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Testicular function and sexuality in adult patients with anorectal malformation☆,☆☆

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ABSTRACT

Purpose: To collect data on sexual and fertility issues in adult male patients with history of anorectal malformations (ARM).
Materials and methods: Thirty adult males born with ARM, cared for at the Pediatric Surgery of Treviso and Padua Hospitals, were enrolled and interviewed about sexual habits and relationships. Testicular ultrasound, evaluation of male sex hormones and semen analysis were performed to assess testicular function and compare data with 15 fertile controls. Presence of erectile dysfunction was evaluated with IIEF-5 questionnaire.
Results: Cryptorchidism and recurrent orchiepididymitis were reported in 33% and 40% of patients, respectively. Average testicular volume resulted significantly lower than fertile controls (11.1 vs 14.3 mL, $p = 0.002$) and 53.5% presented testicular hypotrophy (<10 mL).
Erectile dysfunction was reported by a single patient and ejaculatory anomalies by 46.5%.
Thirteen patients were azoospermic/cryptozoospermic; 6 of them presented a reduced peripheral sensitivity to androgens (ASI > 139). Coital debut resulted delayed at 18 years old (vs 15 years in the control group). Overall 63.5% reported their condition did not affect their sexual sphere.
Conclusions: Evaluation of testicular function is recommended in ARM patients to detect and treat possible infertility disorders, to recognize the clinical conditions which could affect the spermatogenesis since childhood, and to guarantee psychological support.
Level of evidence rating: Prognosis study.
Level III (case–control study).

Anorectal malformations (ARMs) are a spectrum of congenital malformations owing to the abnormal development of the anus and rectum occurring during the hindgut embryonic maturation [1]. The incidence of ARM is about 1 in 2500–5000 live births, without significant gender differences [2].

The etiology of this condition seems to be multifactorial and more than 50% of patients show associated congenital malformations, particularly of the genitourinary tract [3,4]. The adoption of specific surgical approaches [such as the posterior sagittal anorectoplasty (PSARP)] and postoperative techniques of bowel and urinary management has improved the prognosis and quality of life of ARM patients over the years [5]. In spite of these positive aspects, ARM patients require a lifelong follow-up in order to manage fecal and urinary continence, fertility and sexual issues, and to provide psychological support, when necessary [6]. The literature is rich with information about fecal and urinary long-term outcomes but little is known about fertility aspects in both males and females [7].

Aim of the present study was to assess the fertility potential and sexual issues in adult male patients with previous history of ARM once they reach the adult age.

1. Materials and methods

1.1. Patients

Forty-five consecutive male patients, aged ≥18 years, with history of ARM were selected from the registers of all ARM patients treated or followed up in the Departments of Pediatric Surgery of Treviso and Padua University-Hospital in the last 45 years. Thirty of them were enrolled in the study as showed in Fig. 1. Exclusion criteria were recent

Abbreviations: ARM, anorectal malformation; ASI, androgen sensitivity index; IIEF-5, simplified international index of erectile function; PSARP, posterior sagittal anorectoplasty; ED, erectile dysfunction.

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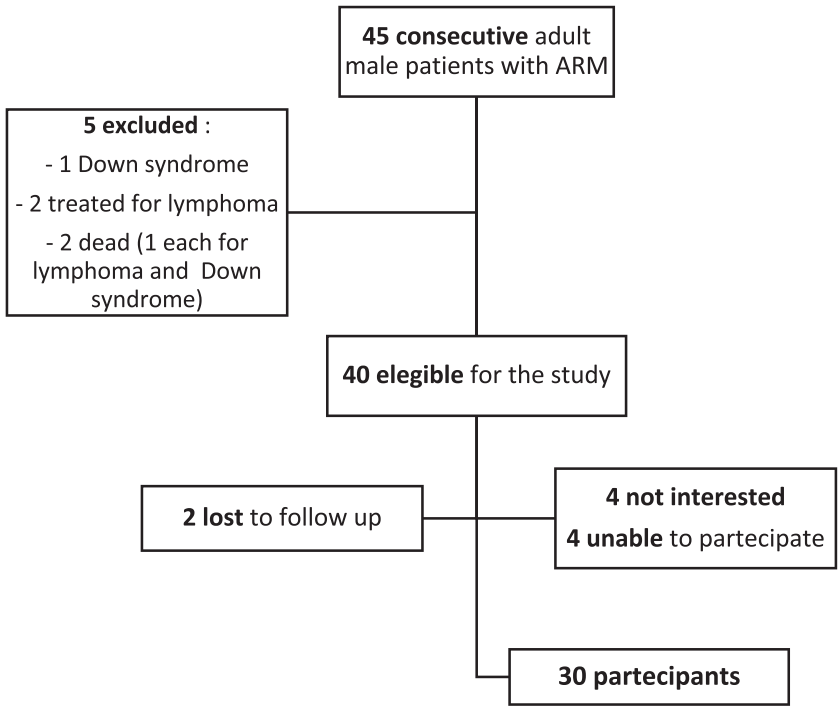

Fig. 1. Flow chart of study selection.

chemoradiotherapy, major mental handicaps and Down syndrome. Mean age was 26 years (range 18–41 years). The study was approved by the independent ethics committees of both institutions and all participants provided written informed consent.

1.2. Clinical and instrumental evaluation

All subjects underwent a complete clinical history and physical examination, including a clinical andrological evaluation of the genitalia, body hair distribution, BMI, presence of gynecomastia, and other secondary sexual characteristics. In addition, a scrotal ultrasound was performed to determine the testicular volume and to observe the presence of cysts, nodules, anomalies of spermatic ducts, hydrocele, and varicocele. A volume of 10 mL was arbitrarily established as cutoff of testicular hypotrophy, as no standardized values are available in literature [8].

Semen samples were collected after 3–5 days of sexual abstinence and parameters analyzed and compared with WHO 2010 normal values [9]; postejaculation urine samples were also collected to evaluate the presence of retrograde ejaculation. Main hormones regulating testicular function (LH, FSH, total testosterone, 17β-estradiol, inhibin B) were measured. In all patients, serum levels of testosterone and LH were utilized to define the Androgen Sensitivity Index (ASI, LH × total testosterone, normal value ≤139) in order to explore the presence of a reduced peripheral sensibility to testosterone. Semen data and hormone levels of ARM patients were compared with data collected from 15 fertile age-matched controls without ARM, i.e. with biological offspring and semen quality parameters within the range reported in the WHO guidelines [9].

Details of sexual activity, considering both functional and psychological aspects, were examined during an oral interview with the andrologist: sexual orientation, relationship status and total number of partners, timing of first sexual experience and frequency of intercourses during the last year. In patients who experienced at least one coitus in the last 6 months, the erectile function was evaluated using the IIEF-5 questionnaire (simplified International Index of Erectile Function), a simplified version of the IIEF-15, more suitable as office diagnostic tool for erectile dysfunction (Table 1). Alternatively, this datum was collected with direct questions about erection and presence of ejaculatory anomalies (i.e. retrograde ejaculation, premature ejaculation, etc.). All patients were asked if they fathered or if they had ever attempted to.

Table 1
IIEF-5 questionnaire and its items.

In the past 6 months	1 point	2 points	3 points	4 points	5 points
1 How do you rate your confidence that you could get and keep an erection?	*Very low*	*Low*	*Moderate*	*High*	*Very high*
2 When you had erections with sexual stimulation, how often were your erections hard enough for penetration?	*Almost never/never*	*A few times (much less than half the time)*	*Sometimes (about half the time)*	*Most times (much more than half the time)*	*Almost always/always*
3 During sexual intercourse, how often were you able to maintain your erection after you had penetrated (entered) your partner?	*Almost never/never*	*A few times (much less than half the time)*	*Sometimes (about half the time)*	*Most times (much more than half the time)*	*Almost always/always*
4 During sexual intercourse, how difficult was it to maintain your erection to completion of intercourse?	*Extremely difficult*	*Very difficult*	*Difficult*	*Slightly difficult*	*Not difficult*
5 When you attempted sexual intercourse, how often was it satisfactory for you?	*Almost never/never*	*A few times (much less than half the time)*	*Sometimes (about half the time)*	*Most times (much more than half the time)*	*Almost always/always*

The IIEF-5 score is the sum of the ordinal responses to the five items. The score can range from 5 to 25: severe (5 – 7), moderate (8 – 11), mild to moderate (12 – 16), mild (17 – 21), and no ED (22 – 25) [11].

Table 2
Types of ARM and main associated anomalies.

Types of ARM (n/30)	
Cloaca exstrophy	**2 (6.5%)**
Rectobladder fistula	**8 (26.5%)**[a]
Rectourethral fistula	**16 (53.5%)**
Bulbar fistula	5 (31%)
Prostatic fistula	3 (19%)
Not specified	8 (50%)
Without fistula	**2 (6.5%)**
Perineal fistula	**1 (3.5%)**
Anal stenosis	**1 (3.5%)**
Associated anomalies (n/30)	
Genitourinary malformations	
Renal anomalies	**6 (20%)**
Cryptorchidism	**10 (33.5%)**[b]
Hypospadias	**4 (13.5%)**
Urethral stenosis	**4 (13.5%)**
Micropenis	**2 (6.5%)**
Genitourinary Infections	
Orchiepididymitis	**12 (40%)**
Urinary tract infections	**11 (36.5%)**
Voiding dysfunctions	
Neurogenic bladder	**4 (13.5%)**
Vesicoureteral reflux	**6 (20%)**[c]
Sacral Anomalies	**12 (40%)**
Tethered cord	**6 (20%)**
Other malformations[d]	**9 (30%)**

[a] One with rectal pouch.
[b] Four with bilateral form and 1 with agenesis of contralateral testis.
[c] Two with bilateral VUR.
[d] Four with cardiac defects, three with esophageal atresia and two with skeletal anomalies.

Finally, we assessed how their initial condition might have influenced their relationships.

1.3. Statistics

Data were normally distributed and expressed as mean ± standard deviation; the *t*-test was used as parametric statistic for data analysis. The Mann–Whitney *U*-Test was used for the subgroup analysis between azoospermic versus nonazoospermic patients' ASI value and data were expressed as median.

A *p*-value <0.05 was considered as statistically significant in both cases.

2. Results

Patients' typology of ARM – according to the Krickenbeck classification [10] – and associated anomalies are outlined in Table 2. The majority of patients (83.5%) underwent PSARP, 6 required a combined perineal and laparotomic approach, and 1 underwent four redo procedures.

2.1. Erectile dysfunction

IIEF-5 questionnaire was administrated to 25 patients (83%) because 2 of them showed a delayed psychosexual development and never experienced sexual activity, 2 had cloacal exstrophy, and 1 patient reached the erection by means of a penile prosthesis required to overcome the consequences of multiple surgical treatments of persistent urethral stenosis. Results are illustrated in Fig. 2.

2.2. Ejaculatory anomalies and semen analysis

Concerning ejaculatory anomalies, 16.5% reported occasional premature ejaculation, 10% loss of urine during ejaculation, and 3.5% soiling immediately after orgasm. Retrograde ejaculation was confirmed in 26.5% by means of urine analysis: 3 showed ARM with rectovesical fistula (one was a pouch-colon), 1 rectobulbar and 4 not specified rectourethral fistula. Moreover, 13 patients (43.5%) showed azoospermia. None of the patients reported to use medications that may have affected the fertility and sexual function. Results of semen analysis, compared to controls values, are reported in Table 3. These results excluded patients with cloacal exstrophy, who sampled semen by catheterism after climax (only agglutinations without sperm cells were found).

2.3. Testicular ultrasound

The ultrasound scan showed testicular hypotrophy in 53.5% (16 patients), 30% bilaterally. Seven of them were diagnosed with cryptorchidism/retractile testicle (4 bilateral) and 8 reported recurrent episodes of orchiepididymitis. Mean testicular volume of ARM patients and controls was 11.10 ± 5.00 and 14.30 ± 2.60 mL, respectively ($p = 0.002$). Frequent anomalies of the epididymis were also detected:

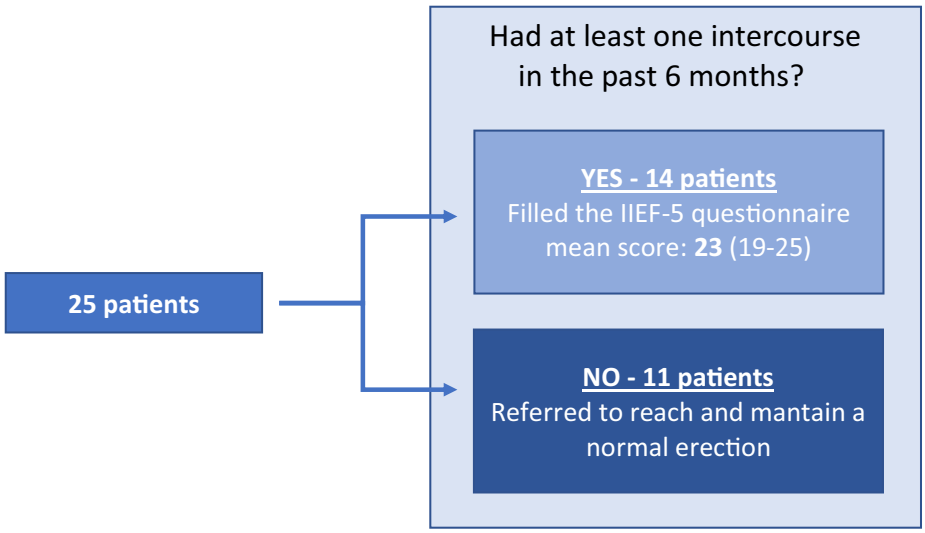

Fig. 2. Graphic representation of the ED evaluation conducted on 25 patients (5 excluded for delayed psychosexual development, cloacal exstrophy and artificial erection). IIEF-5 questionnaire was filled only by patients who had had at least one intercourse in the past 6 months, as requested by the item; a mean score of 23 was obtained, corresponding to absence of ED [11]. Other patients verbally referred to have not ED.

Table 3
Comparison of main seminal parameters between ARM patients and controls (WHO 2010 standards [9]).

Parameters	ARM patients *n*/28	Controls *n*/15	*p*
Azoospermic/cryptozoospermic patients	**13**	**0**	------
Normozoospermic/oligozoospermic patients	**15**	**15**	------
Sperm count ($\times 10^6$/mL)	29.80 ± 25.70	45.80 ± 7.40	**0.03**
Total sperm count ($\times 10^6$)	57.80 ± 54.20	88.60 ± 10.50	**0.04**
Progressive motility (%)	12.00 ± 10.10	68.80 ± 7.40	**0.0001**
Normal morphology (%)	6.70 ± 6.20	56.60 ± 3.20	**0.0001**
Volume (mL)	1.80 ± 1.60	------	------
Ph	7.70 ± 0.40	------	------

63.5% (19 patients) presented cysts and dilations of head, body and/or tail, suggestive of obstructions along the spermatic tract. Signs of previous orchiepididymitis, such as thickening of tunicae, altered echogenicity, and presence of calcifications of testis and epididymis, were detected in 6 patients (20%). The *rete testis*, which is the network of tubules in the hilum of testis between the seminiferous tubules and the efferent ducts, was also greatly altered: it was unilaterally well represented in only 13.5% (4 patients), unilaterally undetectable in 26.5% and bilaterally in 53.5%. Finally, tubular ectasia of *rete testis*, a benign condition with multiple little cysts, was present in one patient. Low grade varicocele (grade 2/3 according to Sarteschi classification) was detected in 7 patients with normal semen analysis.

2.4. Hormone blood levels

Evaluation of hypothalamic–pituitary–gonadal axis by means of dosage of circulating male hormones (FSH and LH) was normal in all but 3 patients in which it was increased, probably owing to testicle hypotrophy. The plasma levels of other sexual hormones (total testosterone and β-estradiol) did not differ between cases and controls (Table 4). ASI, which is an index of peripheral sensitivity to androgens, resulted higher in ARM patients but not statistically relevant (116.60 ± 103.96 vs 87.66 ± 68.94 U × nmol/L^2, $p = 0.34$). However, comparing this value among azoospermic and nonazoospermic ARM patients, we observed a significant difference between the two subgroups (Fig. 3); moreover, 38.5% of azoospermic patients showed a pathological ASI value >139 (Table 5).

2.5. Physical examination

None of the patients presented alterations of body hair distribution and other secondary sexual characters, gynecomastia, or elevated BMI.

2.6. Psychological and sexual evaluation

Seventeen patients (56.5%) declared to have a partner at the time of the enrollment and 7 of them stated to be engaged in a stable relationship (married or living together with the partner), while 8 (26.6%) experienced at least one relationship in the past. Nineteen patients (63.5%) experienced coitus and 3 (10%) reported only sexual activities without penetration; two of these latter patients, born with cloaca exstrophy, pleaded to the fact of having inadequate dimension of penis. On the contrary, 5 patients (16.5%) never experienced sex with a partner: 2 of them because of a delayed psychosexual development owing to a borderline intellectual functioning and 3 because of fear of soiling during intercourse. Mean age of first sexual experience without penetration was 17 years (range 13–22) and 18 with penetration (range 13–22). Only one patient referred scarce libido and one was a homosexual. Four patients (13%) tried to father. Two of them, both with adequate sperm count and motility, succeeded while the others showed severe retrograde ejaculation and poor semen parameters.

Finally, patients were asked to quantify how much their congenital malformation impacted on personal relationships using a scale from 1 to 10 (1 = no impact and 10 = great impact). Mean score was 4.30 ± 3.30. Eleven patients (36.5%) scored ≥6 because of fear of soiling during coitus (6 patients), discomfort with their body image (4 patients) and fear not to be not able to father (1 patient).

All the patients received the results of exams along with a comprehensive report from the andrologist. Azoospermic patients were suggested to return to our centers for further examinations whenever interested to plan a pregnancy.

Table 4
Comparison of hormones blood levels between ARM patients and controls.

Hormones	ARM patients ($n = 30$)	Controls ($n = 15$)	*p*
LH (U/L)	6.00 ± 3.52	4.75 ± 1.34	0.19
FSH (U/L)	6.60 ± 6.91	3.52 ± 0.91	0.09
Total Testosterone (nmol/L)	18.70 ± 7.00	15.70 ± 4.20	0.13
17-β-Estradiol (pmol/L)	96.90 ± 37.86	78.70 ± 39.60	0.14
Inhibin β (ng/L)	196.50 ± 100.11	--------	--------

3. Discussion

Fertility is a heartfelt topic for ARM patients when they grow up and desire to have their own family. Little is known about this aspect in these patients and, in most cases, the clinicians are not able to answer the questions coming from parents and patients about their future sexuality and fertility. Previously published studies mainly focused on psychological aspects of sexuality owing to a low self-esteem [11,12]. Others have reported patients treated in the pre-PSARP era, when the different surgical techniques, consisting of a blind dissection of the pelvis, caused many damages of genitourinary and pelvic nerves [13,14].

This study was conducted to evaluate if male ARM patients, operated in the PSARP era, might have a lower potential for fertility than the general population owing to the congenital and associated malformations. According to the Krickenbeck classification, 80% of patients had a fistula communicating with the urinary tract and 76.5% showed associated anatomical alterations, mainly of the genitourinary tract.

The definition of fertility is the probability for a couple to conceive within a year of attempts without contraception [15]. About 15% of couples worldwide are infertile and in half of the cases this is because of male factors [16,17]. In 2014 Huibregtse et al. conducted a meta-analysis to evaluate the birth rate in couples with at least one partner affected by ARM [18]. Seven of 9 studies distinguished the rate based on the gender of the partner with ARM: 15% for males and 19% for females. The birth rate of our group is lower (6.5%) probably because of the young age of participants (mean age 26 years), which is quite lower than the mean age of Italian men seeking pregnancy (35.3 years) [19].

No erectile dysfunction, except for one patient, was reported in our group as determined by the IIEF-5 questionnaire. This is not in contrast either with previous studies, which reported severe erectile dysfunction in 0–11.8% of cases, even though different methods to evaluate it were used (IIEF-15 [12], Erection angle [20] and Erection Hardness Score [21]), or with the prevalence observed in general Italian population (1.5% in 15–30-year-old males [22]). Physiology of ejaculation is a very complex process that requires the integrity of autonomic nervous system and many anatomic structures [23]; congenital anomalies of the genitourinary tract and sacrum, as well as iatrogenic damages of bladder and urethra could lead to retrograde ejaculation or loss of urine during orgasm in ARM patients, as we found in 26.5% and 10% of cases, respectively. Regardless the surgical approach, the dissection of the fistula in patients with high type fistula implicates a higher risk of pelvic plexus damages: in fact,

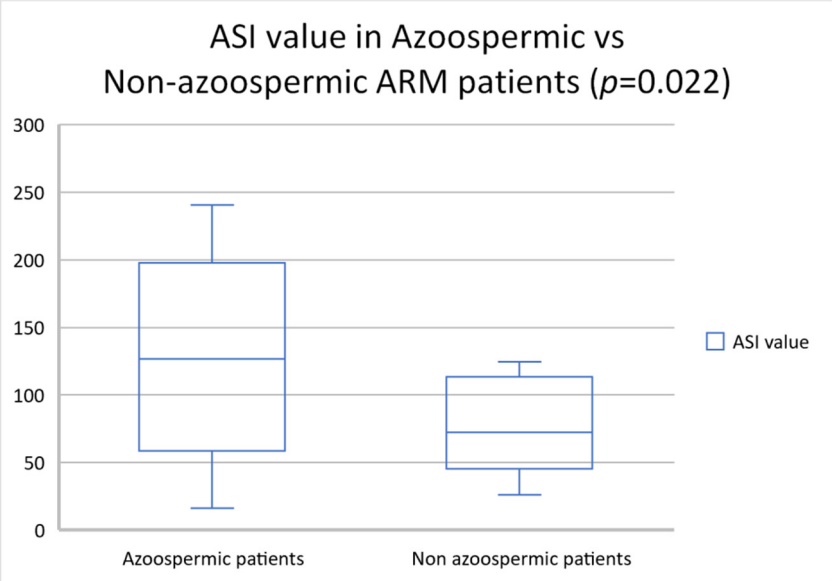

Fig. 3. Comparison between ASI value of 13 azoospermic (126.65 U × nmol/L^2, range: 16.21–568.13) versus 15 nonazoospermic ARM patients (72.28 U × nmol/L^2, range: 25.87–124.6), p = 0.022.

these nerves run tightly close to the fistula, more medially than in the normal population [24]. In addition to this, associated sacral anomalies further increase the risk because of a more inefficient neurological function [24,25]. We observed sacral anomalies in 2 of 8 patients with retrograde ejaculation and 2 of 3 with voiding problems during ejaculation, i.e. sacral hypoplasia with 2 segments remaining in one patient of both groups, unknown in the others.

It was observed that a decreased testicular size indicates impaired spermatogenic potential, considering that 85% of the testicular volume is associated with sperm production [26]. Ultrasound evaluation of the testes showed a statistically significant difference of volumes between our patients and healthy fertile controls, probably owing to personal history of cryptorchidism, recurrent orchiepididymitis, and intrinsic alteration of the *rete testis*. As for other components of the spermatic tract, the *rete testis* develops from mesonephros, the embryogenic organ promoting also the development and maturation of the kidney. The *rete testis* was, indeed, bilaterally undetectable in 73% of patients with congenital kidney anomalies and in the other cases was absent in one testis and poorly visible in the contralateral testis.

ARM patients presented a higher prevalence of semen anomalies than fertile controls, in particular oligozoospermia (with 46% of azoospermia/cryptozoospermia), hypoposia, and asthenozoospermia. Azoospermia is a clinical condition affecting 1% of the worldwide male population and 10%–15% of infertile males [26]. An attempt to investigate the causes of azoospermia in ARM patients distinguishing pretesticular, testicular and posttesticular etiologies was performed.

The pretesticular causes are mainly owing to endocrine disorders and thus sex hormone levels should be tested. In the literature there is only one study investigating this aspect in ARM patients, but neither the type of hormones nor the referral threshold was reported [13]. However, that study did not detect anomalies in male hormones levels. Accordingly, we did not observe any significant alteration of reproductive hormone plasma levels in our patients with respect to fertile controls. Nonetheless, azoospermic patients showed a higher ASI value than others and, in particular, 5 of them showed pathological values of this index, which empirically indicate the sensitivity of the peripheral androgen receptor. An inadequate activity of this receptor leads to an increase of LH secretion and, consequently, to testosterone production by Leydig cells. This condition can be associated to testicular hypotrophy, azoospermia, gynecomastia, and sexual dysfunction. Indeed, 75% of our patients with bilateral testicular hypotrophy showed an elevated ASI. The etiopathogenic role of androgens in ARM is still unclear. Studies on animal models show the rectum and anus are rich of receptors for androgens and estrogens, suggesting that these hormones could play an important role on the embryogenesis of anal sphincters [27]. Also the maternal prenatal exposure to endocrine disruptors such as dybutil

Table 5
Associated anomalies in patients with elevated ASI (n.v.: ≤139).

	Type of fistula	ASI	Main anomaly of semen analysis	Genital anomalies	Hormonal alterations	Cryptorchidism/hypospadias	BMI >25/gynecomastia
1	RU	240.71	Azoospermia	Testicular hypotrophy	↑ LH, ↑ FSH	Hypospadias	Yes
2	RU	234.62	*Not evaluable*	Testicular hypotrophy	↑ E2	-----	Yes
3	RP	184.10	Azoospermia	Normal	-----	-----	No
4	RV	164.74	Azoospermia	Normal	------	Bilateral cryptorchidism	No
5	WF	211.17	Azoospermia	Testicular hypotrophy micropenis	↑ LH, ↑FSH	Bilateral cryptorchidism	Yes
6	CE	568.13	Azoospermia	Testicular hypotrophy micropenis	↑ LH, ↑ FSH, ↑ E2, ↑TT	Bilateral cryptorchidism	No

WF: without fistula, RU: unspecified rectourethral fistula, RP: rectoprosthatic fistula, CE: cloacal extrophy, RV: rectovesical fistula.

phthalate, a common plasticizer that influences the physiological levels of androgens, increased the incidence of ARM on rat [28,29]. Despite absence of human studies, the finding of a partial peripheral resistance to androgens could be not incidental in ARM patients. To this regard, it could be interesting to identify mutations within the whole coding region of the androgen receptor gene in ARM patients, above all in those with elevated ASI.

Cryptorchidism can be considered one of the main causes of secretory azoospermia and in ARM patients the prevalence of this congenital testicular malformation is higher than in the general pediatric population, i.e. 19%–27% vs 2.7% [13,26,30]. Holt et al. observed that 2 out of 3 ARM patients with bilateral cryptorchidism at birth were azoospermic with regular spermatogenesis at testicular biopsy [13]. In this study 38.5% of azoospermic patients presented this anomaly and 3 of them showed also an elevated ASI. In addition, we observed that orchidopexy was performed between the age of 5 and 11 years, quite later than the present recommendation [31]. Apart from the recurrent episodes of orchiepididymitis seen in these patients, there are other rare causes of secretory azoospermia such as varicocele and testicular torsion, seen in a minority of patients.

Posttesticular causes of azoospermia (obstructive forms) in ARM patients are often owing to iatrogenic damages. Holt et al. studied 14 ARM patients (10 azoospermic, 4 aspermic) with vasography, which demonstrated bilateral obstruction of the reproductive tract in 5 and unilateral in 7 patients, possibly owing to the reconstructive procedure [13]. Congenital associated malformations of the spermatic ducts in ARM patients have been described in very few studies but they are, likely, underestimated [32,33]. Two patients in our series presented ectopic *vasa deferens,* one ectasia of the *rete testis*, and 10 epididymal cysts and dilatations. Moreover, one patient was a carrier of CFTR gene mutation that can be associated to congenital bilateral absence of the vas deferens (CBAVD), a clinical condition that typically causes a reduced semen volume (<0.5 mL) [34]. Finally, the patient with cryptozoospermia, born with a rectoprostatic fistula, could present obstruction of the terminal tract of seminal ducts as the result of iatrogenic surgical damage.

The possible association between ARM and the impact on relationship and sexual life of these patients was also investigated. According to WHO, sexuality is a fundamental aspect of the human being that includes many features such as sex, gender identities, sexual orientation, pleasure, intimacy and reproduction. The definition of sexual health is, indeed, not merely the absence of disease or dysfunction, but in general "a state of physical, emotional, mental and social well-being in relation to sexuality" [35]. Previous studies highlighted the negative impact of fecal incontinence on social sphere, self-esteem, and acceptance of physical appearance [11,36]. The mean age at coital debut was 18, which is two years later than in the healthy male population [21,36]. At time of the present study, most patients were engaged, or had had at least one relationship in the past, and experienced sexuality. In our group of patients 63.5% of cases had intercourses, a percentage that is higher when compared to 45% reported by Schmidt et al. [36]. In general, our patients referred to have satisfying relationships, sexual activities and socially acceptable episodes of fecal soiling. However, 36.5% of them considered the ARM as a handicap to their personal life that had deeply interfered with the possibility to find a partner.

The present study demonstrates a reduced fertility potential in a group of male patients treated for ARM. The most frequent semen alteration was azoospermia, owing to secretory and obstructive causes. Furthermore, we observed a partial reduction of the peripheral sensitivity to androgens and a lower representation of the *rete testis*. Strengths of this work are the high number of adult male patients treated with PSARP technique, and the integration of clinical and objective parameters with the psychological aspects. Limits of the study are the potential bias concerning sensitive questions related to sexual activity which patients reported during interviews, the impossibility to correlate the impairment of fertility with severity of ARM and the lack of information concerning complications and iatrogenic damages occurred during the operative procedures.

In brief, this study underlines the importance to perform an accurate evaluation of the genitourinary apparatus during childhood to quickly detect and treat cryptorchidism and recurrent infections, which could lead to fibrosis and obstructions. We also recommend to procede with a strict andrological evaluation, blood test to detect and treat any anomaly in sex hormones levels which could affect the pubertal development and/or the spermatogenetic process, then routinely semen analysis after sexual maturation. Finally, a psychosexual support is fundamental to increase self-esteem and own-body perception, overcome the fear of soiling, and reduce the psychological causes of sexual dysfunctions.

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