Characteristics of female genital restoration surgery for congenital adrenal hyperplasia using a large scale administrative database

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Keywords: congenital adrenal hyperplasia, female genital restoration surgery, clitoroplasty, labiaplasty, vaginoplasty, complications

Abstract
Objectives: To analyze nationwide information on the timing of surgical procedures, cost of surgery, hospital length of stay following surgery and surgical complications of female genital restoration surgery (FGRS) in females with congenital adrenal hyperplasia (CAH).

Methods: We used the Pediatric Health Information System database to identify patients with CAH who underwent their initial FGRS in 2004-2014. These patients were identified by an ICD-9 diagnosis code for adrenogenital disorders (255.2) in addition to a vaginal ICD-9 procedure code (70.x, excluding vaginoscopy only) or perineal ICD-9 procedure code (71.x), which includes clitoral operations (71.4).

Results: 544 (11.8%) females underwent FGRS between 2004 and 2014. Median age at initial surgery was 9.9 months (interquartile range 6.8 – 19.1 months). 92% underwent a vaginal procedure, 48% underwent a clitoral procedure, and 85% underwent a perineal procedure (non-clitoral). The mean length of stay was 2.5 days (standard deviation 2.5 days). The mean cost of care was $12,258 (median $9,558). 30-day readmission rate was 13.8%. 2.0% underwent reoperation before discharge, and one (0.2%) was readmitted for a reoperation within 30 days. 4.0% had a perioperative surgical complication.

Conclusions: Overall, 12% of girls with CAH underwent FGRS at one of a national collaborative of freestanding children’s hospitals. The majority underwent a vaginoplasty.

This is the author's manuscript of the article published in final edited form as:
as a part of their initial FGRS for CAH. Clitoroplasty was performed on less than half the patients. Overall, FGRS for CAH is performed at a median age of 10 months and has low 30-day complication and immediate reoperation rates.

Introduction:

Congenital adrenal hyperplasia (CAH) results in genital virilization in female patients. Many parents still opt to proceed with female genital restoration surgery (FGRS: clitoroplasty, labiaplasty with or without vaginoplasty) early in life, despite recent controversies[1].

When surveyed, the majority of surgeons perform early vaginoplasty[4], and the majority of patients with CAH and their parents prefer early FGRS [6,7,10]. Available analyses of nationwide databases (Pediatric Health Information System [PHIS], Faculty Practice Solutions Center Database) demonstrates that 78-89% surgeries performed for virilized genitalia on CAH patients <2 years of age included vaginoplasty[17].

We hypothesize that the majority of FGRS are performed prior to 12 months of age. We sought to determine the timing of FGRS in patients with CAH using administrative data from a national collaborative of freestanding pediatric hospitals. Additionally, we analyzed the changes over the past ten years, cost of surgery, admission length, reoperations, and complications. The intentions of this study were to establish the age at which surgery is done, the components of the surgeries performed, the cost, surgical complication rate and the changes that have occurred over the 10 years data were analyzed.
Materials & Methods:

Data for this study were obtained from PHIS, an administrative database that contains inpatient, emergency department, ambulatory surgery, and observation data from 43 not-for-profit, tertiary care pediatric hospitals in the United States. Included hospitals are affiliated with the Children’s Hospital Association, a business alliance of children’s hospitals. Data quality and reliability are assured through a joint effort between the Child Health Corporation of America and participating hospitals. The data warehouse function for the PHIS database is managed by Thomas Reuters (Ann Arbor, MI). For the purposes of external benchmarking, participating hospitals provided discharge/encounter data, including demographics, diagnoses, and procedures. Forty-two of these hospitals also submit resource utilization data (e.g. pharmaceuticals, imaging, and laboratory) into PHIS. Data were de-identified at the time of data submission and subjected to a number of reliability and validity checks before being included in the database.

We used PHIS to identify patients with CAH who underwent their initial FGRS between 2004 (the first year when data were available in PHIS) and 2014. We defined our cohort with the following characteristics: 1) born after 2004 (in order to only obtain patients’ initial surgery after birth), 2) had an ICD-9 diagnosis code for adrenogenital disorders (255.2), and 3) a vaginal ICD-9 procedure code (70.x) or perineal ICD-9 procedure code (71.x).
Common vaginal procedure codes include: vaginoscopy (70.21), vaginal reconstruction (70.62), and other repair of vagina (70.79). Common perineal procedure codes included: operations on the clitoris (71.4), other repair of vulva and perineum (71.79), other operations on the vulva (71.8), and other operations on female genital organs (71.9). Perineal procedures were defined as any perineal ICD-9 procedure code 71.x, excluding operations on the clitoris (71.4), which was defined as a clitoral procedure. We excluded patients who underwent vaginoscopy alone.

We abstracted the age at the initial operation, procedure performed (by ICD-9 procedure codes), length of stay, ratio of charge-to-cost (RCC) based cost of each encounter, readmission within 30 days, reoperation before discharge, reoperation within 30 days, and perioperative surgical complications. Analysis for duplicates was performed to identify reoperations. We were not able to assess outpatient follow-up, as outpatient visits are not consistently found in PHIS. We did not assess for long term repeat or redo procedures, i.e., redo vaginoplasties, due to the relatively short window of follow up in the PHIS cohort.

High-volume centers were defined arbitrarily as centers that performed >30 procedures within the 10-year period, which included 3 hospitals accounting for >30% of the cases. Medium-volume centers performed 10-30, and low-volume centers performed <10 procedures (<1 procedure/year).
We used the McNemar’s chi-squared test to examine the change in procedure type over time by comparing the procedural rates in 2004 to the procedural rates in 2014. We performed mixed effects multiple regression (with hospital as a random effect) when determining association between subject demographics (age, hospital volume, ethnicity, race, insurance type) and procedure type, cost, and length of stay. All analyses were completed using the R software package (www.r-project.org). The Institutional Review Board at Indiana University approved this study with exempt status prior to data acquisition or analysis.

Results:

Our query yielded 544 patients who underwent FGRS between 2004-2014 (Figure 1, Table 1). During this time frame, there are 15,497 encounters captured in PHIS for 6,886 unique patients with 4,617 unique females with CAH. With an annual incidence of 1/5,000 - 1/15,000[18] and an annual birthrate of approximately 4,000,000[19], there was an estimated 2,933-8,800 patients born during the study period, indicating 78.3%-100% of patients were captured. Median age at initial surgery was 9.9 months (interquartile range 6.8–19.1 months). There was only one spike in the frequency of surgeries performed at around the age of 10 months (Figure 2).

During the initial FGRS in this cohort, 92.3% underwent a vaginal procedure, 48.3% underwent a clitoral procedure, and 85.3% underwent a perineal procedure (excluding
ICD-9 code 71.4 clitoral procedures). Clitoroplasty varied by hospital volume; high-volume centers performed clitoroplasty 26.7% of the time, while medium- and low-volume centers performed clitoroplasty 56.3% and 60.6% of the time, respectively.

From 2004 to 2014, there was a small change in the type of procedure performed (Figure 3). The change in percentage of procedures over time was a mean -1.8% per year for vaginal procedures alone, mean +2.2% per year for vaginal and clitoral procedures, and a mean -0.2% per year for procedures without vaginal procedures, with a significant difference between vaginal alone vs. vaginal and clitoral procedures (p=0.01). There was no difference between vaginal alone versus perineal/clitoral procedures alone (p=0.94). Therefore, over the past ten years, there has been an increase in the proportion of combination procedure and a decrease in the proportion of vaginal only procedures during initial FGRS, although the shift was relatively small.

Three high-volume centers (centers which performed >30 cases over the ten year period) performed 165/544 procedures (30.3%) (Supplementary Figure 1).

The mean length of stay was 2.5 days (standard deviation 2.5 days). Length of stay was longer in high-volume center: mean 4.3 days, median 4 days (high) vs. 2.4 days, 2 days (medium) vs. 2.4 days, 2 days (low).

The average RCC-based cost of care was $12,258 (median $9,558). On multivariate regression, high-volume centers had a significantly higher cost of care (defined as a
binary variable of >$10,000) compared to low- (OR 0.31, p<0.05) and medium-volume centers (OR 0.21, p<0.05). High-volume centers demonstrated higher unit/room cost: $14,889.99 (high) vs. $6,266.79 (medium) vs. $6,520.19 (low). Operating room costs were comparable between centers: $19,927.50 (high) vs. $20,963.71 (medium) vs. $18,032.22 (low) (Supplementary Figure 2).

Only surgical complications and re-admissions could be considered and “medical” complications were not recorded. Readmission for any reason within 30 days occurred in 75 of 544 subjects (13.8%). On multivariate regression, there was no significant difference between readmission rates in low- (OR 1.99, p=0.09) and medium-volume centers (OR 1.95, p=0.06) compared to high-volume centers. Of those who were readmitted to an inpatient service, the most common admission diagnoses were: CAH (255.2 and 752.49, 21.3%), surgical complication or hemorrhage (998.32, E8788, 959.14, 998.11, V4589, 16.0%), infectious enteritis or gastroenteritis (558.9, 787.03, 86.2, 88.0, 10.7%), and UTI (599.0, 5.3%).

Eleven patients (2.0%) underwent a reoperation before discharge. The ICD-9 procedure codes for these reoperations included: other repair of vagina (70.79, n=7), other cystoscopy (57.32, n=2), vaginoscopy (70.21, n=1), and dilation of anal sphincter (96.23, n=1). One patient (0.2%) was readmitted for a reoperation within 30 days: other cystoscopy (57.32) with other repair of vagina (70.79).
Using the standard PHIS database methodology, any ICD-9 code associated with a surgical complication was flagged. Twenty-two patients (4.0%) were recorded as having a perioperative surgical complication, but our data set did not indicate the type of complication.

Comment:

This study represents a large sample of the current practice patterns for initial FGRS in patients with CAH at United States’ pediatric hospitals. Initial FGRS in CAH patients continues to occur at a young age of 10 months, with a 30-day complication rate of 13.8% and rare immediate reoperation rate (2.0%). It appears that the majority of patients undergo vaginoplasty during their initial reconstructive surgery. While information obtained from this study is valuable in providing evidence of current practice in the units reviewed, it does not provide evidence of surgical or psychological outcomes.

Outcomes in vaginoplasty are difficult to evaluate as the exact surgical technique, patient compliance of steroid replacement, and the initial degree of virilization (Prader score) is seldom reported. Published poor outcomes in vaginoplasty may reflect outdated surgical technique (e.g Fortunoff flap for high confluence urogenital sinuses) or technical error (inadequate vascular supply, inexperienced surgeons). Multiple reports have recommended patients be treated at a center of excellence[20-22]. Less than half
of patients underwent clitoroplasty at their initial surgery, likely reflecting a variety of
Prader stages at presentation and current controversies regarding clitoral
surgery\cite{Hughes2006js, Hughes2006dd, Mouriquand2016cj}.

Although there is controversy in the CAH literature regarding both the timing of the initial
FGRS and what components of FGRS are performed with initial surgery, there is
minimal data on current trends of practices at United States hospitals. In a survey of 61
surgeons (of which 12% were based in the United States), Yankovic et al. reported that
75% perform a combined procedure of clitoroplasty, labiaplasty and vaginoplasty
whereas 8% perform vaginoplasty alone for CAH\cite{4}. The majority of respondents (72%)
supported surgery in the first 2 years of life and 8% advocated for late surgery. Of those
who supported early surgery, 68% would perform all components of reconstruction at
the same time and 43% would delay some components. In comparison, our study
demonstrated that in the United States, 92% of patients with CAH underwent a vaginal
procedure, 48% underwent a clitoral procedure, 85% underwent a perineal procedure.
The majority of patients underwent surgery at a young age (10 months). We presume
that if a clitoroplasty was not necessary due to lower Prader grade (I/II) or a less
prominent clitoris, a surgeon may advise a family to not proceed with this aspect of the
FGRS. Other reasons for lower incidence of clitoroplasty would include potential
miscoding, or a potential recent movement towards delaying clitoroplasty to the age of
consent. Low- and medium-volume centers performed clitoroplasty at a higher rate. The
reasons for this are unclear.
A recent paper that analyzed females with CAH seen at 60 institutions using the Faculty Practice Solutions Center database, demonstrated that the median age for combined clitoroplasty/vaginoplasty was 11.3 months, while median ages for vaginoplasty alone was 53 months and for clitoroplasty alone was 70 months, with histograms for both demonstrating a second peak at adolescence[17]. This study included 577 female patients with CAH (<12 months of age) seen between 2009 and 2011 and 18% underwent feminizing surgery.

Our analysis utilized a cohort of children from large American tertiary children’s hospitals to focus on the current practice of primary FGRS and perioperative outcomes of this initial operation. We found a vaginoplasty rate of 92%, was similar to the previously reported 89% vaginoplasty rate for those who were operated on children at <2 years of age; however, they found a higher rate of clitoroplasty (73% vs. our 48%)[17]. While our study corroborates the previously reported vaginoplasty rate, the reason behind the differences between studies is unclear. It may be due to coding or hospital practice differences between PHIS hospitals and those in the Faculty Practice Solutions Center database. Additionally, this could be due to the differences in number of patients captured, as this study captured 4,617 females while the Sturm et al. study captured 2,614 females with CAH. Interestingly, in following their cohort of those patients who presented at less than 12 months of age, only 18% proceeded with surgery within 1-4 years of follow-up. This may reflect the wide anatomical spectrum observed in females with CAH.
In our analysis, 3 hospitals were responsible for 30% of all surgeries and averaged >3 CAH surgeries per year. This seems to demonstrate a regionalization of CAH surgery to specific centers. Additionally, we demonstrate that high-volume centers had a longer length of stay, reflected in a higher cost to the hospital and higher room/unit costs to patients. This may reflect a higher medical complexity of patients referred to these high-volume centers. Differences in cost could also be related to variation in practice between centers, cost variation based on hospital rather than patient factors, or referral bias stemming from the concentration of more complex reconstruction being performed by a few highly-experienced surgeons.

The limitations of our study include the reliance on administrative data to identify cases of FGRS. Errors in billing and coding may have affected the number of cases and the cost data available. Additionally, given the low use of CPT codes in PHIS, ICD-9 codes were used, and may not properly capture the procedures performed or perioperative complications encountered. As only surgical complications and re-admissions were considered, the complication rate may be underestimated. Further, the inability to pull clinical details, such as level of virilization, affects interpretation of case complexity. Lastly, our data analysis is limited to a subset of free-standing pediatric hospitals, so data may not fully reflect national trends. Another limitation is that the study only includes PHIS institutions and may have missed some patients, however, our data likely captured 78.3-100% of patients with CAH. In addition, our dataset does not include patients who have either decided to delay or forego reconstruction, thus conclusions about age at surgery must be tempered.
This study was designed to describe current FGRS practice in CAH patients in the United States. While the surgeries observed were performed on a large majority of children, this is not evidence that it is correct and should not be taken as such. Should the recommendations of the Chicago consensus\cite{Hughes:2006js, Hughes:2006dd} and more recent recommendations\cite{Mouriquand:2016cj} be more closely followed and surgery after puberty become more desirable, attention must be focused on how to train a cadre of surgeons to be able to perform FGRS following puberty as this does not exist in large numbers at present. As is being done increasingly in health systems in other developed nations like the UK, rare surgeries such as these should be referred to centers of excellence for optimal patient outcomes.

Conclusions:

The majority of patients undergoing treatment at one of a national collaborative of freestanding children’s hospitals underwent a vaginoplasty as a part of their initial FGRS for CAH. Clitoroplasty was performed on less than half the patients. Overall, FGRS for CAH is performed at a median age of 10 months and has low 30-day complications and immediate reoperation rates.

Conflict of interest statement: None
References:


[8] Fagerholm R, Mattila AK, Roine RP, Sintonen H, Taskinen S. Mental health and


Figure Legend:

Figure 1. Subject Selection Strategy.

Figure 2. Frequency of Procedure by Age

Figure 3. Change Over Time in Procedure Type (2004-2014)

Supplementary Figure 1. Number of Cases by Hospital

Supplementary Figure 2. Proportion of Charges, by Category in High-, Medium- and Low-Volume Centers.

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