Factori predictivi pentru succesul MESA la pacienții cu azoospermie obstructivă primară

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Abstract

Introduction The aim of scrotal exploration in patients with obstructive azoospermia (OA) is to perform reconstruction of spermatic tract and to retrieve sperm using microsurgical epididymal sperm aspiration (MESA). Reconstruction is performed only if viable spermatozoa are found in the epididymis. The outcome of scrotal exploration in patients with OA secondary to previous vasectomy largely depends on the interval (in years) between vasectomy and reversal operation. The outcome of primary OA, unrelated to prior vasectomy has been less studied. Normal testicular volume and epididymal distension together with normal FSH are the main clinical argue for OA. To date, no non-invasive clinical criteria has shown to be of predictive value for the outcome of MESA in patients with primary OA.

Objective The objective of this study was to find a correlation between clinical preoperative data and the presence of viable spermatozoa with MESA in patients with primary OA.

Material and methods 30 patients (mean age 32.17, range 26-40 years) were prospectively included between September 2008 and September 2009, using the following criteria for primary OA: vas deferens clinically present; seminal volume ≥1mL, semen pH≥7, seminal fructose present; normal reproductive hormones; at least one testicle with volume ≥10cc and width of epididymis caput ≥5mm as measured by ultrasound. Patients with history of vasectomy, attempted microsurgical reconstruction and congenital absence of vas deferens (CAVD) were excluded. All patients underwent scrotal exploration with the aim to perform MESA and, if possible, reconstruction of the spermatic tract. The entire cohort was divided into 2 groups: group 1 with viable sperm – successful MESA and group 2 with absent/dead sperm – unsuccessful MESA. Correlations of variables with outcome of MESA were calculated using SPSS software and by comparison the 2 groups.

Results The testicles were analyzed independently. MESA was successful in 32 (55.17%) and unsuccessful in 26 (44.82%) testicles (tow patient has solitary testicle). In this cohort the only significant correlation with OA was found with the width of epididymis caput; an epididymal caput > 8.5mm was predictive for finding viable spermatozoa (sensitivity 71.9%, specificity 71.4%).

Conclusion This report aimed to predict the success of MESA using objective clinical variables. So far, only the width of the caput of the epididymis was significantly associated with the presence of viable spermatozoa in epididymis. Nevertheless, as about 30% can be omitted using this parameter (false negative rate), scrotal exploration is still indicated in all patients with fulfilling the criteria for primary OA.

Key words: predictive factors, infertility, microsurgical epididymal sperm aspiration, primary obstructive azoospermia
Introduction
Obstructive azoospermia (OA) is present in 10–20% of infertile men and is characterized by normal testicular volume and normal reproductive hormones indicating normal spermatogenesis\(^1\). Post-vasectomy OA are the most prevalent causes of OA in Western Europe and was extensively reported by many authors. Primary OA, most frequent in East Europe, were the vasectomy is pretty rare, has been less studied. There are two main options for patients with primary OA, microsurgical reconstruction of the spermatic tract and sperm retrieval followed by intracytoplasmatic sperm injection (ICSI). Other options for parenting include donor sperm or adoption. The sperm retrieval could be performed either open, microsurgical epididymal sperm aspiration (MESA) or as a percutaneous procedure (PESA). The reconstruction is performed only if viable spermatozoa are found into epididymis. Clinical examination of genitalia is an important part of patient evaluation when OA is suspected. Normal testicular volume and epididymal distension together with normal FSH are the main clinical argue for OA\(^2\). To date, no non-invasive clinical criteria have shown to be of predictive value for the outcome of MESA in patients with primary OA. Founding predictive criteria would leed to an objective counselling for patients with primary OA.

Objective
The objective of this study was to find a correlation between clinical preoperative data and the presence of viable sperm retrieved by MESA in patients with primary OA.

Material and methods
Patients.
Between September 2008 and September 2009, 30 patients with primary OA were prospectively analyzed. Azoospermia was confirmed on at least 2 semen analyses after centrifugation. The inclusion criteria for primary OA were: vas deferens clinically present; seminal volume ≥1mL, semen pH≥7, seminal fructose present; normal reproductive hormones; at least one testicle with volume ≥10cc and width of epididymis caput ≥5mm as measured by ultrasound. Patients with history of vasectomy, attempted microsurgical reconstruction and congenital absence of vas deferens (CAVD) were excluded. All patients underwent scrotal exploration with the aim to perform MESA and, if possible, reconstruction of the spermatic tract.

Variables
The preoperative recorded variables were level of reproductive hormones (Testosterone, FSH, and LH) and scrotal ultrasound data (testicular volume and thickness of the epididymis).

Microsurgical epididymal sperm aspiration procedure
Surgery was performed under general anesthesia. After creating a longitudinal hemiscrotal incision, the testicles was delivered. The vaginalis tunica was opened and reversed. The tail of the epididymis was identified and an Optitron microscope (optical magnification x12-x40) was brought into the operatory field. A single epididymal tubule was exposed as caudal as possible. The tubule was opened, the epididymal fluid was aspirated (MESA) and, a small amount, was examined immediately by light microscope into operating room for viable sperm. If they were present, the fluid was sent for cryopreservation and intussusception vasoepididymostomy according to Berger\(^3\) was performed when was technicaily possible. If they were not present, more proximal MESA was performed until sperm were identified. The same procedure were performed on opposite hemiscrotum unless there was severe atrophy/absence of testicle.

Statistical analysis
The entire cohort was divided into 2 groups: group 1 with viable sperm – successful MESA and group 2 with absent/dead sperm – unsuccessful MESA. Correlations of variables with outcome of MESA were calculated using SPSS software and by comparison the 2 groups.

Results
The mean age was 32.17 years (range 26-40 years). The etiology of the obstruction was uro-genital tract infection and idiopathic in 53.3% and, respectively, 46.7% of cases. In all patients MESA was performed with the intention to cryopreserve sperm: viable spermatozoa were found in the epididymis (unilaterally or bilaterally) in 20 cases (66.6%). No postoperative complications occurred. IVES was performed in only 11 patients (36.6%), seven unilaterally and four bilaterally. In 63.4% of cases (the remaining 19 men), reconstruction was not possible due to absence of viable spermatozoa in epididymis in 10 men (33.3%), small size of
epididymal tubule in 6 men (20%) and obstruction of the vas deferens in 3 men (10%).

The testicles were analyzed independently. MESA was successful in 32 (55.17%) and unsuccessful in 26 (44.82%) testicles (tow patient has solitary testicle). The mean (range) values for FSH, testosterone, LH, testicular volume and the width of epididymis caput in group 1 and 2 are shown in the Table 1.

Table 1

<table>
<thead>
<tr>
<th>Primary OA MESA (n=58 testicle)</th>
<th>Successful (32)</th>
<th>Unsuccessful (26)</th>
</tr>
</thead>
<tbody>
<tr>
<td>FSH*</td>
<td>3.96 (1.52 – 8.80)</td>
<td>5.70 (1-13.10)</td>
</tr>
<tr>
<td>LH*</td>
<td>2.89 (1.07 – 6.74)</td>
<td>4.58 (1.47 – 9.40)</td>
</tr>
<tr>
<td>Testosterone*</td>
<td>8.12 (2.21 – 22.12)</td>
<td>9.27 (2.88 – 20.16)</td>
</tr>
<tr>
<td>Testicular volume**</td>
<td>13.73 (9.10 – 25.00)</td>
<td>13.27 (7.30 – 21.80)</td>
</tr>
<tr>
<td>Width of epididymis caput***</td>
<td>9.46 (5.00 – 15.00)</td>
<td>7.96 (1.00 – 15.70)</td>
</tr>
</tbody>
</table>

* = IU, ** = cc, *** = mm

Correlations of main variables with end point are depicted in the table 2.

Table 2

<table>
<thead>
<tr>
<th>Parameter</th>
<th>p</th>
<th>Statistical significance</th>
</tr>
</thead>
<tbody>
<tr>
<td>Width of epididymis</td>
<td>0.05</td>
<td>Significant</td>
</tr>
<tr>
<td>Testicular volume</td>
<td>0.39</td>
<td>NS</td>
</tr>
<tr>
<td>FSH level</td>
<td>0.25</td>
<td>NS</td>
</tr>
<tr>
<td>LH level</td>
<td>0.18</td>
<td>NS</td>
</tr>
</tbody>
</table>

In this cohort, the only significant correlation with endpoint was found with the width of epididymis caput; an epididymal caput > 8.5mm was predictive for finding viable spermatozoa (sensitivity 71.9%, specificity 71.4%).

In the group with successful MESA, 8 out of 32 testicles had the volume between 25cc and 15cc; 24 out of 32 testicles had volume lower than 15 cc. In this last group of 24 testicles, 23 testicle had the width of epididymis caput more than 7 mm. This result confirm the possibility that in case of clinical sings of OA a testicle with a volume between 10 and 15 cc could be obstructed if the epididymis is distended over 7 mm. If this is a specific feature for primary OA only, we do not know.

A normal hormonal value was a condition for inclusion in our series. For nonOA is well known the negative correlation between the level of FSH and the success of sperm retrieval. In our cohort mean level of FSH is different in group 1 versus group 2, but, still, non statistically significant.

In spite of apparent difference between two groups in all variables, in this cohort, the only significant correlation with endpoint was found with the width of epididymis caput; an epididymal caput > 8.5mm was predictive for finding viable sperm. The data about value of epididymal distension, as a predictor factor for OA and for success of sperm retrieval, are sparsely. Sukcharoen and al. reported the success of PESA in 49 azoospermia men. They reported a 93.8% success rate of PESA procedure in epididymis with distension (significantly higher than in epididymis without distension 47.1%). In this study the definition of distension was based on pregnancy rates ranging from 27%–49%. Scrotal exploration in patients with supposed primary OA offers the advantage of epididymal sperm retrieval and simultaneous reconstruction with VES. In our study, viable spermatozoa were found in the epididymis (unilaterally or bilaterally) in 20 cases (66.6%) and IVES was performed in only 11 patients (36.6%), seven unilaterally and four bilaterally. Bernardinucci et al. reported a success of MESA in 65% of patients with idiopathic epididymal obstruction. The azoospermic patients were included if a testicular biopsy showed normal spermatogenesis and excluded in case of history of vasectomy or CBAVD. The authors emphasize the limited success rate of MESA in patients with primary OA. In other study, Dohle et al. reported a 65% success rate of MESA in a cohort of 43 patients with suspected primary OA. Our results are similar with the authors cited above and underline moderate success rate of MESA in patients with suspected primary OA.

The cut-off values for normal testicular volume and width of epididymis caput are 15 cc and 5 mm respectively. The EAU guidelines stated that a testicle with decreased volume would be an obstructed testicle with partial loss function. In our series 24 out of 32 testicular units testicular units had a decreased volume (15 cc – 9.1cc). For this group, the majority (23 out of 24) of testicular units, had the width of epididymis caput more than 7 mm. This result confirm the possibility that in case of clinical sings of OA a testicle with a volume between 10 and 15 cc could be obstructed if the epididymis is distended over 7 mm. If this is a specific feature for primary OA only, we do not know.

Discussions

Sperm retrieval and ICSI has dramatically improved the chances for patients with azoospermia to obtain pregnancy. Although ICSI can be used in patient patients with any etiology of OA, microsurgical reconstruction of the genital tract is the preferred approach for epididymal obstruction, with reported patency rates ranging from 67%–85%, and spontaneous
clinical examination only, without other objective measurement. We confirmed this data and, in addition, an objective measurement of epididymal distension by ultrasound was done. In other study, Bromage and al., evaluated sperm retrieval rates in subgroups of men with azoospermia, based on obstructive etiology, testicular volume and FSH. Forty-five out of 106 patients (32%) had clinically distended epididymis. The presence of a distended epididymis did not correlate with either a positive retrieval from PESA or TeSE in group of primitive OA. The patient included in this study have testicular size ranged from 1 cm to 8 cm, median 5 cm, and FSH ranged from 1 IU to 50 IU, median 7 IU. The low testicular size and the high level of FSH would explain the difference with the results of our study.

Microsurgical reconstructive techniques and their widespread availability have made vasectomy reversal a realistic option for many couples. In our series the main limitation for reconstruction was absence of motile sperm into epididymis. Our results would help to adequately counsel azoospermic man about the success rates of sperm retrieval and the chance to perform reconstruction.

The main limitation of our study is the low number of patients with primary OA. Still, because an individual analysis for each testicle was performed, the comparison of the groups accomplishes statistical power.

**Conclusion**

This report aimed to predict the success of MESA using objective clinical variables. So far, only epididymal distension was significantly associated with the presence of viable spermatozoa in epididymis. Finding an epididymal caput by ultrasound larger than 8.5mm has sensitivity and specificity of 71.9% and, respectively 71.4% for successful sperm retrieval by MESA in patients with primary OA. Nevertheless, as about 30% can be omitted using this parameter (false negative rate), scrotal exploration is still indicated in all patients with fulfilling the criteria for primary OA. These dates would help to adequately counsel azoospermic man about their treatment options.

**Biography**