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Refertilization Surgery. A surgeon's experience of over 27 years with nearly 2000 patients

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Aim. **The aim of this paper was to present the experiences of microsurgical refertilization in a single-centre study during a period of 27 years.**

Methods. **Nearly 2000 patients were operated by a single surgeon (JUS). A total of 1708 patients were evaluated in a data base, 1164 were available for a follow-up. Both vasovasostomy (VV) and epididymovasostomy (EV) were carried out in a three-layer technique. Vasectomy reversal (VR) end-to-end VV was performed only if spermatozoa had been demonstrated at the epididymal stump of the vas. In all other cases of VR, EV was done in a preocclusive region of the epididymal tubule. In the cases of postinfectious obstruction (PIO) of seminal pathways, an EV was always carried out.**

Results. **The outpatient procedure of refertilization was associated with a very low complication rate, which underlines its minimal-invasive character. The follow-up rate was 68%, the overall patency rate was 88% for VR and 67% for PIO and the pregnancy rate was 59% for VR and 38% for PIO. Secondary azoospermia was observed in 1% of the patients.**

Conclusion. **In relation to the intervals of obstruction, the patency and pregnancy rates were higher after short-term obstruction than after long-term obstruction. There is a significant discrepancy between patency and pregnancy rates that is likely to be caused by a relevant number of patients with postoperative asthenozoospermia.**

KEY WORDS: Fertilization - Asthenozoospermia - Azoospermia. - Vasovasostomy.

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Obstructive azoospermia (OA) is a possible cause of male infertility. OA is caused by vasectomy, postinfectious scaring or iatrogene lesion of the seminal pathways. The therapy of OA requires microsurgical refertilization (MR) or sperm retrieval and intracytoplasmic sperm injection (ICSI) with epididymal or testicular spermatozoa.

In cases of obstructive azoospermia after vasectomy, MR is performed by end-to-end or side-to-end anastomosis between vas and vas or vas and epididymis. A one- or two-layer technique is generally used for anastomosis. We consequently applied a microsurgical three-layer technique for the end-to-end and side-to-end anastomoses and present this technique and our results over 27 years in terms of clinical outcomes, such as rates of patency and pregnancy. In all patients with not vasectomy related OA (*e.g.* PIO) an EV was necessary for reconstructive surgery, which was carried out also by a three-layer-technique.

Materials and methods

All microsurgical interventions were carried out on an outpatient basis under

general anesthesia. A single shot of ciprofloxacin 500 mg or cefuroxim 500 mg was given perioperatively. The use of an operating microscope was obligatory in all cases. Through a surgical approach of two lateral scrotal incisions (only in a few cases inguinal approach due to inguinal vasectomy) both scrotal cavities are explored. The tunica vaginalis is only opened when epididymal surgery is done. The further operative strategy consists in attempting an end-to-end VV in the cases of VR whenever possible (see below). If there is no sperm outflow from the epididymal stump of the vas (which is mainly the case after long obstructive intervals) or the OA is caused by an postinfectious scaring of the epididymis an end-to-side anastomosis between vas and epididymis is required (EV). Both procedures are carried out using a three-layer technique. The wound is closed with self-dissolving sutures and a pressure dressing is applied for one day.

Intraoperative strategy for vasectomy reversal

At first both ligated stumps of the vas deferens are identified, prepared and trimmed. Patency of the inguinal stump of the vas deferens is checked by injection of 3 mL saline solution. If liquid comes out from the epididymal stump, there is apparently no additional obstruction in the epididymis, caused by the formation of an epididymal granuloma. The fluid pouring out of the vas deferens is examined intraoperatively by microscopic analysis for the presence of sperm and its viscosity. If spermatozoa are demonstrated, VV is realizable. Sperm motility and morphology is of minor importance for the further surgical strategy according to the authors own experience and the literature.[1, 2]

In addition to the presence of spermatozoa, low viscosity of the fluid is a positive prognostic factor for the outcome of the procedure.[1-6]

Vasovasostomy

The VV is performed with a three layer end-to-end technique. At first the interior (mucosal) layer is sutured with 10-12 non-absorbable single-armed 10-0 stitches with a round needle (Figures 1, 2). So many stitches are necessary to compensate for the different lumina of both vasal stumps, to ensure a conical lumen at the point of anastomosis and to avoid a step-like intraluminal formation and any shifting of the

Figure 1.—Vasovasostomy: internal layer between the mucosa of both stumps of the vas deferens, typically presenting relevant luminar difference.

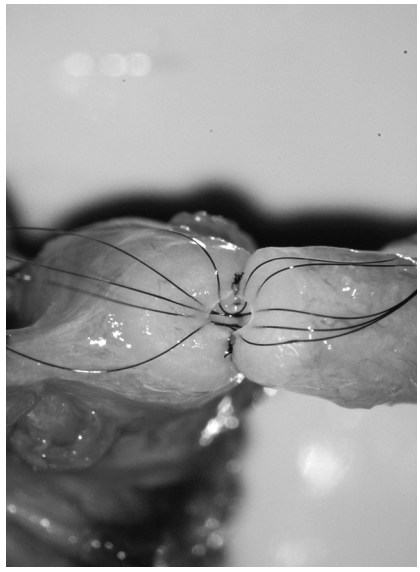

Figure 2.—Vasovasostomy: internal layer.

Figure 3.—Vasovasostomy: first suture of middle layer between the muscular layer of both stumps of the vas deferens.

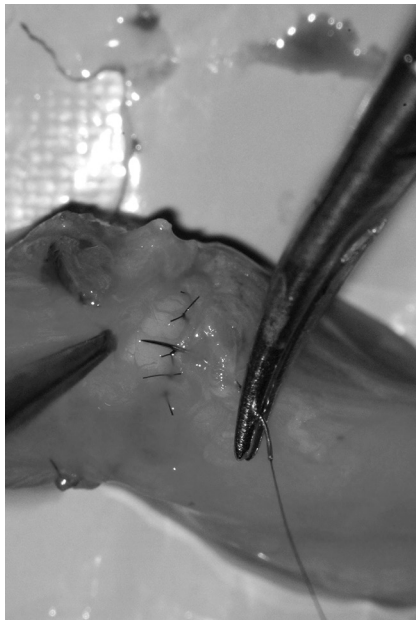

Figure 4.—Vasovasostomy: outer layer between the adventitia of both stumps of the vas deferens.

mucosal layer. This adaptation of the different lumina is crucial for subsequent patency of the anastomosis. The second layer comprises suturing the muscle walls of both vasal stumps. About ten 9-0 single stitches are placed with non-absorbable threads. A sharp spatula needle facilitates the optimal passage through the compact muscular layer (Figure 3).

The third layer comprises the adventitial connective tissue surrounding the vas. About ten 8-0 stitches are placed, preventing any tensile stress to the internal mucosal layer (Figure 4).

Epididymovasostomy

If the fluid that pours from the epididymal stump of the vas has a toothpaste like consistence, normally no or only a few fragments of spermatozoa are found. In this case, as in the case of missing epididymal fluid, an anastomosis at the epididymal stump of the vas deferens does not make sense – a view that is largely non-controversial.[3, 4, 5, 7, 8, 16] Instead, an EV between preocclusive epididymal tubule and abdominal stump of the vas deferens should be done. The strategy for the EV consists the following steps: at first identifying the area of the obstruction of the epididymal tubule, in most cases the obstruction is located in the cauda epididymidis. Then the dilated preocclusive tubule is tangentially incised, which requires a very subtle operating technique. The outflow of epididymal fluid indicates the preocclusive location. The outflowing fluid is analysed by the operating surgeon using a lab microscope. If spermatozoa are identified, a side-to-end anastomosis between epididymal tubule and abdominal stump of the vas deferens is carried out in a three-layer technique.

For the internal layer between the wall of the laterally opened epididymal tubule and the mucosa of the vas deferens 8-10 non-absorbable single-armed 10-0 stitches are placed with a round needle.

This internal layer, including the easily tearable structure of the tubular wall, requires 20-30x magnification with the operating microscope as well as extensive microsurgical experience and utmost concentration of the surgeon (Figure 5). The

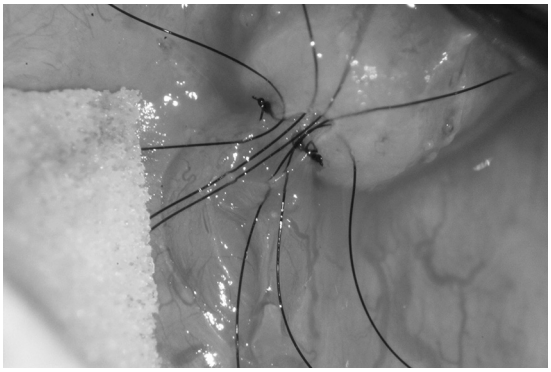

Figure 5.—Epididymovasostomy: internal layer between mucosa of the vas deferens and wall of the epididymal tubule.

second layer is closed between the muscularis of the vas and the epididymal serosa with about ten 9-0 stitches with spatula needle (Figure 6). Complete tension relief is then achieved by suture of the third layer, which is performed between the adventitia of the vas and the epididymal serosa with about ten 8-0 single stitches (Figure 7). For completion of the third layer it is most important that the connective tissue around the vas deferens is well-preserved; excessive denudation should therefore be avoided (see operative technique of VV).

Intraoperative strategy for postinfectious obstruction

The tunica vaginalis is opened and the epididymis is explored microsurgically. If the epididymal tubule is dilatated, a semicircular incision of the vas is performed at the beginning of the straight part of the vas. If liquid is coming out from the epididymal part of the vas, the obstruction must be located more central, which can be evaluated more precisely by injection of saline solution and intraluminal probing. If patency of the abdominal stump can be demonstrated and no sperms are coming from the epididymal stump of the vas deferens, the epididmal cauda is explored step by step to find a dilatated tubular sling, which can be opened for the EV. The EV is carried out in the same three layer technique that is described above (strategy of vasectomy reversal).

Patients

From August 1987 to September 1993 about 250 patients were operated by J. U. Schwarzer at the urological clinic of the Technische Universität München (directed by Prof. Rudolf Hartung). In this period a two-layer-technique was carried out and consequent follow up did not exist, therefore these patients are not included in our scientific evaluation. In October 1993 the three-layer-technique was introduced and a follow up with an exact data base was started, so the patients considered in the present study are treated from 10/93 to 06/14. In this period 1708 patients underwent microsurgical refertilization by one surgeon in a

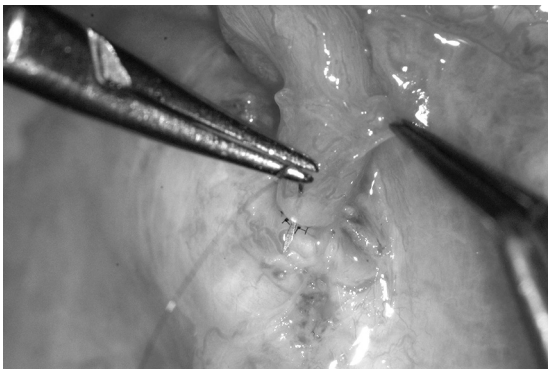

Figure 6.—Epididymovasostomy: middle layer between muscular layer of vas deferens and serosal layer of epididymis.

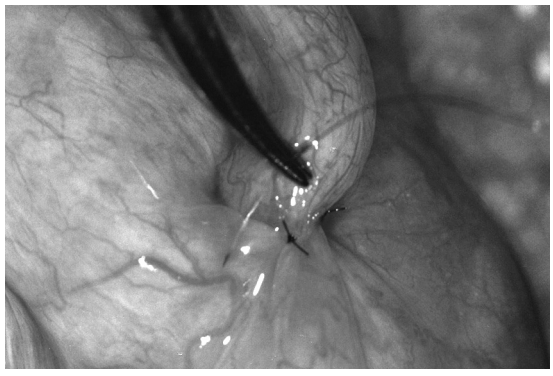

Figure 7.—Epididymovasostomy: outer layer between adventitia of vas deferens and serosal layer of epididymis.

single center for genital microsurgery. The study thus comprises these group of patients who underwent refertilization surgery for VR in 1581 cases and for PIO in 127 cases; 177 out of 1708 (10.4%) required repeat intervention after a previous attempt of refertilization.

All patients were physically examined with palpation of the scrotum, especially for identification of the vasal stump, and a scrotal sonography.

The age of the patients ranged from 20 to 73 years, with an average of 42.9 years. The age of the female partners ranged from 19 to 46 years, with an average of 33.6 years.

The periods of obstruction ranged between 18 hours and 39 years (average 8.7 years). In some cases of PIO the period of obstruction couldn`t be elicited. The study followed ethical guidelines that are established for human subjects by the Department of Urology of the Technische Universität München.

Results

Perioperative course

A total of 1195 patients underwent bilateral VV, 267 patients unilateral VV in combination with contralateral EV. Another 50 patients underwent unilateral VV, 137 patients EV bilaterally and 59 patients EV unilaterally (Table I). In 349 out of 1587 patients with VR (22%) an EV had to be carried out at least at one side according to our strategy as mentioned above.

The operation time ranged from 75 to 180 min for bilateral surgery (average 114 min) and 45 min to 150 min for unilateral surgery (average 65 min).

The complication rate was 0.3% (N.=5) for scrotal haematoma, only one patient had to be reoperated for evacuation of haematoma. Ten (0.6%) had a superficial wound infection, no case of epididymitis was seen. Apart from two cases of allergic reaction to antibiotics, no side effects or complications were ever seen.

Postoperative course

The follow-up was characterized by special problems, *e.g.* that many patients changed their place of residence and were not detectable. Nevertheless, great importance was attached to the follow-up using an individualized database (based on filemaker®). Statistical analysis was done by use of Fisher's exact test.

Patients were urgently asked to have a sperm analysis performed after 3 months and to report the occurrence of a pregnancy. This request was explicitly documented in the medical report to the urologists responsible for further treatment. Unless a response had been received concerning sperm analysis and/or pregnancy, active follow-up consisted of telephone inquiries with patients or urologists one year after the operation, strongly recommending a semen analysis.

Fifty-one patients (3%) had actually no desire to have children or wished to have the operation for other reasons such as chronic pain syndrome or psychic or religious motives. This group of patients was not considered in the follow-up.

TABLE I.—*Microsurgical refertilization: results in relation to the type of anastomosis: epididymovasostomy at least on one side in 22% of patients (total number of patients N.=1708, follow-up N.=1164).*

Operative technique	Patients operated (N.)	Patients follow up (N.)	Patency rate (%)	Pregnancy rate (%)	average age of the female partner (years)
Bilateral vasovaso-stomy	1195	819	92	62	33.7
Vasovasostomy + epididymovasostomy	267	185	78	54	34.2
Bilateral epididymo-vasostomy	137	91	73	45	33.1
Unilateral vasovasostomy	50	31	71	45	33.4
Unilateral epididymovasostomy	59	38	58	31	32.1
Total	1708 (N.)	1164 (N.)	86 (%)	59%	33.6

TABLE II.—*Microsurgical refertilization: patency and pregnancy rates in relation to the cause of obstruction of the seminal pathways in a follow-up of N.=1164 out of 1708 patients (68% follow-up rate).*

Cause of obstruction of the seminal tract	Patients (N.)	Patency rate (%)	Pregnancy rate (%)	Average age of the female partner (years)
Vasectomy	1581	88	59	33.8
Postinfectious, iatrogene, congenital	127	67	38	31.7
	1708	86	59	34.6

The follow-up period comprised at least 3 months.

Altogether, 1164 out of 1708 cases were followed up (68%), showing an overall patency rate of 86% and a pregnancy rate of 59% without any use of IVF (Tables I, II).

Patency was demonstrated by semen analyses according to WHO (2010), performed by the referring urologists or in our andrological centre.

The patency and pregnancy rates include 151 pregnancies that occurred without follow-up semen analyses. This mainly concerns couples who achieved pregnancy within the first 3-4 months after refertilization so they saw no need (and could not be persuaded) to have a sperm analysis performed.

Discussion

In all cases of obstructive azoospermia, methods of microsurgical refertilization (MR) can be used to achieve natural fertility, while the alternative procedure of intracytoplasmic sperm injection (ICSI) is a means of artificial reproduction with a relevant burden to the female partner and higher costs.[6, 9]

Different techniques are used for microsurgical refertilization, and since the last 30 years many papers have been published about these techniques and their results.[1, 6 10-19] We introduced and consequently used a three-layer technique for VV and EV, resulting in single-surgeon experience over 27 years.

In our opinion, the three-layer technique is insignificantly more time-consuming than both the previous one- or two-layer techniques [10, 13, 15, 20, 21] and the robotic techniques currently published.[22-25] One reason for our preference of the three-layer technique over the one- or two-layer technique is the possibility of exact adaptation of the interior layer which typically shows luminal disparity.

Secondly, the third layer of the anastomosis, *i.e.* the connective tissue coat (adventitia), provides tension relief to the internal layer to a greater extent than does the second layer alone. Furthermore, the third layer ensures vascularization of the duct. According to the author's experience, preservation of the connective tissue layer is of essential importance for a successful operation because it prevents hypotrophy of the duct and ensures complete tension relief to the internal layer - an issue that has so far not been considered in the literature. When the stumps of the epididymal duct are prepared, the third layer of connective tissue should be preserved by all means. Excessive or prolonged denudation and loss of the third layer involve a high risk of secondary hypotrophy and fibrotic occlusion of the anastomosis.

Results in comparison with other techniques

Apart from the operative strategy, the aforementioned technical peculiarities of three-layer anastomosis may explain our favorable results. Although these are not better than many others published before, the 1% rate of secondary reocclusions is significantly lower compared with studies reporting rates up to 12% for VV and up to 21% for EV.[2, 3, 26, 27] In our experience the secondary azoospermia rate is not relevantly underestimated, because patients with an initial positive result in semen analysis whose female partner doesn't get pregnant,

will come to reevaluate the ejaculate quality in most cases.

A comparison of our results and those of others should primarily consider a study by Silber & Grotjan [3] who published their findings with two-layer VV and EV in 4010 patients, reporting a high follow-up rate of 86.5% and patency rates of 95% for bilateral VV and 78% for bilateral EV. The problem of low follow-up rates is to be found in many studies on refertilization, reflecting insecurity about whether the patients who were not followed up are statistically equal to those who underwent long-term follow-up.

Importance of epididymovasostomy

We suggest that for successful VR the most important prerequisite even after a long period of obstruction is the consistent implementation of the strategy to perform EV if no sperm is detectable at the epididymal stump of the vas deferens.[28, 29]

In 22% of our patients, predominantly in those with longer periods of obstruction, we encountered the situation that a bypass anastomosis had to be performed at least on one side. So clearly the indication for epididymovasostomy is statistically correlated with the period of obstruction (Table I). This is in accordance with the experiences of many other authors.[30-36]

Epididymal damage

Similar to other studies [2, 3, 37, 38] we found a significant discrepancy between the patency and the pregnancy rates, independently of the interval of obstruction. In most cases this discrepancy was explained by the demonstration of asthenozoospermia or oligoasthenozoospermia in the postoperative semen analyses. This pathologic finding could be caused by epididymal damage due to a long period of obstruction or antisperm antibodies.[39-41]

Spermatogenesis is not altered by the obstruction, which was shown by histological studies in patients with obstructive azoospermia. Only insignificant alterations of spermatogenesis are described, such as interstitial fibrosis [42] and increased sperm DNA fragmentation.[43]

The most relevant damage to the reproductive function that increases with time is the impairment of the epididymis from the obstruction.[44-46] Statistically, this deteriorating effect to the epididymis is related to the interval of obstruction, which finds expression in the necessity of EV. However, individual differences in the resistance to time-related epididymal damage must be presumed because in single cases of normozoospermia complete recovery of the epididymis after refertilization may occur.

Female fertility factor

Another relevant factor for the difference between patency and pregnancy rates may be the relatively high average age of 33.6 years of the female partners, affecting their fertility. But the age of the female partner at the time of operation was not significantly related to the period of obstruction among the male patients.

Furthermore should be realized that with increasing female age abortion rates are most likely also increasing. This should be considered when birth rates are discussed. So birth rates are probably somewhat lower, as was already shown in other studies.[2, 3]

Conclusions

Our results show that the mircrosurgical refertilization surgery provides excellent results for couples seeking fertility treatment in cases of obstructive azoospermie caused by vasectomy as well as postinfectious obstruction of seminal pathways. By microsurgical refertilization surgery the ICSI treatment can be avoided for many couples. So possible morbidity of ICSI and the considerable costs of the gynecological treatment can be avoided.

In our opinion, the three-layer anastomosis is no more time-consuming than a two-layer technique and the patient benefit justifies the higher amount of time compared to the single-layer technique. According to our

experience, this sophisticated reconstruction of the seminal tract using three-layer technique, in the framework of a minimally invasive procedure should be the standard of refertilization surgery against which all other techniques, such as the robotic technology, must be measured.

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Conflicts of interest.—The authors certify that there is no conflict of interest with any financial organization regarding the material discussed in the manuscript.

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