 | .03 | | |
| *Self-employed*[b] | −5.09 | 2.33 | $-.21^{*}$ | | |
| Employed[b] | −3.23 | 2.03 | −.18 | | |
| Other occupation[b] | −1.33 | 2.06 | −.07 | | |
| Gender-related discrimination | .27 | .43 | .06 | | |
| Gender-related rejection | .37 | .31 | .12 | | |
| Gender-related victimization | −.33 | .35 | −.09 | | |
| *Nonaffirmation of gender identity* | .42 | .14 | $.32^{**}$ | | |
| *Internalized transphobia* | .28 | .11 | $.23^{**}$ | | |
| Negative expectations | .11 | .10 | .11 | | |
| Nondisclosure | .03 | .17 | .01 | | |
| Pride | .02 | .11 | .01 | | |
| Community connectedness | −.24 | .18 | −.11 | | |

*Notes.* $^{***}p < 0.001$; $^{**}p < 0.01$; $^{*}p < 0.05$; [a]reference category: transfeminine; [b]reference category: unemployed.

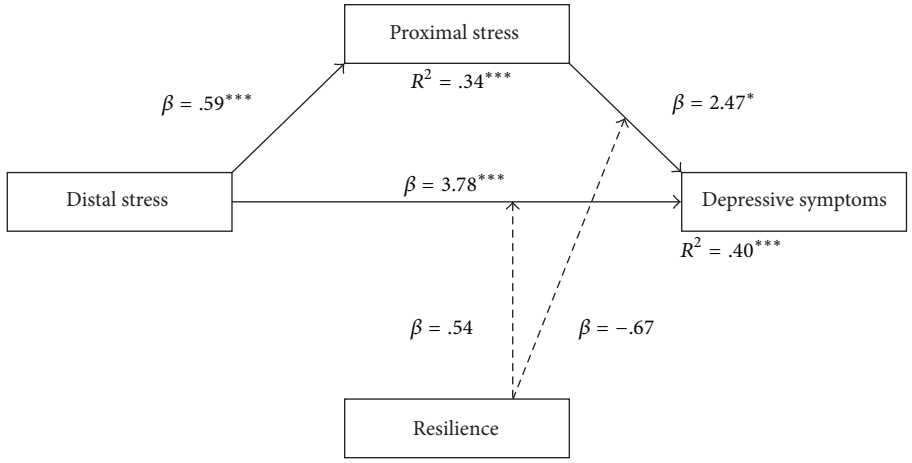


Figure 2: Path model of the direct and indirect effects of proximal and distal stress within the GMSM. Dashed lines represent nonsignificant results. $^{***}p < .001$; $^{*}p < .05$.

research facilitated exploration of the scarcely studied Swiss transpopulation and established an intercultural validity of the proposed biopsychosocial interactions between stigmatization experiences and mental health problems.

*4.1. Validation of the Gender Minority Stress Model.* The overall results indicate the validity of the GMSM. Firstly, distal stressors were highly associated with depressive symptoms. This finding is in line with the large body of previous research about gender-related discrimination, rejection, and victimization [7, 18, 20, 25, 26]. Interestingly, this result confirms the results from the only two studies investigating the effects of nonaffirmation of gender identity [23, 41]. It further indicates that the difficulty for society to recognize the transpersons' gender results in significant negative long-term impact for this group. Perhaps the relationship between society's perception and the transperson's gender is particularly strong in transitioned transpersons. It is possible that the probability of experiencing interpersonal stigma decreases due to the type of GAI undertaken. The problems arising from the nonaffirmation of the own gender (e.g., having to explain one's own gender repeatedly) are difficult to avoid by performing hormonal or surgical measures. Future studies should definitely take the transition time axis more into account and consider the respective minority stressors differently depending on the transition situation. However, comparing results between studies that have investigated distal stressors is problematic because they have used different conceptualizations of the different stressors. To advance

understanding of distal factors, future research should also use validated instruments for the assessment of gender minority stressors.

Secondly, proximal stressors also had the expected association with depressive symptoms. Importantly, internalized transphobia as proximal stressor was strongly associated with depressive symptoms. Our results confirm previous research on proximal stressors [5, 21, 41]. Comparisons to other proximal factors cannot be drawn, as there are no existing published studies. At the same time, studies on the lesbian, gay, and bisexual (LGB) population show that constant confrontation with stigmatizing messages leads to internalization, which, in turn, negatively affects the health status of the person concerned [42, 43], thus indicating that gender and sexual minorities seem to be affected by similar stressors of the GMSM.

However, limitations on the validity of the GMSM should be mentioned. First, the resilience factors in general and particularly pride are limitations of the model. Pride did not significantly correlate with depressive symptoms, rejecting the model's assumptions. To our knowledge, only one other study has assessed pride in the context of stigmatization and mental health [5]. That study used the same questionnaire items to assess pride as this study and its findings aligned with the results of this current study. However, pride was handled as subscale of internalized transphobia in the previous study. So, one may ask if pride is a factor separate from internalized transphobia or if pride is the same construct (positive pole) as internalized transphobia (negative pole) and therefore not contributing significantly in explaining variance. There is some evidence in the literature for both the first [18] and second [5] interpretations. In studies on sexual minorities, pride is a well-established resilience factor [44], so it is assumed that similar mechanisms apply to transpersons. Yet, in contrast to transpersons, LGB persons are able to conceal their sexual orientation from public view, so showing pride becomes an active process that can be measured independently of sexual orientation. This situation is different for transpersons in that they do not want to (and cannot) conceal their gender identity from their environment. Therefore, gender identity and pride interact and mix with each other in such a way that objective and individual measurement of each category is more difficult. Future investigations in the GMSM field must take these concerns into account and suggest a more precise definition and measurement of resilience factors with regard to transpersons.

*4.2. Predictive Factors.* In terms of predictability of the GMSM, this study found primarily distal stressors (nonaffirmation of gender identity) and proximal stressors (internalized transphobia) to contribute to depressive symptoms. This is an interesting finding, as both factors are not related to interpersonal stigma level. While the "nonaffirmation of gender identity" items are more related to structural stigma experiences, the "internalized transphobia" questions clearly indicate a self-stigmatization of the transparticipants. This means that although the body of literature focuses on interpersonal stigmas, such as discrimination and victimization [18, 20, 25, 26], it seems that their importance is diminished in this posttransitioned population.

From a clinical perspective, the relationship between distal experiences of nonaffirmation of gender identity and long-term development of depressive symptoms are well understood. Gender dysphoric states arise from both intrinsic differences (between one's own gender identity and the sexually marked body) and extrinsic differences (between mentally experienced and socially committed sex) [45]. By means of medical transition and initiation of the first GAI (e.g., hormonal treatment and gender affirming surgeries), transindividuals initially primarily contribute to the reduction of the intrinsic, and occasionally of the extrinsic, gender dysphoric source. Currently, there has been very little discussion on how these steps contribute to improving mental health and quality of life of transpersons [46].

However, in cases where there is no reduction of extrinsic suffering, gender nonaffirmation of the person concerned acquires a special meaning. It has been argued that for a "successful" affirmation of gender identity, the perception of one-self and of other persons' perception of that person needs to be congruent [47]. If this congruence is undermined, the nonaffirmation of their own gender identity can have long-term detrimental effects on a transperson's well-being. Due to the pressure to conform to a binary gender system, it is not surprising that some posttransitioned transpersons are satisfied after their first medical transition steps and seek further GAI such as facial feminization. According to our data, this dynamic is particularly evident in nonbinary transpersons. The mix of pronounced binary stigma and lack of suitable GAI is strongly related to the high level of depression in this population.

Furthermore, the relationship between internalized transphobia and depressive symptoms found in this study fits well into the existing knowledge body of the GMSM [5, 18, 21, 41]. Once again, it is important to note that the positive effects of GAI do not appear to affect all subsequent problems of stigmatization to the same extent. Therefore, it is important that individuals who exhibit a high degree of self-stigmatization do not exclusively perform somatic treatments to minimize their gender dysphoric symptoms. In order to strengthen their own transidentity, these individuals should be in contact with transcommunity-based care and psychotherapeutic services [48, 49].

In addition to all of the stigma-related factors, the control variable occupational status (with the category "unemployed") also reached predictive significance. The association between unemployment and depressive symptoms is well established in other populations as well [37]. In this sense, the investigated Swiss transpopulation, which has an unemployment rate four times higher than the general population [50], seems to confirm this negative correlation.

*4.3. Moderating/Mediating Effects of Stigma.* Findings suggesting the occurrence of a moderated mediation for the GMSM are partially supported. For distal and proximal stressors, there was a mediation of proximal stressors between distal stressors and depressive symptoms. This study partly confirms the few previous studies examining the mediating

effects of gender minority stressors. In a study by Breslow et al. [21], internalized transphobia did not significantly mediate, but they assessed a construct called stigma awareness (consisting of negative expectations and nondisclosure) that did mediate the relationship between distal stressors and depressive symptoms. Since we did not distinguish between individual proximal stressors to assess the mediation, we cannot say how the different proximal stressors contributed to the mediating effect. Our hierarchical linear regression analysis indicated that internalized transphobia may be the most important proximal stressor.

However, the resilience factors failed to confirm the model's assumed moderation of the relationship between distal and proximal stressors and depressive symptoms (there were no significant interactions). This raised the question of what were the resilience factors influencing, since they explained only 1% of the variance. Based on previous studies that have assessed community connectedness, it is clear that the assumed relevance of resilience factors is usually not confirmed [19, 27] and the validity of using community connectedness as a resilience factor should be further examined. Using community connectedness as a resilience factor can have a protective effect on some transpersons [28, 29], whereas it has a pejorative effect on other groups [21], suggesting that other mechanisms are involved with this resilience factor. Similar to handling issues with assessing the effects of pride as mentioned above, future studies should use a more appropriate operationalization of the "community connectedness" concept.

*4.4. Strengths and Limitations.* A substantial limitation of this study is the cross-sectional design, which only allows us to draw correlational, not causative, conclusions. In light of a better understanding of the GMSM, future studies should address this limitation by considering a longitudinal study design. Another aspect to consider is that study participants were asked to concentrate on a questionnaire for 45 minutes. This aspect could have jeopardized the generalizability of the study, as transpersons with severe mental health problems may not have had the cognitive ability to concentrate for that amount of time and were therefore underrepresented. The last limitation concerns two issues with operationalization. Firstly, for this study, mental health was only assessed through self-assessment of depressive symptoms. Even though we used a validated instrument, it only serves as screening test, so a prevalence estimate of depressive disorders could not be calculated. Secondly, the gender-related discrimination, rejection, and victimization scales were retrospectively answered (before age of 18, after age of 18, and in the last year). Since it has been suggested that recent events of interpersonal stigmatization are more likely to affect a transperson's mental health [25], the operationalization of these scales may not be accurate and should be changed.

Despite the limitations, the major strength of this study was that it approached the GMSM systematically with all proposed stressors and resilience factors. Furthermore, this is the first report to record the long-term stigmatization experiences of a considerable number of nonbinary transpersons in Central Europe.

## 5. Conclusions

In summary, the GMSM provides a heuristic approach when examining the impact of stigmatization on the mental health of transpersons. However, the proposed resilience factors should be revised, as they do not exhibit a consistent moderating effect. Future studies working on GMSM should improve the operationalization and, consequently, the measurement of resilience factors. From a clinical perspective, the history of experiences with stigmatization should be given high priority when in contact with transitioned transpersons. It is also important to note that structural and self-stigmatization episodes frequently occur in this group. In cases where these stigmatization experiences are the basis for the initiation of further GAI measures, especially transpersons exhibiting a high degree of self-stigmatization, transpersons should be supported by a community-based services or psychotherapy.

## Conflicts of Interest

The authors declare that they have no conflicts of interest.

## Authors' Contributions

Tiziana Jäggi and Lena Jellestad contributed equally to this work.

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*Research Article*

# Quality of Life in Transitioned Trans Persons: A Retrospective Cross-Sectional Cohort Study

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*Background*. Medical gender-affirming interventions (GAI) are important in the transition process of many trans persons. The aim of this study was to examine the associations between GAI and quality of life (QoL) of transitioned trans individuals. *Methods*. 143 trans persons were recruited from a multicenter outpatient Swiss population as well as a web-based survey. The QoL was assessed using the Short Form (36) Health Survey questionnaire (SF-36). Depressive symptoms were examined using the Short Form of the Center for Epidemiologic Studies-Depression Scale (ADS-K). Multiple interferential analyses and a regression analysis were performed. *Results*. Both transfeminine and transmasculine individuals reported a lower QoL compared to the general population. Within the trans group, nonbinary individuals showed the lowest QoL scores and significantly more depressive symptoms. A detailed analysis identified sociodemographic and transition-specific influencing factors. *Conclusions*. Medical GAI are associated with better mental wellbeing but even after successful medical transition, trans people remain a population at risk for low QoL and mental health, and the nonbinary group shows the greatest vulnerability.

## 1. Introduction

Gender incongruence (GI) is a condition in which the gender identity or gender expression of a person is discordant with their assigned sex characteristics. GI is often accompanied by clinically relevant psychological distress, then called gender dysphoria (GD) [1]. Individuals with a GI are usually referred to as trans persons. This umbrella term covers persons whose gender identity is the opposite of their assigned sex (transmen and transwomen). It also includes persons who place themselves between or outside the binary gender categories (nonbinary persons).

GD can present with a strong rejection of the anatomical characteristics—primarily the sexual features [1]. Furthermore, because of the ubiquitous social stigma that trans persons experience [2], GD can lead to negative self-image and mental health problems [3–5]. In particular, many trans individuals experience depressive episodes during their lifetime, which in the worst case are associated with suicidal behavior [3]. To overcome this feeling of GD, many trans persons seek medical help and undergo gender-affirming interventions (GAI) (e.g., sex hormonal treatment or gender-affirming surgery). Nowadays, it is generally accepted that both hormonal and surgical interventions can alleviate GD [6–8].

Previous evidence on the negative psychological and QoL effects of GAI is rare and is based on older studies [9, 10]. In contrast, the positive effects on psychological wellbeing and QoL in trans persons have been reported more frequently [7, 8, 11–17]. Several studies have shown that a medical transition can positively impact the social status of treated trans persons [18]. However, it is also known that various psychosocial factors such as old age [7], unemployment [7, 19], being single [7, 20], having a low level of education [7], and depressive disorders [12] can negatively influence QoL. Many GAI require long-term care and follow-up, which can have a negative impact on wellbeing [21]. Consequently, the QoL of transitioned trans persons remains low compared to the general population [16, 22].

The literature is unclear regarding potential gender differences within the trans population. While some authors found no considerable differences in QoL scores between transwomen and transmen [12, 23], others noted significant divergences. For example, Parola et al. reported that transwomen have a better QoL in different mental and physical domains than transmen [14]. In contrast, Motmans et al. [7] found lower QoL scores in transwomen compared to transmen. Similar conflicting evidence is found in studies on mental health comparisons between trans persons. While some studies demonstrated worse mental health in transwomen [24], others found no gender-related differences [25].

Furthermore, this previous outcome research mainly used binary assumptions about gender identities and focused on either transfeminine or transmasculine individuals. There is little research on gender nonbinary persons [26]. This situation is caused by many factors but is particularly related to the theoretical and methodological issues of earlier study designs [27]. However, this unique subpopulation of trans persons seems to be especially prone to stigmatization [2], poor self-rated health [28], and high rates of affective disorders [29].

Therefore, the aim of this present study was to examine the associations between GAI and QoL in transitioned trans individuals. In particular, we investigated potential psychological and social factors that could influence the wellbeing of trans persons. We emphasized a broader gender spectrum by including gender nonbinary persons. For the first time, this provides a simultaneous comparison between different transitioned trans subgroups in terms of QoL.

## 2. Methods

We performed a retrospective cross-sectional multicenter study on persons self-identified as being trans. The study was performed in collaboration with the Department of Plastic, Reconstructive, Aesthetic, and Hand Surgery at Basel University Hospital, the Department of Psychiatry and Psychotherapy of the University Hospital Zurich, the Department of Psychiatry and Psychotherapy of the University Hospital Bern, and the Psychiatric Services Hospitals of the Canton of Solothurn.

*2.1. Sample.* We applied two ways of recruitment. Trans persons who had formerly presented to the outpatient clinic of the collaborating hospitals were invited by post to participate in the study and could choose between a paper-based form and a web-based survey. To maximize the number of participants, recruiting was expanded to the larger Swiss trans community via advocacy groups. These participants could only use the web-based survey. Data was collected anonymously in both ways of recruitment. The inclusion criteria included a minimum age of 18 years, a good command of the German language, and self-identification of being transitioned, that is, participants defining their medical transition to be completed independent of the extent of medical affirming interventions performed. Here, we defined the latter by the absence of psychiatric treatment associated with gender dysphoria, a minimum of one year of hormonal treatment, and no planned surgical intervention for the upcoming year. The exclusion criterion was an unfinished medical transitioning process. The study was approved by the Ethics Committee of Basel.

### 2.2. Measurements

*2.2.1. Quality of Life.* The Short Form (36) Health Survey questionnaire (SF-36) is a widely used self-reported questionnaire on QoL and health status which assesses four mental domains of health (vitality, social functioning, emotional role functioning, and mental wellbeing) and four physical domains of health (physical functioning, physical role functioning, bodily pain, and general health). The two global measures can be derived from all physical and all mental domains, respectively, and are referred to as the physical component summary (PCS) and the mental component summary (MCS). Answers were transformed via a standardized measure according to the predefined scoring algorithm to yield a total score ranging from zero to 100; higher values indicate a higher subjective quality of life. Cronbach's alpha is an indicator of internal consistency and yielded a high score of .87.

In addition to group comparisons, we performed a *t*-test group comparison of the mean scores of transfeminine and transmasculine individuals with mean scores of men and women in the German general population. The SF-36 German general population data were taken from the 1995 German population survey [30]. No standard values exist for nonbinary individuals.

*2.2.2. Depressive Symptoms.* The Allgemeine Depressionsskala (ADS-K) is a validated German short form adaptation of the Center for Epidemiologic Studies Depressions Scale (CES-D), a screening instrument for depressive symptoms [31, 32]. It covers 15 items on affective, motivational, psychosocial, somatic, and cognitive symptoms. The total score ranges from zero to 45, with higher values indicating more severe depressive symptoms. A score $\geq 18$ is the cut-off for clinically relevant depressive disorders [33]. For reliability analysis, Cronbach's alpha was calculated to assess the internal consistency of the ADS-K questionnaire in our sample. With a Cronbach's alpha value of .85, the internal consistency of the questionnaire is high and comparable with the reported value of $\alpha = .88–.95$ in the ADS-K manual [31].

Table 1: Sociodemographic characteristics. [a]One-way ANOVA. [b]Chi-square test.

| | Transfeminine | Transmasculine | Nonbinary | $p$ |
|---|---|---|---|---|
| Age (M (SD)) | 51.51 (17.06) | 35.95 (12.79) | 42.16 (24.41) | <0.01[a] |
| Level of education ($n$ (%)) | | | | |
| Primary school | 3 (3.9%) | 0 | 0 | |
| Secondary school | 3 (3.9%) | 4 (10%) | 2 (8%) | |
| Apprenticeship | 28 (36.8%) | 15 (37.5%) | 3 (12%) | 0.06[b] |
| A-levels | 9 (11.8%) | 7 (17.5%) | 8 (32%) | |
| University/technical college | 33 (43.4%) | 12 (30%) | 11 (44%) | |
| Other | 0 | 2 (5%) | 1 (4%) | |
| Relationship status ($n$ (%)) | | | | |
| Single | 41 (53.9%) | 17 (42.5%) | 11 (44%) | |
| In a relationship | 33 (43.4%) | 23 (57.5%) | 7 (28%) | <0.01[b] |
| Other | 2 (2.6%) | 0 | 7 (28%) | |
| Work situation ($n$ (%)) | | | | |
| Self-employed | 15 (19.7%) | 5 (12.2%) | 4 (16.7%) | |
| Employed | 27 (35.5%) | 25 (61%) | 6 (25%) | 0.07[b] |
| Unemployed | 15 (19.7%) | 3 (7.3%) | 5 (20.8%) | |
| Other | 19 (25%) | 8 (19.5%) | 9 (37.5%) | |
| Housing situation ($n$ (%)) | | | | |
| With family | 13 (17.1%) | 9 (22%) | 3 (12%) | |
| With friends/shared flat | 7 (9.2%) | 3 (7.3%) | 7 (28%) | |
| With partner | 22 (28.9%) | 13 (31.7%) | 2 (8%) | 0.1[b] |
| Alone | 31 (40.8) | 15 (36.6%) | 13 (52%) | |
| Other | 3 (3.9%) | 1 (2.4%) | 0 | |

*2.2.3. Sociodemographic Characteristics.* The sociodemographic survey was thematically divided into three categories: general, trans-specific, and transition-specific. In the general part, participants self-reported their age, current housing situation, relationship status, level of education, and current work situation. The trans-specific variables included gender assigned at birth and preferred gender label. The transition-specific variables included prior hormonal and surgical affirming interventions.

*2.3. Data Analysis.* We used SPSS version 22.0 for all statistical analysis. Frequency distributions were analyzed using chi-square tests. A set of $t$-tests and one-way ANOVA tests were calculated to compare the mean scores between gender groups. We performed multiple multivariate regression analyses to identify predictor variables to QoL. We considered two-tailed $p$ values $< 0.05$ to be significant.

## 3. Results

*3.1. Sample.* We contacted 373 individuals from outpatient clinics via a written form and asked them to participate in the study; 66 completed questionnaires were returned (response rate of 18.0%). There were 201 web participants, of whom 77 individuals completed it. There was an inclusion rate of 38%. In total, 143 individuals completed the questionnaire and were included. In this study, we defined a transfeminine person as an individual self-identified as female with a male sex assigned at birth and a transmasculine person as an individual self-identified as male with a female sex assigned at birth; a gender nonbinary person is an individual self-identified in-between male and female gender or self-identified as no gender, independent of the assigned sex at birth. The majority of our sample was transfeminine ($n = 77$; 53.8%) followed by transmasculine ($n = 41$; 28.7%) and nonbinary gender ($n = 25$; 17.5%). Within the group of nonbinary individuals, 7 persons (28%) had a male sex assigned at birth and 17 persons (68%) had a female sex assigned at birth. One person stated to have an "other" sex assigned at birth.

*3.2. Sociodemographic Characteristics.* Participants' age ranged from 18 to 75 years (Table 1). Transfeminine individuals were older than transmasculine individuals and nonbinary individuals; the difference between transfeminine and transmasculine individuals was significant ($p < 0.01$). There was no significant difference in the level of education, relationship status, work, and housing situation between groups. Post hoc test of the variable relationship status provided no significant differences between groups (data not shown).

*3.3. Transition-Specific Characteristics.* Compared to transmasculine individuals, transfeminine individuals were significantly ($p < 0.01$) older at coming out and proceeded

Table 2: Transition-specific data. [a]One-way ANOVA.

| | Transfeminine ($n$ = 77) | Transmasculine ($n$ = 41) | Nonbinary ($n$ = 25) | $p$ |
|---|---|---|---|---|
| Age at coming out (M (SD)) | 34.8 (14.66) | 22.73 (22.32) | 28.04 (10.88) | <0.01[a] |
| First steps in transition (M (SD)) | 35.12 (14.23) | 27.12 (10.31) | 27.62 (10.91) | <0.01[a] |
| Current hormone therapy ($n$) | 63 | 41 | 12 | |
| Hormone therapy in years ($n$) | | | | |
| 0–5 | 22 | 17 | 6 | |
| 6–10 | 4 | 4 | 1 | |
| 11–20 | 8 | 1 | 1 | |
| >20 | 6 | 2 | 0 | |
| Overall gender-affirming surgery ($n$) | 65 | 39 | 10 | |
| Mammoplasty ($n$) | 45 | 38 | 10 | |
| Genital reconstruction ($n$) | 50 | 12 | 1 | |

Table 3: Mean scores (M (SD)) of SF-36 domains and global measures and group comparison by one-way ANOVA.

| | Transfeminine | Transmasculine | Nonbinary | $p$ |
|---|---|---|---|---|
| Physical | | | | |
| Physical functioning | 88.16 (21.52) | 94.27 (9.46) | 91.25 (9.47) | 0.1 |
| Physical role | 81.91 (32.81) | 92.31 (20.0) | 76.0 (37.14) | 0.04 |
| Bodily pain | 80.57 (27.06) | 82.66 (23.06) | 74.16 (27.8) | 0.45 |
| General health | 74.13 (22.73) | 72.58 (20.09) | 53.36 (26.75) | <0.01 |
| Mental | | | | |
| Vitality | 56.76 (24.47) | 59.87 (17.88) | 40.2 (20.23) | <0.01 |
| Social functioning | 77.17 (27.3) | 79.69 (28.0) | 65.0 (31.66) | 0.16 |
| Mental health | 72.72 (22.78) | 72.11 (19.93) | 52.5 (21.44) | <0.01 |
| Emotional role | 75.32 (37.62) | 89.47 (25.83) | 46.67 (45.13) | <0.01 |
| Component summary | | | | |
| Physical (PCS) | 53.05 (8.44) | 53.76 (5.88) | 53.75 (7.9) | 0.87 |
| Mental (MCS) | 46.37 (12.48) | 49.8 (10.25) | 35.18 (14.13) | <0.01 |

faster into the transition process (transmasculine individuals after 4.39 years versus transfeminine individuals after 0.32 years) (Table 2). On one hand, nonbinary individuals showed distinctly different traits representing a population "in-between" transfeminine and transmasculine individuals concerning distribution of age at coming out and first steps into transition. On the other hand, by making the first steps of medical transition before actually coming out, the nonbinary group significantly differed from the binary trans people. The same dichotomous pattern between binary and nonbinary trans persons was also found in current hormone treatment and the overall demand for gender-affirming surgical interventions. Within the binary group, an analysis of the surgical interventions performed showed gender-specific patterns. While mastectomy was very common (92.6%) and phalloplasty was less used (29.2%) in men, breast augmentation (58.4%) and vaginoplasty (64.9%) were reported in a more similar frequency in women.

*3.4. ADS-K.* Gender had a significant effect on ADS-K scores between groups ($F = 5.98$; $p \leq 0.01$). Post hoc tests demonstrate that gender nonbinary individuals rated significantly higher (M (SD): 18.04 (10.17)) compared to transfeminine (M (SD): 10.76 (7.80)) and transmasculine (M (SD): 12.59 (10.16)) individuals. This suggests higher affective distress in this population. The difference between transfeminine and transmasculine individuals was statistically nonsignificant.

*3.5. SF-36.* Transfeminine individuals scored worse than transmasculine individuals did in both the somatic and mental domains (Table 3), except in the domains general health and mental health. However, these differences were not significant. Nonbinary individuals performed worse than the other two groups in seven out of eight domains with significant results in the domains physical role, general health, vitality, mental health, and emotional role. In addition, the mental component summary (MCS) score of the nonbinary persons was significantly lower than that in the other groups.

In comparison to the German general population, both transfeminine and transmasculine individuals scored lower in the mental component summary score (MCS) of the SF-36 (Table 4). In transfeminine individuals, the mental domains social functioning, emotional role, and the MCS showed significantly reduced values compared to the general female population. Transmasculine individuals rated the mental domains vitality and social functioning significantly lower than the general male population.

Table 4: $t$-test comparison of mean scores (M (SD)) of SF-36 domains between groups and the general German population.

| | Transfeminine | Cis women | $p$ | Transmasculine | Cis men | $p$ |
|---|---|---|---|---|---|---|
| Physical | | | | | | |
| Physical functioning | 88.16 (21.52) | 82.71 (23.17) | 0.03 | 94.27 (9.46) | 89 (20.15) | <0.01 |
| Physical role | 81.91 (32.81) | 80.41 (33.02) | 0.69 | 92.31 (20.0) | 87.3 (29.62) | 0.13 |
| Bodily pain | 80.57 (27.06) | 75.99 (27.68) | 0.14 | 82.66 (23.06) | 82.47 (26.56) | 0.96 |
| General health | 74.13 (22.73) | 66.64 (19.67) | 0.01 | 72.58 (20.09) | 69.59 (20.63) | 0.35 |
| Mental | | | | | | |
| Vitality | 56.76 (24.47) | 60.62 (18.47) | 0.18 | 59.87 (17.88) | 66.17 (18.01) | 0.04 |
| Social functioning | 77.17 (27.3) | 87.02 (18.92) | <0.01 | 79.69 (28.0) | 90.67 (17.51) | 0.02 |
| Mental health | 72.72 (22.78) | 71.44 (16.29) | 0.65 | 72.11 (19.93) | 76.55 (16.06) | 0.18 |
| Emotional role | 75.32 (37.62) | 88.77 (26.34) | <0.01 | 89.47 (25.83) | 92.06 (24.58) | 0.54 |
| Component summary | | | | | | |
| Physical (PCS) | 53.05 (8.44) | 49.09 (10.6) | <0.01 | 53.76 (5.88) | 51.42 (9.62) | 0.03 |
| Mental (MCS) | 46.37 (12.48) | 50.71 (8.39) | 0.01 | 49.8 (10.25) | 52.44 (7.7) | 0.15 |

The physical component summary scores were significantly higher in both trans groups compared to the general population. Within all the physical domains, QoL was rated higher compared to the general population in both transfeminine and transmasculine individuals. Among these, scores in the domain physical functioning were significant in both transfeminine and transmasculine individuals compared to the general population. Transfeminine individuals also rated general health significantly higher than the general population.

*3.6. Interferential Analysis.* Factors that have a significant negative influence on quality of life in the global measures include young age, having an "other" relationship status (different from being in a relationship and being single), being unemployed, and having an "other" work situation (different from being employed or unemployed) (Table 5).

Medical transition measures such as hormone therapy and gender-confirmation surgery have strong implications on the mental wellbeing and self-rated quality of life depicted by significantly reduced MCS values (Table 6).

*3.7. Multiple Regression Analysis.* A block-wise multiple regression analysis was performed to estimate the relationships between MCS and gender, medical affirming interventions, work situation, and relationship status (Table 7). The full model explained 20% of the variance ($R^2$ = .196, $F(8/113 = 4.68)$, and $p < 0.001$) with only gender and employment having significant regression weights. Gender contributed more to the model than employment.

## 4. Discussion

This study expanded research into the associations between gender-affirming interventions (GAI) and quality of life (QoL) of transitioned trans persons. Compared to the general population, these findings indicate poor quality of life in trans persons who had performed those medical interventions that they deemed necessary for their transition. However, not all trans persons are affected to the same extent by this situation: among trans people, the nonbinary group scored significantly worse on QoL and depressive symptoms than the transfeminine and transmasculine participants. First interferential analysis identified different sociodemographic and transition-specific influencing factors on the QoL of transitioned trans persons. Multiple regression analysis, however, failed to validate a relevant correlation between GAI and QoL. The model only confirmed a significant correlation between gender, work situation, and QoL.

*4.1. Comparison to the General Population.* To the best of our knowledge, this is the first study to evaluate QoL in both transfeminine and transmasculine individuals compared to the general population. In agreement with previous findings in transwomen [13] and transmen [7, 16, 20], the participants showed worse scores than the general population in virtually all measurement ranges of mental QoL. Of particular note is the significant difference in the social functioning domain of the SF-36, which was found in both genders. A possible explanation for this difference might be the still prevalent gender-binary model of western societies which reinforces the social stigma of trans persons [34]. These experiences of stigmatization constitute a specific so-called minority stress, which in turn affects the social functioning, the physical and mental health, and ultimately the QoL of trans persons [35].

A different picture is provided with regard to the physical dimensions of the QoL. We found a significantly increased physical component summary (PCS) score in both transfeminine and transmasculine participants compared to the general population. In addition, both groups showed a significant difference in the "physical functioning" domain. This concurs with observations that found physical-related QoL to be higher in transwomen [11, 13]. Ainsworth and Spiegel [11] suggested higher rates of chronic and acute disease in the general population as an underlying cause for this discrepancy. Following this argument, another possible explanation for this finding might be a selection bias of physically healthier individuals in our sample as most of

Table 5: Descriptive results of SF-36 global measures and sociodemographic data with group comparison of mean scores (M (SD)) by one-way ANOVA.

| | PCS | $F$ (df) | $p$ | MCS | $F$ (df) | $p$ |
|---|---|---|---|---|---|---|
| Age | | | | | | |
| 18–35 years ($n$ = 40) | 53.22 (7.41) | | | 41.17 (13.99) | | |
| 36–50 years ($n$ = 32) | 55.76 (4.74) | 2.29 (2) | 0.11 | 46.61 (13.4) | 3.02 (2) | 0.05 |
| >50 years ($n$ = 45) | 52.04 (9.17) | | | 46.61 (13.4) | | |
| Level of education | | | | | | |
| Primary school | 46.94 (15.16) | | | 43.13 (12.83) | | |
| Secondary school | 50.68 (7.27) | | | 45.90 (10.35) | | |
| Apprenticeship | 51.59 (8.98) | 1.66 (5) | 0.15 | 45.29 (13.42) | 1.14 (5) | 0.34 |
| A-levels | 54.39 (5.86) | | | 40.04 (14.75) | | |
| University/technical college | 55.14 (6.6) | | | 47.05 (12.59) | | |
| Other | 53.79 (3.32) | | | 54.39 (8.37) | | |
| Relationship status | | | | | | |
| Single | 52.63 (7.32) | | | 44.17 (14.15) | | |
| In a relationship | 53.97 (7.86) | 0.61 (2) | 0.55 | 47.82 (11.61) | 4.45 (2) | 0.01 |
| Other | 55.03 (9.6) | | | 33.15 (13.17) | | |
| Work situation | | | | | | |
| Employed | 55.5 (5.89) | | | 49.18 (11.06) | | |
| Unemployed | 49.94 (9.31) | 6.24 (2) | <0.01 | 40.92 (11.58) | 7.47 (2) | <0.01 |
| Other | 51.57 (8.24) | | | 40.12 (14.94) | | |
| Housing situation | | | | | | |
| With family | 54.05 (7.19) | | | 44.26 (10.89) | | |
| With friends/shared flat | 55.45 (3.77) | | | 39.37 (17.05) | | |
| With partner | 54.89 (7.1) | 1.67 (4) | 0.16 | 49.64 (10.73) | 2.23 (4) | 0.07 |
| Alone | 51.29 (8.83) | | | 44.01 (13.71) | | |
| Other | 57.6 | | | 59.88 | | |

Table 6: Descriptive results of SF-36 global measures and transition-specific datawith $t$-test comparison of mean scores (M (SD)).

| | PCS | $p$ | MCS | $p$ |
|---|---|---|---|---|
| Current hormone therapy | | | | |
| Yes | 54.03 (6.43) | 0.19 | 46.76 (11.89) | 0.04 |
| No | 50.94 (11.2) | | 39.39 (16.04) | |
| Overall gender-affirming surgery | | | | |
| Yes | 53.83 (6.69) | 0.59 | 46.81 (12.02) | 0.01 |
| No | 52.67 (10.24) | | 39.76 (15.33) | |

Table 7: Block-wise multiple regression analysis displaying the predictive value of transition-specific and sociodemographic factors on mental quality of life.

| Block | Predictor | MCS | | | |
|---|---|---|---|---|---|
| | | $\beta$ | $p$ | Corrected $R^2$ | $R^2$ change |
| 1 | Transfeminine | .373 | .005 | .144 | .158 |
| | Transmasculine | .390 | .005 | | |
| 2 | Overall gender-affirming surgery | .026 | .814 | .139 | .002 |
| 3 | Hormonal therapy | .029 | .786 | .135 | .003 |
| 4 | In a partnership | .091 | .600 | .135 | .014 |
| | Single | .030 | .860 | | |
| 5 | Employment | .299 | .003 | .196 | .071 |
| | Unemployment | .038 | .701 | | |

the participants underwent surgical GAI, which are generally only amenable to largely physically healthy patients. Other studies, however, described no statistically significant differences in physical functioning compared to the general population [7, 16, 20].

*4.2. Comparison between Transfeminine and Transmasculine Persons.* In line with the findings of Auer et al. [23] and Gorin-Lazard et al. [12, 36], we found no significant differences in QoL between transfeminine and transmasculine persons. However, this contrasts with previous observations showing physical functioning and general health domains to be better in transmen than in transwomen and bodily pain to be better in transwomen than in transmen [7]. The

latter result coincides with the clinical experience that masculinizing surgical procedures in the genital region are more complex to perform, are associated with more complications, and cause more discomfort. The fact that in our sample much less transmasculine than transfeminine persons have undergone a genital-confirming operation suggests that some transmen have decided against carrying out a phalloplasty in order not to endanger their own QoL. In this sense, the small number (12 cases) could have contributed to minimizing this gender-specific difference.

At the same time, there are studies (e.g., Parola et al. [14]) suggesting that the transmasculine population has better social functioning and mental health than the transfeminine population. In literature, this difference is attributed to the different ways in which society deals with transwomen and transmen. While transwomen must perform a good, if not perfect, (cis) passing, society gives transmen more freedom in this regard [37]. The fact that we have not established this gender difference cannot be explained with complete certainty. Nevertheless, it can be assumed that some of the transient transwomen develop mechanisms over time such that these stigmatizing situations do not affect their QoL.

*4.3. Nonbinary Trans Persons.* Our results show considerably different characteristics within the group of trans participants. While we did not detect significant differences in the QoL between transfeminine and transmasculine participants, persons with a nonbinary gender identity presented the lowest rates of wellbeing. They showed significantly worse values in five of eight QoL domains as well as in the mental component summary (MCS) compared to both binary groups. Moreover, a nonbinary gender identity was associated with significantly more depressive symptoms compared to the transfeminine and transmasculine groups.

The reasons for these clear group differences should be determined on different levels. First, nonbinary persons reported specific needs regarding medical GAI. Thus, approximately half of this group decided not to seek medical treatment. This diversity in terms of the GAI undertaken has been confirmed by other studies [38]. The comparatively worse QoL of the nonbinary participants could therefore be related to the lack of a standardized treatment and accordingly suitable GAI, which cover the specific needs of this group [39]. Second, the nonbinary group most clearly questions the binary gender norm that exists in western societies. As a result, nonbinary individuals are more likely to be confronted with stigmatization experiences, which can lead to higher minority stress levels [26] and increased self-reported disability [28]. This in turn has a negative impact on mental health [28] and especially the emergence of clinically relevant depressive [2] and anxiety disorders [29], which ultimately affects QoL.

*4.4. Influencing and Predictive Factors.* The one-way ANOVA and the $t$-test comparisons show significant associations between participants' mental QoL and certain sociodemographic factors (age, work situation, and relationship status) and GAI factors (hormone treatment and surgical measures). These findings support the investigations of Motmans et al. [7] who revealed the influence of these sociodemographic factors on QoL in female and male trans persons. Beyond that, an association between these sociodemographic factors and QoL was also outlined among the general population [40]. With regard to GAI and QoL, the positive relationship is well documented [11–14].

However, surprisingly, none of these variables had a relevant predictive impact on the mental QoL in our model. Only the categories gender and work situation had significant regression weights, but these could only explain a small fraction of the MCS variance. But neither the hormonal nor the surgical obtained any predictive significance regarding QoL. This result is, on one hand, in accordance with the findings of Gómez-Gil et al. [19] who found employment to be a (minor) predictive factor of QoL. On the other hand, this contrasts with previous work by Motmans et al. [7] who identified not only gender but also age and relationship status as influencing factors.

The reasons for these disparate observations are complex and difficult to determine. In principle, they can be related to definition, methodological, and conceptual issues. Due to the multiple changes that the trans phenomenon has undergone over time [1, 41, 42], the inclusion criteria of the respective trans populations in various studies differ greatly [13, 14, 16, 28]. This is particularly evident in the visibility of nonbinary trans persons, where the explicit coupling of inclusion and ICD-10 transsexualism definition criteria leads to automatic exclusion. In addition, many previous studies have examined trans persons regardless of their transition stage. Accordingly, a transparent comparison of the results is impossible due to these differences in definitions. The absence of a significant correlation of GAI and QoL in our model might stem from the biased narrowing of our sample. Given that being in an initial phase of transition [43] or not yet having begun planned medical GAI [44] is associated with worse mental health, the decision to include only trans persons who were actually able to carry out the interventions they wished could have led to loosening of the link between mental QoL and GAI. Furthermore, it might be that the SF-36 questionnaire does not sufficiently display the QoL concerns of trans persons. Even if it is a widely used and validated instrument on QoL [7, 11–14, 20], the SF-36 questionnaire might focus too much on irrelevant aspects of this population's wellbeing.

These difficulties raise the conceptual question: which factors actually impact the QoL of transitioned trans persons? Our results indicate that the wellbeing of trans individuals must depend on factors other than GAI. Thus, while medical interventions are crucial to the transition of trans persons, they do not define the endpoint of stabilizing QoL [45]. Here, stigmatization and its resulting gender minority stress [35] might play an essential role as further influencing factors. This is in accordance with Başar et al. [46] who claimed perceived personal discrimination to predict QoL and Bockting et al. [47] who found social stigma to be positively associated with psychological distress. In this sense, the future exploration of QoL of trans persons should consider not only the impact of medical measures but also the psychosocial consequences of the minority position of trans persons.

*4.5. Limitations and Strengths.* Our data cannot be generalized to the entire trans population. Due to our study design, only trans persons who have undergone a medical transition participated in this study. Thus, the findings cannot be applied to trans persons who decline the use of GAI. Likewise, trans persons who have not yet started a medical transition or are currently in the process of such measure were excluded. Therefore, our data does not allow any statements regarding this group of trans persons. At the same time, our inclusion criteria led to homogenization of the group, which was clearly missing in some previous studies.

A further limitation of our study is the missing information on the participants' current level of gender dysphoria. This could be an important predictive factor for the QoL of trans persons. Concurrently, the trans people enrolled here defined their medical transition as "completed." In this sense, we can assume that no trans person who participated hoped to improve their QoL by initiating further medical measures. In addition, the cross-sectional design of this study does not allow further comparison of the QoL before the medical transition of the participants. Accordingly, no statements can be made as to whether the GAI changed the QoL of the trans persons or not. However, this study design allowed for many trans persons to be made aware of the ongoing investigation. By using two ways of recruitment and cooperating with trans organizations, we executed one of the largest surveys of trans persons in Central Europe.

## 5. Conclusions

The results emphasize that trans individuals are at greater risk of decreased QoL and increased mental health problems than the general population. We provide evidence that gender nonbinary individuals comprise a particularly vulnerable group within the trans population and have worse mental health and, for the first time, we could identify limited QoL in this group. Therefore, somatic as well as psychosocial QoL aspects should be addressed in the medical consultation and education of trans persons. Particularly important are measures that allow the nonbinary persons to identify themselves as such and to report on their specific situation.

Finally, our data show that medical GAI are a key factor in transition and are associated with better mental wellbeing. Yet, taking into account the fact that we did not find significant correlations between GAI and QoL in our sample of transitioned trans people, future research should seek to adapt the QoL concept to the specific needs of this population. In particular, the impact of other potential influencing factors such as stigma should be investigated.

## Conflicts of Interest

The authors declare that they have no conflicts of interest.

## Authors' Contributions

Lena Jellestad and Tiziana Jäggi share equal contribution.

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*Research Article*

# Spermatogenesis Abnormalities following Hormonal Therapy in Transwomen

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*Objective*. To measure spermatogenesis abnormalities in transwomen at the time of sex reassignment surgery (SRS) and to analyze the association between hormonal therapy duration and infertility severity. *Design*. Retrospective study. *Setting*. University hospital. *Patients*. One-hundred seventy-three transwomen who underwent SRS from January 2000 to December 2015. *Interventions*. All orchidectomy specimens were retrospectively reviewed and classified. History of hormonal therapy duration was retrieved from medical records. *Main Outcome Measures*. Histological examinations of orchidectomy specimens were performed to assess spermatogenesis. *Results*. One-hundred seventy-three orchidectomy specimens were evaluated. Histological examinations showed maturation arrest in 36.4%, hypospermatogenesis in 26%, Sertoli cell-only syndrome in 20.2%, normal spermatogenesis in 11%, and seminiferous tubule hyalinization in 6.4% of the specimens. Spermatogenesis abnormality severity was not associated with the total therapy duration ($P = 0.81$) or patient age at the time of surgery ($P = 0.88$). Testicular volumes and sizes were associated with spermatogenesis abnormality severity ($P = 0.001$ and $P = 0.026$, right testicle and left testicle, resp.). *Conclusion(s)*. Feminizing hormonal treatment leads to reductions in testicular germ cell levels. All transwomen should be warned about this consequence, and gamete preservation should be offered before starting hormonal treatment.

## 1. Introduction

The therapeutic approach to gender dysphoria consists of many treatment options, including psychological support and hormonal and surgical treatments [1]. The goal of hormonal therapy is to suppress endogenous hormone levels and to replace exogenous sex hormone levels with those of the desired gender. Using hormonal therapy may lead to adverse effects such as venous thromboembolism, hypertriglyceridemia, weight gain, and gallstones [2]. Therefore, hormonal therapy should be administered under the care of qualified health professionals such as endocrinologists. For the best possible care, information regarding irreversible physical changes should be provided before the initiation of treatment [1]. Studies have shown that almost all Thai transsexuals self-medicate with hormonal therapy that includes hormones that are usually bought directly from the pharmacy without any prescription; therefore, transwomen are not warned about the loss of reproductive function [3, 4].

The objectives of this study were to identify spermatogenesis abnormalities in transwomen at the time of sex reassignment surgery (SRS) and to analyze the association between the level of infertility and duration of hormonal therapy.

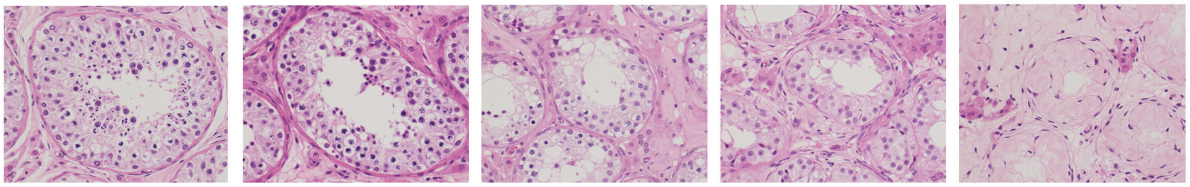


Figure 1: Classification of human spermatogenesis.

## 2. Materials and Methods

This study was approved by the Committee of Research Affairs, Faculty of Medicine, Chulalongkorn University (project number 081/59). All orchidectomy specimens obtained during SRS at King Chulalongkorn Memorial Hospital from January 2000 until December 2015 were retrospectively reviewed by an experienced pathologist. Clinical data such as age at the time of surgery, duration of hormonal therapy, and hormonal therapy type were retrieved from the medical records. Our practice requires all patients to discontinue hormonal treatment for 4 weeks prior to surgery.

Orchidectomy specimens were examined histologically under light microscopy. Slides were evaluated for seminiferous tubules, germ cells, Sertoli cells, basement membrane thickness, and other abnormalities. Then, specimens were classified histologically as follows (Figure 1) [8]:

(i) *Normal testicular biopsy*: it is complete spermatogenesis during the entire biopsy and presence of normal intertubular tissue.

(ii) *Hypospermatogenesis*: all stages of spermatogenesis are present but reduced to a varying degree. This includes a mixed pattern with some tubules showing Sertoli cells only or hyaline sclerosis, with other tubules containing complete spermatogenesis.

(iii) *Maturation arrest*: it is complete arrest at a particular stage. This occurs most often at the spermatogonial or primary spermatocyte stage. If rare spermatids are present focally, then the lesion is classified as severe hypospermatogenesis rather than arrest.

(iv) *Sertoli cell-only*: tubules contain only Sertoli cells and there is a complete absence of germ cells.

(v) *Seminiferous tubule hyalinization*: it is thickening of the peritubular membranes due to fibrosis and basement membrane-like material and the absence of intratubular germ cells and Sertoli cells.

In some cases, right and left testicular biopsy results showed discordant patterns. Regarding the clinical implications for fertility, patients who had discordant patterns in their testicular biopsy results were classified according to the less abnormal category. The number and percentage of each spermatogenesis classification were calculated using IBM SPSS Statistics 22. Categorical variables were compared using $\chi^2$ tests. One-way analysis of variance was used to compare continuous variables among these five histological groups. Kaplan-Meier curves were used to analyze the association of the duration of hormonal therapy and histological findings.

Table 1: Spermatogenesis classification of testicular specimens.

| Classification | $n$ | % |
|---|---|---|
| Normal spermatogenesis | 19 | 11 |
| Hypospermatogenesis | 45 | 26 |
| Maturation arrest | 63 | 36.4 |
| Sertoli cell-only syndrome | 35 | 20.2 |
| Seminiferous tubule hyalinization | 11 | 6.4 |
| Total | 173 | 100 |

## 3. Results

A total of 173 transwomen underwent SRS at King Chulalongkorn Memorial Hospital between January 2000 and December 2015. The mean patient age on the day of the surgery was 26.09 ± 5.37 years. The mean testicular volume was 10.48 ± 7.46 ml in the right testicle and 9.89 ± 7.62 ml in the left testicle. The details of histopathological classification from the specimens are presented in Table 1. The most common abnormality was maturation arrest (63 patients; 36.4%). Normal spermatogenesis was found in 19 patients (11%). Three patients had discordant patterns as follows: normal and Sertoli cell-only, Sertoli cell-only and maturation arrest, and hypospermatogenesis and maturation arrest.

According to the available data, the mean duration of hormone use was 8.51 ± 4.67 years. The contraceptive pills used were Diane-35®, Sucee®, Yasmin®, Androcur®, Premarin®, and Progynova®; the contraceptive injection Progynon® was also used. Antiandrogens combined with estrogen were used for 18 patients (10.4%). Estrogen-only therapy was used for 38 patients (22%). Spironolactone and estrogen were used for one patient (0.6%). However, there were missing data regarding the types of hormones used for 57 patients (39%). The durations of hormonal treatments for each group are shown in Table 2. The mean ages between groups were not different ($P = 0.88$), and neither was the duration of hormonal exposure ($P = 0.81$). The Kaplan-Meier estimator in Figure 2 shows the duration of hormonal therapy that led to the absence of spermatozoa in testicular

Table 2: Different hormonal treatments sorted by spermatogenesis classification.

| | Normal $n = 19$ (11%) | Hypospermatogenesis $n = 45$ (26%) | Maturation arrest $n = 63$ (36.4%) | SCO $n = 35$ (20.2%) | Seminiferous tubule hyalinization $n = 11$ (6.4%) | $P$ |
|---|---|---|---|---|---|---|
| *Age* | 25.95 ± 3.98 | 26.04 ± 3.55 | 26.62 ± 6.62 | 25.49 ± 4.74 | 25.45 ± 7.76 | 0.88 |
| *Hormonal duration* | 9.40 ± 3.18 | 8.49 ± 3.99 | 8.09 ± 5.24 | 8.35 ± 3.88 | 10 ± 8.79 | 0.81 |
| *Testicular volume (ml)* | | | | | | |
| Right | 15.02 ± 2.50 | 12.14 ± 9.04 | 10.18 ± 6.07 | 7.43 ± 3.76 | 7.22 ± 3.50 | 0.001 |
| Left | 13.98 ± 10.0 | 10.38 ± 5.93 | 10.17 ± 9.06 | 7.21 ± 4.35 | 7.76 ± 5.16 | 0.026 |

SCO, Sertoli cell-only.

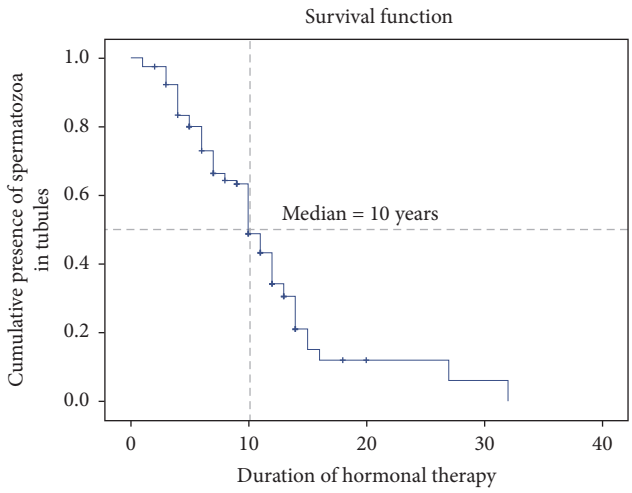


Figure 2: Kaplan-Meier curve shows the duration of hormonal therapy and the absence of spermatozoa in testicular tubules.

tubules (maturation arrest, Sertoli cell-only, and seminiferous tubule hyalinization). The mean duration was 10 years (95% confidence interval [CI], 9.03–10.97). The severity of abnormal spermatogenesis was directly associated with smaller volumes in both testes ($P = 0.001$ and $P = 0.026$).

## 4. Discussion

Although the number of scientific publications regarding the various treatments related to gender affirmation surgery is increasing, specific studies regarding spermatogenesis abnormalities following hormonal therapy in transwomen at the time of SRS are very limited, and the number of patients reported in these studies is very low [5, 6, 9, 10].

A case report of a transgender patient receiving estrogen showed a decreased amount of sperm in the semen after high-dose estrogen use for just 2 weeks [11]. Schneider et al. [6] examined the variations in spermatogenesis abnormalities in 46 testicular specimens from transwomen patients receiving the same antiandrogen and estrogen medications, as recommended by feminizing hormone guidelines, and their findings were similar to those of our study. However, in studies by Schneider et al. [6, 7], the proportion of those with normal (complete) spermatogenesis was higher than that of our study (26% versus 11%). This may be due to early hormonal exposure for Thai transwomen. When comparing the mean patient ages, we found that Thai transwomen involved in those studies who had undergone surgery were younger (26 versus 42 years). The estimated age of hormone initiation in our study was 17.59 ± 4.52 years; however, these data were lacking in the German study [7].

In the present study, morphological changes following prolonged hormonal usage were found in Leydig cells, Sertoli cells, and spermatogonia. The abnormality most commonly found was maturation arrest (36.4%), followed by hypospermatogenesis (26%) and Sertoli cell-only syndrome (20.2%). Seminiferous tubule hyalinization, which has the worst reproductive prognosis, was found in only 6.4% of patients. Eleven percent of patients had normal spermatogenesis. Our patients discontinued hormonal treatment before surgery, which may have affected spermatogenesis to some degree. Regardless, the results resembled those of the study by Schulze [9]. Table 3 compares our findings with those of similar studies. When comparing groups with spermatozoa still in the tubules (normal and hypospermatogenesis groups combined versus other groups: 37% versus 63%), the results were close to those of a study performed in Singapore (focal or normal spermatogenesis, 3 patients; absent spermatogenesis, 7 patients) [5].

Decreased testicular volume appeared to be related to the severity of the spermatogenesis abnormality (Table 2), and smaller-than-normal testes were observed in Thai males with abnormalities in the same age groups (right: 10.48 ml versus 17.2 ml; left: 9.89 ml versus 17.2 ml) [12]. This result was similar to that of the study by Schneider et al. [7] in which the testicular weight decreased with the severity of spermatogenesis and was correlated with serum testosterone level.

The 2009 guidelines for endocrine treatment of transsexual people stated variable timing of male sexual dysfunction after starting hormonal treatment [2]. Currently, the microdissection testicular sperm extraction technique (micro-TESE) can retrieve sperm at hypospermatogenesis maturation arrest and from the Sertoli cell-only group, but the success rate is low [13–17]. Therefore, we advocate informing transsexual patients before the commencement of hormonal therapy.

Table 3: Comparison of spermatogenesis abnormalities in transsexual women in various studies.

| Year | Studies | *N* | Country | Spermatogenesis | | | | |
|---|---|---|---|---|---|---|---|---|
| | | | | Normal | Hypospermatogenesis | Maturation arrest | SCO | Seminiferous tubule hyalinization |
| 1987 | Thiagaraj et al. [5] | 10 | Singapore | ⟵ 30% ⟶ | | | ⟵ 70% ⟶ | |
| 2013 | Schneider et al. [6] | 36 | German | 26% | 28% | 33% | 11% | 2% |
| 2015 | Schneider et al. [7] | 108 | German | 24.07% | 24.07% | 35.17% | 14.81% | 1.85% |
| 2017 | Current study | 173 | Thailand | 11% | 26% | 36.4% | 20.2% | 6.4% |

SCO, Sertoli cell-only.

Because our study was retrospective, all patients were from Thailand, and patients were not followed by physicians during hormonal therapy. Data regarding hormonal usage were reported by patients; therefore, they might be somewhat inaccurate. To the best of our knowledge, this study is the largest series presenting spermatogenesis in a population of transwomen undergoing SRS following hormonal usage.

## 5. Conclusion

Feminizing hormonal treatment before SRS results in spermatogenesis abnormalities and loss of reproductive function. Maturation arrest was the most common abnormality encountered in our study (36.4%). Other abnormalities were hypospermatogenesis (26%) and Sertoli cell-only syndrome (20.2%). Normal spermatogenesis was present in only 11%. All transwomen should be advised about this adverse effect. Furthermore, cryopreservation of sperm before the initiation of hormonal treatment should be offered and discussed routinely.

## Conflicts of Interest

The authors declare that there are no conflicts of interest regarding the publication of this article.

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