

Urological, Sexual, and Quality of Life Evaluation of Adult Patients With Exstrophy-Epispadias Complex: Long-term Results From a Dutch Cohort



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OBJECTIVE	To assess urological function, sexual function, and quality of life in patients with exstrophy or epispadias. Little is known regarding these outcomes in adult patients; our aim is to determine where improvements are needed for long-term management.
METHODS	The study population comprised adult (>18 years) patients. Demographic data were gathered and patients were asked to fill out 4 validated questionnaires: (1) International Consultation on Incontinence Questionnaire urinary incontinence form (ICIQ-UI) regarding continence; (2) International Prostate Symptom Score (IPSS) for men and International Consultation on Incontinence Questionnaire-Female Lower Urinary Tract Symptoms (ICIQ-FLUTS) for women regarding lower urinary tract symptoms; (3) 12-Item Short Form Health Survey regarding quality of life; (4) International Index of Erectile Function for men and Female Sexual Function Index for women regarding sexual function.
RESULTS	Seventeen patients were included (9 men and 8 women) with a median age of 36 years (range 19-73). Median score on ICIQ-UI was 5/21. Median IPSS score was 7/35 and median quality of life score was 1 (=pleased). Median scores per domain within ICIQ-FLUTS were 7 for storage, 0 for voiding, and 6 for urinary incontinence with bother scores of 4, 0, and 2.8, respectively. Scores for 12-Item Short Form Health Survey in the study population were comparable with those of the Dutch population, except for Physical Component Summary in women. For sexual function, no difference was found between those in the general population and our participants except for the domain "pain" in Female Sexual Function Index.
CONCLUSION	Adult patients with exstrophy or epispadias have a high rate of incontinence and lower urinary tract symptoms with relatively low to some degree of bother. When compared with the general population, quality of life, and sexual function of our patients were more or less similar. UROLOGY 136: 272–277, 2020. © 2019 Elsevier Inc.

The exstrophy-epispadias complex (BEEC) consists of 3 disorders: bladder exstrophy, epispadias, and cloacal exstrophy. Epispadias is the least severe defect of the group, characterized by failure of the urethra to close normally, and as a result, the inner lining of the urethra lays flat and exposed on the dorsal surface of the penis in boys and in girls there is a nonclosed urethral plate. Patients with bladder exstrophy will also have epispadias. However, isolated epispadias is less common than classical bladder exstrophy and is diagnosed in 1 in 200,000-400,000 live births.^{1,2} Bladder exstrophy is classically characterized

by an open, inside-out bladder on the surface of the lower abdominal wall and an open exposed dorsal urethra. Bladder exstrophy usually involves several organ systems in the body, including the urinary tract, the reproductive tract, the muscles, and the skin of the lower abdominal wall, and the muscles and bones of the pelvis. The reported incidence is 1 per 20,000-33,000 live births.^{1,2}

Cloacal exstrophy, the most severe defect, is classically characterized by exstrophy of the urinary bladder and large intestine (hindgut) through an abdominal wall defect, anal atresia, and possibly hypoplasia of the colon, omphalocele, and anomalous genitalia. In some cases, there may also be hypoplasia of the small intestine and severe pelvic bone abnormalities. The vertebral column (backbone) and spinal cord are also often abnormally developed.

Little is known concerning adult patients with exstrophy or epispadias as prevalence is limited and long-term follow-up is scarce.³ In this study, we aim to collect data in these patients regarding continence, lower urinary tract

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symptoms (LUTS), quality of life, and sexual function. This may give us insight in where improvements are needed with respect to long-term management and may provide useful tools for better counselling. Because of relatively small sample size and a varying surgical history, our goal is to present the overall result of treatment of BEEC and follow-up, not the result of any particular surgical technique.

MATERIALS AND METHODS

Study Design

We received local ethical committee approval before starting the study and all patients provided written consent (METC No 17-319c).

After consent, the patients with exstrophy or epispadias were asked to fill out 4 validated questionnaires:

- 1) International Consultation on Incontinence Questionnaire urinary incontinence form (ICIQ-UI) regarding continence.⁴
- 2) International Prostate Symptom Score (IPSS) for men⁵ and International Consultation on Incontinence Questionnaire-Female Lower Urinary Tract Symptoms (ICIQ-FLUTS) for women⁶ regarding LUTS.
- 3) 12-Item Short Form Health Survey (SF-12) regarding quality of life.⁷
- 4) International Index of Erectile Function (IIEF) for men⁸ and Female Sexual Function Index (FSFI) for women⁹ regarding sexual function.

A separate questionnaire was sent to patients to assess outcomes such as education level, employment status, relationship status, sexually activity (yes/no), and children (yes/no).

Medical history and previous treatment were obtained from electronic medical records.

Study Population

The study population comprised adult (>18 years) patients with BEEC from the department of Urology of University Medical Center Utrecht, the Netherlands. The primary treatment of these patients did not necessarily take place in Utrecht. In order to be eligible to participate in this study, patients had to be proficient in the Dutch language and were willing to fill out questionnaires.

Primary Outcomes

Continence was evaluated with the abovementioned ICIQ-UI. It is a 4-item questionnaire with a score range from 0 to 21. A score of 0 is continent, and high scores indicate more severity of incontinence.

To determine LUTS, IPSS and ICIQ-FLUTS were used. IPSS consists of 7 questions with a maximum score of 35 (range 0-35, 35 = most possible complaints), and a quality of life score with a maximum score of 6 (range 0-6, 6 = very unsatisfied). The ICIQ-FLUTS consists of 12 questions with 5 subscales of frequency of occurrence (never to always) with a maximum score of 48, regarding storage,²⁻⁵ voiding,⁶⁻⁸ and urinary incontinence,⁹⁻¹³ and a bother score with a maximum score of 10 linked to each answer.

Quality of life was measured with SF-12. The SF-12 consists of a subset of 12 items from the SF-36 Health Survey covering the same 8 domains of health outcomes, including physical functioning, role-physical, bodily pain, general health, vitality, social functioning, role-emotional, and mental health. Two subscales

are derived from the SF-12: the Physical Component Summary (PCS) and the Mental Component Summary (MCS). These summary scales based on the SF-12 correlate very highly with the SF-36 versions.¹⁰ Results were compared with outcomes of the Dutch population.¹¹

Sexual function was measured with questionnaires FSFI and IIEF. Higher scores indicate a better overall sexual function. The FSFI is a brief questionnaire of 19 questions, designed to measure sexual functioning in women. It was developed for the specific purpose of assessing domains of sexual functioning (eg, desire, arousal, lubrication, orgasm, satisfaction, and pain) in clinical trials. The total score ranges between 2.0 and 36.0. The IIEF addressed the relevant domains of male sexual function (erectile function, orgasmic function, sexual desire, intercourse satisfaction, and overall satisfaction).

Statistical Analysis

Filled-out questionnaires were collected and answers were entered into a database. Analyses were performed using SPSS 25 (IBM Corp, Armonk, NY). Mean values with standard deviation (SD) and median values were calculated. Mean scores on SF-12, FSFI, and IIEF were compared with the general Dutch population using Student's *t* test. Correlation between variables was sought using Pearson correlation. A *P* value of <.05 was considered significant.

RESULTS

Patient Characteristics

In total, 39 BEEC patients were contacted from our outpatient clinic. Twenty of these 39 (51.3%) patients gave their consent. Seventeen patients (43.6%) filled out the questionnaires and data from those patients were included in this study, see [Table 1](#).

The median age was 36 years (range 19-73). Male/female ratio was 9:8. Most had classical bladder exstrophy (*n* = 12), followed by epispadias (*n* = 4), and cloacal exstrophy (*n* = 1). Most patients were highly educated, employed, had a committed relationship, and were sexually active. Thirteen of the 17 patients did not have children, although 10 of them had a child wish.

As for bladder augmentation, 6 underwent ileocystoplasty, 1 sigmoidocystoplasty, and 4 had a continent urinary reservoir. At the time of the survey, 5 voided spontaneously, 11 applied intermittent self-catheterization (3 per urethram and 8 via stoma) and 1 had an ileal conduit (who did not fill out ICIQ).

Continence and LUTS

The individual data are presented [Supplementary Figures 1 and 2](#) and the total data are presented in [Table 2](#). In all, the median score on the ICIQ-UI was 5/21 (range 0-19). Five patients were continent (score = 0) of which 4 were men. As for LUTS, the median IPSS score was 7/35 (range 1-18) and the median quality of life score was 1 (=pleased). The overall median score on the ICIQ-FLUTS was 21/48 (range 2-28). The median scores per domain were 7 for storage, 0 for voiding, and 6 for urinary incontinence. The median bother scores were 4, 0, and 2.8, respectively.

Quality of Life and Sexual Function

For Dutch women aged 30-39 the mean MCS score of the SF-12 is 49.8 and the mean PCS score is 52.7. For Dutch men aged 30-39 the mean score is 52.4 and 54.9, respectively.¹¹ In the study population, scores for PCS and MCS were comparable with those of the Dutch population, except for PCS in women, see [Tables 3 and 4](#).

Table 1. Characteristics of the study population

	Women (n = 8), n (%)	Men (n = 9), n (%)	Total (n = 17)
Education level			
Master/bachelor degree	6 (75)	5 (55.6)	11 (64.7)
Nonacademic degree	1 (12.5)	2 (22.2)	3 (17.6)
Secondary school	0	2 (22.2)	2 (11.8)
Primary school	1 (12.5)	0	1 (5.9)
Employment			
No	2 (25)	1 (11.1)	3 (17.6)
Yes	6 (75)	8 (88.9)	14 (82.4)
Relationship			
No	3 (37.5)	2 (22.2)	5 (29.4)
Yes	5 (62.5)	7 (77.8)	12 (70.6)
Sexually active			
No	3 (37.5)	0	3 (17.6)
Yes	5 (62.5)	9 (100)	14 (82.4)
Having child (ren)			
No	6 (75)	7 (77.8)	13 (76.5)
Yes	2 (25)	2 (22.2)	4 (23.5)
Child wish			
No	4 (50)	3 (33.3)	7 (41.2)
Yes	4 (50)	6 (66.7)	10 (58.8)
Bladder augmentation or substitute			
No	3 (37.5)	3 (33.3)	6 (35.3)
Ileocystoplasty	3 (37.5)	3 (33.3)	6 (35.3)
Sigmoidocystoplasty	0	1 (11.1)	1 (5.9)
Continent urinary reservoir	2 (25)	2 (22.2)	4 (23.5)
Catheterizable stoma			
No	5 (62.5)	4 (44.4)	9 (52.9)
Yes	3 (37.5)	5 (55.6)	8 (47.1)
Voiding manner			
Spontaneously	2 (25)	3 (33.3)	5 (29.4)
CISC per urethram	3 (37.5)	0	3 (17.6)
CISC via catheterizable stoma	2 (25)	6 (66.7)	8 (47.1)
Ileal conduit	1 (12.5)	0	1 (5.9)

CISC, clean intermittent self-catheterization.

For sexual function, no difference was found between those in the general population and our participants except for the domain "pain" in the FSFI, that is, women in our group experienced more pain.

Relationship Between Continence, LUTS, Sexual Function, and Quality of Life

Men with higher scores on IPSS scored lower on PCS ($P = .008$). A trend was seen as women with higher scores on ICIQ-UI scored lower on FSFI ($P = .096$).

DISCUSSION

BEEC is a serious congenital disorder with significant burden on patients and inevitable consequences in adulthood. To our knowledge, this is one of the few studies in adults with BEEC exploring multiple outcomes including continence, LUTS, quality of life, and sexual function. One of the strengths of this study is the long-term follow-up. Future research will involve other parameters such as renal function and fertility as well. In general, our data suggest that despite the high rate of incontinence and

Table 2. Median scores on continence and LUTS questionnaires

	Women (range)	Men (range)
ICIQ-UI	6 (0-19)	3.5 (0-17)
Bother score	3 (0-8)	1.5 (0-8)
IPSS	-	7 (1-18)
Quality of life	-	1 (0-3)
ICIQ-FLUTS, storage	7 (2-10)	-
Bother score	4 (0-6.8)	-
ICIQ-FLUTS, voiding	0 (0-9)	-
Bother score	0 (0-1.3)	-
ICIQ-FLUTS, urinary incontinence	6 (0-20)	-
Bother score	2.8 (0-7.2)	-

ICIQ-FLUTS, International Consultation on Incontinence Questionnaire-Female Lower Urinary Tract Symptoms; ICIQ-UI, ICIQ urinary incontinence form; IPSS, International Prostate Symptom Score.

Table 3. Scores SF-12 and FSFI in women

	Study Population	Dutch Population ^{11,25}	P Value
SF-12			
PCS	46.5	52.7	.01
MCS	43.2	49.8	.052
FSFI			
Desire	3.1	3.6	.38
Arousal	4.6	5.4	.14
Lubrication	5.3	6	.29
Orgasm	5.8	5.0	.18
Satisfaction	5.1	5.2	.96
Pain	4.2	6	.0026
Total	28.1	31	.28

FSFI, Female Sexual Function Index; MCS, Mental Component Summary; PCS, Physical Component Summary; SF-12, 12-Item Short Form Health Survey

LUTS, adults with BEEC are usually healthy and well-adjusted individuals functioning well in society. These findings support that BEEC is a mostly isolated urogenital midline malformation and does not necessarily impair psychological and cognitive development.

In the present study, education level was above the population average,¹² with almost two-third having received a master and/or bachelor degree. This finding is consistent with previous studies.¹³⁻¹⁵ In all, 71% of the participants were in a committed relationship, which is higher than reported by some authors^{16,17} but comparable with others.^{14,18} It should be noted that good performance in school and occupation does not need explicit announcement about BEEC, but to have a committed relationship does require open communication between patients and partners. Apparently, these patients have the skills to cope with their condition.

It is still a matter of debate how continence is defined in BEEC and what the best way is to achieve it. In this study, the severity of incontinence is not defined in terms of, for example, quantity of pads needed. Nevertheless, despite the high scores on ICIQ-UI, IPSS and ICIQ-FLUTS, both scores were surprisingly low in both women and men. This suggests that the patients have developed adequate coping mechanisms. However, as expected, men with more severe LUTS scored lower on PCS and women with high ICIQ-UI scores tend to have lower FSFI scores.

Nevertheless, incontinence and LUTS were not correlated with SF-12 scores, maybe partially due to the sample size.

For quality of life, some studies demonstrated that patients with BEEC scored equally high as the normative population. Bujons et al evaluated questionnaires from 19 patients with BEEC and found that SF-36 reported general quality of life was comparable with that of the general population in 5 out of 8 items. Differences were seen in the mental health, emotional role, and physical functioning items ($P < .001$).¹⁴ Wittmeyer et al also used SF-36 in their analysis of 25 adult patients with BEEC and observed lower than norm based scores on only 2 of the 8 health concepts. Patient scores did not differ in regard to gender, number of interventions, sexual life, cosmesis, or renal function.¹⁵ Feitz et al studied the psychosexual and socio-economic development of 22 adult patients with BEEC and found that 19 of the 22 scored better or were in accordance with standard scores.¹⁹ In contrast, Deans et al reported significant poorer sexual function scores and quality of life when compared with normative data based on their analysis of 28 patients.¹⁸

Our data based on the SF-12 show that male participants had comparable quality of life, but in women both PCS and MCS were lower when compared with the Dutch population from the same age group. Clear explanation for this is lacking and therefore it needs to be confirmed in larger studies. It would actually be expected that men with BEEC would score lower on the PCS because the appearance of the genitals is generally different despite multiple surgical corrections.²⁰ It would be interesting to determine outcomes in a larger group of male patients combined with a penile perception score as used in hypospadias follow-up.²¹

Sexual function is an important health domain to assess in adults with BEEC, because sexual function may be severely affected. In our study, 82.4% of the patients were sexually active, comparable with other recent reports.^{14,18,22} In addition, IIEF scores were comparable with the general population. However, it should be mentioned that men from the reference study were aged 52 on average and therefore were somewhat older.²³ The total FSFI score in our study population was 28.1 whereas values of less than 26.55 indicate a risk of sexual

Table 4. Scores SF-12 and IIEF in men

	Study Population	Dutch Population ^{11,22}	P Value
SF-12			
PCS	52.6	54.8	.27
MCS	48.5	52.4	.18
IIEF			
Erectile function	19.9	22.3	.53
Orgasmic function	8.7	8.2	.67
Sexual desire	7.1	6.9	.72
Intercourse satisfaction	7.3	9.0	.39
Overall satisfaction	6.9	7.5	.52

IIEF, International Index of Erectile Function; MCS, Mental Component Summary; PCS, Physical Component Summary; SF-12, 12-Item Short Form Health Survey

dysfunction.²⁴ So, female patients with BEEC might require consultation of a sexologist and this should be offered when indicated. Notably, women in our cohort reported more pain during intercourse. Possible explanations are inadequate anatomic reconstruction, vaginal stenosis, uterine prolapse, and scars. However, the true etiology for this cannot be determined from the data presented and this will be matter of research in the future.

Limitations

A limitation of the present study is the small sample size and the low response rate of 43.6%. The latter is however comparable with some other studies.^{14,25} Although the University Medical Center Utrecht is a third line referral center for BEEC patients, this cohort probably is representative for the group of adult BEEC patients in the Netherlands. However, the design of postal questionnaires, together with the intimate content of the questions, introduces selection bias and responder bias by its nature. The cross-sectional design might also lead to biased results and longitudinal follow-up is therefore warranted.

In addition, BEEC patients form a rare and heterogeneous group, and therefore confounding should be taken into account as considerable variability exists in previous surgical treatments. Although we did not find any significant differences in outcomes, it should be mentioned that the 3 subgroups within BEEC are physically, and some would say mentally as well, different. Lastly, urological and gynecologic management is likely to have changed during time as primary urinary deviation is seldom the treatment of first choice nowadays. Outcomes of this cohort might therefore not be projected onto a younger group of patients.

CONCLUSION

Our data showed that adult men and women with BEEC have a high rate of incontinence and LUTS with relatively low to some degree of bother. Men reported a higher score on quality of life as compared to women and no difference was found between men with BEEC and men from general population. For those who were sexually active, scores within the different domains were comparable with the general population with the exception that women with BEEC experienced more pain during intercourse. We also found that in men LUTS correlated with lower physical quality of life, and that in women incontinence appears to be correlated with lower sexual function. We did not identify other correlations, partly due to the small sample size.

SUPPLEMENTARY MATERIALS

Supplementary material associated with this article can be found in the online version at <https://doi.org/10.1016/j.urology.2019.10.011>.

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