

*Research Article*

## **Aesthetic, functional and psychological outcomes of reconstructive surgery for disorders of sexual development in the paediatric population**

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**Aim of the study:** Aim of this study is to retrospectively evaluate all the paediatric patients affected by DSD (Disorders of Sexual Development) surgically treated at our Department of analysing their diagnosis, treatment and both surgical and psychological outcomes.

**Materials and Methods:** All patients affected by DSD who underwent to reconstructive surgery at our Department from January 2009 to September 2020 were included. Two questionnaires were proposed to them: CBCL (Child Behavioural Check List) and YSR (Youth Self-Report) were used to evaluate their quality of life and the eventual development of emotional and behavioural disorders; PedsQL 4.0 (Pediatric Quality of Life) to analyse the long-term psychological outcomes of surgery in term of daily activities, school grades and social interactions.

**Results:** All 29 paediatric patients presented satisfied aesthetic and functional outcomes. Eight (27.5%) patients were selected to complete the questionnaires and 6 of them (75%) filled in them. 5 of 6 patients (83%) showed alterations of quality of life, 1 (16%) suffered from anxiety, 2 (33%) showed borderline values for anxiety and emotional disturbances.

**Conclusions:** According to our experience, satisfied aesthetic, surgical and functional outcomes were described. Psychological consequences developed after reconstructive surgery for DSD patients. It seems to be useful propose a psycho-diagnostic screening to all patients affected by DSD and treated with a surgical approach in order to evaluate their quality of life and recognise possible emotional and behavioural disorders due to this changing process.

**Keywords:** Disorders of sexual development, Children, Reconstructive surgery, Adrenogenital syndrome, Urinary infections

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## INTRODUCTION

The purpose of this study is to define both the physical and psychological implications of surgical management in patients treated for DSD, taking into account demographic variables as well as therapeutic strategies.

Disorders of Sexual Development (DSD) represent a large and heterogeneous group of rare congenital pathological conditions characterised by abnormal sexual development (Lee et al., 2016).

DSD remain a significant challenge to healthcare professionals (Barbaro et al., 2011). In 2006, a consensus conference on DSD was held in Chicago to define a standardised approach in the treatment of this group of patients (Hughes et al., 2006). A multidisciplinary management approach is required to define the correct sex, to identify the most appropriate treatment modality and to prevent potential complications (Moran et al., 2012). This vulnerable group of patients demands a long-term follow-up as outcomes can often only be fully evaluated during adolescence, when patients are able to verbally express and report their subjective feelings, have developed their personality and their sexual identity (Wang et al., 2015).

A limited group of studies concerning post-operative DSD follow-up are available in the literature, most of which focus on the evaluation of the morphology of the external genitalia, genital function, and intercourse satisfaction (Machado et al., 2016). The lack of long-term studies on psychological outcomes necessitates the definition a new, practical, method to assess the Quality of Life (QoL) in patients affected by DSD (Selveindran et al., 2017). Recently, several studies have looked into this topic, however reviews have shown poor and inconsistent results (Bennecke et al., 2017).

## MATERIALS AND METHODS

A retrospective, monocentric, study was performed, in which we included all patients with DSD who were treated at the Paediatric Surgical Clinic of Siena between January 2009 and September 2019.

### The following data was assessed

Demographic factors (diagnosis, age at diagnosis, attributed gender and gender of rearing), surgical factors (surgical technique and post-operative assigned gender), outcomes (aesthetic and functional results, including presence of erections, changes in micturition, urinary infections, psychopathological profile, and QoL). An informed consent was signed by patients and their parents. Parents were contacted by telephone. Patients who were included in the study were requested to complete two questionnaires (described below), for subjective feedback assessment.

### Paediatric Quality of Life inventory (PedsQL)

Quality of life was assessed using the Paediatric Quality of Life version 4.0 generic core scales (PedsQL) questionnaire, in the Italian language (Trapanotto et al., 2009). This is a self-assessment questionnaire that is divided into two sections: The first section consists of a generic and standardised evaluation

of the influence of objective clinical measures on the individual patient, i.e. regarding health. The second section considers the subjective perception of the pathology and the impact on patients and their parents, i.e. the Health-Related Quality of Life (HRQOL) (Varni et al., 1999 and Gkoltsiou et al., 2008).

The questionnaire includes 23 items, grouped into 4 scales: Physical functioning (8 items), emotional functioning (5 items), social functioning (5 items) and school functioning (5 items). For each item, a score of up to 5 points is given, as a representation of how much of a problem that item has been over the last month (0=is never a problem; 1=is almost never a problem; 2=is sometimes a problem; 3=is often a problem; 4=is almost always a problem). The value for each response is converted into a score between 0-100 (0=100, 1=75, 2=50, 3=25, 4=0). Thus, a higher score on PedsQL 4.0 indicates a better HRQOL. The results comprise of two general scores: Physical health and psychosocial health. The physical health score is the same as the physical functioning scale. The psychosocial health score is obtained by the sum of the scores on the emotional, social, and educational scales, divided by the number of items answered on these three scales (15 items).

### Child Behaviour Checklist (CBCL)

The Achenbach System of Empirically Based Assessment (ASEBA) Child Behaviour Checklist (CBCL) is a useful tool, developed by Achenbach to obtain information on children's and adolescents' adjustment, skills, behavioural and emotional problems, detectable in everyday situations (Kweon et al., 2016 and Achenbach et al., 2000). For children up to the age of 5, the CBCL 1½-5 is used, which is filled in by parents or legal guardians. For older children and adolescents there are 2 versions: the CBCL 6-18, which is also filled out by parents or legal guardians, and the Youth Self-Report 11-18 (YSR), which the adolescent fills out independently (Achenbach et al., 2000).

### The questionnaires are structured in 4 parts

Personal data; 113 short statements about the child's behaviour, emotions, and any physical or social problems; 7 items for older children concerning their participation in physical and social activities, and their scholastic skills; and a final section where parents can comment on the best aspects of their child and express their concerns. To complete the items, the parent is asked to consider the child's behaviour, giving an evaluation according to a 3-point scale: (0) if the statement is not true; (1) if the statement is partly or sometimes true; (2) if the statement is mostly true. Several scales can be obtained from these questionnaires, including competence-related scales, syndromic scales and scales related to the Diagnostic and Statistical Manual of Mental Disorders (DSM V) (Andreoli et al., 2007). The competence scales concern the more mature age groups and are derived from 20 items, which investigate three different areas: 1) the activity scale assesses the quantity and quality of the child's participation in sports, hobbies, games and activities, the quantity and quality of work and/or chores, 2) the social scale assesses the child's ability to get along with others, their friendships, as well as their behaviour in a social setting and during independent activity and 3) the school scale assesses the child's performance at school and the psychopathological profile of the child's behavioural problems, if present. The syndrome scale scores provide a qualitative

measure of the possible problem area grouped broadly into internalising behavioural problems and externalising behavioural problems. (Dominguez-Lara et al., 2017). The six DSM V oriented scales associate particular problems and behaviours with a corresponding DSM V category. The CBCL uses a normative sample to create standard scores. From the responses to the various items, raw scores are obtained for each scale, which are then transformed into standardised values for sex and age (T scores), which facilitate interpretation and comparison. The standard scores are rescaled so that 50 is the mean for age and sex, with a standard deviation of 10 points. Higher scores indicate greater problems. Scores are interpreted as falling into the normal, borderline or clinical range. Any score falling below the 93rd percentile is considered normal, scores between the 93-97th percentiles are borderline, and any score above the 97th percentile is in the clinical range. The data we obtained was treated anonymously, in accordance with current privacy legislation.

## RESULTS

A total of 29 patients with DSD were included in this study:

### Demographic factors

None of the patients included were diagnosed prenatally. The age at diagnosis ranged from 3 months to 21 years, with a mean age of 8.3 years and a standard deviation of 5.3 years. The sex of rearing was female in 22 patients (76%), and male in 7 patients (24%). Only 3 patients (10, 35%) had a different attributed sex to the sex of rearing, 2 female patients and 1 male patient changed their sex (Table 1).

**Table 1.** Demographic data including prenatal diagnosis, age at diagnosis, gender at birth and attributed gender for each patient included in the study.

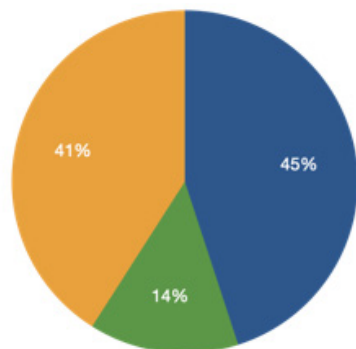
DSD type	Pre-natal diagnosis	Age at the diagnosis	Sex of breeding	Attributed sex
DSD 46, XX deficit of 21-hydroxylase	no	6 y.o.	F	F
DSD 46, XX deficit of 21-hydroxylase	no	8 y.o.	F	F
DSD 46, XX deficit of 21-hydroxylase	no	11 y.o.	F	F
DSD 46, XX deficit of 21-hydroxylase	no	2 y.o.	F	F
DSD 46, XX deficit of 21-hydroxylase	no	3 y.o.	M	F
DSD 46, XY deficit of 5- $\alpha$ reductase	no	9 y.o.	M	M
DSD 46, XY deficit of 5- $\alpha$ reductase	no	15 y.o.	F	M
DSD 46, XY deficit of 5- $\alpha$ reductase	no	21 y.o.	F	M
DSD 46, XY deficit of 5- $\alpha$ reductase	no	4 y.o.	M	M

DSD 46, XY deficit of 5- $\alpha$ reductase	no	14 y.o.	M	M
DSD 46, XY deficit of 5- $\alpha$ reductase	no	5 y.o.	M	M
DSD 46, XY deficit of 5- $\alpha$ reductase	no	6 y.o.	F	F
DSD 46, XY deficit of 5- $\alpha$ reductase	no	9 y.o.	F	F
DSD 46, XY deficit of 5- $\alpha$ reductase	no	2 y.o.	F	F
DSD 46, XY partial gonadal dysgenesis	no	3 y.o.	F	F
DSD 46, XY partial gonadal dysgenesis	no	3 y.o.	F	F
DSD 46, XY partial gonadal dysgenesis	no	5 y.o.	F	F
DSD 49, XXXXY variant of klinefelter syndrome	no	3 y.o.	F	F
DSD 45, X0/46, XY ovotesticular dysgenesis	no	7 y.o.	F	F
DSD 45, X0/46, XY ovotesticular dysgenesis	no	12 y.o.	M	M
DSD 46, XX abnormalities of müllerian ducts	no	14 y.o.	F	F
DSD 46, XX abnormalities of müllerian ducts	no	8 y.o.	F	F
DSD 46, XX abnormalities of müllerian ducts	no	17 y.o.	F	F
DSD 45, X0 turner syndrome	no	13 y.o.	F	F
DSD 46, XX HWW syndrome	no	15 y.o.	F	F
DSD 46, XX HWW syndrome	no	10 y.o.	F	F
DSD 46, XX HWW syndrome	no	12 y.o.	F	F
DSD 46, XX bilateral gonadal dysgenesis	no	3 y.o.	F	F
DSD 46, XX persistent cloaca	no	At birth	F	F

**Note:** y.o. indicates year old.

Patients were divided into three groups according to the classification introduced by the 2006 consensus conference in Chicago: 13 patients had a 46, XX karyotype (45%), 12 had 46, XY (41%) and 4 had chromosomal abnormalities (14%).

Among the 13 patients with DSD 46, XX, there were 5 cases of adrenogenital syndrome, 3 abnormalities of the Müllerian ducts, 3 cases of Herlyn-Werner-Wunderlich syndrome, 1 case of bilateral gonadal dysgenesis and 1 case with persistent cloaca. Among the 12 patients with DSD 46, XY, there were 9 cases of 5 $\alpha$ -reductase deficiency syndrome and 3 cases with partial gonadal dysgenesis. Among the 4 patients with DSD associated with chromosomal abnormalities, there were 2 cases of ovotesticular dysgenesis with mosaicism 45 XO/46 XY, 1 variant of klinefelter syndrome with karyotype 49 XXXXY and 1 case of turner syndrome with karyotype 45 X0 and bilateral gonadal dysgenesis (Figure 1).



**Figure 1.** Percentage of each type of DSD. 41% DSD 46 XX, 14% DSD chromosomal abnormalities and 45% DSD XY. **Note:** (•): DSD 46, XX; (•): DSD Chromosomal Abnormalities; (•): DSD 46, XY.

### Surgical factors

The surgical approach varied depending on the type of DSD. Patients with DSD 46, XX underwent clitoridoplasty or vaginoplasty. Concerning the patients with adrenogenital syndrome, 4 underwent clitoridoplasty with removal of 3/4 of the corpora cavernosa and reduction of the glans with relative de-epithelialisation and preservation of the neurovascular bundle. Only in one patient was it not possible to perform a clitoridoplasty, due to previous amputation. All patients affected by anomalies of Mullerian ducts underwent vaginal reconstruction with a sigma tract anastomosed to the uterus proximally and the vulvar epithelium distally. The patient with bilateral gonadal dysgenesis underwent cystovaginostomy. The three patients with Herlyn-Werner-Wunderlich underwent vaginostomy, and the patient with persistent cloaca underwent both vaginoplasty and anoplasty. Patients with DSD 46, XY underwent urethroplasty, scrotal reconstruction and/or orchidopexy. In female patients with a deficit of 5 $\alpha$ - reductase, a gonadectomy was performed, whereas in male patients affected by a deficit of 5 $\alpha$ - reductase, the vagina was resected and orchidopexy with perineal hypospadias was performed. Patients affected by partial gonadal dysgenesis underwent clitoridoplasty, labio-vulvoplasty and gonadectomy. Among the patients with DSD associated with chromosomal abnormalities, those with DSD 45 XO, 46 XY with ovotesticular dysgenesis underwent clitoridoplasty and vuvlo-vaginoplasty, and patients with 49 XXXXY with Klinefelter syndrome and DSD 45 XO with Turner Syndrome underwent bilateral gonadectomy and bilateral female external genital asportation.

### Outcomes

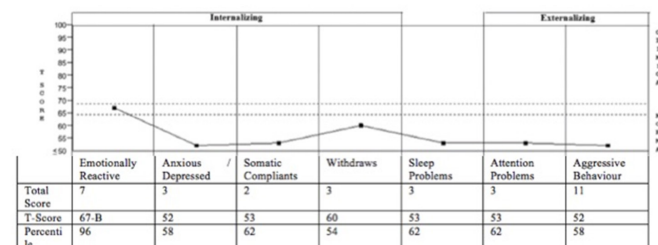
Of the 8 patients selected for psychological evaluation, only 6 completed the questionnaires (Table 2).

**Table 2.** Characteristics of the sample to which questionnaires were administered and related questionnaires.

DSD type	Age	CBCL and YSR questionnaires	PedsQL questionnaires
DSD 45, X0/46, XY	16 y.o.	CBCL 6-18 YSR 11-18	PedsQL 13-18 y.o.
DSD 45, X0/46, XY	15 y.o.	CBCL 6-18 YSR 11-18	PedsQL 13-18 y.o.
DSD 45, X0	15 y.o.	CBCL 6-18 YSR 11-18	PedsQL 13-18 y.o.
DSD 46, XX	13 y.o.	CBCL 6-18 YSR 11-18	PedsQL 13-18 y.o.
DSD 46, XX	13 y.o.	CBCL 6-18 YSR 11-18	PedsQL 13-18 y.o.
DSD 46, XX	16 y.o.	CBCL 6-18 YSR 11-18	PedsQL 13-18 y.o.
DSD 46, XX	4 y.o.	CBCL 1.5-5	PedsQL 2-4 y.o.
DSD 46, XX	10 y.o.	CBCL 6-18	PedsQL 8-12 y.o.

**Note:** y.o. indicates year old.

We collected: 1 CBCL questionnaire for ages 1.5-5, 5 CBCL questionnaires for ages 6-18, 2 YSR questionnaires for ages 11-18, 6 PedsQL questionnaires for ages 13-18, 1 PedsQL questionnaire for ages 8-12 and 1 PedsQL questionnaire for ages 2-4. The 4-year-old patient for whom the CBCL 1.5-5 years questionnaire was completed presented borderline results for the emotional reactivity scale (Figure 2), as well as for internalising problems (Table 3). According to the DSM V classification, no relevant data was found (Table 4).



**Figure 2.** T score and percentile of the syndromic scale related to the 4 year old patient (CBCL 1.5-5 y.o.).

**Table 3.** Result of the syndromic scale compartmentalized in internalizing problems.

Patients	Internalizing problems
1 (10 y.o.)	46
2 (16 y.o.)	50
3 (15 y.o.)	58
4 (16 y.o.)	63 B
5 (13 y.o.)	52
6 (4 y.o.)	61 B

**Note:** y.o. indicates year old.

**Table 4.** Results related to the DMS IV oriented scale (CBCL 1.5-5 y.o.).

Patient	T score			
	Emotional problems	Anxiety problems	Pervasive development issues	ADHD problems
6 (4 y.o.)	56	54	63	51

As shown in Table 5, among the five 6-18 years-old patients who filled in CBCL questionnaires, none of them showed clinically significant values for the social and school scales. On the activity and total competence scales, two of five patients showed pathological values.

**Table 5.** Results of the competence scale (CBCL 6 y.o.-18 y.o.).

Patient	T score		
	Activity scale	Sociality scale	Scholastic scale
1	31 B	44	41
2	46	54	55
3	27 C	41	50
4	27 C	35 B	55
5	25 C	43	37

From the table above, we can see that there are no clinically relevant results apart from a borderline value for social disorders in one of the two patients as previously mentioned. According to DSM V (Table 6), only 1 patient had clinically significant values in the field of anxiety disorders, with borderline values for attention/hyperactivity disorder (Figure 3). Another patient had values belonging to the normal range in all fields, with the exception of anxiety problems, where borderline values are reached (Table 6). As can be seen from Table 7, no clinically relevant data is reported with regards to Post Traumatic Stress Disorder (PTSD).

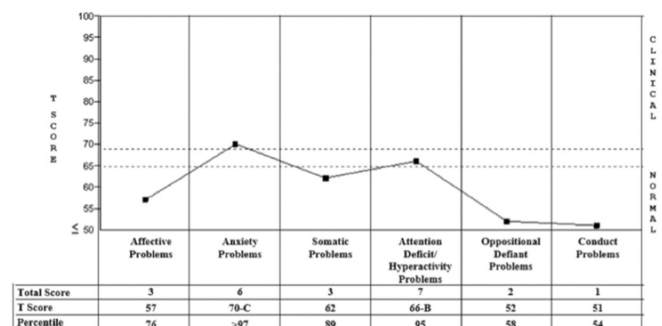


Figure 3. T-score and percentile of the patients that presented alterations relatively to DMS IV oriented scale (CBCL 6-18 y.o.).

**Table 6.** Results of the DMS V oriented scale (CBCL 6 y.o.-18 y.o.).

Patients	T score				
	Emotional problems	Anxiety problems	Somatic problems	ADHD problems	Opposite rebel problems
1	50	51	50	50	51
2	50	55	50	51	51
3	59	66 B	56	50	50
4	57	70 C	62	66 B	52
5	50	60	50	58	52

**Table 7.** Results of PedsQL regarding physical and psychosocial health.

Patient	Physical health	HRQOL
1	Mildly problematic	Mildly problematic
2	Non problematic	Non problematic
3	Problematic	Problematic
4	Problematic	Problematic
5	Problematic	Mildly problematic
6	Significantly problematic	Significantly problematic

Of the 6 patients to whom the YSR version was administered, 2 responded, both aged 16 years. The scales analysed by this questionnaire are the same as those of the CBCL version 6-18 years. With regards to QoL assessment, 6 patients were given the PedsQL 13-18 questionnaire, 1 patient the PedsQL 8-12 questionnaire and 1 patient the PedsQL 2-4 questionnaire. Scholastic skills analysed with the PedsQL questionnaire described lower QoL scores for 5 of 8 patients (62.5%) and, in general, lower scores were reported for DSD patients than for healthy controls.

## DISCUSSION

Numerous previous studies concerning the follow-up of children affected by DSD have been conducted. The majority mainly concern surgical strategies, genital function and personal satisfaction. The issue is extremely important, in fact many surgeons have emphasized how both functional and aesthetic outcomes could be reduced after this type of surgery (Cuomo et al., 2019). This study aims to evaluate different aspects of short- and long-term follow-up, considering not only the best surgical technique and aesthetic results, but also the psychological well-being of patients with DSD, the impact on QoL and the emergence of possible behavioural disorders. It is fundamental to consider the sexual identity of the child and their psychological evaluation to determine the appropriate sex. After identifying the sex, it is then appropriate to identify the relevant surgical approach. We used the CBCL questionnaire to assess the psychopathology of DSD patients managed surgically, and noticed that only one of them had anxiety/attention/hyperactivity disorder, and one had a predisposition for future anxiety. Syndromic scales were used to identify

behavioural implications and showed only one case of social problems. No patient fit the diagnosis of PTSD. DSD patients were found to have inferior scholastic skills than those of healthy controls. These results can be explained by the fact that DSD is not only a chronic disabling disease that is difficult to be shared and discussed with peers, but it is also often a part of a more complex syndrome. The perception of this disease can be altered, as patients often do not consider themselves as sick people. Self-administered YSR questionnaires did not show significant results. In contrast, we did find significant results with the CBCL questionnaires administered to parents. In particular, QoL seemed to be the most affected. QoL was evaluated considering both physical and psychological health and was not altered for most of our patients. Thus, even if surgery allowed patients to achieve excellent functional and aesthetical results, gender transitioning negatively affected children's QoL and their self-perception. Thus far, there has not been an established and precise diagnostic and therapeutic pathway for patients with DSD, however it is recognised that a multidisciplinary and individualised management approach is needed for early diagnosis, to choose the best possible treatment option and to support patients and their families from a psychological point of view. The multidisciplinary team should include paediatricians, paediatric surgeons, geneticists, and psychologists. Clinicians must examine the anatomical features of each patient, understand their perspective in relation to their genotype, and understand their psyche, their hormonal balance, as well as their social and cultural background. The end goal of this individualised and multidisciplinary approach is to not only optimise surgical decision making and functional results, but also to minimise the risk of compromising QoL and undesirable emotional and behavioural implications.

## CONCLUSION

Our results show that outcomes of surgical intervention for DSD, in terms of aesthetic and functional results, are excellent. We conclude that a multidisciplinary team with expertise in treating patients with DSD is fundamental. However, this is not always sufficient to ensure optimal results, particularly with regards to QoL and psychosocial outcomes. A long-term psychological support system for this vulnerable group of patients and their families is required to reduce the risk of potential behavioural disorders. Demographic and psychologic considerations are helpful in identifying the appropriate therapeutic strategy, including the optimal time of surgical intervention, while also reducing potential complications.

We propose the application of the CBCL questionnaire as a valid and reproducible strategy to screen and assess the psychological state of paediatric patients affected by DSD. We also suggest the application of the PedsQL questionnaire as a valuable tool to evaluate their behavioural characteristics.

## LIMITATIONS

We encountered instances where data was missing due to patients who were lost to follow up or due to issues with age, i.e., some patients were not within the age range included in the assessment questionnaires, which were validated exclusively for subjects from the first year of life up to 18 years of age.

We recognise that further studies including larger groups of paediatric patients with DSD are needed to prove the viability of our protocols. Furthermore, patients should be ideally followed-up in both the short and long term.

## DECLARATIONS

### Ethical approval

Not applicable.

### Consent for publication

The consent for publication was obtained from the parents or legal guardians of the children involved in the study, *via* a consent form.

### Availability of data and materials

Please contact authors for data requests.

### Funding sources

We have no funding to declare.

### Competing interests

The authors have no competing interests.

### Author contributions

FM and MM carried out the surgical procedures. RA proposed the questionnaire to fill in. FM, MM and RA conceived the study and participated in its design and coordination. FN and GC participated in the design of the study, performed the statistical analysis and helped to draft the manuscript. TC, GV, GF, VB, VS, ST helped to draft the manuscript.

### Conflict of interest

The authors have no conflicts of interest to declare.

### Acknowledgments

Not applicable.

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