

XXIII Congresso Brasileiro de
Reprodução Assistida

31 de julho a 03 de agosto de 2019
ExpoUnimed - Curitiba - Paraná



Falha de Fertilização e Implantação: O papel do Espermatozoide

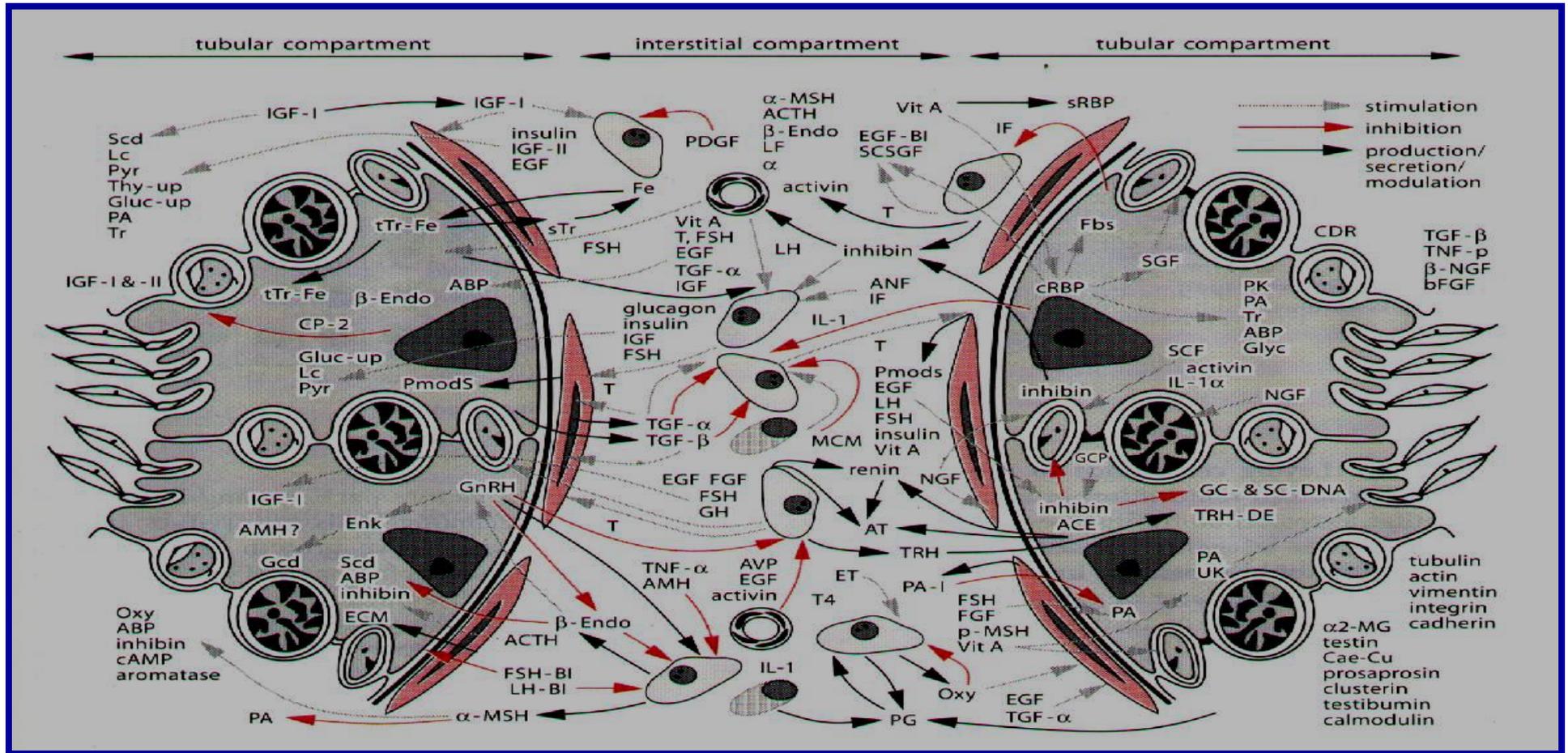
Declaração:

Declaro o recebimento de honorários para palestras e /ou ensaios clínicos da Merck, Ferring e Abbott (não relacionados ao assunto desta palestra).

Nenhum outro conflito de interesse para divulgar.

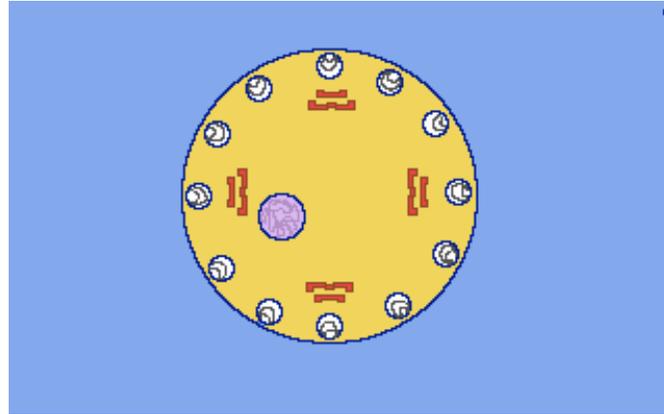
**Resolução do Conselho Federal de Medicina
nº 1.595/2.000**

Túbulo Seminífero



- 65 dias: espermatogônia - espermatozoide
- 3 mitoses + 2 meioses: 10^{12} - 10^{13} espermatozoides
- perda + 75% céls. produzidas

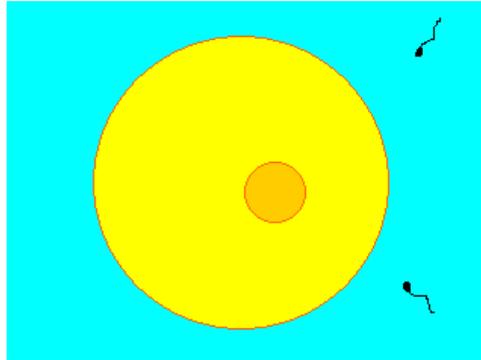
Mecanismos do “efeito paterno” no desenvolvimento embrionário pré-implantacional



EFEITO PATERNO PRECOCE:

- ➔ anormalidades do centríolo e da ativação oocitária
- ➔ fecundação e divisão embrionária inicial

Mecanismos do “efeito paterno” no desenvolvimento embrionário pré-implantacional



EFEITO PATERNO TARDIO:

- ➔ relacionado com a fragmentação do DNA espermático
- ➔ divisão embrionária tardia
- ➔ implantação
- ➔ desenvolvimento embrionário / fetal



espermatogênese
espermiogênese

maturação



capacitação
hiperativação



interação zona
pelúcida



reação acrossômica



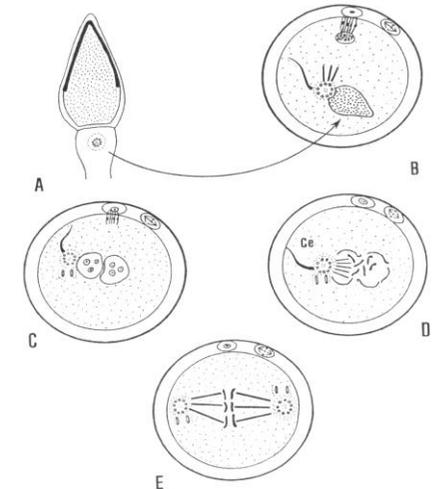
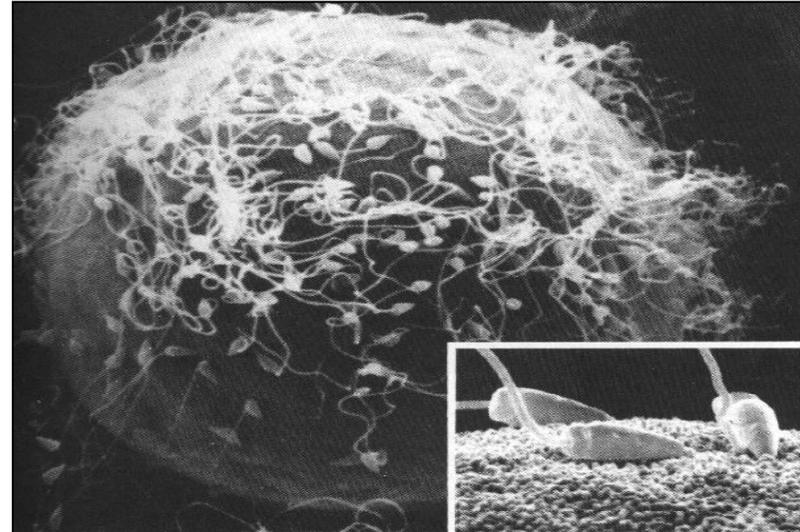
descondensação
pronúcleo



fusão
espermatozóide
óvulo



penetração zona
pelúcida



FERTILITY

espermatogênese
espermio gênese



maturação



capacitação
hiperativação



interação zona
pelúcida



reação acrossômica



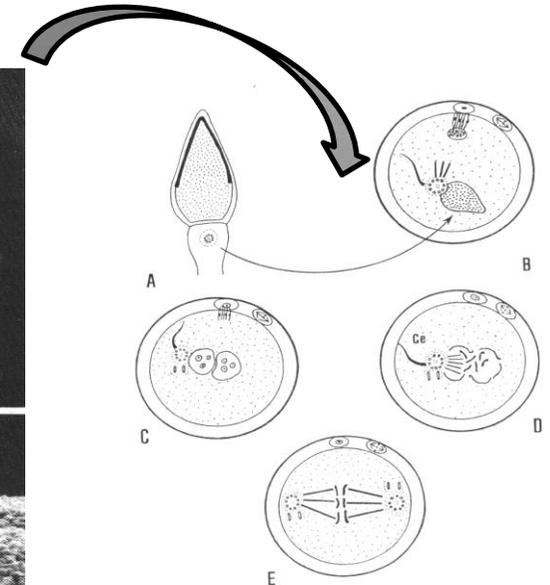
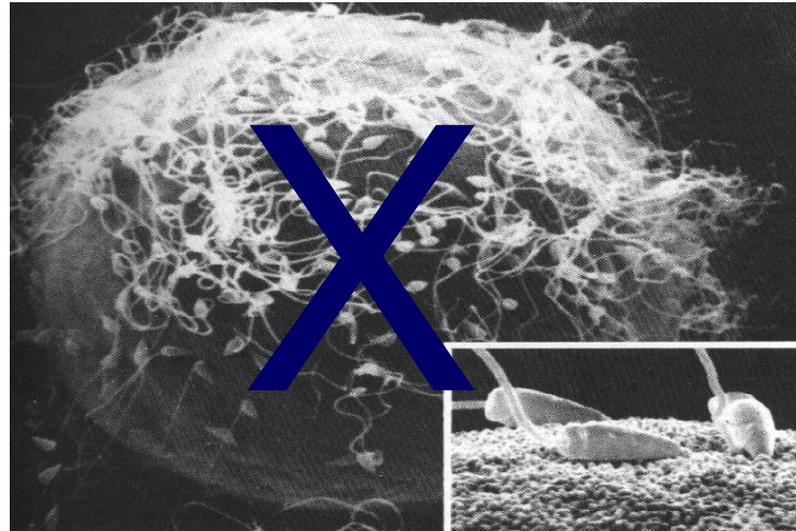
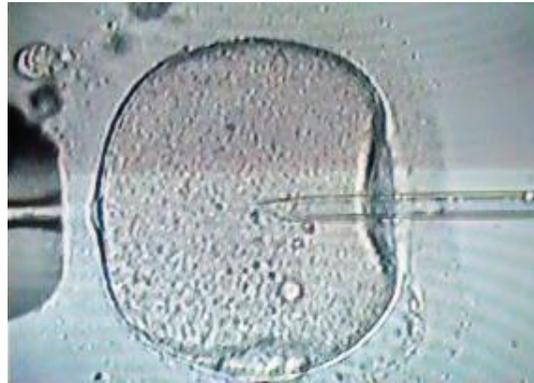
descondensação
pronúcleo



fusão
espermatozóide
óvulo



penetração zona
pelúcida



FERTILITY

Qualidade seminal e resultados de T.R.A.



ANDROLOGI
**The out
plasmic**

R. Mercan, S. E
The Howard and Ge
Virginia Medical Sch

Andrology: The
three basic sperm pa
Z.P. Nagy, J. Liu, H. Joris, G. Verhe
Human Reproduction, Volume 10,
<https://doi.org/10.1093/oxfordjo>



Journal Article
tion is not related to any of the

ACCEPTED: SEPTEMBER 16, 1997

**following intracyto-
ed by semen quality**

sher and S. Oehninger
of Obstetrics and Gynecology Eastern

Consequências da Alteração Espermática

- menores taxas de
- desenvolvimento
- maiores taxas de
- piores condições
- maior incidência
- maiores taxas de

Slama et al, 2005, Nybo Andersen et al, 2006, Wyrobek et al, 2006,



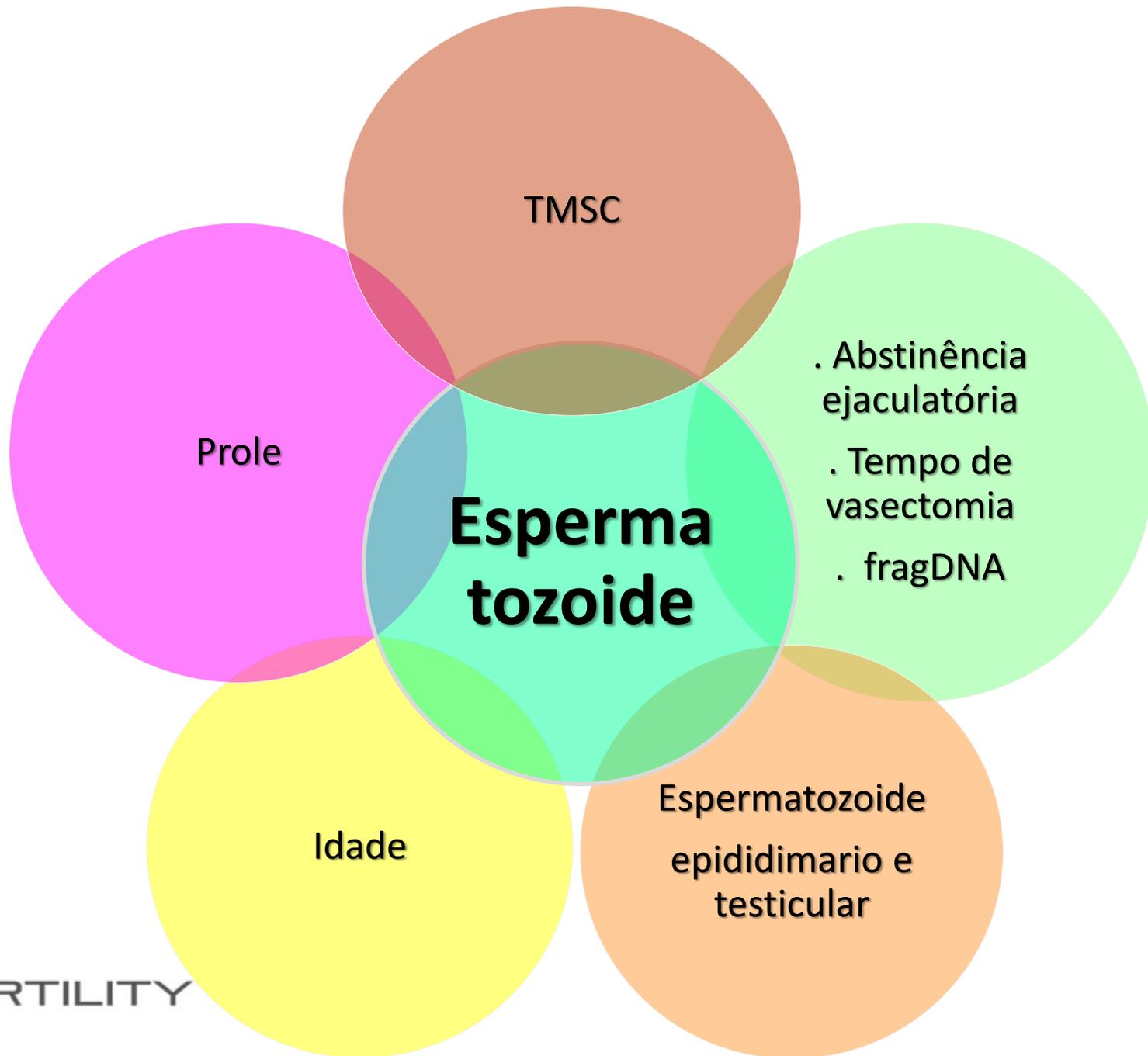
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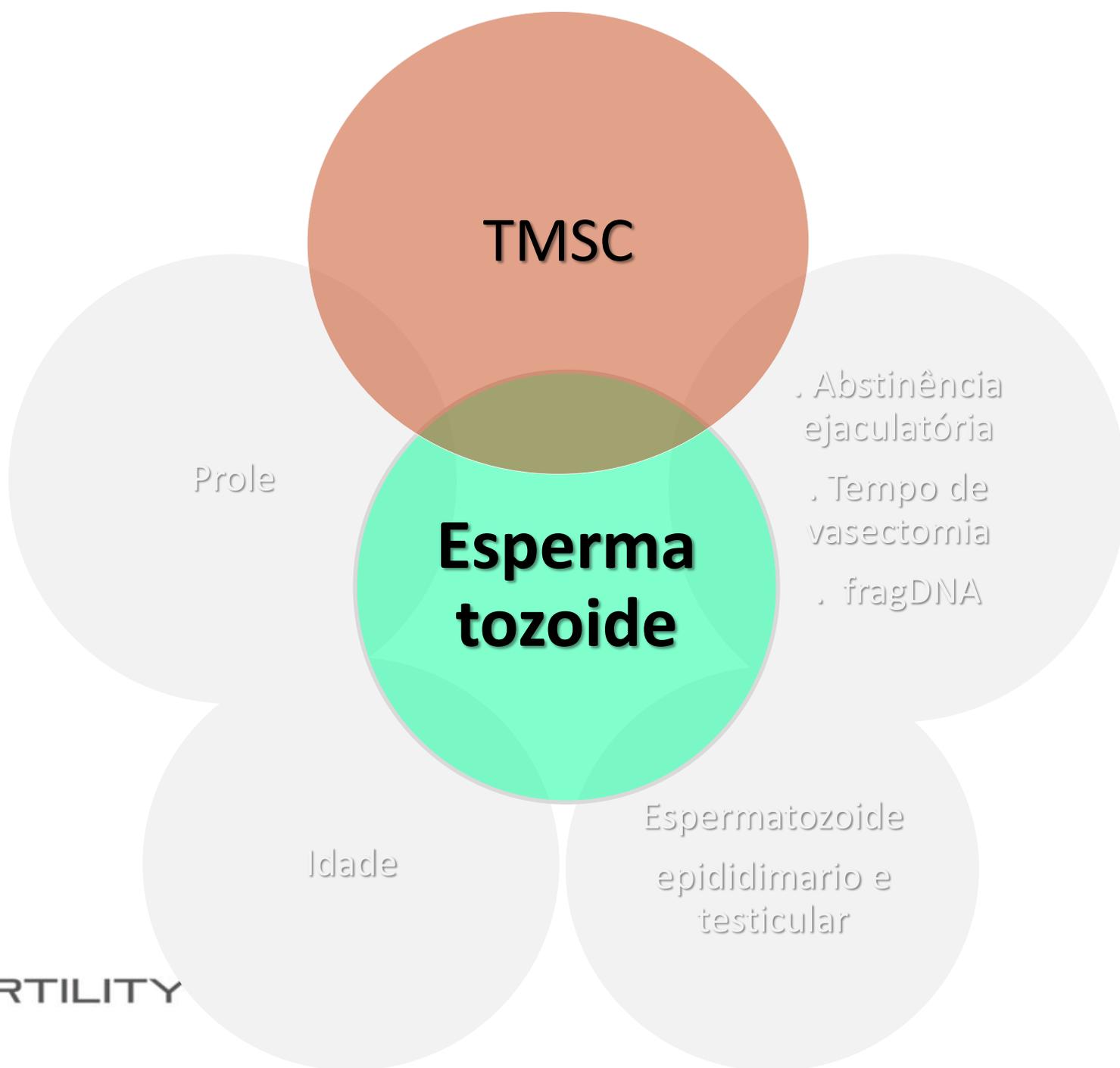
éticas

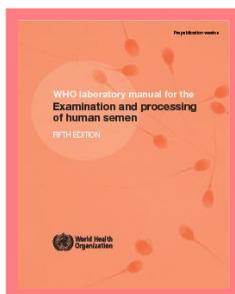
2005, Nieschlag et al, 2004, Tesarik et al, 2005, et al, 2008 ...



FERTILITY







World Health Organization reference values for human semen characteristics[‡]

Trevor G. Cooper^{1,10}, Elizabeth Noonan², Sigrid von Eckardstein³, Jacques Auger⁴, H.W. Gordon Baker⁵, Hermann M. Behre⁶, Trine B. Haugen⁷, Thinus Kruger⁸, Christina Wang⁹, Michael T. Mbizvo^{3,1}, and Kirsten M. Vogelsong^{3,1}

Table II Distribution of values, lower reference limits and their 95% CI for semen parameters from fertile men whose partners had a time-to-pregnancy of 12 months or less (n= 1953)

	N	Centiles										
		2.5	(95% CI)	5	(95% CI)	10	25	50	75	90	95	97.5
Semen volume (ml)	1941	1.2	(1.0–1.3)	1.5	(1.4–1.7)	2	2.7	3.7	4.8	6	6.8	7.6
Sperm concentration (10 ⁶ /ml)	1859	9	(8–11)	15	(12–16)	22	41	73	116	169	213	259
Total number (10 ⁶ /Ejaculate)	1859	23	(18–29)	39	(33–46)	69	142	255	422	647	802	928
Total motility (PR + NP, %)*	1781	34	(33–37)	40	(38–42)	45	53	61	69	75	78	81
Progressive motility (PR, %)*	1780	28	(25–29)	32	(31–34)	39	47	55	62	69	72	75
Normal forms (%)	1851	3	(2.0–3.0)	4	(3.0–4.0)	5.5	9	15	24.5	36	44	48
Vitality (%)	428	53	(48–56)	58	(55–63)	64	72	79	84	88	91	92

*PR, progressive motility (WHO, 1999 grades a + b); NP, non-progressive motility (WHO, 1999 grade c).

The values are from unweighted raw data. For a two-sided distribution the 2.5th and 97.5th centiles provide the reference limits; for a one-sided distribution the fifth centile provides the lower reference limit.

ORIGINAL ARTICLE

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*These authors contributed equally to this manuscript.

Keywords:

intracytoplasmic sperm injection, infertility, sperm count, sperm motility, spermatozoa

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Total motile sperm count has a superior predictive value over the WHO 2010 cut-off values for the outcomes of intracytoplasmic sperm injection cycles

^{1,2}*E. Borges Jr, ^{1,2}*A. S. Setti, ^{1,2}D. P. A. F. Braga, ¹R. C. S. Figueira and ^{1,2}A. Iaconelli Jr

- ➔ 518 ciclos de ICSI
- ➔ OMS / TMSC
- ➔ TMSC normal: > 20 milhões



Table 4 Comparison of ICSI outcomes between normal and abnormal TMSC groups

Variables	Normal TMSC group (<i>n</i> = 328)	Abnormal TMSC group (<i>n</i> = 190)	<i>p</i> -value
Paternal age (year-old)	37.4 ± 4.8	38.1 ± 6.1	0.187
Maternal age (year-old)	35.4 ± 3.9	33.5 ± 4.0	<0.001
Number of aspirated follicles	17.8 ± 9.7	20.8 ± 11.2	0.002
Number of obtained oocytes	12.7 ± 7.2	15.1 ± 8.1	0.001
Number of mature oocytes	9.7 ± 5.5	11.2 ± 6.2	0.003
Number of injected oocytes	9.4 ± 4.3	10.2 ± 4.9	0.067
Fertilization rate (%)	84.9 ± 14.4	81.1 ± 15.8	0.016
Number of obtained embryos	8.2 ± 3.8	8.7 ± 4.4	0.204
Number of transferred embryos	2.2 ± 0.6	2.2 ± 0.5	0.469
Implantation rate (%)	25.1 ± 36.0	25.8 ± 35.2	0.832
Pregnancy rate (%)	134/328 (40.9)	94/190 (49.5)	0.060
Miscarriage rate (%)	29/162 (17.9)	23/78 (29.5)	0.041

SD, standard deviation; TMSC: total motile sperm count.

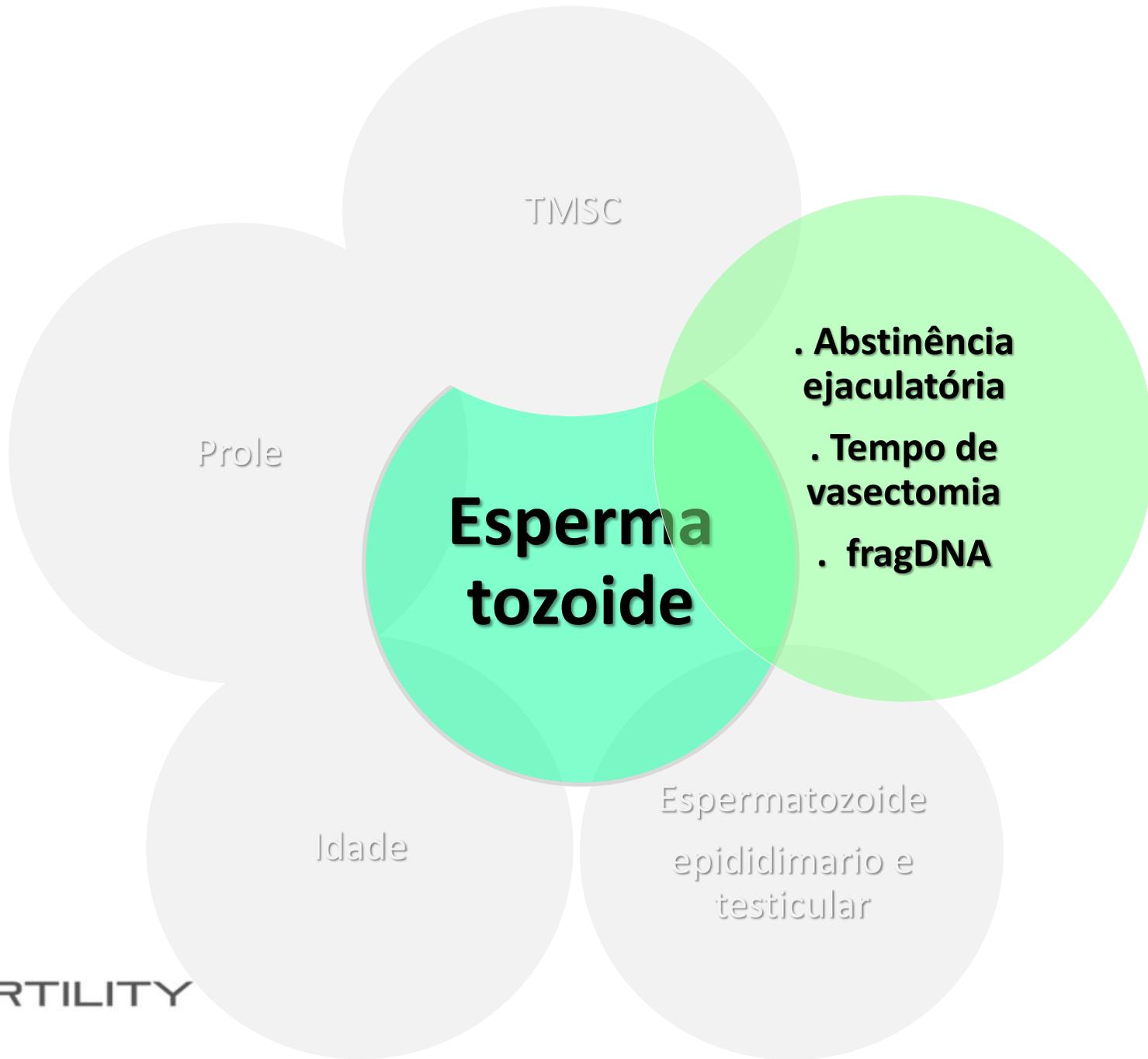


Table 5 Linear and binary regression analysis results for the influences of TMSC and WHO cut-off values on ICSI outcome

Variables	Method	OR or RC	CI or R^2	p -value
Fertilization rate	Concentration	3.994	1.4%	0.015
	Motility	0.097	0.0%	0.957
	Progressive motility	2.299	0.5%	0.163
	Morphology	8.735	0.9%	0.047
	TMSC	3.784	1.5%	0.013
	Normal TMSC	-0.253	0.1%	0.592
Formation of high-quality zygotes on D1	Concentration	1.64	1.09–2.46	0.018
	Motility	1.34	0.85–2.12	0.208
	Progressive motility	1.22	0.80–1.85	0.355
	Morphology	0.89	0.65–1.22	0.461
	TMSC	1.13	1.01–1.28	0.049
	Normal TMSC	0.99	0.97–1.02	0.629
Formation of high-quality embryos on D2	Concentration	0.93	0.76–1.09	0.101
	Motility	0.91	0.79–1.06	0.222
	Progressive motility	1.06	0.92–1.22	0.420
	Morphology	0.84	0.60–1.18	0.314
	TMSC	1.18	1.03–1.35	0.013
	Normal TMSC	0.97	0.94–1.01	0.098
Formation of high-quality embryos on D3	Concentration	0.91	0.79–1.06	0.229
	Motility	0.93	0.79–1.09	0.379
	Progressive motility	1.00	0.85–1.17	0.969
	Morphology	1.18	0.83–1.67	0.354
	TMSC	1.12	1.07–1.29	0.037
	Normal TMSC	0.98	0.95–1.02	0.319
Formation of blastocyst on D5	Concentration	1.11	0.97–1.27	0.116
	Motility	1.03	0.90–1.19	0.660
	Progressive motility	0.91	0.70–1.23	0.303
	Morphology	1.13	0.83–1.55	0.427
	TMSC	1.16	1.04–1.26	0.011
	Normal TMSC	1.00	0.97–1.04	0.802

Blastocyst expansion grade on D5	Concentration	0.83	0.66–1.05	0.120
	Motility	1.01	0.79–1.29	0.948
	Progressive motility	1.08	0.85–1.38	0.533
	Morphology	0.99	0.57–1.71	0.962
	TMSC	1.27	1.01–1.60	0.042
	Normal TMSC	1.03	0.98–1.07	0.287
Implantation rate	Concentration	2.387	0.1%	0.492
	Motility	–2.916	0.1%	0.453
	Progressive motility	–1.754	0.0%	0.616
	Morphology	6.084	0.0%	0.502
	TMSC	–0.688	0.0%	0.833
	Normal TMSC	1.705	1.0%	0.222
Pregnancy	Concentration	0.71	0.49–1.05	0.083
	Motility	0.77	0.50–1.19	0.242
	Progressive motility	0.72	0.49–1.05	0.089
	Morphology	2.17	0.78–6.07	0.132
	TMSC	1.40	0.98–2.01	0.066
	Normal TMSC	0.94	0.86–1.03	0.200
Miscarriage	Concentration	0.57	0.30–1.08	0.089
	Motility	1.32	0.61–2.85	0.478
	Progressive motility	1.05	0.54–2.05	0.886
	Morphology	0.84	0.17–4.08	0.826
	TMSC	0.52	0.28–0.90	0.045
	Normal TMSC	1.12	0.91–1.26	0.084

CI, confidence interval; OR, odds ratio; RC, regression coefficient; TMSC, total motile sperm count; WHO, World Health Organization.



ORIGINAL ARTICLE

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Keywords:

Ejaculatory abstinence, ICSI, semen quality, sperm DNA fragmentation

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Revisiting the impact of ejaculatory abstinence on semen quality and intracytoplasmic sperm injection outcomes

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¹Fertility Medical Group, Sao Paulo, Brazil, and ²Sapientiae Institute, Sao Paulo, Brazil



**Linear model analysis of the association between sperm parameters and
EA length (n = 818)**

SEMEN PARAMETER	R	SLOPE	R² (%)	P-VALUE
Semen volume (mL)	0.1405	1.62102	5.28	<0.001
Sperm count (x10 ⁶ /mL)	3.1261	52.2206	2.59	<0.001
Total sperm count (x10 ⁶)	18.941	170.650	8.37	<0.001
Total sperm motility (%)	-0.3355	19.0885	0.23	0.212
Progressive sperm motility (%)	-0.1895	19.1802	0.07	0.483
TMSC (x10 ⁶)	9.6396	102.629	6.14	<0.001
Morphology (%)	0.0227	1.29926	0.23	0.215
SDF (%)	0.5355	9.34201	2.57	<0.001

Linear model analysis of the association between sperm parameters and EA length (n = 818)

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Total sperm count (x10 ⁶)	18.941	170.650	8.37	<0.001
Total sperm motility (%)	-0.3355	19.0885	0.23	0.212
Progressive sperm motility (%)	-0.1895	19.1802	0.07	0.483
TMSC (x10 ⁶)	9.6396	102.629	6.14	<0.001
Morphology (%)	0.0227	1.29926	0.23	0.215
SDF (%)	0.5355	9.34201	2.57	<0.001

Table 5 GzLM results for the association between ICSI outcomes and EA length ($n = 483$)

Continuous ICSI outcomes	B	95% CI	<i>p</i> -value
Fertilization rate ^a	-0.983	-1.954 to -0.011	0.047
High-quality embryos rate on day 3 ^a	-0.090	-0.207 to 2.284	0.131
Blastocyst formation rate on day 5 ^a	-2.384	-4.552 to -0.216	0.031
Implantation rate ^{ab}	-3.299	-5.388 to -1.260	0.002
Continuous ICSI outcomes	Exp(B)	95% CI	<i>p</i> -value
Pregnancy rate ^{ab}	0.506	0.290-0.882	0.016
Miscarriage rate ^{ab}	0.736	0.458-1.185	0.207

GzLM: generalized linear model; ICSI: intracytoplasmic sperm injection; EA: ejaculatory abstinence; B: unstandardized regression coefficient; CI: confidence intervals; Exp(B): exponentiation of the B coefficient. ^aAdjusted for maternal and paternal ages, smoking habits and body mass index, seminal parameters, total dose of FSH administered, estradiol levels on the day of hCG administration, number of oocytes and mature oocytes; ^bAdjusted for number of transferred embryos.



ORIGINAL ARTICLE

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Keywords:
Ejaculatory abstinence, ICSI, semen quality,
sperm DNA fragmentation

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and ^{1,2}A. S. Setti

¹Fertility Medical Group, São Paulo, Brazil, and ²Sapientiae Institute, São Paulo, Brazil



Abstinência ejaculatória \leq 4 dias:

- Frag DNA espermático significativamente menor, maiores taxas de fertilização, embriões de alta qualidade no dia 3, desenvolvimento a blastocisto, implantação e gestação quando comparados ao grupo de abstinência ejaculatória \geq 4 dias.
- Taxas de implantação significativamente maiores e taxas de gestação tendendo a serem maiores com *um dia de abstinência ejaculatória*, comparado a 2 – 4 de abstinência ejaculatória.

ARTICLE

The obstructive interval predicts pregnancy rates in post-vasectomy patients undergoing ICSI with surgical sperm retrieval



BIOGRAPHY

Edson Borges Jr obtained his MD degree in 1984 (University of Campinas), PhDs in urology in 2005 (Federal University of São Paulo) and in gynaecology in 2007 (São Paulo State University). He is founder and managing partner of Fertility Medical Group and director at Sapientiae Institute, São Paulo, Brazil.

Edson Borges Jr^{1,2,*}, Daniela Paes de Almeida Ferreira Braga^{1,2}, Assumpto Iaconelli Jr^{1,2}, Amanda Souza Setti^{1,2}

TABLE 2 INFLUENCE OF THE OBSTRUCTIVE INTERVAL ON SSR OUTCOMES

SSR parameter ^a	Estimate (β)	SE	P-value	95% CI	
				Lower bound	Upper bound
Presence of spermatozoa during PESA	-0.032	0.012	0.009	-0.056	-0.009
Presence of motile spermatozoa during PESA	-0.031	0.012	0.010	-0.054	-0.008
Need to convert to TESA	0.012	0.004	0.003	0.004	0.019

CI = confidence interval; PESA = percutaneous epididymal sperm aspiration; SE = standard error; SSR = surgical sperm retrieval; TESA = testicular sperm aspiration.

^a Adjusted for paternal age, smoking habit, previous vasectomy reversal attempt, hormonal profile and abnormalities found in the male partner physical examination.

TABLE 4 INFLUENCE OF THE OBSTRUCTIVE INTERVAL ON THE OUTCOMES OF ICSI WITH SSR

ICSI outcome	Estimate (β)	SE	P-value	95% CI	
				Lower bound	Upper bound
Fertilization rate ^a	-0.098	0.302	NS	-0.696	0.500
Day 2 high-quality embryos rate ^a	-0.001	0.003	NS	-0.007	0.005
Day 3 high-quality embryos rate ^a	0.001	0.003	NS	-0.003	0.007
Blastocyst development rate ^a	-0.011	0.004	0.014	-0.019	-0.002
Clinical pregnancy rate ^b	-0.016	0.007	0.031	-0.031	-0.001
Implantation rate ^b	-1.107	0.530	0.039	-2.157	-0.056
Miscarriage rate ^b	0.006	0.009	NS	-0.012	0.025

^a Adjusted for maternal and paternal ages, paternal smoking habit, previous vasectomy reversal attempt, paternal hormonal profile and abnormalities found in the male partner physical examination, and number of retrieved oocytes.

^b Adjusted for the same variables cited above plus number of transferred embryos. CI = confidence interval; ICSI = intracytoplasmic sperm injection; NS = not significant; SE = standard error; SSR = surgical sperm retrieval.

Intervalos de vasectomia > 17 anos mostraram efeitos prejudiciais na chance de gravidez clínica

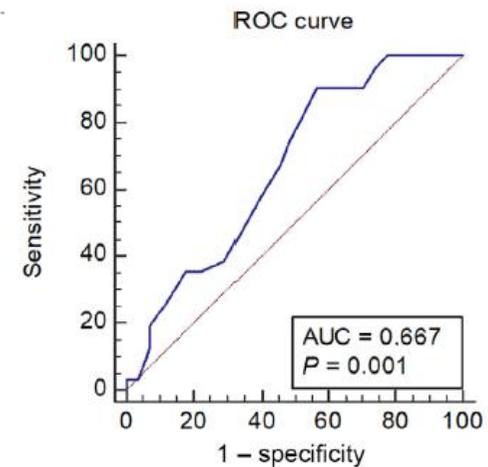


FIGURE 1 Receiver operating characteristic (ROC) curve for predicting clinical pregnancy using obstruction interval as test variable.

Sperm DNA fragmentation is correlated with poor embryo development, lower implantation rate, and higher miscarriage rate in reproductive cycles of non–male factor infertility

Edson Borges Jr., M.D., Ph.D.,^{a,b} Bianca Ferrarini Zanetti, Ph.D.,^{a,b} Amanda Souza Setti, M.Sc.,^{a,b} Daniela Paes de Almeida Ferreira Braga, Ph.D.,^{a,b} Rodrigo Rosa Provenza, B.Sc.,^a and Assumpto Iaconelli Jr., M.D.^{a,b}

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- ➔ 475 ciclos de ICSI / ausência de fator masculino
- ➔ fragDNA espermático $\geq 30\%$ x $< 30\%$
- ➔ Estudo coorte prospectivo



Sperm DNA fragmentation is correlated with poor embryo development, lower implantation rate, and higher miscarriage rate in reproductive cycles of non-male factor infertility

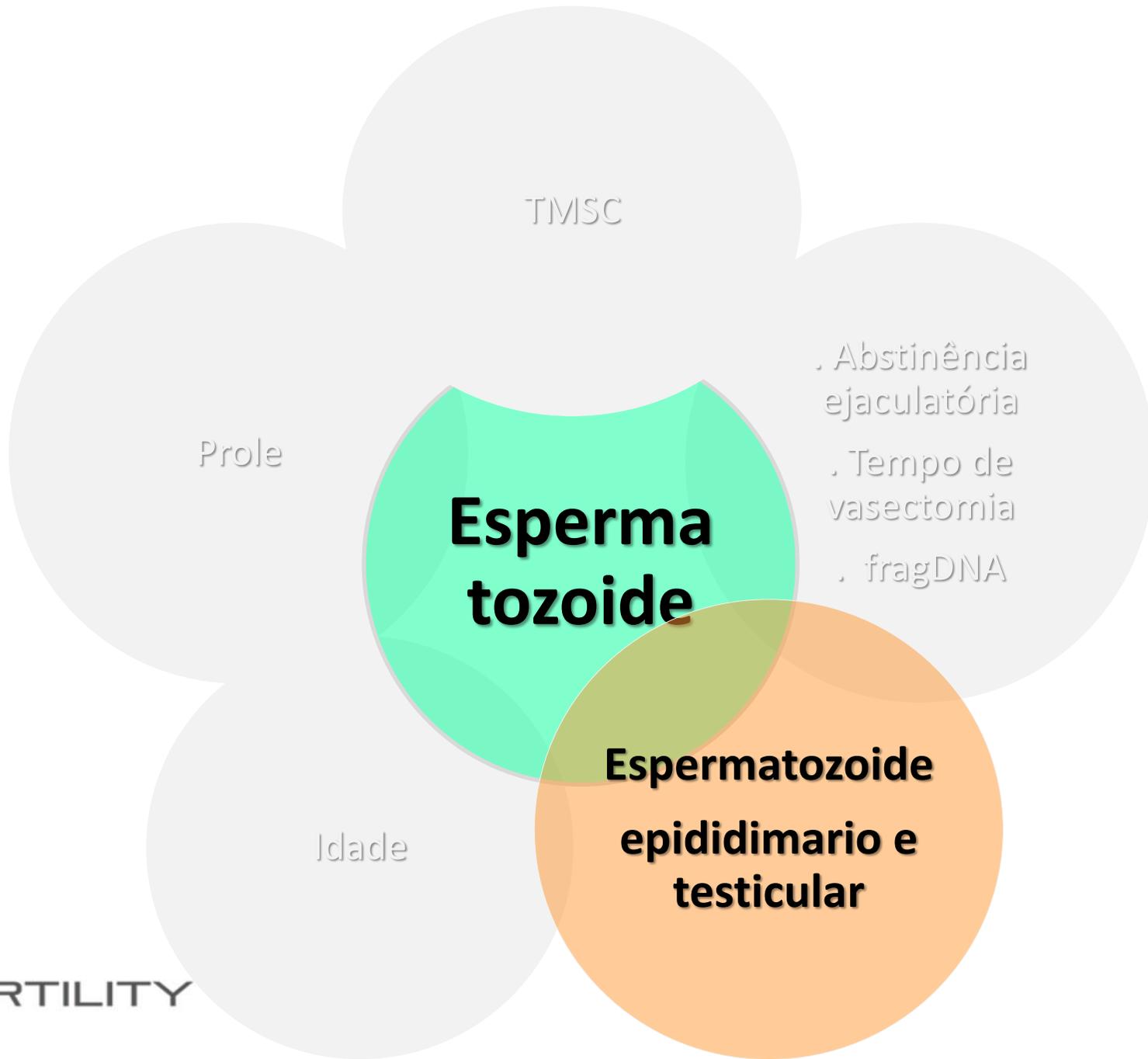
Effect of SDF on laboratory and clinical outcomes.

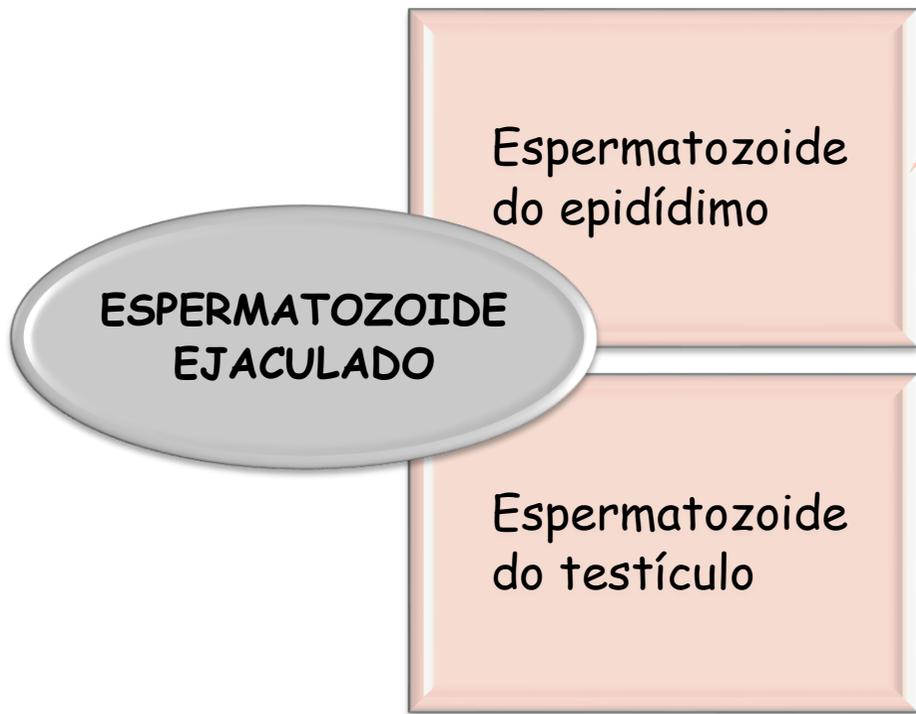
Variable	< 30% SDF (n = 433)	≥30% SDF (n = 42)	P value
Laboratory outcomes ^a			
Fertilization rate	90.10 ± 3.50	85.67 ± 1.03	.226
Normal cleavage speed rate	72.16 ± 1.30	61.56 ± 4.40	.010
High-quality embryos at day 3 rate	36.47 ± 1.51	23.89 ± 5.51	.021
Blastocyst rate	56.25 ± 2.01	39.01 ± 1.40	.016
Blastocyst quality rate	30.54 ± 2.27	11.32 ± 7.72	<.001
Clinical outcomes ^b			
Implantation rate	46.09 ± 0.55	33.21 ± 1.96	<.001
Chemical pregnancy rate	34.99	33.11	.940
Clinical pregnancy rate	32.42	30.33	.774
Miscarriage rate	17.8	39.9	.018

^a Adjusted for maternal age, maternal BMI, total FSH dose, number of retrieved oocytes, and paternal age.

^b Adjusted for maternal age, maternal BMI, total FSH dose, number of retrieved oocytes, paternal age, number of transferred embryos, endometrial thickness.

Borges. Sperm DNA fragmentation and ICSI outcomes. *Fertil Steril* 2019.





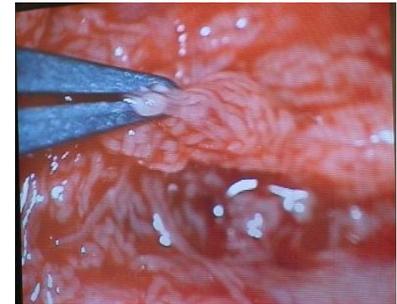
PERCUTANEOUS
EPIDYDIMAL
SPERM
ASPIRATION

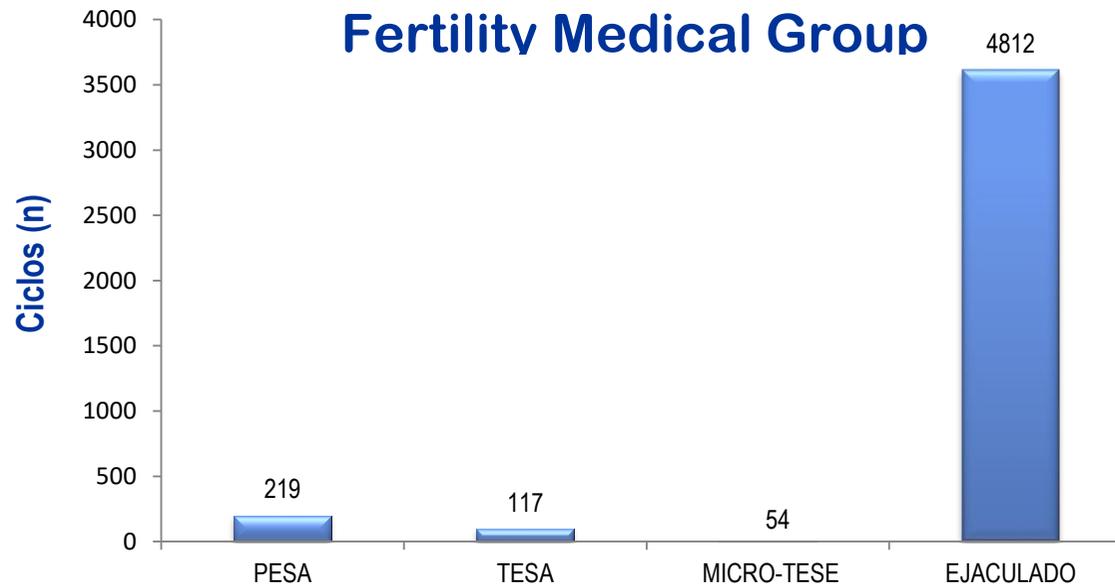


TESTICULAR
SPERM
ASPIRATION
EXTRACTION



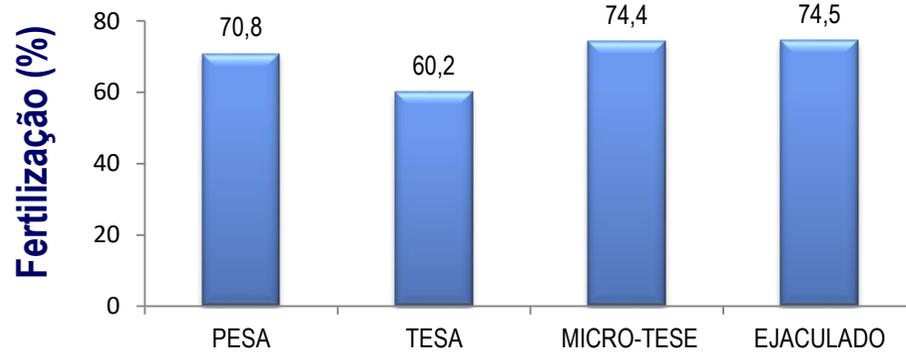
MICRO
TESTICULAR
SPERM
EXTRACTION





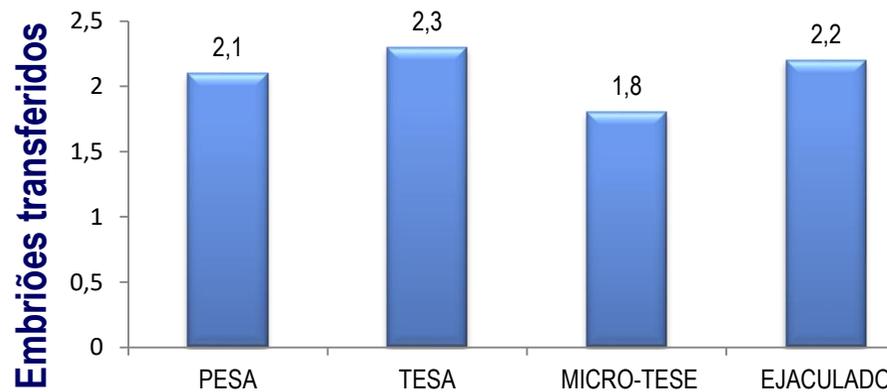
	PESA	TESA	MICRO-TESE	EJACULADO
Ciclos (n)	219	117	54	4812
Idade ± DP	34.9 ± 4.6	34.8 ± 5.4	32.2 ± 2.7	35.8 ± 4.7
Folículos ± DP	20.4 ± 15.4	18.1 ± 11.3	15.9 ± 14.4	15.8 ± 12.4
Oocitos recuperados ± DP	14.2 ± 10.8	13.3 ± 9.3	11.0 ± 11.4	11.0 ± 9.0
Oocitos micromanipulados ± DP	9.8 ± 6.4	8.9 ± 5.1	8.0 ± 6.9	7.8 ± 5.8

Fertility Medical Group



	P
PESA VS TESA	< 0.001
PESA VS MICRO-TESE	> 0.05
PESA VS EJACULADO	> 0.05
TESA VS MICRO-TESE	> 0.05
TESA VS EJACULADO	< 0.001
MICRO-TESE VS EJACULADO	> 0.05

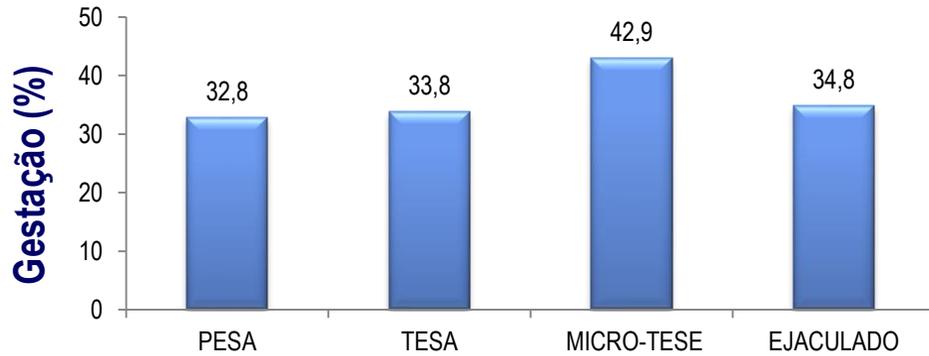
ANOVA



	P
PESA VS TESA	> 0.05
PESA VS MICRO-TESE	> 0.05
PESA VS EJACULADO	> 0.05
TESA VS MICRO-TESE	> 0.05
TESA VS EJACULADO	> 0.05
MICRO-TESE VS EJACULADO	> 0.05

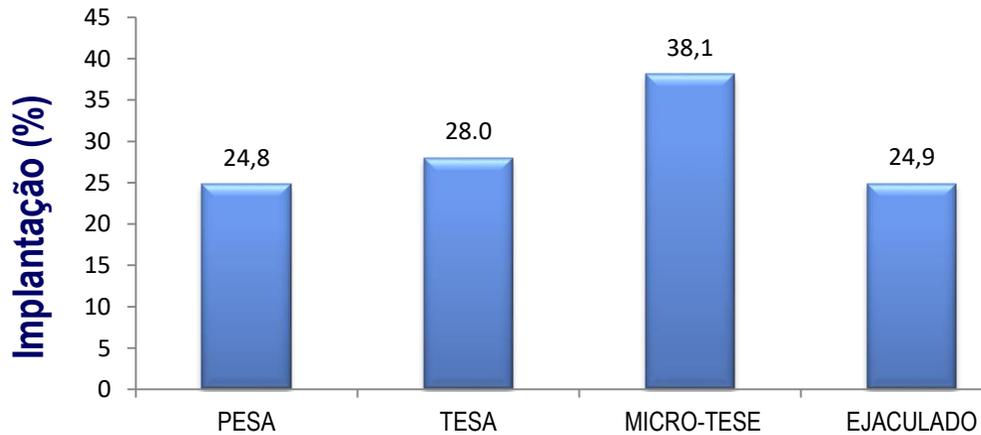
ANOVA

Fertility Medical Group



	P
PESA VS TESA	> 0.05
PESA VS MICRO-TESE	> 0.05
PESA VS EJACULADO	> 0.05
TESA VS MICRO-TESE	> 0.05
TESA VS EJACUALDO	> 0.05
MICRO-TESE VS EJACULADO	> 0.05

QUI-QUADADRO



	P
PESA VS TESA	> 0.05
PESA VS MICRO-TESE	> 0.05
PESA VS EJACULADO	> 0.05
TESA VS MICRO-TESE	> 0.05
TESA VS EJACUALDO	> 0.05
MICRO-TESE VS EJACULADO	> 0.05

ANOVA



FERTILITY

¹Fertility – Assisted Fertilization Center, São Paulo, SP, Brazil, ²Sapientiae Institute – Educational and Research Center in Assisted Reproduction, São Paulo, SP, Brazil, and ³Institute of Biotechnology – Caxias do Sul University, Caxias do Sul, RS, Brazil

ORIGINAL ARTICLE

Assisted reproductive technology outcomes in azoospermic men: 10 years of experience with surgical sperm retrieval

Table II. ICSI outcomes from patients with obstructive azoospermia when the injected sperm were retrieved from the testicle (TESA) or epididymis (PESA).

Variable	Study group		p value
	OA-TESA (n=103)	OA-PESA (n=171)	
Normal fertilization rate (%)	57.9 ± 9.5 (48.5–67.5)	65.2 ± 4.1 (54.7–69.3)	0.0017
Abnormal fertilization rate (%)	13.2 ± 6.3 (6.5–19.5)	12.7 ± 5.3 (7.9–18.0)	0.9437
Fertilization failure rate (%)	28.9 ± 8.9 (20.2–37.8)	22.1 ± 6.0 (15.8–28.1)	0.1081
Non-cleaved rate (%)	9.87 ± 5.9 (4.2–15.8)	7.46 ± 3.9 (3.5–11.4)	0.4406
Pregnancy rate (%)	31.9 ± 9.0 (23.0–41.0)	32.5 ± 7.5 (25.9–40.0)	0.8803
Abortion rate (%)	38.8 ± 9.6 (29.6–48.4)	18.0 ± 5.8 (12.2–23.8)	0.0387
Implantation rate (%)	9.4 ± 5.6 (3.8–15.0)	10.5 ± 4.0 (5.5–14.5)	0.6054

Values in percentage expressed as mean ± SD (confidence interval of the frequencies).



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ORIGINAL ARTICLE

Assisted reproductive technology outcomes in azoospermic men: 10 years of experience with surgical sperm retrieval

Table IV. ICSI outcomes when the injected sperm were retrieved from the testicle (TESA) of patients with obstructive (OA) or non-obstructive (NOA) azoospermia.

Variable	Study group		p value
	OA-TESA (n=103)	NOA-TESA (n=102)	
Normal fertilization rate (%)	57.9 ± 9.5 (48.5–67.5)	50.4 ± 9.3 (40.3–59.7)	0.0050
Abnormal fertilization rate (%)	13.2 ± 6.3 (6.5–19.5)	13.98 ± 6.8 (7.3–20.7)	0.4421
Fertilization failure rate (%)	28.9 ± 8.9 (20.2–37.8)	35.65 ± 11.8 (27.6–47.4)	0.0023
Non cleaved rate (%)	9.87 ± 5.9 (4.2–15.8)	16.1 ± 17 (8.9–23.1)	0.0034
Pregnancy rate (%)	31.9 ± 9.0 (23.0–41.0)	29.7 ± 9.2 (21.1–38.9)	0.4166
Abortion rate (%)	38.8 ± 9.6 (29.6–48.4)	37.0 ± 9.4 (27.6–46.4)	0.9992
Implantation rate (%)	9.4 ± 5.6 (3.8–15.0)	9.65 ± 6.1 (4.2–15.8)	0.8519

Values in percentage expressed as mean ± SD (confidence interval of the frequencies).



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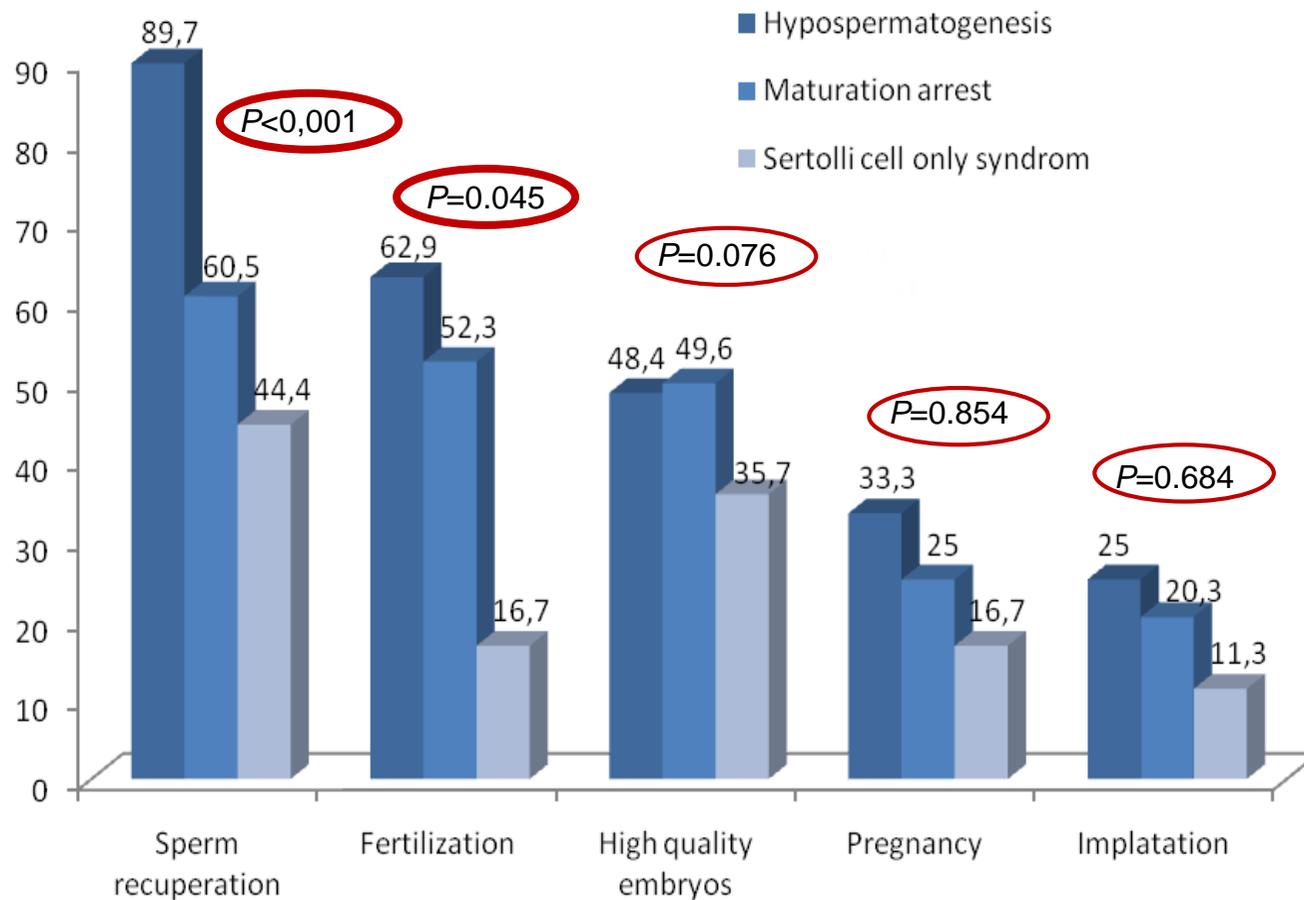
Values in percentage expressed as mean ± SD (confidence interval of the frequencies).

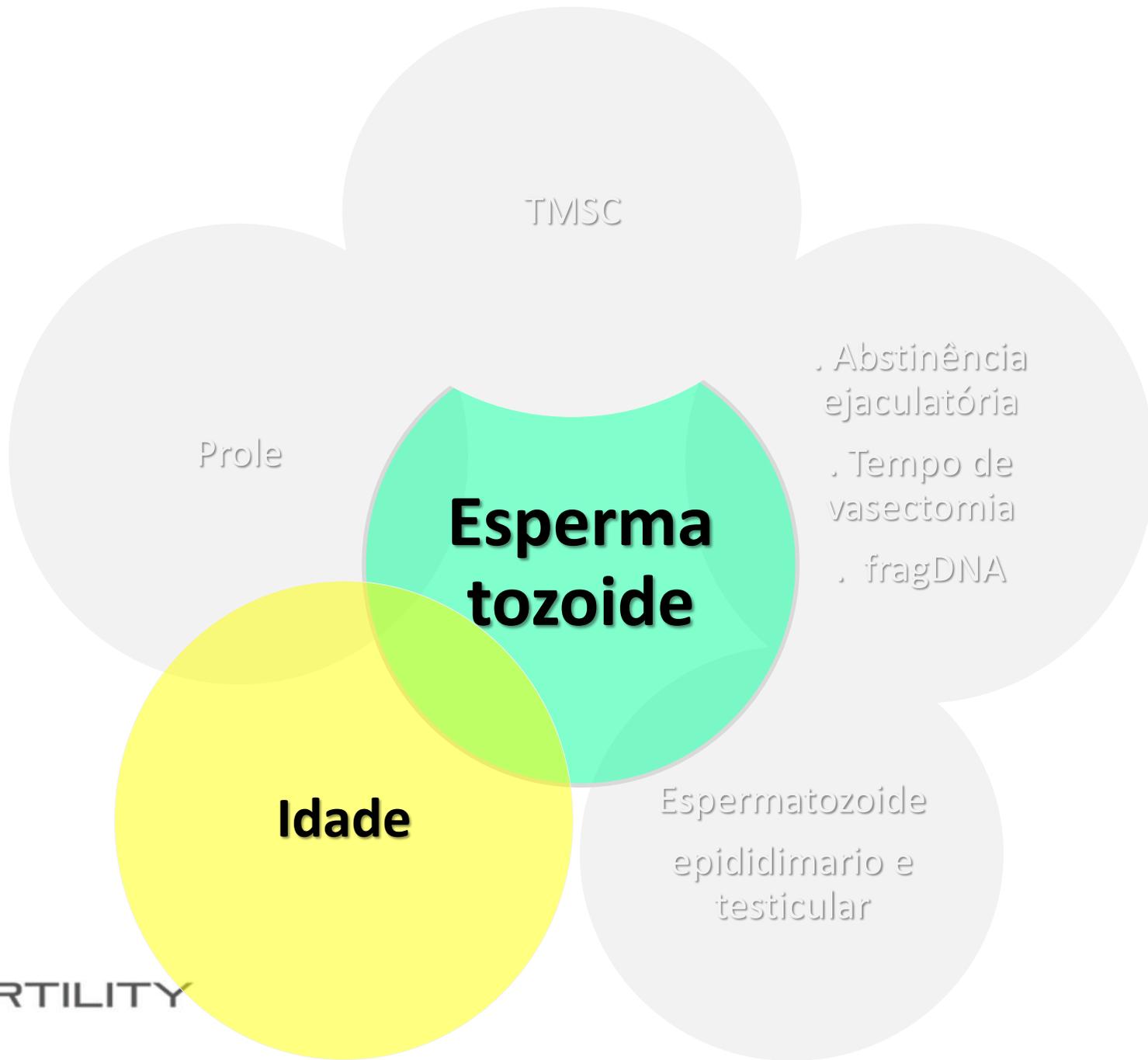


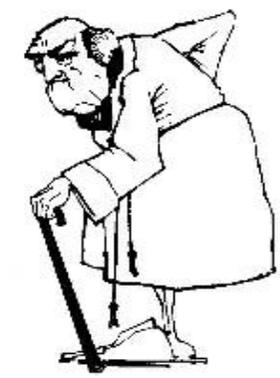
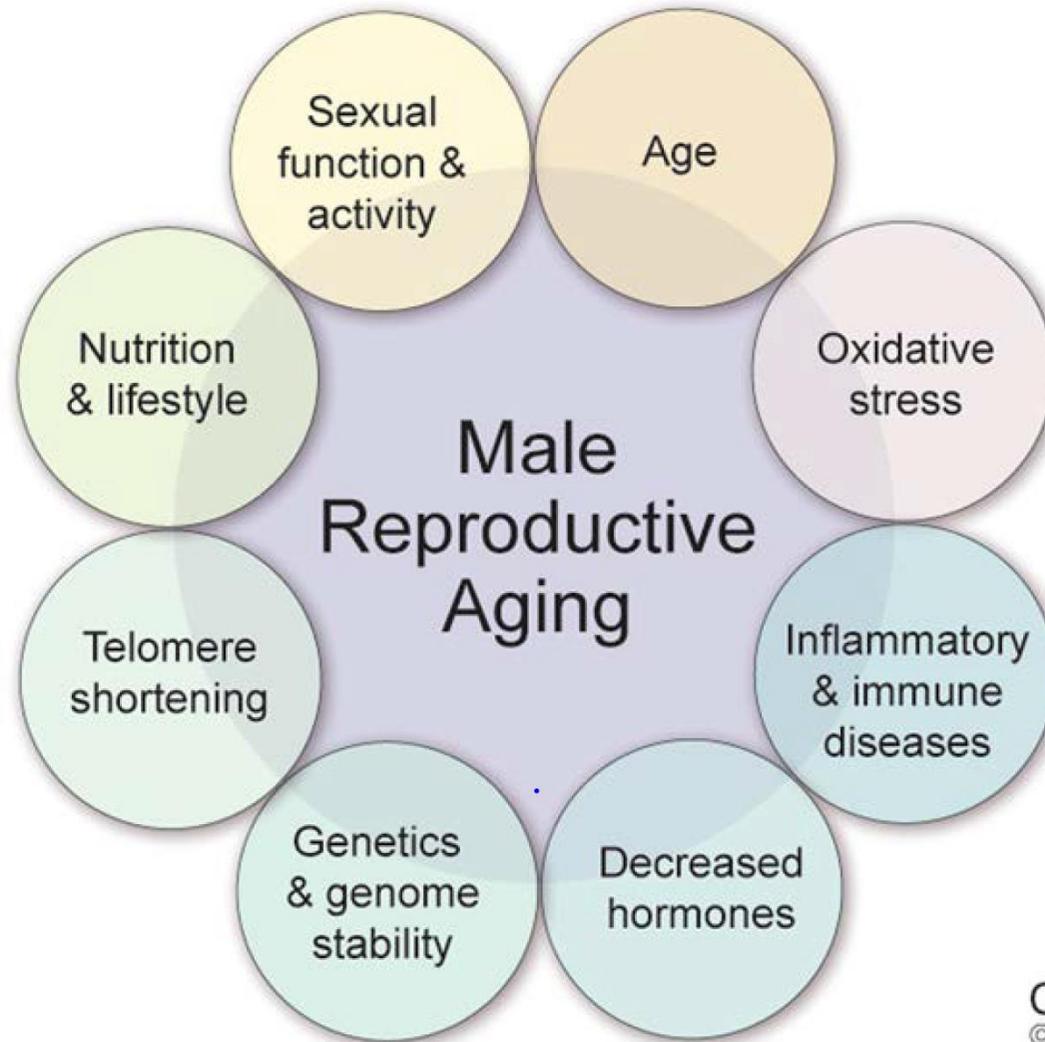
The prognostic value of the testicular histopathological pattern for sperm retrieval and intracytoplasmic sperm injection outcomes in non-obstructive azoospermic patients

O valor prognóstico do padrão histopatológico testicular na recuperação de espermatozóides e nos resultados da injeção intracitoplasmática de espermatozóides em pacientes com azoospermia não-obstrutiva

Edson Borges Jr. ^{a,b}, Daniela Paes de Almeida Braga ^{a,b}, Rita de Cássia Savio Figueira ^a, Amanda Souza Setti ^b, Assumpto Iaconelli Jr. ^{a,b}, Fabio Firmbach Pasqualotto ^c







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Figure 1 Main factors involved in impaired male infertility due to reproductive aging.

The effect of paternal factors on perinatal and paediatric outcomes: a systematic review and meta-analysis

Nan B. Oldereid ^{1,*}, **Ulla-Britt Wennerholm**², **Anja Pinborg**³,
Anne Loft⁴, **Hannele Laivuori**^{5,6,7,8}, **Max Petzold**⁹,
Liv Bente Romundstad^{10,11}, **Viveca Söderström-Anttila**¹²,
and **Christina Bergh**¹³

¹Livio IVF-klinikken Oslo, Sørkedalsveien 10A, 0369 Oslo, Norway ²Department of Obstetrics and Gynaecology, Institute of Clinical Sciences, Sahlgrenska Academy, Gothenburg University, Sahlgrenska University Hospital East, SE 416 85 Gothenburg, Sweden ³Department of Obstetrics and Gynecology, Hvidovre Hospital, Institute of Clinical Medicine, Copenhagen University Hospital, Copenhagen, Denmark ⁴Fertility Clinic, Section 4071, Copenhagen University Hospital, Rigshospitalet, Blegdamsvej 9, DK-2100 Copenhagen, Denmark ⁵Department of Obstetrics and Gynecology, Tampere University Hospital, Teiskontie 35, FI-33521 Tampere, Finland ⁶Faculty of Medicine and Life Sciences, University of Tampere, Arvo Ylpön katu 34, FI-33520 Tampere, Finland ⁷Medical and Clinical Genetics, University of Helsinki and Helsinki University Hospital, Haartmaninkatu 8, FI-00290 Helsinki, Finland ⁸Institute for Molecular Medicine Finland, Helsinki Institute of Life Science, University of Helsinki, Tukhomankatu 8, FI-00290 Helsinki, Finland ⁹Swedish National Data Service and Health Metrics Unit, University of Gothenburg, 405 30 Gothenburg, Sweden ¹⁰Spiren Fertility Clinic, Norwegian University of Science and Technology, Trondheim NO-7010, Norway ¹¹Department of Public Health, Norwegian University of Science and Technology, Trondheim, Norway ¹²Mehiläinen Felicitas, Mannerheimintie 20A, 00100 Helsinki, Finland ¹³Department of Obstetrics and Gynaecology, Institute of Clinical Sciences, Sahlgrenska Academy, Gothenburg University, Reproductive Medicine, Sahlgrenska University Hospital, SE-413 45 Gothenburg, Sweden

➔ 14.371 artigos, 238 incluídos, 81 para a meta-análise

➔ Idade, estilo de vida, peso, altura, gordura corporal, cigarro



Table XI Summary results of the meta-analyses of the association between paternal factors and perinatal and paediatric outcomes.

Exposure	Outcome	Pooled estimate (with 95% CI)	Certainty of evidence GRADE
Paternal age	PTB	1.02 (1.00–1.05)	⊕⊕○○
	Low BW	1.00 (0.97–1.03)	⊕⊕○○
	Stillbirth	1.19 (1.10–1.30)	⊕⊕○○
	★ Children with any birth defects	1.05 (1.02–1.07)	⊕⊕⊕○
	★ CHDs	1.03 (0.99–1.06)	⊕⊕⊕○
	Orofacial clefts	0.99 (0.95–1.04)	⊕⊕○○
		1.14 (1.02–1.29)*	
	★ Gastroschisis	0.88 (0.78–1.00)	⊕⊕⊕○
	★ Spina bifida	0.97 (0.90–1.04)	⊕⊕⊕○
	★ Trisomy 21	1.13 (1.05–1.23)	⊕⊕⊕○
	★ Acute lymphoblastic leukaemia	1.08 (0.96–1.21)	⊕⊕⊕○
	★ Autism and ASDs	1.25 (1.20–1.30)	⊕⊕⊕○
★ Schizophrenia	1.31 (1.23–1.38)	⊕⊕⊕○	
Paternal BMI	No meta-analysis		
Paternal smoking	PTB	1.16 (1.00–1.35)	⊕⊕○○
	Low BW	1.10 (1.00–1.21)	⊕⊕○○
	SGA	1.22 (1.03–1.44)	⊕⊕○○
	CHDs	1.75 (1.25–2.44)	⊕⊕○○
	Orofacial clefts	1.51 (1.16–1.97)	⊕⊕○○
	Brain tumours	1.12 (1.03–1.22)	⊕⊕○○



*Exposure: Paternal age >45 years.

Paternal age and reproduction

Gideon A. Sartorius^{1,2} and Eberhard Nieschlag^{1,3}

¹Centre of Reproductive Medicine and Andrology of the University, Domagkstrasse 11, D-48149 Muenster, Germany ²Present address: ³University Women's Hospital Basel, Spitalstrasse 21, CH-4031 Basel, Switzerland

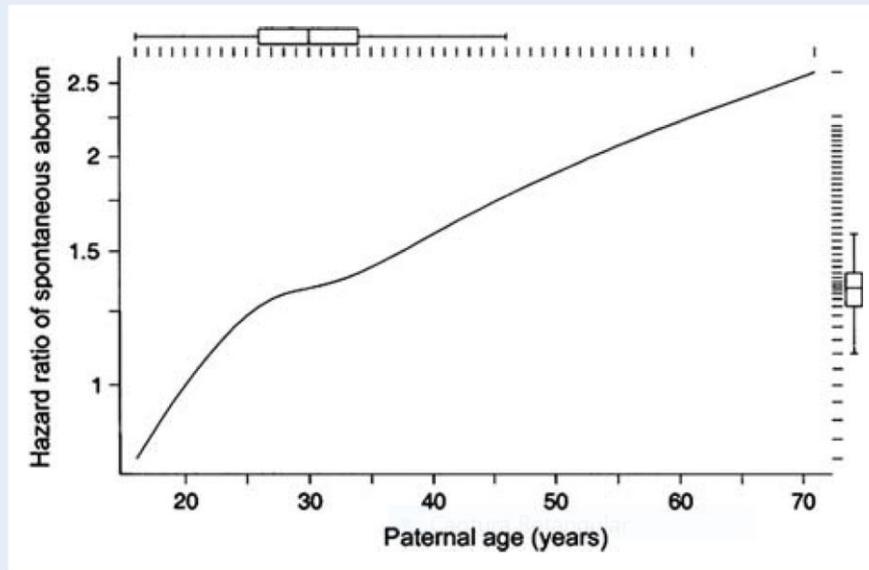


Figure 3 Hazard ratios of spontaneous miscarriages between 6 and 20 weeks according to paternal age adjusted for different confounders including maternal age (using prospective data from 5121 Californian women, men aged 20 years as referent).

Boxplots along the top and right side indicate data distribution according to each axis (with permission from Slama *et al.*, 2005).

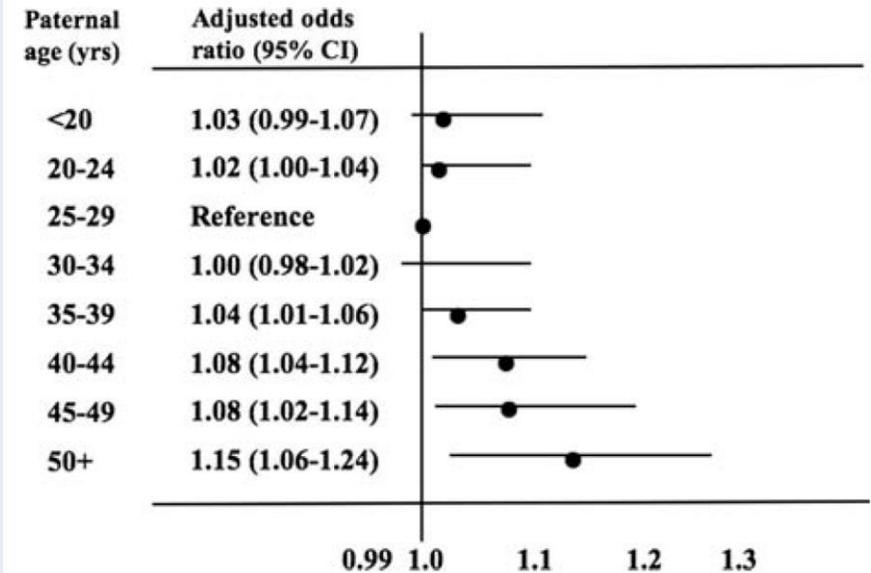
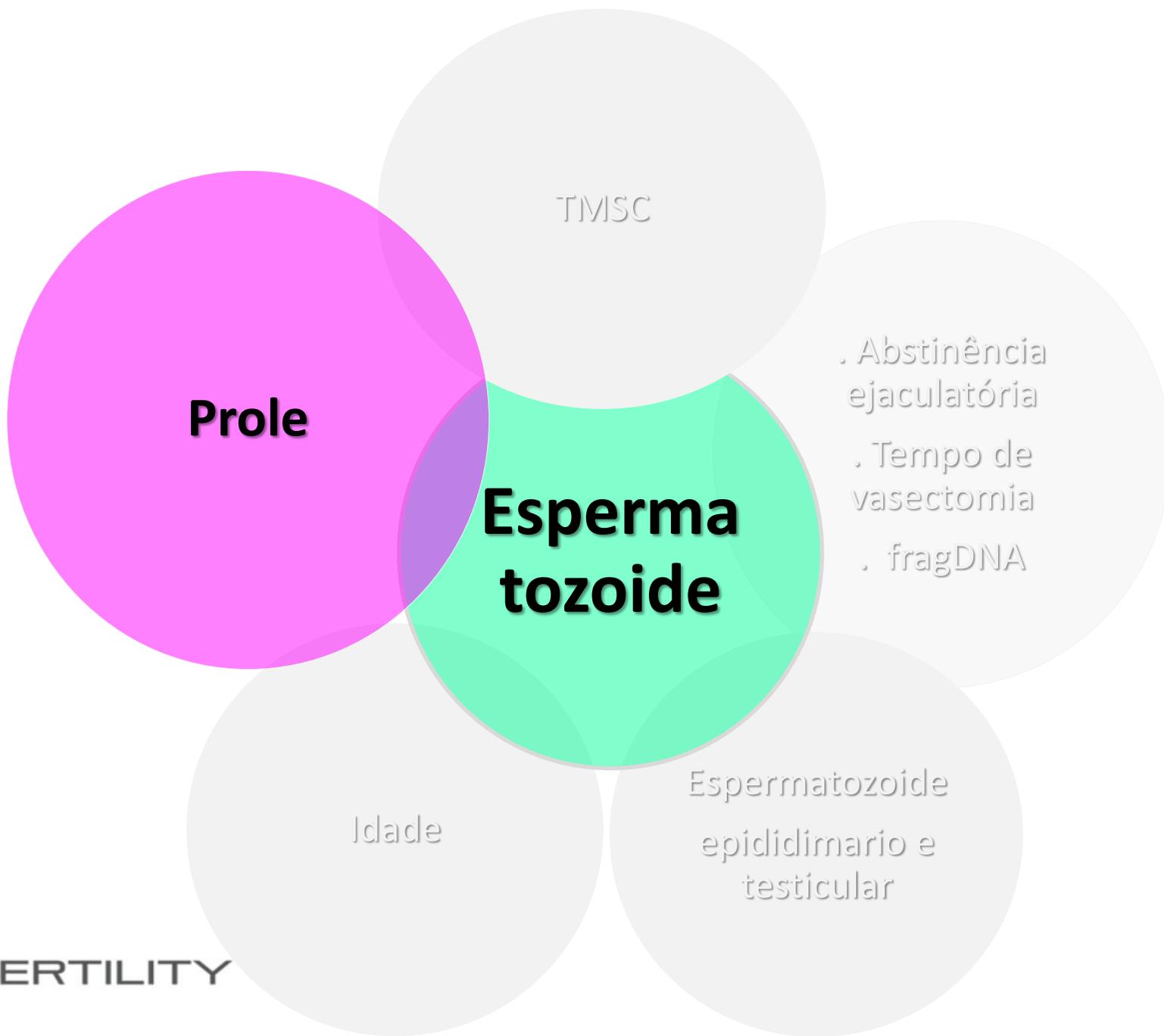


Figure 4 Relative risk of birth defects depending on paternal age. Retrospective analysis of 5 213 248 subjects in the USA. Increased risk for heart defects, circulatory/respiratory defects, diaphragmatic hernia, tracheo-oesophageal fistulas, musculo-skeletal anomalies (data extracted from Yang *et al.*, 2007).



Effect of the male factor on the clinical outcome of intracytoplasmic sperm injection combined with preimplantation aneuploidy testing: observational longitudinal cohort study of 1,219 consecutive cycles

VOL. 108 NO. 6 / DECEMBER 2017

Rossella Mazzilli, M.D.,^{a,b} Danilo Cimadomo, M.Sc.,^{b,c} Alberto Vaiarelli, M.D.,^{b,d} Antonjo Capalbo, Ph.D.,^{b,e} Lisa Dovere, Ph.D.,^b Erminia Alviggi, M.Sc.,^f Ludovica Dusi, Ph.D.,^g Carlo Foresta, M.D.,^h Francesco Lombardo, M.D.,ⁱ Andrea Lenzi, M.D.,ⁱ Herman Tournaye, M.D.,^j Carlo Alviggi, M.D.,^k Laura Rienzi, M.Sc.,^{b,f,g} and Filippo Maria Ubaldi, M.D.^{b,f,g}

- ➔ O fator masculino grave prejudica a competência embrionária precoce em termos de taxa de fertilização e potencial de desenvolvimento.
- ➔ No entanto, a taxa de euploidia e o potencial de implantação dos blastocistos obtidos são independentes da qualidade espermática, assim como os eventos obstétricos e perinatais



The risk of birth defects is not associated with semen parameters or mode of conception in offspring of men visiting a reproductive health clinic

Alexander W. Pastuszak^{1,†,*}, Amin S. Herati^{2,†}, Michael L. Eisenberg³, Cenk Cengiz^{4,5}, Peter H. Langlois⁶, Taylor P. Kohn⁷, Dolores J. Lamb⁸, and Larry I. Lipshultz^{4,5}

Table III Adjusted association of semen parameters with birth defects in offspring, Texas 1999–2009, additionally requiring that men have testicular failure and using hierarchical modeling. Includes adjustment for using type of infertility treatment (drugs etc., assisted reproductive technology, none).

Characteristic	Categories examined	Odds ratio, adjusted for all covariates ^a		Odds ratio, adjusted for father covariates ^b		Odds ratio, adjusted for mother covariates ^c	
		Estimate	(95% CI) ^d	Estimate	(95% CI)	Estimate	(95% CI)
Concentration	< 15 ≥ 15	1.07	(0.63–1.83)	1.08	(0.64–1.82)	0.99	(0.59–1.68)
Motility	< 40 ≥ 40	0.91	(0.52–1.59)	0.90	(0.52–1.55)	0.82	(0.47–1.41)
Volume	< 1.5 ≥ 1.5	1.08	(0.52–2.22)	1.10	(0.54–2.24)	1.05	(0.52–2.13)
Total sperm count	< 39 ≥ 39	0.89	(0.51–1.53)	0.89	(0.53–1.51)	0.84	(0.49–1.41)
Total motile count	< 9 ≥ 9	1.21	(0.70–2.08)	1.18	(0.69–2.01)	1.09	(0.64–1.85)

^aFather's age, birthplace, education, race/ethnicity; mother's age, birthplace, education, race/ethnicity; infant's birth year, plurality of the pregnancy, type of infertility treatment.

^bFather's age, birthplace, education, race/ethnicity; infant's birth year, plurality of the pregnancy, type of infertility treatment.

^cMother's age, birthplace, education, race/ethnicity; infant's birth year, plurality of the pregnancy, type of infertility treatment.

^d95% confidence interval.



INVITED SESSION

SESSION 01: KEYNOTE SESSION

Monday 2 July 2018

Forum (Auditorium)

08:30–09:30

O-001 Human Reproduction Keynote Lecture - Semen quality of young adult ICSI offspring: The first results

F. Belva¹, M. Bonduelle¹, M. Roelants², D. Michielsen³, A. Van Steirteghem⁴, G. Verheyen⁴, H. Tournaye⁴

- ➔ UZ Brussel, entre 03/2013 – 04/2016, 54 jovens
- ➔ Saúde reprodutiva e metabólica de jovens 18-22 anos, nascidos de ICSI com espermatozóide ejaculado x concepção natural (CN)

O-001 Human Reproduction Keynote Lecture - Semen quality of young adult ICSI offspring: The first results

F. Belva¹, M. Bonduelle¹, M. Roelants², D. Michiels³, A. Van Steirteghem⁴, G. Verheyen⁴, H. Tournaye⁴



→ ICSI:

- menor concentração espermática/mL, total, TMSC (17,7 mil/ml, 31,9 mil e 12,7 mil) que os nascidos por **CN** (37 mil/ml; 86.8 mil; 38.6 mil)
- **CN**: dobro na concentração espermática/mL (ratio 1.9, 95% CI 1.1-3.2)
- **ICSI**: duas vezes menor concentração espermática total (ratio 2.3, 95% CI 1.3-4.1) e TMSC (ratio 2.1, 95% CI 1.2-3.6)

→ ICSI:

- 3X menor chance de ter concentração espermática/mL (15 mil/mL) abaixo OMS (AOR 2.7; 95% CI 1.1-6.7)
- 4X menor chance de ter concentração espermática total (39 mil) (AOR 4.3; 95% CI 1.7-11.3)

Considerações (1)



- ➔ **TMSC parece estar mais relacionada com o potencial reprodutivo do espermatozoide;**
- ➔ **Menor tempo de abstinência ejaculatória associada a melhora dos parâmetros seminais, da fragDNA e do potencial reprodutivo do espermatozoide;**
- ➔ **Quanto maior o tempo de obstrução nos homens vasectomizados, pior a qualidade embrionária, menores as taxas de implantação e gestação e maiores as taxas de aborto;**
- ➔ **A fragDNA espermático nos homens normozoospermios está relacionada com o desenvolvimento embrionária, com as taxas de implantação, gestação e aborto;**



Considerações (2)



- ➔ A alteração seminal e a origem do espermatozoide interferem nas taxas de fertilização e abortamento, não sendo afetados o desenvolvimento embrionário, as chances de implantação e gestação;
- ➔ A taxa de aneuploidia dos embriões não parece estar relacionada com a gravidade da alteração seminal, como também sem consequências nos desfechos obstétricos e perinatais;
- ➔ A idade do homem está relacionada aos desfechos perinatais e a saúde de sua prole;
- ➔ Filhos de homens tratados com ICSI têm maior probabilidade alteração seminal.