

## Original Article

# Quality of life among postoperative patients with disorders of sex development: a long-term perspective

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**Abstract:** Objective: Quality of life (QOL) among patients with disorders of sex development (DSD) is important aspect of their care. In our study, we evaluated the long-term QOL of postoperative DSD patients compared with the control. Design: A cross-sectional study utilizing a standardized questionnaire. Patients and Methods: Thirty-five patients with DSD (seven with congenital adrenal hyperplasia, six with 46,XY gonadal dysgenesis, and twenty-two with androgen insensitivity syndrome) participated in this study. They all underwent different surgical treatments. A long-term follow up was carried out after surgeries including postoperative QOL and sexual life quality, which were assessed through SF-12 questionnaire and Chinese version of Female Sexual Function Index (CVFSFI) for patients with DSD and 35 controls matched for sex, age, and education level etc. Results: The mean follow-up time was 3.98 (0.3-11.2) years. Compared to the 46,XX healthy women, patients with DSD reported significantly lower mental health scores ( $P<0.05$ ) while other domains were not significantly different ( $P>0.05$ ). And two patients received psychotherapy after surgery. There were no significant differences ( $P>0.05$ ) regarding the eight domains between patients with different types of DSD ( $P>0.05$ ). We observed no differences in QOL between patients with androgen insensitivity syndrome (AIS) who underwent gonadectomy in adolescence or adulthood ( $P>0.05$ ). Among all patients, only 8 women (22.8%) reported sexual activity with lower orgasm and total FSFI scores ( $P<0.05$ ). Conclusion: A skilled multidisciplinary team is necessary and especially more attention should be paid to the treatment of psychological and sexual problems experienced by patients with DSD to improve their QOL.

**Keywords:** Quality of life, disorders of sex development, surgical treatment, sexual dysfunction

## Introduction

The term “disorder of sex development” (DSD) is defined as a congenital condition in which the development of chromosomal, gonadal, or anatomical sex is atypical according to the international consensus established in Chicago in 2005. The term includes a heterogeneous group of conditions and can be divided into sex chromosome DSD, 46,XY DSD, and 46,XX DSD according to the consensus [1]. DSDs are rare, and the incidence is approximately 1:4,500-5,000 [2, 3]. The rarity of DSD limits the relevance of the literature when conducting a medium to long-term follow-up study of affected patients.

Quality of life (QOL) is a term utilized to describe an individual's perception of their position in life in the context of the culture and value systems in which they live and in relation to their goals, expectations, standards and concerns,

according to the Quality of Life Group of the World Health Organization [4]. QOL is indeed crucial to outcome studies involving patients with DSD. QOL measurements provide an overview of multiple dimensions regarding patient well-being and influence patient management. Although a few articles have assessed QOL for patients with DSD during the last decade, DSD is a heterogeneous condition that can be quite variable [5-7].

In our study utilizing the SF-12 survey, we evaluated the QOL of Chinese patients with DSD who underwent surgical treatments compared to normal individuals matched for sex, age, and education level etc.

## Material and methods

### Patients and comparison group

This study was conducted at the Obstetrics and Gynecology Hospital of Fudan University. We

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**Table 1.** Basic characteristics of patients with DSD

	N	%
Age		
Mean	22.94 (4.90)	
Range	14-32	
Follow-up time (years)		
Mean	3.98 (3.19)	
Range	0.3-11.2	
Social gender	Female	
Diagnosis		
Congenital adrenal hyperplasia	7	20
Gonadal dysgenesis	6	17.1
Androgen insensitivity syndrome		
CAIS	17	48.6
PAIS	5	14.3
Educational level		
Middle school degree	19	54.3
High school degree or above	16	45.7
Marriage		
Married	8	22.9
Unmarried	27	77.1
Employment		
Employed	17	48.6
Unemployed	4	11.4
Schooling	14	40.0

CAIS: Complete androgen insensitivity syndrome; PAIS: Partial androgen insensitivity syndrome.

invited 58 DSD patients from different regions of China who received surgical treatments in our hospital between February 2005 and November 2015 to participate this study. Among the 58 patients, 35 (60%) agreed to participate. These patients were well informed and signed consent forms. For 5 (9%) patients, their parents rejected the invitation because they had not informed their children about their diagnosis and considered them too young to understand their condition. The remaining 18 (31%) patients did not reply to our invitation.

All 35 patients had definite diagnosis following comprehensive examinations, including physical examinations, laboratory tests, ultrasonography and pathological results following surgery. Despite of their diagnosis, all patients or their parents chose female as the final social sex. The mean follow-up time for these patients was 3.98 years (0.3-11.2 years). We collected data regarding age, clinical diagnosis, education level, marriage, employment, the age at

operation, the scores of the SF-12 questionnaire and all treatments they received including surgery, medicine and psychological therapy.

The control group was recruited from women who came to the health examination center at our hospital and several girls from nearby schools with complete medical records indicating no past or present illness. The controls were matched for sex, age (n=35, age: 22.97±4.94, range: 15-33 years), education level, marriage, employment and were informed about the nature of our study.

### Methods

The SF-12 questionnaire is a reasonable alternative to SF-36. The Chinese version is available at <http://www.qualitymetric.com>, and further information can be obtained from the International Quality of Life Assessment Project [8]. The SF-12 questionnaire consists of 12 questions that measure health in 8 domains: physical functioning, physical roles, bodily pain, general health, vitality, social functioning, emotional roles, and mental health. The scale scores are calculated by summing the responses across scale items and then transforming the raw scores to a 0-100 scale (higher scores indicate better health) [9]. Such questionnaires have been widely utilized to assess the impact of a variety of diseases or interventions on general health [10, 11].

### Statistical analysis

The data were analyzed using PASW Statistics for Windows, Version 19.0 (SPSS Inc., Chicago, IL, USA). The continuous data are presented as means ± standard deviations, and the categorical data are presented as counts and percentages. Independent sample t tests were used to compare the differences between patient and control groups. A one-way ANOVA was used to compare differences based on age and diagnosis. A P value of less than 0.5 was considered significant.

### Results

Thirty-five patients with DSD and thirty-five healthy women (control group) were recruited to participate in this study. Among the patients with DSD, 7 had congenital adrenal hyperplasia, 6 had 46,XY gonadal dysgenesis, and 22 had androgen insensitivity syndrome. All

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**Table 2.** SF-12 scores for patients with different types of DSD versus the control group

Groups	General health	Physical function	Role physical	Mental health	Role emotional	Bodily pain	Vitality	Social function
DSD (n=35)	66.71±19.33	97.86±7.10	82.86±29.56	68.29±17.06	72.86±30.54	82.86±16.90	65.14±21.33	78.57±17.30
Control (n=35)	57.14±23.17	97.14±8.07	75.71±32.93	73.43±12.59	68.57±29.92	85.00±18.39	65.14±16.34	87.86±12.68
P	0.368	0.433	0.207	0.047	0.729	0.409	0.067	0.587

**Table 3.** Comparison of SF-12 scores for DSD subgroups

Subgroups	General health	Physical function	Role physical	Mental health	Role emotional	Bodily pain	Vitality	Social function
CAH (n=7)	69.29±22.81	100.00±0.00	78.57±26.73	70.00±19.15	78.57±39.34	89.29±13.36	74.29±19.02	85.71±19.67
46XY GD (n=6)	62.50±22.08	95.83±10.21	83.33±40.83	68.33±21.37	91.67±20.41	87.50±13.69	66.67±24.22	83.33±12.91
AIS (n=22)	67.05±18.24	97.73±7.36	84.09±28.40	67.73±16.02	65.91±28.40	79.55±18.32	61.82±21.30	75.00±17.25
F	0.198	0.551	0.166	0.044	1.930	1.166	0.921	1.316
P	0.821	0.582	0.848	0.957	0.162	0.324	0.408	0.282

CAH: Congenital adrenal hyperplasia; 46XY GD: 46,XY gonadal dysgenesis; AIS: Androgen insensitivity syndrome.

**Table 4.** CVFSI scores for patients with DSD and the control group

Group	Desire	Arousal	Lubrication	Satisfaction	Orgasm	Sexual pain	Total
DSD (n=8)	3.38±0.71	4.08±1.37	4.84±0.91	4.05±1.16	3.10±1.51	4.75±0.84	24.20±5.30
Control (n=14)	3.69±0.57	4.24±0.86	5.04±0.66	4.37±0.85	3.91±0.74	4.46±0.35	25.71±2.81
P	0.393	0.053	0.421	0.232	0.017	0.233	0.048

CVFSI: Chinese version of the Female Sex Life Index.

**Table 5.** Comparison of SF-12 scores for AIS groups based on the age at operation

Age at operation	General health	Physical function	Role physical	Mental health	Role emotional	Bodily pain	Vitality	Social function
<18 (n=14)	62.06±23.98	97.06±8.30	73.53±35.87	61.76±20.38	58.82±31.80	82.35±17.15	60.00±25.50	73.53±16.47
≥18 (n=8)	71.54±12.97	98.08±6.93	92.31±18.77	74.62±11.98	92.31±18.78	80.77±18.13	69.23±17.54	88.46±16.51
P	0.109	0.475	0.002	0.028	0.087	0.937	0.134	0.411

patients were reared as female. The mean patient age was 22.94 years (SD 4.90, range: 14-32 years). The mean follow-up time was 3.98 years (range: 0.3-11.2 years). In total, 19 patients (54.3%) had achieved a middle school degree, and the other patients had achieved high school degree or above. Seventeen patients (48.6%) are employed, four patients (11.4%) are unemployed and others are schooling. Seven patients (22.7%) are married. The basic characteristics of the patients are presented in **Table 1**.

The scores from the SF-12, including 8 domains (physical functioning, physical role, bodily pain, general health, vitality, social functioning, emotional role, and mental health) were calculated for the patients with DSD and controls. The scores were transformed to a 1-100 scale.

Compared to the 46,XX healthy women, patients with DSD reported significantly lower

scores for mental health ( $P<0.05$ ) but not the other domains ( $P>0.05$ ) (**Table 2**). As shown in **Table 3**, the data were analyzed via a one-way ANOVA. Regarding the eight domains, we observed no significant differences between the different DSD subgroups. Among all patients, 8 women (22.8%) were sexually active and the ratio is lower than the control group in which the ratio is 40% (14/35). We also evaluated their sexual life quality using the Chinese version of the Female Sex Life Index (CVFSI). In contrast with the control group, patients with DSD reported significantly lower orgasm and total FSFI score ( $P<0.05$ ) (**Table 4**).

All thirty-five patients had undergone different surgical treatments, including gonadectomy, clitoroplasty, vaginoplasty and constructive genital surgery in accordance with their conditions. We compared the QOL among patients diagnosed with androgen insensitivity syndrome who had undergone a gonadectomy during

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adolescence or adulthood. We observed no differences between these two groups (**Table 5**).

### Discussion

Our study is a cross-sectional investigation of the QOL of patients with DSD. In agreement with other studies reported previously [12-14], DSD does not affect some aspects of life, such as general health, physical function and bodily pain according to our results. The general health scores for patients with DSD were even higher than the scores for healthy women (but not significant). The patients may feel that they are better followed and medically protected because of the necessity of long-term follow-up in clinical settings. Other hypotheses may also account for these differences. Perhaps exposure to prenatal androgen positively affects a woman's physical well-being. Additionally, women with DSD are not exposed to the immense hormonal fluctuations that other women experience during "normal" female pubertal changes [14]. Further studies are needed to better understand these results. Patients with CAH and 46,XX and 46,XY-virilized DSD reported a poorer QOL according to a case-control study [15]. However, we did not observe any differences among the three different DSD sub-groups in our study. This inconsistency may be due to different patient groups, cultural environments, or questionnaires.

Patients with DSD scored significantly lower on the mental health domain compared to healthy women. And only two patients received psychotherapy. This result raises concern. Franco et al. [16] investigated the QOL and psychological adjustment of 34 Italian females with 46,XY DSD. These women were more likely to be depressed and anxious, showing more withdrawal and aggressive behaviors and having more thought and attention problems than the women in the comparison group. Accordingly, the ESPE/LWPES guidelines emphasized the importance of a clinical psychologist as a key member of the multidisciplinary team to provide proper management for patients with DSD patients and their families [17].

The timing of surgical interventions, especially gonadectomy for patients with 46,XY DSD is controversial. Currently, the common practice is to remove the testes of patients diagnosed with AIS after their feminization is complete.

Feminization occurs when peripheral androgen is converted to estrogen. The malignancy risk associated with AIS gonads is relatively low [18, 19]. However, some doctors still recommend that gonadectomy should be performed soon after diagnosis due to the potential for malignant transformation [20]. Among all 22 AIS patients in our study, only 1 (4.54%) patient had dysgerminoma. This patient was first diagnosed with CAIS and underwent gonadectomy at the age of 22. We evaluated the QOL of patients diagnosed with AIS who had undergone gonadectomy during adolescence or adulthood and found no difference between these two groups. The removal of the gonads in AIS patients can be deferred until adolescence due to the low malignancy rate and unaffected QOL. Moreover, better awareness of one's medical condition during adolescence may contribute to better psychological adjustment [21].

In this study, we also evaluated the sexual life quality of patients with DSD using the Chinese version of FSFI (CVFSFI) which has been previously validated [22]. However, only 8 women (22.8%) reported any lifetime sexual activity while 14 (40.0%) women had sexual activity in control group. The low ratio may be due to the young age and conservative traditional beliefs of the patient population. Moreover, a higher degree of sexual and social anxieties for patients with DSD (e.g., fear of sexual contact) may delay or decrease sexual activity compared to the healthy women [12, 23, 24]. In contrast with the control group, patients with DSD had significantly lower orgasm and total FSFI scores and the scores of other domains were also lower but not significant. Based on the cut-off scores of the CVFSFI established by Jiehua Ma et al. [25], 4 patients (50%) were sexually dysfunctional (total score  $\leq 23.5$ ); 2 (22.2%) patients had low desire; 2 (22.2%) patients had an arousal disorder; 2 (22.2%) patients had a lubrication disorder; 6 (66.7%) patients had an orgasm disorder, and 1 (11.1%) patient had sexual pain. These findings agree with some previous studies in which patients with DSD were more likely to be sexually dysfunctional [26, 27]. More attention should be given to the sexual problems of these patients in addition to their medical management.

There were several limitations to this study that should be mentioned to interpret the results

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cautiously. (1) The study response rate was only 60%, and it is possible that the most ill or distressed patients did not participate. Hence, the sample size of our study is small. (2) Our study may have a selection bias. The data were collected in a gynecological hospital, and all of the patients were reared as female. Not all DSD types were represented in our study. (3) Because our follow-up study was cross-sectional in regards to QOL, we could not investigate how the QOL of the patients had evolved over time. We also could not investigate the impact of other potentially adverse life events.

### Conclusion

In conclusion, a skilled multidisciplinary team is necessary to care for patients with DSD, especially regarding their psychological and psychosexual counseling and education, to reduce the degree of psychological and sexual problems and improve patient QOL by better understanding their condition and best treatment options.

### Disclosure of conflict of interest

None.

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