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Review

A Review of Sexual Outcomes in Female XX Patients with Congenital Adrenal Hyperplasia Following Early Surgical Revision

Sonja Klumpp [1], Elnaz Guivatchian [1], Ana M. Moser [2,*] and Aron Liaw [2]

[1] School of Medicine, Wayne State University, Detroit, MI 48201, USA
[2] Department of Urology, Wayne State University, Detroit, MI 48201, USA
* Correspondence: hw7357@wayne.edu

Abstract: Most genotypically XX females born with congenital adrenal hyperplasia (CAH) have undergone feminizing genital reconstructive surgery within their first few years of life or in early childhood. Reconstructive surgery may impact the sexual function of patients later in life, including their satisfaction with sexual activity. A review of the sexual function of CAH patients with previous reconstructive surgery was conducted through PubMed using several search terms, including (((sexual function) AND (female)) AND (congenital adrenal hyperplasia)) AND (reconstruction), and focused on articles published within the past 25 years. Relevant cited references within these articles were reviewed as well. Most studies demonstrated worse sexual function in female CAH patients compared to controls, while some showed comparable sexual function between the two groups. Further research is necessary to clarify these conflicting findings and improve long-term care of these patients, especially as it relates to their sexual health.

Keywords: congenital adrenal hyperplasia; sexual function; surgical outcomes

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1. Introduction

Congenital adrenal hyperplasia (CAH) is the clinical expression of a group of genetic disorders that result in variations in adrenal gland function and its hormone products. These genetic disorders are caused by deficiencies in different enzymes that are a part of adrenal steroidogenesis. These autosomal recessive disorders range in severity, depending on which enzyme is deficient. The three enzyme deficiencies that commonly result in female virilization include 21-hydroxylase, 11β-hydroxylase, and 3β-hydroxysteroid dehydrogenase, with 21-hydroxylase being the most commonly deficient. The variation in clinical presentations and time of presentation among these deficiencies is broad. For instance, a deficiency of 21-hydroxylase can cause earlier onset of disease in the classical form or a later onset in the nonclassical form. In these patients, steroidogenesis is shunted towards progesterone and 17-hydroxyprogesterone, thus increasing subsequent products, including 5α-pregnane-3α and 17α-diol-20-one, which are then converted to dihydrotestosterone (DHT). This final product, DHT, influences the virilization of XX patients. 21-hydroxylase deficiency not only promotes the excessive production of DHT but also 21-deoxycortisole, 11-ketoandrostenedione, and several other steroid hormones [1].

It is important for CAH caused by 21-hydroxylase deficiencies to be identified at birth. Immediate identification of enzymatic disorders can prevent serious complications like hyponatremia, hyperkalemia, and hypotension. Moreover, gender assignment at birth can be confounded by the presence of ambiguous genitalia. Ambiguous genitalia in XX CAH patients may present as clitoromegaly and a rugated labia majora that may be fused [1]. Presently, surgical reconstruction is often performed in these patients with the goal of restoring the anatomy and function of XX female genitalia [2].

This review article discusses general sexual function and satisfaction in female patients diagnosed with CAH in childhood, with respect to surgical outcomes.

2. Anatomic Presentation of CAH and Surgical Options

CAH due to 21-hydroxylase deficiency is classified into salt-wasting, simple virilization, or nonclassical forms depending on the severity of enzyme deficiency and resulting phenotype. In XX patients, external genitalia can present with a spectrum of virilization depending on the amount and timing of exposure to androgens. These patients do, however, form a typical proximal vagina and uterus as well as fallopian tubes and ovaries. Prader scores are used to characterize the degree of virilization of the genitalia, with XX females of scores between three and five (five being more severe) usually undergoing surgical reconstruction.

Surgery on the external female anatomy (Figure 2) is often performed for both cosmetic and functional reasons, but the timing and necessity of such surgeries are becoming more in question. In one study by AbouZeid and Abdelhamid, 10 patients with CAH underwent surgery at a young age to correct external genitalia with the plan to delay vaginal reconstruction until puberty to prevent complications such as scarring, fibrosis, and ultimately vaginal stenosis. Immediate outcomes following surgery were satisfactory to doctors and parents when considering the cosmetic result and lack of complications such as voiding problems [3]. Not only has delaying vaginal reconstruction until puberty been found to help mitigate such complications, but it also allows for greater patient autonomy and decision-making in the matter.

However, gender assignment in such patients, and indeed in many patients with ambiguous genitalia, remains a controversial topic [3–6]. Clinical practice in the past has favored early surgery for healing and developmental considerations, but this is increasingly falling out of favor among clinicians, with many choosing to delay surgery until the patients themselves can participate in an informed manner [3,4]. Surgical options for these patients vary depending on severity but commonly include clitoroplasty, labioplasty, and/or feminizing genitoplasty, with the stages of the latter shown in Figure 1 [2,7]. When these surgeries are conducted in early childhood, there can be immediate complications, but issues with sexual function do not present until later in patients' lives [7]. Delayed problems related to eventual sexual function include issues with clitoral sensitivity, stenosis of the vagina, and reduced overall sexual satisfaction [5].

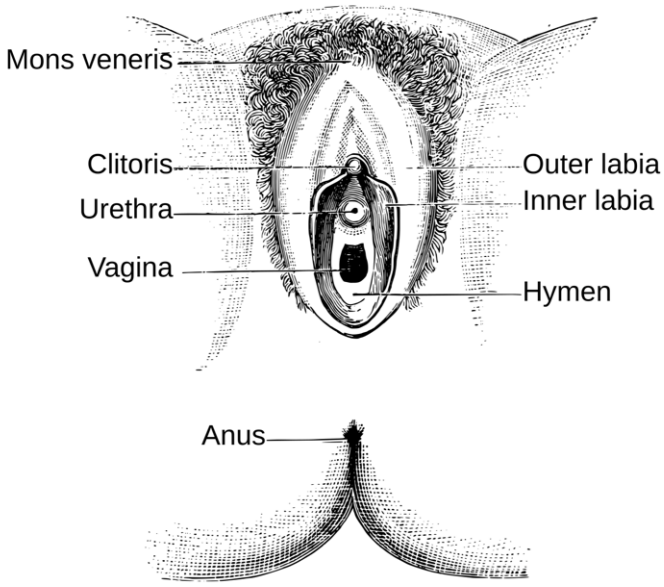

Figure 1. External female anatomy showing the labia majora, clitoris, and vaginal introitus, all frequently operated on in patients with congenital adrenal hyperplasia (CAH) [8,9]. Reprinted from Handbook of Obstetric Nursing, by Francis W.N. Haultain and James Haig Ferguson, 1889.

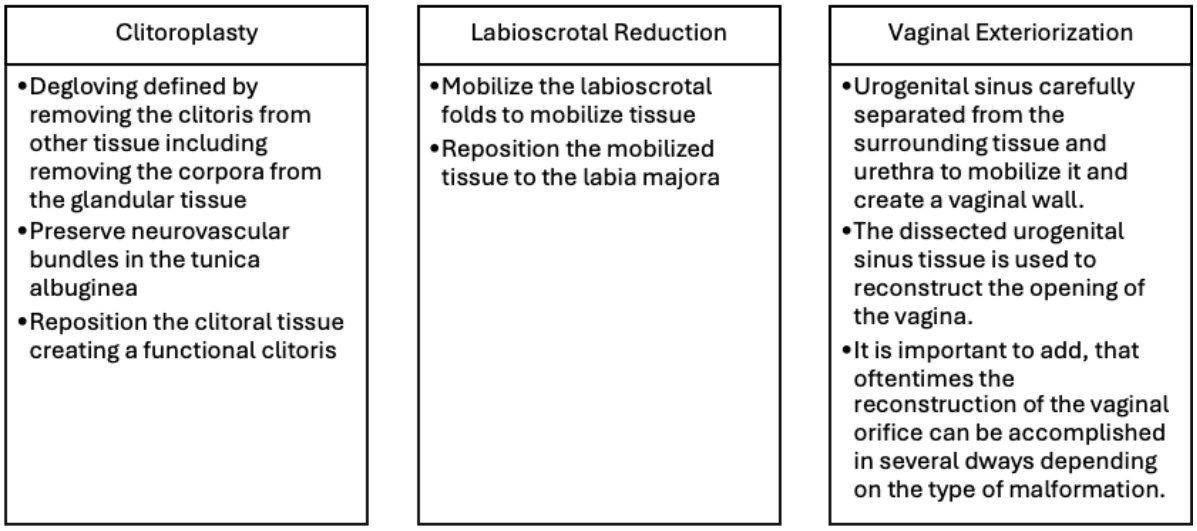

Figure 2. Stages of a feminizing genitoplasty based on standard single-stage surgery as outlined by Kudela et al. [8].

3. Defining Sexual Function

Sexual function is a broad concept, but it is often used as a marker of successful genitoplasty in patients with CAH. Several studies examine sexual function in CAH patients who underwent these surgeries as children; however, definitions of success vary widely (Table 1). In one paper by Wang et al., sexual function was focused on clitoral sensitivity and nerve preservation in patients and how it contributes to sexual satisfaction [5]. Many articles measure sexual function by using standardized measures like the Female Sexual Function Index (FSFI) score, which is based on a 19-part questionnaire focused on sexual satisfaction, discomfort, pain, ability to orgasm, lubrication, arousal, desire, and stimulation, with higher scores indicating better sexual function (a score of 36 being the highest) [10]. Another article by Tjalma et al. focused instead on the ability of women to have orgasms after these surgeries as a measure of sexual function [11]. Most articles reviewed in this paper utilized the FSFI.

Table 1. Measures of sexual function used by studies in this paper.

Study Authors [Reference Number]	Definition of Sexual Function	Brief Description
Wang et al. [5]	Presence of complications	Changes in clitoral sensitivity, vaginal stenosis, need for surgical revisions, and rate of urinary tract infections (UTIs)
Gastaud et al. [10]	Female Sexual Function Index (FSFI)	*
Tjalma [11]	Orgasm	Ability of patient to achieve orgasm following surgery
Dwiggins et al. [12]	FSFI	*
Fagerholm et al. [13]	FSFI	*
Sircili et al. [14]	Presence of complications	Need for surgical revisions, need for dilators, vaginal stenosis, dyspareunia, and inability to have sexual intercourse
Wolffenbuttel et al. [15]	Presence of complications	Hypersensitivity, pain, or cosmetic concerns
Dobrowolska-Glazar et al. [16]	FSFI	*

Table 1. *Cont.*

Study Authors [Reference Number]	Definition of Sexual Function	Brief Description
Nordenström et al. [17]	120-item questionnaire, McCoy sexual rating scale	Questions about lubrication, appreciation of clitoral and vaginal touching, interest and activity; McCoy sexual rating scale focused on sexuality and sexual function with an emphasis on menopausal women
Crouch et al. [18]	Golombok–Rust Inventory of Sexual Satisfaction (GRISS)	‡
Nidal et al. [19]	FSFI	*
Seyam et al. [20]	FSFI	*
Preston et al. [21]	FSFI	*
Stikkelbroeck et al. [22]	Interview and visual analog scales with a female sexologist	Questions regarding frequency of sexual intercourse, vaginal/urologic symptoms, clitoral sensitivity, lubrication, and dyspareunia
Binet et al. [23]	Sexual fulfillment	Open-ended questions
Almasri et al. [24]	FSFI, GRISS	*, ‡
Trachta et al. [25]	Lower urinary tract symptoms (ICIQ-FLUTS), GRISS	Questionnaire evaluating 18 different aspects of female lower urinary tract symptoms and quality of life, ‡
Baskin et al. [26]	Presence of complications	Vaginal stenosis, adhesions, UTIs, and urinary retention
Dangle et al. [27]	Presence of complications	UTIs, stenosis, incontinence, need for revision, and requirement of vaginal dilators
Stites et al. [28]	Presence of complications	Urinary continence outcomes
Ibrahim et al. [29]	Presence of complications	Vaginal stenosis and recurrent UTIs
Jesus [30]	FSFI, GRISS	*, ‡

* 19-part questionnaire including questions about satisfaction, discomfort, pain, ability to orgasm, lubrication, arousal, desire, and stimulation. ‡ 28-item questionnaire evaluating presence and severity of sexual problems.

4. Vaginal Caliber and Need for Surgical Revisions

There are a few factors most emphasized in the literature that contribute to the sexual functioning of XX patients with CAH and previous genital reconstruction, one being vaginal caliber. Vaginal caliber refers simply to the diameter of the vaginal canal, which is often impacted in individuals who undergo vaginal reconstruction at a young age. In a study performed by Dwiggins et al., 36 patients with CAH and 27 controls underwent a gynecologic examination and filled out validated questionnaires, including the Female Sexual Function Index [12]. Patients with CAH were more likely to have sexual dysfunction, defined as a score of $\leq$26.55 on the FSFI. Specifically, 37% of controls versus 71% of patients with CAH met criteria for sexual dysfunction. CAH patients were more likely to have pain with intercourse, poorer self-body image, smaller vaginal calibers, or absence of sexual activity altogether. Through further analysis, decreased vaginal caliber was the anatomic finding most predictive of sexual dysfunction [12]. These differences can also help explain the common need for surgical revision in many CAH patients. Revision surgeries often focus on the need for vaginal dilation because of stenosis of the vaginal introitus. In one article, researchers found that revision rates in certain samples were up to 75%, although these were from surgeries in the 1960s and 70s [5]. Another article by Fagerholm et al. found that 9 of 16 patients struggled with penetrative sex, resulting in the need for vaginal dilations [13]. A similar rate was noted by Sircili et al., with 15 of 20 patients needing revisions and dilations later in life as patients reached puberty and became more sexually active [14]. More recent studies suggest that revision rates run anywhere from 3 to 36% [5].

Thus, decreased vaginal caliber and the need for surgical revisions remain significant barriers to the sexual health and well-being of female patients with CAH.

5. Pain and Clitoral Sensitivity

With vaginal stenosis certainly contributing, increased pain for various reasons is an important factor leading to worsened sexual function in these patients. In a retrospective chart review, six patients ranging from 4 to 21 years old (median age 13) presented to their physician (some with their parents) with clitoral complaints, like clitoral pain or hypersensitivity, following a feminizing reconstructive surgery [15]. In all six of these patients, the glans clitoris was found to be completely exposed. With subsequent clitoral hoodplasty, the postoperative covering of the glans was complete in five patients and only partial in one. All patients reported being pleased with the cosmetic result, and patients who were having pain or hypersensitivity reported resolution of these symptoms after the procedure. For instance, parents of one of the patients had previously endorsed their child's discomfort during diaper changes, a problem that resolved following clitoral hoodplasty [15]. In another study consisting of nine patients with CAH compared to 10 adult female controls, sexual function was found to be comparable in both groups in most domains except for pain, which was significantly higher in CAH participants [16]. Similarly, in a cross-sectional study performed by Gastaud et al., 81% of patients with CAH (n = 22) and previous genital reconstruction had pain with penetration versus about 17% (n = 69) in controls [10]. Pain for any reason, whether it be due to vaginal stenosis and decreased vaginal caliber, exposed clitoral tissue, or inadequate lubrication, evidently impacts the sexual functioning of XX CAH patients after reconstruction, and strategies to minimize pain with sex should be assigned great importance in the care of these patients.

Loss of clitoral sensitivity was also discussed in several articles as a measure of sexual outcomes in patients with CAH. In one study conducted by Nordenström et al., CAH patients were compared with age-matched controls on several variables [17]. Researchers used cotton swabs to compare sensitivity in study subjects' thighs versus that of their clitoris to determine if there was loss of sensitivity in CAH patients versus controls. They found that it was the patient's initial degree of virilization and the type of surgery they had that determined their preservation of sensitivity, with more favorable outcomes in partial resection surgeries [17]. In another study by Crouch et al., researchers used a genitosensory analyzer and von Frey filaments to analyze clitoral sensitivity in patients with CAH; all six patients evaluated were found to have decreased clitoral sensitivity, indicating worsened sexual function [18]. Researchers further emphasized that this loss of clitoral sensitivity negatively impacted CAH patients' ability to orgasm [18]. In conclusion, both pain and changes in clitoral sensitivity have been shown to impact and possibly worsen sexual function in CAH patients following genital reconstruction surgery.

6. Sexual Activity and Satisfaction

The level of sexual activity is also an important marker of sexual function, considering both the frequency and quality of a patient's sexual encounters. Unlike with vaginal caliber and pain, most studies reviewed found female CAH patients with previous genital reconstruction to have a comparable level of sexual activity and satisfaction to controls. In a study by Nidal et al., about 80% of CAH patients who underwent feminizing genitoplasty at their institution reported regular sexual intercourse and positive self-image [19]. In another study, researchers found that within their group of 21 CAH patients across three centers, there was no difference in patients' sexual fulfillment when compared to controls, suggesting that successful genitoplasty may have played a part in improving the sexual function of patients [6]. Seyam et al. also found no significant difference in sexual function scores (as measured by the FSFI) or in the number of children CAH patients had compared to controls [20]. Finally, Preston et al., Strikkelbroeck et al., and Binet et al. came to similar conclusions that, for the most part, female CAH patients with a history

of genitoplasty have regular intercourse and are generally as satisfied as their non-CAH counterparts [21–23].

Some studies, however, have had less definitive outcomes. For instance, Fagerholm et al. found that CAH patients tended to begin sexual activity at a later age than healthy controls and engaged in intercourse with their partners less frequently [13]. Despite these differences, both cohorts had similar sexual function as indicated through FSFI scores, with the ability to achieve orgasm being an issue in both groups [13]. Additionally, one study reported that while most CAH patients were sexually active, less than half described their sexual experiences as comfortable [24]. Similarly, Dwiggins et al.'s study, among many others, suggests that rates of sexual dysfunction are higher in patients with CAH than in controls when using the FSFI [12].

7. Urinary Tract Infections

Urinary tract infections (UTIs) can affect sexual outcomes of patients, influencing not only their overall health but also their comfort and ability to engage in sexual activity. Some researchers looked at the incidence of UTIs in patients with CAH who underwent surgical interventions. In one such study by Wang et al., researchers found that UTI rates in CAH patients were not significantly different from those in females without CAH [5]. This study also noted that UTI rates were consistent across different surgical procedures, including partial urogenital sinus mobilization, total urogenital sinus mobilization, and the Passerini-Glazel genitoplasty [5]. Similarly, in a systematic review by Almasri et al., UTIs were not commonly reported in female XX patients with previous genital reconstruction [24]. Likewise, a retrospective study conducted by Trachta et al. found no significant difference in urinary tract symptoms between cases (median age 25.5 years old) and healthy controls, although it only included 32 patients [25]. Some studies, however, do suggest an increased rate of UTIs in children following surgery; a cohort study conducted by Baskin et al. found that two patients with CAH who underwent surgical reconstruction had UTIs post-surgery compared to none among participants who did not receive early surgery, although the difference in UTI rate was not statistically significant ($p = 0.59$) [26]. Dangle et al. conducted a retrospective review of 26 CAH patients following early reconstructive surgery and found that two developed UTIs over an average six-year follow-up, while urinary continence was achieved in all patients [27]. Notably, however, one patient required suprapubic tube insertion for urinary retention. Stites et al., on the other hand, studied 24 female CAH patients who underwent vaginoplasty and found that 2/10 patients who underwent total urogenital mobilization had serious incontinence issues like dysfunctional voiding [28]. Finally, both Sircili et al. and Ibrahim et al. found that female CAH patients with early reconstruction frequently experienced recurrent UTIs in childhood, some even requiring surgical revision for this reason [14,29]. Overall, a review of the literature suggests that UTIs and continence issues can impact the lives of these patients, particularly in childhood but perhaps less so once a patient reaches the age of sexual maturity and becomes sexually active. However, studies do have conflicting results, and UTIs and urinary tract symptoms likely still impact sexually active adult patients in a clinically significant, and sometimes statistically significant, way.

8. Ethical Considerations of Feminizing Genitoplasties

While alluded to briefly in other sections of this paper, it is important to dive deeper into the ethical debate surrounding the treatment of patients with CAH and differences in sex development (DSD) as a whole. As healthcare advances and surgeons are capable of more complex treatments, questions will inevitably arise regarding the ethicality of procedures like a feminizing genitoplasty in patients unable to make their own informed decisions. Many modern techniques have started to be questioned by ethics and advocacy groups who argue that genitoplasty should be deferred until a child is mature enough to make their own decision regarding treatment [6]. Even more significant, some groups have considered such surgeries on minors with DSD to be a violation of human rights altogether.

Political institutions like the European Parliament, Council of Europe, Commissioner for Human Rights, and the United Nations Rapporteur on torture and other cruel, inhuman or degrading treatment or punishment have recently taken this stance [31]. However, large governing bodies such as these do not necessarily share the same viewpoint as the patients affected by DSD. For instance, in a multicenter study including six European countries, Bennecke et al. surveyed 459 patients, 192 of whom had CAH. The survey probed their level of agreement with statements about genital surgery, for which 66% of CAH individuals agreed that surgery is appropriate to have in infancy or childhood. Only 12% thought they would have been better off without any surgery in childhood or adolescence [31]. However, individuals with different DSD diagnoses varied greatly in their level of agreement with survey statements, demonstrating the broad range of views held by patients. This highlights the need for individualized and situational medical decision-making instead of a blanket moratorium on genital surgery in early childhood. There is also evidence that delaying surgery until a child is older is an acceptable alternative. A pilot study by Bougnères et al. followed seven patients with CAH ranging from 1 to 8 years old who did not undergo reconstructive surgery. None of the patients developed UTIs, and neither the patients nor their parents expressed significant concerns about postponing surgery [32]. However, it remains uncertain whether these concerns will eventually arise as the patients grow older. Still, there remains a scarcity of studies on the consequences of raising severely virilized children or even avoiding surgery altogether, leaving little basis for comparison with current practices in these scenarios [30]. In addition, urological societies generally support the practice of early genitoplasty as they argue it allows for better tissue healing, lower risk of complications, and reduced psychological impact [6]. Overall, sexual outcomes aside, the ethicality of performing genital surgery on children is increasingly being interrogated.

9. Conclusions and Future Directions

Sexual function can impact the well-being of any individual, especially those with disorders affecting sexual hormone levels such as CAH. Numerous studies have suggested that sexual function is worse in XX patients with CAH who underwent feminizing genital surgery when they were younger compared to controls, especially as it pertains to vaginal caliber and need for surgical revisions, pain with penetrative intercourse, and overall satisfaction with sexual activity. On the other hand, a few studies, albeit smaller in size, have found no significant difference in sexual function between XX CAH patients and controls. These conflicting results suggest the need for more robust research in this area with longer-term follow-up and perhaps a further discussion about how to address and mitigate patients' sexual concerns once they present to their physician. In addition, limited data exists on the sexual function of female XX CAH patients who undergo delayed surgery which is crucial for understanding the potential benefits of postponing surgery. On a separate note, many studies suggest that care for these patients is fragmented, with no clear designation of a specialist responsible for their long-term care. For instance, female patients with CAH likely interact with urologists, gynecologists, and endocrinologists without having a clear "home base" or center of their care. Care must also be taken to determine the best timing for reconstructive surgery, as choosing an individualized surgical and care plan with an optimal balance between reconstruction and sexual organ/skin preservation will ultimately be what improves long-term sexual health in females with CAH. Finally, growing concerns about the ethics of early genitoplasties, along with potential subsequent legislation, will undoubtedly affect the lives and health of these patients and must be considered in their complex healthcare management.

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References

1. Auer, M.K.; Nordenström, A.; Lajic, S.; Reisch, N. Congenital Adrenal Hyperplasia. *Lancet* **2023**, *401*, 227–244. [CrossRef] [PubMed]
2. Lynn Canalichio, K.; Ahn, J.; Elizabeth Amies Oelschlager, A.-M.; Yvonne Fechner, P.; McCauley, E.; Ramsdell, L.; Merguerian, P.; Shnorhavorian, M. Feminizing Genitoplasty in Congenital Adrenal Hyperplasia: 20-Year Experience of Regional Comprehensive Care. *IJCU* **2020**, *4*, 45. [CrossRef]
3. AbouZeid, A.A. Feminizing Genitoplasty in Childhood: Aiming for Achievable Outcomes. *Ann. Pediatr. Surg.* **2020**, *16*, 34. [CrossRef]
4. Liaw, A.; Ziaullah, A.; Wang, M. Long-Term Outcomes of Gender Assigned at Birth in Differences of Sex Development. *J. Sex. Med.* **2023**, *20*, 709–711. [CrossRef]
5. Wang, L.C.; Poppas, D.P. Surgical Outcomes and Complications of Reconstructive Surgery in the Female Congenital Adrenal Hyperplasia Patient: What Every Endocrinologist Should Know. *J. Steroid Biochem. Mol. Biol.* **2017**, *165*, 137–144. [CrossRef]
6. Harris, R.M.; Chan, Y.-M. Ethical Issues with Early Genitoplasty in Children with Disorders of Sex Development. *Curr. Opin. Endocrinol. Diabetes Obes.* **2019**, *26*, 49–53. [CrossRef]
7. Gurgov, S.; Bernabé, K.J.; Stites, J.; Cunniff, C.M.; Lin-Su, K.; Felsen, D.; New, M.I.; Poppas, D.P. Linking the Degree of Virilization in Females with Congenital Adrenal Hyperplasia to Genotype. *Ann. N. Y. Acad. Sci.* **2017**, *1402*, 56–63. [CrossRef]
8. Kudela, G.; Gawlik, A.; Koszutski, T. Early Feminizing Genitoplasty in Girls with Congenital Adrenal Hyperplasia (CAH)-Analysis of Unified Surgical Management. *Int. J. Environ. Res. Public. Health* **2020**, *17*, 3852. [CrossRef]
9. Haultain, F.W.N.; Ferguson, J.H. Female Organs of Generation. In *Handbook of Obstetric Nursing*; Young J. Pentland: Edinburgh, Scotland; London, UK, 1889; p. 26. Available online: https://wellcomecollection.org/works/xgwypp6b/items?canvas=48 (accessed on 21 November 2024).
10. Gastaud, F.; Bouvattier, C.; Duranteau, L.; Brauner, R.; Thibaud, E.; Kutten, F.; Bougnères, P. Impaired Sexual and Reproductive Outcomes in Women with Classical Forms of Congenital Adrenal Hyperplasia. *J. Clin. Endocrinol. Metab.* **2007**, *92*, 1391–1396. [CrossRef]
11. Tjalma, W.A. Assembling a Functional Clitoris and Vulva from a Pseudo-Penis: A Surgical Technique for an Adult Woman with Congenital Adrenal Hyperplasia. *J. Pediatr. Adolesc. Gynecol.* **2017**, *30*, 425–428. [CrossRef]
12. Dwiggins, M.; Brookner, B.; Fowler, K.; Veeraraghavan, P.; Gomez-Lobo, V.; Merke, D.P. Multidimensional Aspects of Female Sexual Function in Congenital Adrenal Hyperplasia: A Case-Control Study. *J. Endocr. Soc.* **2020**, *4*, 11. [CrossRef] [PubMed]
13. Fagerholm, R.; Santtila, P.; Miettinen, P.J.; Mattila, A.; Rintala, R.; Taskinen, S. Sexual Function and Attitudes Toward Surgery After Feminizing Genitoplasty. *J. Urol.* **2011**, *185*, 1900–1904. [CrossRef] [PubMed]
14. Sircili, M.H.P.; Bachega, T.S.S.; Madureira, G.; Gomes, L.; Mendonca, B.B.; Dénes, F.T. Surgical Treatment after Failed Primary Correction of Urogenital Sinus in Female Patients with Virilizing Congenital Adrenal Hyperplasia: Are Good Results Possible? *Front. Pediatr.* **2016**, *4*, 118. [CrossRef] [PubMed]
15. Wolffenbuttel, K.; Menon, V.; Grimsby, G.; ten Kate-Booij, M.; Baker, L. Clitoral Hoodplasty in Females with Disorders of Sex Development. *J. Pediatr. Urol.* **2017**, *13*, 61.e1–61.e5. [CrossRef] [PubMed]
16. Dobrowolska-Glazar, B.; Honkisz, I.; Sulislawski, J.; Tyrawa, K.; Wolnicki, M.; Chrzan, R. Sexual Function and Health Status in Adult Patients with Congenital Adrenal Hyperplasia. *J. Pediatr. Urol.* **2020**, *16*, 464.e1–464.e6. [CrossRef]
17. Nordenström, A.; Frisén, L.; Falhammar, H.; Filipsson, H.; Holmdahl, G.; Janson, P.O.; Thorén, M.; Hagenfeldt, K.; Nordenskjöld, A. Sexual function and surgical outcome in women with congenital adrenal hyperplasia due to CYP21A2 deficiency: Clinical perspective and the patients' perception. *J. Clin. Endocrinol. Metab.* **2010**, *95*, 3633–3640. [CrossRef]
18. Crouch, N.S.; Minto, C.L.; Laio, L.M.; Woodhouse, C.R.; Creighton, S.M. Genital sensation after feminizing genitoplasty for congenital adrenal hyperplasia: A pilot study. *BJU Int.* **2004**, *93*, 135–138. [CrossRef]
19. Nidal, S.; Kocherov, S.; Jaber, J.; Levi-Khademi, F.; Farkas, A.; Chertin, B. Sexual Function and Voiding Status Following One Stage Feminizing Genitoplasty. *J. Pediatr. Urol.* **2020**, *16*, 97.e1–97.e6. [CrossRef]
20. Seyam, R.M.; Bissada, N.K.; Abdul-Aaly, M.; Sakati, N.A.; Al Taweel, W.; Alkhudair, W.K. Long-Term Outcome of Genital Reconstruction of Middle Eastern Women with Congenital Adrenal Hyperplasia. *Urol. Ann.* **2013**, *5*, 277–282. [CrossRef]
21. Preston, M.; Morris, A.; Villegas, R.; Huston, J.; Heloury, Y.; Grover, S. Surgical Timing and Complications, with Body Image, Quality of Life, Sexual Function and Genital Sensation in Patients with Congenital Adrenal Hyperplasia. *J. Pediatr. Urol.* **2024**, *20*, 442.e1–442.e8. [CrossRef]

22. Stikkelbroeck, N.M.; Beerendonk, C.C.; Willemsen, W.N.; Schreuders-Bais, C.A.; Feitz, W.F.; Rieu, P.N.; Hermus, A.R.; Otten, B.J. The Long Term Outcome of Feminizing Genital Surgery for Congenital Adrenal Hyperplasia: Anatomical, Functional and Cosmetic Outcomes, Psychosexual Development, and Satisfaction in Adult Female Patients. *J. Pediatr. Adolesc. Gynecol.* **2003**, *16*, 289–296. [CrossRef] [PubMed]
23. Binet, A.; Lardy, H.; Geslin, D.; Francois-Fiquet, C.; Poli-Merol, M. Should We Question Early Feminizing Genitoplasty for Patients with Congenital Adrenal Hyperplasia and XX Karyotype? *J. Pediatr. Surg.* **2016**, *51*, 465–468. [CrossRef] [PubMed]
24. Almasri, J.; Zaiem, F.; Rodriguez-Gutierrez, R.; Tamhane, S.U.; Iqbal, A.M.; Prokop, L.J.; Speiser, P.W.; Baskin, L.S.; Bancos, I.; Murad, M.H. Genital Reconstructive Surgery in Females With Congenital Adrenal Hyperplasia: A Systematic Review and Meta-Analysis. *J. Clin. Endocrinol. Metab.* **2018**, *103*, 4089–4096. [CrossRef] [PubMed]
25. Trachta, J.; Mushtaq, I.; Petrasova, N.; Hradsky, O.; Skaba, R. Lower Urinary Tract Symptoms in Adult Females after Feminizing Genitoplasty for Congenital Adrenal Hyperplasia. *J. Urol.* **2021**, *205*, 1483–1489. [CrossRef]
26. Baskin, A.; Wisniewski, A.B.; Aston, C.E.; Austin, P.; Chan, Y.M.; Cheng, E.Y.; Diamond, D.A.; Fried, A.; Kolon, T.; Lakshmanan, Y.; et al. Post-operative complications following feminizing genitoplasty in moderate to severe genital atypia: Results from a multicenter, observational prospective cohort study. *J. Pediatr. Urol.* **2020**, *16*, 568–575. [CrossRef]
27. Dangle, P.P.; Lee, A.; Chaudhry, R.; Schneck, F.X. Surgical complications following early genitourinary reconstructive surgery for congenital adrenal hyperplasia—interim analysis at 6 years. *Urology* **2017**, *101*, 111–115. [CrossRef]
28. Stites, J.; Bernabé, K.J.; Galan, D.; Felsen, D.; Poppas, D.P. Urinary continence outcomes following vaginoplasty in patients with congenital adrenal hyperplasia. *J. Pediatr. Urol.* **2017**, *13*, 38.e1–38.e7. [CrossRef]
29. Ibrahim, H.; Lachkar, A.A.; Bidault, V.; Delcour, C.; Paye-Jaouen, A.; Peycelon, M.; El-Ghoneimi, A. Genito-urinary reconstruction in female children with congenital adrenal hyperplasia: Favorable surgical outcomes can be achieved by contemporary techniques and a dedicated multidisciplinary management. *J. Pediatr. Surg.* **2024**, *59*, 1851–1858. [CrossRef]
30. Jesus, L.E. Feminizing Genitoplasties: Where Are We Now? *J. Pediatr. Urol.* **2018**, *14*, 407–415. [CrossRef]
31. Bennecke, E.; Bernstein, S.; Lee, P.; van de Grift, T.C.; Nordenskjöld, A.; Rapp, M.; Simmonds, M.; Strueli, J.C.; Thyen, U.; Wiesemann, C. Early Genital Surgery in Disorders/Differences of Sex Development: Patients' Perspectives. *Arch. Sex. Behav.* **2021**, *50*, 913–923. [CrossRef]
32. Bougnères, P.; Bouvattier, C.; Cartigny, M.; Michala, L. Deferring surgical treatment of ambiguous genitalia into adolescence in girls with 21-hydroxylase deficiency: A feasibility study. *Int. J. Pediatr. Endocrinol.* **2017**, *2017*, 3. [CrossRef]