Sperm Surgery

When and how to retrieve sperm in ***AZOOSPERMIA***

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Milestones in the treatment of Azoospermia

Temple-Smith et al. – **Micro Epididymal Sperm Aspiration (MESA) and IVF** ⟹ Pregnancy
J IVF-ET 2:119, 1985

Schoysman et al. – **MESA and Testicular Sperm by biopsy and ICSI**
Lancet 342:1237, 1993 6 cases ⟹ one pregnancy

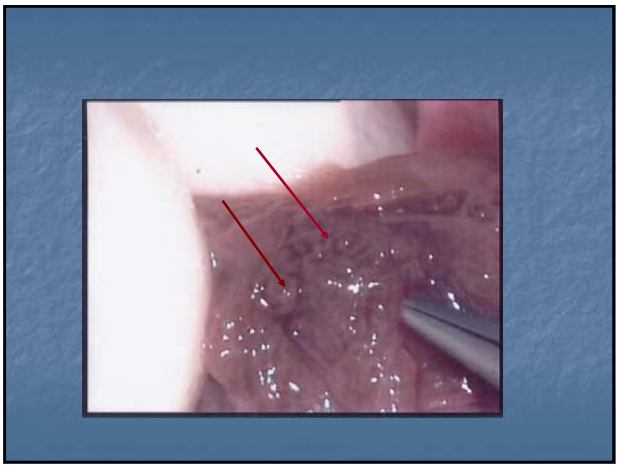
Silber, Devroey & Van Steirteghem – **MESA and ICSI**
HR 9:1705, 1994 17 cases ⟹ **47% pregnancy rate**

Silber, Van Steirteghem, Tournaye & Devroey – **Testicular Biopsy**
HR 10:148, 1995 **Testicular Sperm Extraction (TESE)** in Obstructive cases where epididymal sperm was not achievable
⟹ **43% pregnancy rate**

Tsirigotis and Craft -
HR 10:748, 1995 **Percutaneous Epididymal Sperm Aspiration (PESA)** and ICSI
HR 10:1623, 1995 **Percutaneous Testicular Sperm Aspiration (TESA)** and ICSI

Mile stones in the treatment of Azoospermia

Schlegel – **Micro Dissection – Micro TESE** Improves sperm retrieval rate
HR, 14:131, 1999



Azoospermia

Topics

- Mode of sperm retrieval
- Sperm retrieval rates
- Timing of retrieval in relation to OPU
- Repetitive trials
- Time interval between TESE procedures
- Damage to the testis

Mode of Sperm Retrieval

Obstructive Azoospermia

Non Obstructive Azoospermia

Obstructive Azoospermia

MESA Temple-Smith et al. *J IVF-ET 2:119, 1985*

PESA Tsirigotis and Craft - *HR 10:748, 1995*

"Results with PESA are not less good than with MESA"

Craft HR 10:1623,1995

Retrieval rate in Obst Azoospermia 98-100%

Outcome of ICSI in Azoospermia treated cases

In Obstructive Azoospermia

Category : - Epididymal vs Testicular Sperm; PESA vs TESA

Meta - analysis on 10 reports, *Nicopoullus et al. F&S, 82:691,2004*

Fertilization rate	**Epididymal vs. Testicular**	CI 0.97-1.18, RR 1.1
Pregnancy rate	**Epididymal vs. Testicular**	CI 0.81-1.25, RR 1.0
Ongoing pregnancies	**Epididymal vs. Testicular**	CI 0.71-1.36, RR 0.9 P<0.05 (36% vs 13%) Bulfat et al. *HR 21:1018,2006*

Mode of Sperm Retrieval

Obstructive Azoospermia

ASPIRATION

Sperm Retrieval in Non Obst Azoospermia

Aspiration ?

TESA with same efficiency as in Obst Azoospermia

Craft HR 10:1623,1995

Testicular Fine Needle Aspiration - TEFNA:

The alternative method for sperm retrieval in non-obstructive azoospermia.

Mean of 15 punctures and aspirations

Lewin HR et al. 14:1785, 1999

Gun Needle biopsy

Tuuri et al. HR, 14:1274,1998

Testicular Biopsy ?

How many biopsies?

Sperm Retrieval in Non-Obstructive Azoospermia

	cases	aspiration	biopsy	
		sperm present	no. of biopsies/ testes	sperm present
Friedler HR 12:1448 1997	37	4 (11%)	3	16 (43%)
Ezeh HR 13:3075, 1998	35	5 (14%)	1	22 (63%)
Mercan HR 15:1548, 2000	452	63 (14%)	4-5	228 (50%)
El-Haggar Int J Androl, Website 2007	100	10 (10%)	mTESE	54 (54%)
Total	624	81 (13%)		320 (51%)

P<0.001

The damage of TEFNA

Number of biopsies per testis to be performed ?

	no.of biopsies
Tournaye HR, 1996	up to 12
Friedler HR,1997	up to 3 in each testis

	no. biopsies	%positive TESE biopsies
Amer HR,1999	2	61%
	3	96%
	4	100%
Hauser et al., 1998	3	100%

Demonstrating that

by 3 biopsies per testis, the reliability to find sperm will reach 96 %

Therefore, further search would be of little benefit

Mode of Sperm Retrieval

Obstructive Azoospermia	Non Obstructive Azoospermia
ASPIRATION	*Testicular biopsy*

Sperm Retrieval rates

Frequency of Successful Testicular Sperm Retrieval in Patients With NOA

REFERENCE	Sperm available in TESE	
Turek et al., 1999	20/21	95%
Devroey et al, 1995	13/15	87%
Eckardstein et al.,1999	34/52	65%
Ezeh et al., 1998	22/35	63%
Schlegel et al., 1997	10/16	62%
Silber et al., 1997	39/63	62%
Ben Josef et al., 1999	33/55	60%
Ostad et al., 1998	47/81	58%
Kahraman et al., 1996	14/29	48%
Friedler et al., 1997	18/41	43%
Schlegel et al., 1999	10/22	45%
Westlander et al.,1999	27/86	31%
Kahraman et al., 1999	22/86	31%
TOTAL	**309/602**	**51%**

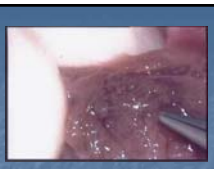
Retrieval rate should be given according to the findings of **first TESE cycles**

Results of outcome may be overestimated by reallocating successful repeated cases

REFERENCE	Sperm available on TESE	Retrieval rate
Vernaeve et al., *HR, advance access Feb,2006*	261/628	41.6%
Ron-El et al. *2006*	77/172	44.7%

* Cases without Klinefelter sy.

Micro TESE



Schlegel P, HR 14:131, 1999

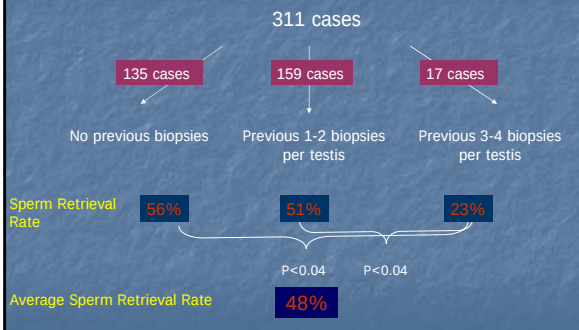
"The technique identifies sperm containig regions before their removal"

Sequential study first 22 cases with TESE, then 27 cases with mTESE

	conventional TESE	m TESE
Sperm retrieval	**45%** (10/22)	**63%** (17/27)

Sperm retrieval with m TESE in failed TESE - 35%

Micro TESE



Ramasamy & Schlegel J Urol 177:1447,2007

Comparison Between TESE and Micro-TESE

Comparative study

	Micro-TESE	Conventional TESE
No. of cycles	56	37
Cycles with Retrieved Sperm	43%	35%

Tsujimura et al. HR 17:2924,2002

Assaf Harofeh, Tel Aviv University, 2000-2007

	Micro-TESE	Conventional TESE
No. of cycles	73	427
Cycles with Retrieved Sperm	35 (48%)	248 (56%)

Ron-El, unpublished data

The chance to find sperm in failed 1st TESE trial ?

Sperm was available
in One out of 9 patients
who insisted to have a repeated TESE
(~10%)

Friedler, Ron-El et al., HR 17: 2356,2002

No repeated TESE is performed after 1st failed TESE

Vernaeve et al., HR advance, 2006

Timing of retrieval in relation to OPU

Few available studies

Retrospective study

Heterogeneous groups of Obst and Non Obst Azoospermia

Sperm Retrieval	Cases	Motile Sperm	Pregnancies
Day of OPU	23	61%	35%
One day before OPU	19	63%	29%

Levran F&S 76:380,2001

Repeated TESE

How many patients with non-obstructive azoospermia who failed will need **further treatment** ?

Patients with available sperm	42%
Couples who achieved pregnancy	28%
Meaning that, cycles with conception are (28% out of 42%)	12%
Additional pregnancies using frozen thawed testicular sperm	10-15%

~70% of the couples will seek for further treatment

What should be the time interval to repeat TESE procedure?

Interval to repeated TESE	<6 months		≥6 months	
	patients	available sperm	patients	available sperm
Schlegel & Su, *HR 12:1688,1997*	4	25%	15	80%

Interval to repeated TESE	<3 months		≥3 months	
	patients	available sperm	patients	available sperm
Amer et al., *HR 14:3030,1999*	8	75%	19	95%

Successful Sperm Retrieval Rate in First and Repetitive TESE

Study period: Oct 1995 - Dec 1999

TESE trial	1st TESE	Repetitive
# of patients	83	39
Sperm found	32 (39%)	33 (85%)

Friedler et al., HR 17: 2356,2002

Study period: Jan 1995 – Dec 2003

TESE trial	1st TESE	Repetitive
# of patients	628	156
Sperm found	384 (42%)	123 (79%)

Vernaeve et al., HR advance, 2006

Successful Sperm Retrieval Rate in First and Repetitive TESE

TESE trial	2nd TESE	3rd TESE	4th TESE	5th TESE
# of patients	22	8	6	3
Sperm found	**17 (77%)**	**8 (100%)**	**5 (83%)**	**3 (100%)**

Friedler et al., HR 17: 2356,2002

TESE trial	2nd TESE	3rd TESE	4th TESE	5th TESE	6th TESE
# of patients	103	34	11	5	2
Sperm found	**77 (75%)**	**28 (82%)**	**11 (100%)**	**3 (82%)**	**2 (100%)**

Vernaeve et al., HR advance, 2006

Complications

In Assaf Harofeh

	Conventional TESE	Micro TESE
Complications		
Extratunica Hematoma	6/429	3/73
Intratunica Hematoma	2/429	3/73
Total	8 (1.9%)	6 (8.2%)

In the repetitive TESE: There were no difficulty or complications

With TEFNA: scar tissue in an unknown occurrence

In the literature: safe procedure

Discussion

which is the best sperm retrieval technique in Obst and Non Obst azoospermia ?

Cochrane Database Jul 2006

"There is insufficient evidence to recommend any specific sperm retrieval mode

Donso, Tournaye, Devroey HR Update, Nov-Dec, 2007 (Pub-Med)

3 outcome measures were assessed for the sperm retrieval techniques in **NOA**:

- sperm retrieval rate (SRR)
- complications
- live birth rate

Discussion

No available RCT's. Only Descriptive studies

Higher sperm retrieval rate with Conventional TESE than FNA (especially in cases of SCO and MA)

Micro TESE performs better than Conventional TESE (In SCO)

Micro TESE appears to be the safest technique regarding post-operative complications

No evidence which technique has better influence on live birth rate

Donso, Tournaye Devroey HR Update, Nov-Dec, 2007 (Pub-Med)

In Summary

Sperm retrieval rate should be considered of first cycles only (42%)

In Obst Azoospermia – Aspiration should be the chosen method for sperm retrieval

In Non Obst Azoospermia – Testicular biopsy should be the method used for sperm retrieval

There is no clear advantage of Micro TESE over TESE by now

Repeated TESE is feasible but to a limited number

Assaf Harofeh Infertility IVF Unit:

Clinicians	Embryologists	Biologists	
Friedler S.	Bern O.	Kaufman S.	Schlegel P.
Raziel R.	Komsky A.	Omanski A.	Cornell University,
Schachter M.	Kasterstein E.		New York
	Komarovsky D.		
	Maslansky B.		
	Starssburger D.		

thank you

Azoospermia – *Testicular biopsy and Aspiration*

treated cycles in Assaf Harofeh Medical Center,Tel Aviv University

	Number of cycles	incidence
First cycles	299	4.7% (299/6300)
Fresh cycles First and repeated	393	6.2% (393/6300)
Fresh and frozen cycles	692	11.0% (393/6300)

15700 testicular biopsies and aspiration

are performed per year in Europe and the United States

Presence or absence of sperm among patients with Yq microdeletions

	cases	Azoospermia	Crypto-zoospermia	Severe Oligozoospermia
AFZa	1	1		
AZFb	3	2	1	
AZFc	27	16	6	5
AZFb+c	5	5		
AZFa+b+c	2	2		
Total	38	26 (68%)	7 (18%)	3 (13%)

Stouffs et al. HR 20:1887, 2005

Outcome of ICSI in Azoospermia treated cases

In Non Obstructive Azoospermia - Fresh vs. Frozen

	Fresh	Frozen-thaewd
No. of patients	18	9
No. of cycles	25	14
Fertilization rate	47%	44%
Pregnancy rate	6/23 26%	3/11 27%
Ongoing pregnancy	5/23 22%	1/11 9%

No statistical significance

Friedler et al., F&S, 68:892,1997

The two largest registries of ICSI cycles

lately published were:

2001 Results

		OPU'S
ART in Europe	*HR,20:1158,2005*	103538
SART	*CDC Report, USA, December, 2003*	38928
Total		142466

How many azoospermia patients were treated by testicular biopsy or aspiration ?

Prevalence of treated azoospermic patients

First treatment cycles

Epididymal and Testicular

In VUB (1995-2003)

Sperm aspiration/ ICSI cases	2.1%	(381/18000)
Testicular biopsy/ICSI cases	3.5%	(628/18000)
	5.6%	

In Assaf Harofeh: (1995-2003)

Sperm aspiration/ ICSI cases	1.5%	(98/6300)
Testicular biopsy/ ICSI cases	3.1%	(201/6300)
	4.7%	

Prevalence of *first* treatment of azoospermic patients

Presuming that the treated azoospermic patients comprise 5% of the ICSI program

The number of firstly treated cases with azoospermia according to the American and European Registry in 2001 would be:

7123 patients (5% from 142466 cases) with azoospermia\year will have their first treatment

Prevalence of treated azoospermic patients

First and repeated fresh cycles

Epididymal and Testicular

In VUB (1995-2003)

Sperm aspiration/ ICSI cases	3.3%	(597/18000)
Testicular biopsy/ICSI cases	4.4%	(784/18000)
	7.7%	

In Assaf Harofeh: (1995-2003)

Sperm aspiration/ ICSI cases	1.7%	(106/6300)
Testicular biopsy/ ICSI cases	4.6%	(287/6300)
	6.3%	

Prevalence of *first and repeated fresh* treatments of azoospermic patients

Presuming that the treated azoospermic patients comprise 7% of the ICSI program

The number of fresh and repeated treated cases with azoospermia according to the American and European Registry in 2001 would be:

9972 patients (7% from 142466 cases) with azoospermia\year will have their first & repeated fresh treatments

Outcome of ICSI in Azoospermia treated cases

In Obstructive Azoospermia

Category : - Fresh vs. Frozen

Epididymal and testicular sperm

	cycles	Fertilization rate	E.T.	Pregnancy rate
Fresh	*96*	61%	*93* 97%	36.6%
Frozen-thawed	*167*	53%	*147* 88%	34.6%
		P<0.001	P<0.03	NS

Ron-El et al., 2006

Outcome of ICSI in Azoospermia treated cases

In Non Obstructive Azoospermia - Fresh vs. Frozen

First results showed similar outcome when using fresh or frozen testicular sperm

Nagy et al., 1995; Silber et al., 1995; Devroey et al., 1995

Gil-Salom et al., 1996; Podsiadly et al., 1996

conclusion :

oocyte\ICSI procedure **can be disassociated from** sperm retrieval without compromising the chances of pregnancy

Outcome of ICSI in Azoospermia treated cases

In Non Obstructive Azoospermia

Ron-El et al. – Assaf Harofeh

First cycles		Transferred embryos	Pregnancy rate per ET
All first cycles	177		
Cycles with sperm	77 (44.7%)	2.8±1.75	28.6%

First & repeated cycles			
All cycles	287		
First & repeated cycles with sperm	141(49.4%)	121 transfers 2.9±1.61	34.7%

Outcome of ICSI in Azoospermia treated cases

In Non Obstructive Azoospermia

Ron-El et al. – Assaf Harofeh

Fresh cycles

cycles	Cycles with sperm		Fert. rate	transfers	Pregnancy /ET	
287	141	49.4%	53%	121	42	34.7%

Frozen thawed cycles

131	116	88.5%	47%	116	31	26.7%

P < 0.0001 P< 0.03 NS

Outcome of ICSI in Azoospermia treated cases

In Non Obstructive Azoospermia

Results of outcome may be overestimated

by

reallocating successful repeated cases

Reliable results of ICSI in NonObstructive cases should be of first cycles only

	First cycles with sperm found	Fertilization rate	Pregnancy rate per ET	
Vernaeve et al. F&S, 79:529, 2003	306	48.5%	72/262	27.5%
Ron-El et al. 2006	77	47.7%	22/77	28.6%

Outcome of Repetitive TESE-ICSI Cycles, by the Number of Trial

TESE trial	2nd TESE	3rd TESE	4th TESE	5th TESE
# of ICSI cycles	17	8	5	3
Fertilization rate (%)	48	50	44	54
# of embryos replaced /ET	3.4±1.8	5±4.8	4.5±1.4	4.7±0.6
Implantation rate (%)	3/56 (5)	2/32 (6)	1/10 (10)	0/14
Clinical preg. rate/ET (%)	3/17 (18)	1/7 (14)	1/4	0/3

Friedler et al., HR 17: 2356,2002

The outcome of repeated TESE cycles was not given in Vernaeve's study