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# Maximizing surgical outcomes with gender affirming hormone therapy in gender affirmation surgery

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# ABSTRACT

Gender Affirmation Surgery (GAS) is a super specialized subset within the field of plastic and reconstructive surgery (PRS) that is ever evolving and of increasing interest to the PRS community. It is a multifaceted process which, in addition to surgical therapy, involves mental health therapy and hormonal therapy. One rapidly emerging interest within GAS is the role that gender affirming hormone therapy (GAHT) plays in enhancing surgical outcomes. GAHT has been used adjunctively with GAS as a comprehensive therapy to ameliorate gender dysphoria. This literature review will examine the positive effects of GAHT on the surgical outcomes on GAS, as well as other important considerations prior to surgery. As such, the primary objective of this literature review is to evaluate and assess the current evidence concerning the efficacy and safety of GAHT, as it relates to Gender Affirmation Surgery procedures.

## Introduction

Gender affirmation surgery (GAS) is a series of surgical procedures that assist gender diverse people in obtaining physical characteristics that align with their gender identity. This is crucial to treating Gender Dysphoria (ICD-10 F64.2), a condition defined by the tenth edition of the World Health Organization's International Statistical Classification of Diseases and Related Health Problems. Currently, many academic centers around the world follow the Standards of Care guidelines recommended by the World Professional Association of Transgender Health (WPATH SOC) to treat patients with gender dysphoria [1].

The most common gender affirming surgical procedures among transgender and gender non-conforming patients are facial feminization/masculinization, feminizing chest surgeries, and masculinizing chest surgeries. [2] The primary objective of gender affirmation surgery is to modify an individual's physical attributes in order to harmonize them with their affirmed or authentic gender identity. GAS includes facial, genital, and whole-body procedures as a way to create a phenotype that aligns with one's gender identity [3]. The treatment for Gender Dysphoria (GD) typically requires a multidisciplinary approach with mental, hormonal and surgical therapies that are equally important in alleviating GD and enhancing overall well-being [4]. The goal is to minimize the dysphoria with these therapies; however, all therapies may not be required to accomplish this goal.

Gender Affirming Hormone Therapy (GAHT) is an important component of GAS for transgender patients. The significance of this cannot be emphasized enough, as GAHT exhibits a crucial role in adopting a holistic approach to gender transition and optimizing overall surgical outcomes [5]. It is important to ensure a safe and effective hormone regimen that can help suppress the natural production of sex hormones based on an individual's genetic and gonadal sex, while maintaining sex hormone levels within the normal range for the person's affirmed gender [6]. GAHT has been shown to be safe and effective with concurrent GAS, with higher rates of satisfaction reported among those individuals undergoing GAS with GAHT than in those without GAHT [6].

This literature review aims to summarize the different surgical treatments for gender affirmation, the role of GAHT on the outcome of these procedures, and the treatment protocols with special considerations related to these surgeries.

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### Methods and materials

A comprehensive literature search was utilized across two major electronic databases (ClinicalTrials.gov, PubMed) to identify pertinent research papers on the benefits of hormone replacement before and after GAS for our literature review. Our search strategy is exhibited in Table 1. Keywords used were "gender affirmation surgery," "cross-sex hormone therapy," and "hormone replacement therapy." Key outcomes were benefits or drawbacks of gender affirming hormone therapy before and after GAS. The inclusion criteria consisted of research papers on Transgender Voice and Communication, Feminizing Chest surgery (Breast augmentation with or without Mastopexy), Masculinizing Chest Surgery (Bilateral Mastectomy), Penile Inversion Vaginoplasty, Transfeminine Bottom Surgeries, Colon Vaginoplasty, Orchiectomy, Transmasculine Surgeries, Metoidioplasty. Bottom Phalloplasty. Hysterectomy, Estrogen, Testosterone, and GnRH published in English. The exclusion criteria consisted of low evidence literature, experimental animal studies, and adolescents (Table 2).

# Transgender voice and Communication: GAHT guidelines and considerations for surgery

Transgender and gender non-conforming individuals should be recognized as a diverse group as it relates to subjective gender identity, desired gender expression, self-perception of gender congruency through voice, external perceptions of gender, and satisfaction levels regarding the gender-related aspects of personal vocal experiences. [7] Many of these individuals have dissatisfaction or express dysphoria with features of individual vocal circumstances, and may necessitate the assistance of trained professionals to ameliorate GD.

The impact of hormone therapy on voice is significantly more pronounced in transmasculine individuals, as opposed to those undergoing feminizing transitions, who often sustain minimal impact from their feminizing hormonal therapy. [8] Alternatively, individuals undergoing feminizing transitions rely on surgical procedures and voice therapy to address the physiological changes associated with this process, as feminine vocal attributes are infrequently observed. This can be attributed to the permanent anatomical modifications that may have already taken place in the larynx during the pubertal stage characterized by male development. [9,10] After the cessation of testosterone, there is only a small occurrence of muscle and mucosal atrophy, and there are no substantial alterations observed in the formant ranges and vocal pitch [11].

Treatment with testosterone represents the principal medical therapy for masculinizing voice therapy. The administration of androgen therapy leads to an increase in muscle mass and thickening of the pharyngeal and laryngeal tissues. This results in a natural alteration in pitch by lowering the mean fundamental frequency (MF0) of the voice to resemble the deepened voice pitch of a cisgender male. These changes usually begin within a few weeks of initiating testosterone therapy, achieving maximum results of a decreased voice pitch at around 12 months of therapy [10,11].

Androgen therapy along with behavioral modifications frequently yields an acceptable outcome in terms of developing a masculine voice, thus rarely requiring surgical intervention. [8] This is in contrast to

Table 1	
Study Search Strategy.	

PubMed	Clinicaltrials.gov
(((("gender affirmation surgery" [Title/Abstract]) OR ("hormone replacement transgender" [Title/ Abstract])) OR ("hormone replacement before and after gender affirmation surgery"[Title/Abstract] NOT (adolescents[Title])))	Conditions: "Gender reassignment surgery"
Filters: 10 years, English, Adults	Filters: Adults

## Table 2

Literature Review Inclusion and Exclusion Criteria.

Study Characteristics	Inclusion Criteria	Exclusion Criteria
Study design	Any research-based evidence	Low evidence-based studies
Population	Adult patients requesting GAS	Animals, patients without need of GAS, adolescents
Interventions	Transgender Voice and Communication, Feminizing Chest surgery (Breast augmentation with or without Mastopexy), Masculinizing Chest Surgery (Bilateral Mastectomy), Penile Inversion Vaginoplasty, MtF Bottom Surgeries, Colon Vaginoplasty, Orchiectomy, FtM Bottom Surgeries, Metoidioplasty, Phalloplasty, Hysterectomy, Estrogen, Testosterone, GnRH, FFS, Facial Masculinizing Procedures	None
Outcomes	Successful transition (gender congruence achieved)	Unsuccessful transition (gender congruence not achieved)
Language	English	Non-English

transfeminine individuals who commonly will undergo voice therapy, and occasionally feminizing voice surgery, for modification of their voice as there is minimal to no hormonal influence to induce a feminized high-pitched voice [10].

# Feminizing chest surgery (Breast augmentation with or without Mastopexy) and masculinizing chest surgery (Bilateral Mastectomy): GAHT guidelines and considerations for surgery

### The role of hormones in breast development

Breast development is a key feature in the perception of femininity and therefore an important component to feminizing transition [3]. It is not exactly known when breast development starts after initiating GAHT or how much growth may be expected, as no clinical or laboratory data were found that predict the role of GAHT on breast development [12]. GAHT in transfeminine chest surgery or augmentation with or without mastopexy, includes estrogen, either alone or in conjunction with an androgen receptor antagonist (AR antagonist) and/or progesterone. This treatment modality serves to induce breast development, facilitate the acquisition of a feminine adipose tissue body composition, and softens the skin texture [13]. Earlier studies suggested oral natural progesterone, when incorporated into the hormonal treatment of transfeminine individuals, to have additional feminizing effects, such as increased breast and areolar size [14,15,16]. The WPATH SOC acknowledges the use of progestins and micronized progesterone in transfeminine individuals. However, they emphasize a lack of evidence on beneficial effects and potential side effects, as the potential role for progesterone in breast development has not been investigated in larger randomized controlled trials [16].

Estrogen is the cornerstone of the endocrine treatment for transfeminine individuals and a key factor in the process of human breast development, as it stimulates the proliferation of breast ducts, enhances the accumulation of adipose tissue, and facilitates the creation of stromal connective tissue in the breasts. The expression of progesterone receptors is increased by estrogen, leading to the induction of prolactin [23]. Prolactin, in collaboration with progesterone, assists in stimulating the formation of breast lobuloalveolar tissue [23]. Again, the generalization of these findings to transgender women warrants scrutiny, as one must consider the modified structure of their breasts along with the intricate hormonal environment in individuals with a male sex assigned at birth undergoing estrogen therapy and/or androgen suppression, as many still produce endogenous testosterone [13].

#### Feminizing augmentation mammaplasty

The degree of breast enlargement under estrogen therapy is often limited [12]. As such, many transfeminine patients often believe that a breast augmentation will increase how they are perceived in terms of femininity [5]. The onset of breast growth with estrogen treatment has been observed to occur within a range of 3 to 6 months following the commencement of hormonal therapy. It is anticipated that the development of breasts will reach its maximum extent after approximately 2 vears, accompanied by an advancement to Tanner stage 3 [15]. Some transfeminine patients feel this does not offer enough to improve personal sexual and psychosocial well-being, which leads to a personal desire for an augmentation mammaplasty. (Figs. 1a and b) This procedure is very effective in achieving a greater improvement in gender dysphoria for these individuals. Interestingly enough, decreased patient satisfaction related to augmentation mammoplasty was observed in patients utilizing GAHT for a greater length of time, and in those with a higher body mass index (BMI) [3].

Surgical techniques for augmentation mammaplasty in transfeminine patients include the placement of breast implants, fat grafting, and autologous flap surgery. There has yet to be a formal study on the minimum amount of time GAHT should be utilized prior to performing surgical procedures on the breast, but most surgeons agree that six months of GAHT prior to breast augmentation in transfeminine patients achieves the most optimal aesthetic results [1].

Surgical considerations with augmentation mammaplasty should include discussions on complications such as scarring, infection, extrusion, and/or hematoma development. Considering these possible complications, some patients may opt to achieve their goals via hormone treatment alone [15].

#### Masculinizing top surgery

Testosterone is an important component for individuals with a



**Fig. 1a.** Preoperative view of transgender woman following 3 years of hormonal therapy and prior to undergoing bilateral breast augmentation procedure.

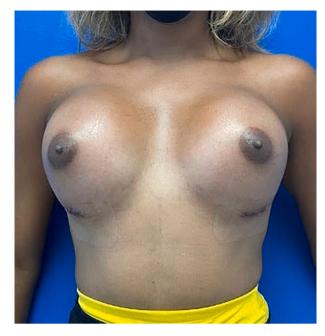


Fig. 1b. Postoperative view of transgender woman 1 year following bilateral round silicone implant placement in the subpectoral position.

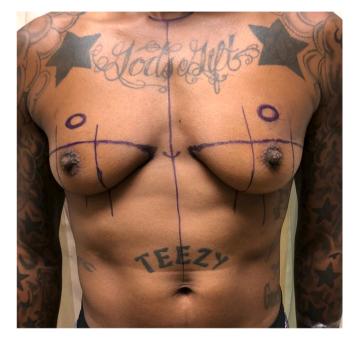
female sex assigned at birth who identify as transmasculine, and who are undergoing GAHT to achieve physiological masculinization. The targeted outcomes typically include the development of body hair (chest and abdomen), and the alteration of the muscle-fat ratio [12,17]. The administration of therapeutic amounts of testosterone has been observed to result in a reduction in breast glandular tissue and total adipose tissue, while concurrently leading to an increase in breast fibrous connective tissue, however, patients will continue to require surgical extirpation of the chest for masculinization. [17,19] Masculinizing top surgery, also known as chest masculinization surgery, is a critical component of care for patients wishing to undergo the masculinizing transition through GAS. For this subset of patients, GAHT has been shown to have very little impact on breast size [1]. Because of this, the procedure of choice for those wishing to undergo masculinizing top surgery is typically a subcutaneous mastectomy. In our literature review, we were not able to find studies showing if testosterone has a positive impact on aesthetic outcomes in these patients, but we have observed with patients in our own practice that the increased muscle growth expedited with the use of testosterone subjectively facilitates desirable aesthetic results [18,19]. (Figs. 2a and b.).

# Genital feminization Surgeries: GAHT guidelines and considerations for surgery

### Penile inversion Vaginoplasty

For the transfeminine patient, the role of pre- and post-operative GAHT is important for genital feminization surgery considerations. Many individuals first receive GAHT alone, without surgical interventions. However, this is not always sufficient to change the phenotype of the genitalia, as desired. For these transfeminine individuals, surgery may subsequently be used to support transition. Currently, there is uncertainty about the value of GAHT as a sole intervention, or when combined with surgery, for feminizing transition [21]. Anti-androgen medications like spironolactone or finasteride are commonly used to block the effects of testosterone, helping to mitigate masculinizing effects. Some considerations with anti-androgen medications include the consideration that anti-androgens may affect penile and scrotal tissue. Long-term use of anti-androgens can also result in

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**Fig. 2a.** Preoperative view of transgender man following 3 years of hormonal therapy and prior to undergoing chest masculinization.



**Fig. 3a.** Preoperative view of transgender woman after undergoing 5 years of hormonal therapy and prior to penile inversion vaginoplasty.



Fig. 2b. Postoperative view of transgender man 16 months after bilateral mastectomy with free nipple grafts.

some degree of penile and scrotal atrophy. This can be beneficial in terms of tissue availability for penile inversion vaginoplasty (PIV). (Figs. 3a and b.) However, it is essential to discuss the potential impact with the surgeon [20,24]. Although estrogen therapy is the mainstay therapy for feminization, its specific benefits on PIV are unclear. However, it does exert a certain effect on subcutaneous fat redistribution during the feminizing transition, which typically enhances the appearance of the pelvic area to a more feminine form. It also displays some benefits on skin texture [25]. Additionally, some studies have demonstrated the presence of estrogen receptors in *cis*-male genital skin through immunohistochemistry staining, suggesting that topical



Fig. 3b. Immediate postoperative view of transgender woman after penile inversion vaginoplasty.

estrogen therapy applied to the neovagina could aid in wound healing and tissue health [22]. Clinical data on the effects of estrogen therapy as it relates to the histology and microbiota of the neovagina is very limited and no specific studies on this subject were found. Therefore, the need for more research in this area is critical to understand the specific medical needs and to set additional guidelines for gender affirming medical care. This provision of inclusive healthcare will concordantly reduce the disparities experienced by transgender and gender nonconforming communities [21].

The timing of GAHT and genital feminization/masculinization surgery is also an important topic. Many surgeons recommend a minimum period of GAHT before surgery to allow for optimal tissue changes. This duration can vary but is often around 6 months [1]. Some surgeons may advise temporarily discontinuing GAHT before surgery due to potential effects on blood coagulation and the potentiation of thrombi. However, this practice can vary, and it's crucial to follow the specific guidelines provided by the surgical team. Once the patient has sufficiently recovered from surgery, GAHT can be resumed. The specific regimen may be adjusted based on postoperative considerations and the individual's overall health [30].

In summary, the coordination of GAHT and PIV involves a collaborative effort between the patient, hormone prescriber, and surgeon. The goal is to optimize both the feminizing effects of GAHT and the surgical outcomes, taking into account individual health factors and preferences. The length of hormonal therapy, a high BMI, or a history of circumcision has no impact on complications [30]. Regular communication and follow-up between the healthcare team and the patient are critical to ensuring a safe and successful gender transition process.

#### Orchiectomy

The complete suppression of testosterone production in some patients may be difficult or even impossible with standard medical therapies. In cases of persistent elevations in the setting of maximal antiandrogen dosing with good medication compliance, the option of surgically removing the testes is an alternative to achieve the desired level of feminization. Undisclosed exogenous testosterone (i.e. to maintain erectile function), as well as autologous endogenous production (i.e. tumor) should be considered prior to surgery [38]. An evaluation to rule out testicular neoplasm should be performed, along with laboratory testing for elevated serum human chorionic gonadotropin (hCG), lactate dehydrogenase (LDH), and alpha-fetoprotein (AFP) levels, in addition to possible scrotal imaging [25,37]. A study conducted by Korpaisarn and Safer examined suggestions pertaining to hormonal transition in individuals undergoing pre- and postorchiectomy [23].

In order to attain the desired estradiol level and sustain folliclestimulating hormone (FSH) within the range typical for people with a female sex, transgender women and gender nonconforming transfeminine individuals need estradiol doses that closely resemble those administered prior to undergoing orchiectomy [23]. The recommended dosage range of oral 17-beta estradiol for those who have undergone post-orchiectomy feminization affirming surgery is 1–5 mg [23,36]. This dosage range aligns with the guidelines for transfeminine individuals who have not undergone orchiectomy, which is typically 2–6 mg [23,36]. Additionally, Spironolactone, a medication commonly administered to block androgen receptors, may be discontinued following the orchiectomy procedure [4,23].

# Genital masculinization Surgeries: GAHT guidelines and considerations for surgery

GAHT in transmasculine individuals is intended to induce virilization, the development of male secondary characteristics. Testosterone is the principal hormonal treatment for transmasculine individuals. GAHT prior to any gender affirmation surgery not only is strongly recommended as the standard of care in daily evidence-based primary care, but it is also necessary to achieve the aesthetics, and at times, the functionality of some of the gender affirmation surgeries [25,26].

#### Metoidioplasty

Metoidioplasty is another option available for genital masculinization surgeries. It involves the reconstruction of a hormonally enlarged clitoris treated preoperatively with testosterone. Such treatment will grow the clitoris into a small phallus, commonly known as a "micropenis". This is a single stage procedure which uses local tissue, to create

the male appearance of the genitalia and the ability to void in a standing position, while preserving the erogenous sensation. [26,27] The small phallus grows to approximately 1-3 in. in length and with a girth close to the size of a thumb [27]. Thus, hormonal pretreatment to enlarge the clitoris is an important aspect of the procedure. The recommended preoperative protocol includes the topical application of dihydrotestosterone gel, in conjunction with the use of a vacuum pump to promote additional clitoral growth. This protocol should be followed for at least one year prior to undergoing metoidioplasty, in order to maximize clitoral growth and enhance postoperative outcomes [27,28]. Although GAHT in this specific procedure is beneficial and necessary preoperatively, testosterone therapy should be paused one month prior to surgery to avoid possible coagulopathies. In accordance with the WPATH SOC, individuals undergoing GAS are encouraged to have completed a minimum duration of 6 months on hormone replacement treatment [1].

### Phalloplasty

Phalloplasty is another option for genital surgical procedures available for transmasculine and gender non-conforming individuals. It involves the creation of a phallus using a flap. There are several techniques used to create such flaps which include a free flap or a pedicled flap of skin (radial forearm free flap RFFF), the anterior lateral thigh (anterior lateral pedicle flap phalloplasty, ALT), an innervated gracilis flap, tube flaps from the abdomen, fibula flaps, latissimus dorsi flaps (Figs. 4a and b.), and vertical rectus abdominis myocutaneous flaps. All offer a distinct approach to harvesting the flap along with related morbidities [4,29].

Similar to other genital procedures for transmasculine individuals, the WPATH SOC recommends patients receive 6 continuous months of GAHT prior to any gonadectomy to allow for a period of reversible changes in appearance before committing to irreversible surgery [1,30].

As discussed in previous sections, the use of GAHT has been proven to not only enhance the aesthetic outcomes of the surgical procedures but also will improve the overall wellbeing of the patients [1,30]. However, certain considerations before and after the procedures must be



**Fig. 4a.** Preoperative view of transgender man following 2 years of hormonal therapy and prior to removal of reproductive organs and gender affirmation surgery with latissimus dorsi phalloplasty 1 year later.

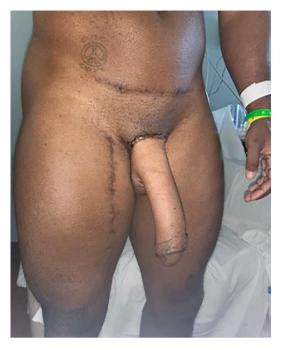


Fig. 4b. Gender affirmation surgery with latissimus dorsi phalloplasty 1 year later.

taken into account, in order to improve surgical outcomes. As it currently stands, there is no clear evidence available on the risk of developing venous thromboembolism under testosterone treatment for transgender male patients [31,32]. Erythrocytosis is the most serious risk while under androgenic therapy, and it has been observed to occur in a small percentage of transmasculine patients [35]. It is mostly associated with supraphysiological levels of testosterone, but can also be observed in patients with normal male sex range testosterone levels. Thus, therapy cessation at least 2 weeks prior to surgery is recommended. GAHT can be resumed safely after 2 weeks from surgery, with different protocols applied on a case-by-case basis. [31,32].

# Hysterectomy and other internal genitalia procedures

As mentioned previously, the aim of medical gender transitioning is to modify bodily functions and appearance in order to become more gender congruent. In transmasculine individuals, this includes external as well as internal procedures. Both evidence and clinical observations show that transgender and gender non-conforming patients can have a wide range of motivations to seek surgical care. GAS of the internal genitalia can include hysterectomy and/or oophorectomy. Motivation for patients to pursue these procedures can include body image dysphoria, unwanted menses (possibly difficult to suppress hormonally), the desire to avoid having to undergo future cervical exams, and/or a desire to remove estrogen-producing gonads. It is important for transgender and gender non-conforming individuals to consider fertility preservation prior to initiating hormone replacement therapy and prior to the removal of uterus and gonads [33].

Testosterone therapy suppresses circulating estrogen and can lead to changes in the vaginal epithelium that are reminiscent of the postmenopausal period in individuals assigned female at birth. As a result of these changes, transmasculine individuals undergoing testosterone therapy could potentially suffer from vaginal atrophy which will contribute to vaginal discomfort. Colpectomy, or vaginectomy, is a consideration for individuals desiring to possibly avoid this side effect. Unfortunately, the overall effect of gender-affirming medical care on the vagina of transmasculine individuals continues to be poorly character-ized. [21,33].

#### Facial feminization surgery

Facial feminization surgery (FFS) is a transformative surgical approach designed to align the facial features of individuals with a male sex assigned at birth with physical characteristics aligned with their gender identity [34]. It targets both the bony framework and soft tissue elements of the face. While GAHT primarily affects the soft tissue elements, the bony framework remains relatively unchanged. By modifying the facial supportive skeleton, FFS aims to accentuate feminine facial traits and reduce the psychological burden of incongruence. This has been shown to lessen gender dysphoria, contributing to improved mental health and overall well-being for transfeminine individuals [34]. Although the WPATH SOC does not set forth criteria needed prior to FFS, many providers prefer patients to have undergone mental health evaluation and GAHT prior to facial surgery. GAHT prior to these procedures has proven beneficial in achieving some of the desired aesthetic results, such as enhancing the texture of the skin, while diminishing facial hair in the transfeminine individuals.

FFS typically encompasses a comprehensive set of procedures targeting the most sexually dimorphic facial regions. These include the forehead, orbits, nose, chin, jaw, and neck, which exhibit distinct differences between male and female individuals. Masculine faces tend to feature square and angular contours, prominent jawlines, and chins, while feminine faces exhibit softer, more oval-shaped characteristics with delicate chins. By employing a combination of surgical techniques such as frontal sinus setback, supraorbital contouring, hairline lowering, brow lift, rhinoplasty, mandibular angle reduction, genioplasty, malar fat grafting, fat removal, upper lip lift, lip augmentation, and tracheal shave, FFS aims to achieve a more feminine appearance [33,34].

#### Gender affirming hormone therapy complications

GAHT does not present without complications. When initiating GAHT prior to GAS, the preoperative management should take into consideration some of the clinical data reflecting that transgender patients undergoing GAHT may have an increased susceptibility to venous thrombosis. This condition can result in severe consequences, including pulmonary embolism, chronic venous insufficiency accompanied by edema, or the development of chronic leg ulcers [32]. This condition is more common in transfeminine individuals undergoing estradiol therapy. There is currently no documented evidence of venous thrombosis occurring in transmasculine patients undergoing testosterone therapy. In the absence of empirical data or substantiating proof, it is advisable to halt gender affirming hormonal medication two weeks before undergoing GAS [12,32].

Following GAS, it is recommended to resume hormonal therapy in order to ensure the overall health of the patient and mitigate the potential adverse effects of sex steroid deficiency [12]. The postoperative period is characterized by a gradual reduction in the risk of venous thromboembolism over a span of two weeks [32]. In the lack of empirical evidence, it is advisable to suggest a delay of 3 to 4 weeks following surgery before initiating hormone medication, or alternatively, until the patient has achieved complete mobilization [6,32].

## Conclusion

The integration of gender affirming hormone therapy (GAHT) with gender-affirming surgery (GAS) stands as a comprehensive and beneficial approach for individuals seeking alignment between their gender identity and physical appearance. GAHT, whether it involves testosterone or estrogen, induces profound changes in secondary sex characteristics, which not only leads to increased patient satisfaction, but improved aesthetic and surgical outcomes.

In our literature review, we found that when coupled with GAS procedures in the realm of feminizing augmentation mammaplasty, genital feminization surgeries, and genital masculinization surgeries,

GAHT is excellent in maximizing surgical outcomes. While much of the literature is limited on the true impact of GAHT and surgical outcomes, we were able to illustrate that the combination of GAHT and GAS exemplifies a patient-centered approach that recognizes and addresses the multifaceted nature of gender identity, while also positively impacting the physical and mental well-being of the patients involved. This literature review not only shows the positive impact of GAHT on GAS, but it aims to open more doors into future research on the topic.

#### Consent

Consent has been obtained from patients for utilization of photographs, and a copy of the consent with personally identifiable information removed has been uploaded.

#### CRediT authorship contribution statement

**Desha Gelles-Soto:** Writing – review & editing, Writing – original draft. **Danielle Ward:** Writing – review & editing, Writing – original draft, Investigation. **Taylor Florio:** Writing – review & editing, Writing – original draft. **Konstantinos Kouzounis:** Writing – review & editing, Writing – original draft. **Christopher J. Salgado:** Writing – review & editing, Conceptualization.

#### Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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