Surgically acquired sperm use for assisted reproductive technology: trends and perinatal outcomes, USA, 2004–2015

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Received: 14 December 2017 / Accepted: 5 April 2018 / Published online: 26 April 2018

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Abstract

Purpose To compare national trends and perinatal outcomes following the use of ejaculated versus surgically acquired sperm among IVF cycles with male factor infertility.

Methods This retrospective cohort includes US fertility clinics reporting to the National ART Surveillance System between 2004 and 2015. Fresh, non-donor IVF male factor cycles ($n = 369,426$ cycles) were included. We report the following outcomes: (1) Trends in surgically acquired and ejaculated sperm. (2) Adjusted risk ratios comparing outcomes for intracytoplasmic sperm injection (ICSI) cycles using surgically acquired (epididymal or testicular) versus ejaculated sperm. (3) Outcomes per non-canceled cycle: biochemical pregnancy, intrauterine pregnancy, and live birth (≥ 20 weeks). (4) Outcomes per pregnancy: miscarriage (< 20 weeks) and singleton pregnancy. (5) Outcomes per singleton pregnancy: normal birthweight (≥ 2500 g) and full-term delivery (≥ 37 weeks).

Results Percentage of male factor infertility cycles that used surgically acquired sperm increased over the study period, 9.8 (2004) to 11.6% (2015), $p < 0.05$. The proportion of cycles using testicular sperm increased significantly over the study period, 4.9 (2004) to 6.5% (2015), $p < 0.05$. Among fresh, non-donor male factor ART cycles which used ICSI ($n = 347,078$ cycles), cycle, pregnancy, and perinatal outcomes were statistically significant but clinically similar with confidence intervals approaching one between cycles involving epididymal versus ejaculated sperm and between testicular versus ejaculated sperm. Results were similar among cycles with a sole diagnosis of male factor (no female factors), and for the subset in which the female partner was < 35 years old.

Conclusion Among couples undergoing ART for treatment of male factor infertility, pregnancy and perinatal outcomes were similar between cycles utilizing ejaculated sperm or surgically acquired testicular and epididymal sperm.

Keywords TESE · PESA · IVF · Perinatal outcomes · Trends

Introduction

Since the first in vitro fertilization (IVF) baby was born in 1978, assisted reproductive technology (ART) has continued to allow an increasing number of infertile couples to have biologically related children. Because conventional IVF requires motile sperm, men with non-motile or poorly motile sperm following surgical sperm retrieval from the testis or epididymis are not good candidates for conventional IVF. The development of intracytoplasmic sperm injection (ICSI), which allows for the fertilization of an egg with non-motile sperm, broadened the autologous IVF options for men with male factor infertility.

The use of ICSI has increased steadily over the past 25 years [1]. Sperm used for ICSI may be ejaculated or surgically retrieved by epididymal aspiration, testicular biopsy, or

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Fig. 1 Trends among fresh autologous IVF cycles with a male factor diagnosis—percentage of cycles with surgically acquired sperm, 2004–2015. *IVF= *in vitro* fertilization, $p < 0.05$ for both epididymal and testicular sperm

testicular extraction with or without microscopic assistance. As men with azoospermia are often faced with a decision regarding whether or not to undergo a surgical sperm retrieval to facilitate IVF with autologous sperm, additional data regarding IVF cycle outcomes using surgically acquired sperm may be helpful in guiding their counseling and decision-making. To our knowledge, only a few single-center studies have been published detailing the outcomes among cycles using surgically acquired sperm [2–6], particularly in comparison to those using ejaculated sperm [7, 8], among men with male factor infertility. Some of these studies specifically investigated outcomes among cycles for which sperm was acquired from either the epididymis [9–12] or the testes [10, 13–20], but were limited by small sample size. Additionally, prior studies using national data focused primarily on IVF cycle outcomes rather than perinatal outcomes [21].

We used the National ART Surveillance System (NASS) data from 2004 through 2015 to calculate the trends in use of surgically acquired sperm among all IVF cycles carrying a diagnosis of male factor infertility during this time period. We also investigated the association between use of surgically acquired versus ejaculated sperm and cycle and pregnancy outcomes among fresh autologous IVF ICSI cycles including a male factor infertility diagnosis.

Methods

As a result of the Fertility Clinic Success Rate and Certification Act of 1992, over 95% of US ART clinics report all ART cycles to the Centers for Disease Control and Prevention's National ART Surveillance System (NASS) annually, including patient and cycle characteristics, treatment procedures, and cycle outcomes [22]. Using NASS data from

2004 through 2015, we included all fresh, non-donor IVF cycles with a diagnosis of male factor infertility ($n = 369,426$ cycles). Donor sperm and donor oocyte cycles were excluded. We used the Cochran Armitage test to assess trends in proportions of surgically acquired sperm use (testicular or epididymal) among all fresh, non-donor cycles with a diagnosis of male factor infertility over the study period.

Among fresh, non-donor IVF cycles with male factor infertility, we compared the distribution of patient and cycle characteristics in each of the sperm acquisition categories, surgically acquired (testicular or epididymal) and ejaculated (standard), using Pearson's chi-square test. Cycles using surgically acquired sperm in which ICSI was not reported ($n = 678$) were excluded as ICSI is required for fertilization using non-motile testicular sperm resulting in inclusion of 368,499 cycles. Using multivariable log binomial regression to estimate relative risk, among cycles using intracytoplasmic sperm injection (ICSI) ($n = 347,078$ cycles), we investigated the relationship between use of epididymal or testicular sperm and cycle/pregnancy outcomes including (1) outcomes per transfer: biochemical pregnancy, intrauterine pregnancy, and live birth (≥ 20 weeks), (2) outcomes per pregnancy: miscarriage (< 20 weeks) and singleton pregnancy, and (3) outcomes per singleton pregnancy: normal birth weight (≥ 2500 g) and full-term delivery (≥ 37 weeks). Cycles were restricted to those involving ICSI to help ensure that the comparison groups were less heterogeneous; the subset of male factor infertility cycles using ejaculated sperm that did not use ICSI may have had very mild male factor infertility and would not be an ideal comparison to cycles in which men required surgical sperm acquisition. Potential confounders associated with both the exposure and the outcome were selected a priori; we adjusted for the following variables: embryo stage, number of embryos transferred, number of supernumerary embryos

Table 1 Patient characteristics by sperm source, fresh autologous IVF cycles with a male factor diagnosis, 2004–2015

	Surgically acquired		Surgically acquired		Standard	
	Epididymal aspiration		Testicular biopsy		Ejaculated	
	<i>n</i>	%	<i>n</i>	%	<i>n</i>	%
Total	17,903	4.9	19,095	5.2	331,501	89.9
Patient characteristics						
Female age [§]						
< 35	9184	51.3	10,415	54.5	166,198	50.1
35–37	3890	21.7	3941	20.6	73,754	22.3
38–40	3054	17.1	3032	15.9	58,240	17.6
≥ 41	1775	9.9	1707	8.9	33,309	10.1
Female race/ethnicity [§]						
Non-Hispanic White	9361	52.3	8927	46.8	158,397	47.8
Non-Hispanic Black	695	3.9	780	4.1	13,770	4.2
Asian Pacific Islander	1033	5.8	1069	5.6	26,782	8.1
Hispanic	936	5.2	1165	6.1	18,104	5.5
Other	14	<0.1		0.1	417	0.1
Missing	5864	32.8	7137	37.4	114,031	34.4
Female BMI [§]						
Underweight < 18.5 kg/m ²	268	1.5	259	1.4	5141	1.6
Normal weight 18.5–24.9 kg/m ²	5540	30.9	5771	30.1	100,011	30.2
Overweight 25–29.9 kg/m ²	2609	14.6	2726	14.3	43,550	13.1
Obese ≥ 30 kg/m ²	1694	9.5	1996	10.6	34,679	10.5
Missing	6984	43.6	8343	43.6	148,120	44.7
Additional infertility diagnosis						
Diminished ovarian reserve [§]						
No	15,358	85.8	16,501	86.4	271,731	82.0
Yes	2545	14.2	2594	13.6	59,770	18.0
Endometriosis [§]						
No	17,314	96.7	18,479	96.8	303,336	91.5
Yes	589	3.3	616	3.2	28,165	8.5
Ovulatory dysfunction [§]						
No	16,834	94.0	17,934	93.9	286,637	86.5
Yes	1069	6.0	1161	6.1	87	13.5
Tubal factor [§]						
No	17,246	96.3	18,392	96.3	297,771	89.8
Yes	657	3.7	703	3.7	33,730	10.2
Uterine factor [§]						
No	17,442	97.4	18,527	97.0	317,351	95.7
Yes	461	2.6	568	2.9	14,150	4.3
No Additional Diagnosis (male factor only) [§]						
No	5461	30.5	5932	31.1	168,792	50.9
Yes	12,442	69.5	13,163	68.9	162,709	49.1
Surgical sterilization [§]						
If yes, vasectomy	447	21.5	538	32.0	0	0.0
If yes, tubal ligation	1613	77.7	1126	67.1	4559	100.0
If yes, both	15	0.7	15	0.9	0	0.0
Maximum female serum FSH* [§]						
< 5 mIU/mL	2848	22.1	3631	26.4	56,087	22.4

Table 1 (continued)

	Surgically acquired		Surgically acquired		Standard	
	Epididymal aspiration		Testicular biopsy		Ejaculated	
	<i>n</i>	%	<i>n</i>	%	<i>n</i>	%
5.1–9.9 mIU/mL	7864	61.0	7836	57.0	148,316	59.2
≥ 10.0 mIU/mL	2171	16.9	2286	16.6	46,133	18.4
Number of prior IVF cycles [§]						
0	10,4236	57.2	10,432	54.7	190,389	57.5
1	3550	19.8	3802	19.9	64,506	19.5
2+	4110	23.0	4834	25.4	76,330	23.3
Number of prior pregnancies						
0	13,360	74.8	14,262	74.9	245,013	74.1
1	3048	17.1	3516	18.5	68,193	20.6
2+	1445	8.1	1258	6.6	17,351	5.3
Number of prior spontaneous abortions [§]						
0	14,485	81.3	15,488	81.5	246,794	74.8
1	2534	14.2	2659	14.0	58,987	17.9
2+	809	4.5	863	4.5	24,330	7.4
Number of prior preterm births [§]						
0	17,389	97.6	18,492	97.4	321,286	97.5
1	378	2.2	457	2.4	7544	2.3
2+	42	0.2	42	0.2	715	0.2
Number of prior full-term births [§]						
0	13,616	76.3	14,603	76.7	251,007	76.0
1	2913	16.3	3300	17.3	64,055	19.4
2+	1315	7.4	1129	5.9	15,336	4.6

IVF in vitro fertilization, FSH follicle stimulating hormone, mIU milli international units, LB live birth

*Missing 25%, remainder of variables missing is < 1% except for race/ethnicity and BMI

§ Pearson's chi-square, $p < 0.05$

cryopreserved, and prior history of vasectomy. Subgroup analyses were also performed among ICSI cycles with a diagnosis of male factor infertility only (i.e., no documented female infertility factors) ($n = 11,491$ cycles) and among cycles with male factor infertility only with a female partner age under 35 years ($n = 6721$ cycles). These subgroup analyses were performed in an attempt to isolate male factor, by removing female factors and female age from the equation.

All analyses were conducted using SAS version 9.4 (SAS Institute Inc.). p values less than 0.05 were considered statistically significant. The Centers for Disease Control and Prevention institutional review board approved this study.

Results

Over the study period, 369,426 IVF fresh non-donor cycles with a diagnosis of male factor infertility were performed in the USA. The number involving surgically acquired sperm

(testicular plus epididymal) ranged from 2896 cycles in 2004 to 3152 cycles in 2015, and the proportion of cycles using surgically acquired sperm increased from 9.8% in 2004 to 11.6% in 2015, $p < 0.05$ (data not shown). The number of cycles involving ejaculated sperm ranged from 26,755 cycles in 2004 to 24,146 cycles in 2015. Among cycles with male factor infertility, 37,925 cycles involved surgically acquired sperm. The proportion of cycles using testicular sperm source increased significantly from 4.9% in 2004 to 6.5% in 2015, and the proportion using epididymal source fluctuated from 4.9% in 2004 to 5.1% in 2015, $p < 0.05$ (Fig. 1).

Among the included 368,499 fresh non-donor cycles, the female partners of those using surgically acquired sperm were significantly less likely than those using ejaculated sperm to have an additional infertility diagnosis, or to have had a prior spontaneous abortion (Table 1). Patterns in female partner age, race/ethnicity, body mass index, number of prior IVF cycles, and number of prior pregnancies were similar between cycles using surgically acquired vs. ejaculated sperm; statistical

Table 2 Cycle characteristics by sperm source, fresh autologous IVF cycles with a male factor infertility diagnosis, 2004–2015

	Surgically acquired		Surgically acquired		Standard	
	Epididymal aspiration		Testicular biopsy		Ejaculated	
	<i>n</i>	%	<i>n</i>	%	<i>n</i>	%
Total	17,903	4.9	19,095	5.2	331,501	89.9
Cycle cancelation between retrieval and transfer [§]						
No	16,314	91.1	17,036	89.2	300,180	90.6
Yes	1589	8.9	2059	10.8	31,321	9.4
Stimulation type [§]						
None (natural cycle)	44	0.3	130	0.3	1861	0.3
Oral Meds + gonadotropins	161	0.9	183	0.5	4037	0.6
Gonadotropins only (antagon)	17,405	49.4	18,471	49.2	323,219	49.5
Gonadotropins only (no suppression)	17,564	49	18,693	48.7	320,041	49.1
Gonadotropins only (flare)	24	0.1	24	0.1	514	0.1
Gonadotropins only (standard lupron)	391	2.2	582	3.1	8643	1.3
Number of oocytes retrieved [§]						
0–4	1742	9.7	1770	9.3	35,989	10.9
5–9	4689	26.2	4980	26.1	90,538	27.5
≥ 10	11,471	64.1	12,344	64.7	203,322	61.4
Ovarian hyperstimulation						
No	17,633	98.5	18,830	98.6	327,029	98.6
Yes	270	1.5	265	1.4	4472	1.4
Number of embryos transferred [§]						
1	2,5	16.4	2696	15.8	45,857	15.3
2	8591	52.7	9119	53.5	157,899	52.6
≥ 3	5051	31.0	5218	30.7	96,360	32.1
Use of intracytoplasmic injection (ICSI) ^{# §}						
No	0	0	0	0	23,043	7.0
Yes	17,903	100.0	19,095	100.0	306,684	92.5
Use of assisted hatching ^{#§}						
No	9741	59.7	10,331	60.6	176,673	58.9
Yes	6573	40.3	6705	39.4	123,507	41.1
Embryo stage at transfer ^{#*§}						
Days 2/3	9603	58.9	10,556	62.0	169,948	56.6
Days 5/6	6322	38.8	6097	35.8	122,326	40.8
Other	383	2.4	380	2.2	7841	2.6
Number of supernumerary embryos cryopreserved [§]						
0	11,054	62.0	12,233	64.6	197,058	60.1
1–2	2828	15.9	2754	14.5	49,845	15.2
3–4	1911	10.7	1874	9.9	35,982	11.0
5+	2050	11.5	2082	11.0	45,022	13.7

[#] Per non-canceled cycles for which a transfer was performed^{*}Does not sum to 100% due to exclusion of transfers on days other than 2, 3, 5, or 6[§] Pearson's chi-square, $p < 0.05$

significance for these comparisons likely reflects the very large sample size. With regard to cycle level characteristics, cycle cancelation was most common among cycles with testicular biopsy-acquired sperm (Table 2). Female ovarian

stimulation regimens, resultant oocyte yield, and incidence of ovarian hyperstimulation were similar among all cycle types; statistical significance for these comparisons was probably due to the very large sample size; with very large sample

Table 3 Cycle and pregnancy outcomes by sperm source, fresh autologous male factor IVF cycles with ICSI, 2004–2015

	Ejaculated sperm–standard ejaculation *		Surgically acquired sperm–epididymal aspiration		Surgically acquired sperm–testicular biopsy			
	(n, %)		(n, %)	RR (95% CI)	aRR (95% CI)	(n, %)	RR (95% CI)	aRR (95% CI)
IVF-ICSI cycles	313,737		16,308			17,033		
Per transfer								
Biochemical pregnancy rate	23,509 (8.4)		1386 (8.5)	1.01 (0.96–1.07)	1.02 (0.97–1.08)	1342 (7.8)	0.94 (0.89–0.99)	0.95 (0.90–1.00)
Intrauterine pregnancy	130,236 (46.5)		7599 (46.6)	1.00 (0.98–1.02)	1.02 (1.01–1.04)	7881 (46.3)	0.99 (0.98–1.01)	1.04 (1.02–1.05)
Live birth (≥ 20 weeks)	107,915 (38.5)		6297 (38.6)	1.00 (0.98–1.02)	1.03 (1.01–1.05)	6517 (38.3)	0.99 (0.97–1.01)	1.03 (1.02–1.06)
Per pregnancy								
Miscarriage (< 20 weeks)	19,325 (14.8)		1092 (14.4)	0.97 (0.92–1.02)	0.96 (0.91–1.02)	1193 (15.1)	1.02 (0.97–1.08)	1.00 (0.96–1.06)
Singleton pregnancy	76,024 (58.4)		4468 (58.8)	1.00 (0.98–1.02)	1.00 (0.98–1.02)	4618 (58.6)	1.00 (0.98–1.02)	1.00 (0.97–1.02)
Per singleton pregnancy								
Normal birth weight (≥ 2500 g)	67,929 (89.4)		4012 (89.8)	1.00 (0.99–1.02)	1.01 (1.00–1.02)	4115 (89.1)	0.99 (0.99–1.01)	1.00 (0.99–1.01)
Full-term delivery (≥ 37 weeks)	66,957 (88.0)		3952 (88.5)	1.00 (0.99–1.02)	1.01 (1.00–1.02)	4079 (88.3)	1.00 (0.99–1.01)	1.00 (0.99–1.01)

Models adjusted for embryo stage, number of embryos transferred, number of supernumerary embryos cryopreserved, and vasectomy

RR relative risk, aRR adjusted relative risk

*Referent column

size, statistical significance is achieved when the absolute difference between groups is small and when clinical significance may not exist (Table 2). ICSI was used in over 92% of all male factor infertility cycles. ICSI was used more frequently in cycles involving surgically acquired sperm (98.1% in the testicular sperm group, 97.1% in the epididymal sperm group, and 92.5% in the ejaculated sperm group). With respect to number and timing of embryo transfer, two-embryo transfer and embryo transfer at the cleavage stage were most frequent in all groups. Use of assisted hatching was approximately 40% in all groups. Number of supernumerary embryos cryopreserved was highest in the ejaculated group.

Among fresh, non-donor ICSI cycles with male factor infertility ($n = 347,078$ cycles), use of epididymal, as compared to ejaculated, sperm was not associated with a difference in rate of biochemical pregnancy (aRR = 1.02, CI = 0.97–1.08); however, epididymal sperm use was associated with a statistically increased rate of intrauterine pregnancy (aRR = 1.02, CI = 1.01–1.04) and live birth (aRR = 1.03, CI = 1.01–1.05) (Table 3). Use of sperm acquired by testicular biopsy, as compared to ejaculated sperm, was not associated with increased rate of biochemical pregnancy (aRR = 0.95, CI = 0.90–1.00) but was associated with increased rates of intrauterine pregnancy (aRR = 1.04, CI = 1.02–1.05) and live birth (aRR = 1.03, CI = 1.02–1.06). The likelihood of miscarriage was not different for epididymal or testicular sperm, as compared to ejaculated sperm (aRR = 0.96, CI = 0.91–1.02 and aRR = 1.00, CI = 0.96–1.06, respectively). The same was true for singleton pregnancy (aRR = 1.00, CI = 0.98–1.02 for epididymal sperm and aRR = 1.00, CI = 0.97–1.02 for testicular sperm). Among singleton pregnancies, there was no difference in likelihood of normal birth weight delivery or of full-term delivery in the surgically acquired sperm groups, as compared to the ejaculated sperm group.

In the subgroup analysis of fresh, non-donor cycles with only a male factor infertility diagnosis ($n = 166,171$), there were no significant differences between each surgically acquired sperm group and the ejaculated group for any of the investigated outcomes (Table 4). In the subgroup analysis of fresh, non-donor cycles with only a male factor diagnosis with a female partner under 35 years of age ($n = 6721$ cycles), there were no significant differences between each surgically acquired sperm group and the ejaculated sperm group for any of the investigated outcomes (data not shown).

Discussion

The percentage of cycles with a male factor infertility diagnosis that used surgically acquired sperm increased over the study period and was mostly driven by the increase in surgically acquired testicular sperm. Among transfers in fresh, non-donor ICSI cycles with a male factor infertility diagnosis,

Table 4 Cycle and pregnancy outcomes by sperm source, fresh autologous male factor only IVF cycles with ICSI, 2004–2015

	Ejaculated sperm–standard ejaculation*		Surgically acquired sperm–epididymal aspiration			Surgically acquired sperm–testicular biopsy		
	(n, %)		(n, %)	RR (95% CI)	aRR (95% CI)	(n, %)	RR (95% CI)	aRR (95% CI)
IVF-ICSI cycles		142, 743	11,491			11,937		
Per transfer								
Biochemical pregnancy rate	11,800 (8.3)		968 (0.4)	1.01 (0.96–1.09)	1.03 (0.96–1.09)	927 (7.8)	0.93 (0.88–1.00)	0.95 (0.89–1.01)
Intrauterine pregnancy	71,154 (49.9)		5717 (49.8)	1.00 (0.98–1.02)	1.02 (1.00–1.04)	5845 (49.0)	0.98 (0.96–1.00)	1.02 (1.00–1.04)
Live birth (≥ 20 weeks)	60,160 (42.2)		4830 (42.0)	1.00 (0.98–1.02)	1.02 (1.00–1.04)	4915 (41.2)	0.98 (0.96–1.00)	1.02 (1.00–1.04)
Per pregnancy								
Miscarriage (< 20 weeks)	9429 (13.3)		734 (12.8)	0.97 (0.90–1.04)	0.96 (0.90–1.03)	807 (13.8)	1.04 (0.97–1.11)	1.03 (0.96–1.10)
Singleton pregnancy	42,033 (59.1)		3418 (59.8)	1.01 (0.99–1.03)	1.01 (0.99–1.03)	3439 (58.8)	1.00 (0.97–1.02)	0.99 (0.97–1.02)
Per singleton pregnancy								
Normal birth weight (≥ 2500 g)	37,771 (89.9)		3082 (90.2)	1.00 (0.99–1.02)	1.01 (0.99–1.02)	3075 (89.4)	1.00 (0.98–1.01)	1.00 (0.98–1.01)
Full-term delivery (≥ 37 weeks)	37,331 (88.8)		3034 (88.8)	1.00 (0.99–1.01)	1.00 (0.99–1.01)	3043 (88.5)	0.99 (0.98–1.01)	1.00 (0.98–1.01)

Models adjusted for embryo stage, number of embryos transferred, number of supernumerary embryos cryopreserved, and vasectomy

RR relative risk, aRR adjusted relative risk

*Referent column

pregnancy, and perinatal outcomes were clinically similar (confidence intervals included or approached 1) between cycles involving epididymal versus ejaculated sperm and testicular versus ejaculated sperm. Results were similar among cycles with a sole diagnosis of male factor infertility, and for the subset of such cycles in which the female partner was under 35 years old.

While prior studies have investigated cycle level outcomes such as fertilization rate, implantation rate, and pregnancy rate for surgically acquired sperm used in IVF cycles [9–21], this is one of the first studies to use national US ART data to explore perinatal outcomes including miscarriage, term delivery, and normal birth weight delivery. Several prior studies with smaller sample sizes also showed similar neonatal outcomes between infants conceived using either testicular or ejaculated sperm [23–26]. The clinical similarity in pregnancy and live birth rates per transfer, miscarriage per pregnancy, and favorable perinatal outcomes (term delivery and normal birth weight delivery) between IVF cycles in which sperm was surgically acquired, from the testis or epididymis, versus ejaculated sperm, is reassuring for couples with severe male factor infertility who may be considering the use of surgically acquired sperm. More specifically, this study affirms the findings of a prior national retrospective study using 2004 to 2008 data that compared live birth rates among male factor ICSI cycles, which found no difference in live birth rate per cycle between those with male factor infertility only, compared to those with tubal factor only infertility [21]. Building upon the previously published results, our study uses recent data, specifically investigates sperm acquisition source, and investigates perinatal outcomes in addition to live birth.

The study is strengthened by the inclusion of 97% of ART cycles performed in the USA, its generalizability to other couples undergoing IVF in the USA, the large number of included cycles, and the validation of a select number of clinic responses conducted annually as part of routine data validation procedures in NASS. Additionally, we were able to control for confounders, such a prior vasectomy, that may impact cycle, pregnancy, and perinatal outcomes.

The study is limited by the lack of information regarding more detail of underlying male infertility diagnosis, such as non-obstructive azoospermia, obstructive azoospermia, or another semen parameter abnormality. Future NASS data collection will incorporate some of these additional characteristics, and it is possible that future analyses will demonstrate differences in pregnancy and perinatal outcomes with respect to varying etiology and severity of male factor infertility. This study also does not address surgical technique. Surgical skill and technique vary from one urologist to another; some use microsurgical technique and others do not, which could also influence the choice of sperm acquisition source. Finally, the study is subject to the weaknesses associated with large retrospective database studies such as the inability to randomize

patients and consequent possibility of bias. The results are reliant on input from individual clinics; the 768 cycles with surgically acquired sperm that did not include ICSI likely reflect data entry error and were excluded from the outcomes analysis. Additionally, statistical significance can be determined but may not be representative of clinical importance. The confidence intervals that so closely approach 1 in a study involving thousands of cycles are unlikely to reflect clinical relevance.

Since severity of semen parameter abnormality can affect how sperm are obtained for IVF, men with male infertility can be reassured that IVF cycle and perinatal outcomes are similar between testicular or epididymal and ejaculated sperm. Involvement of a urologist with infertility subspecialty training is a reasonable consideration in men with severely abnormal semen parameters. Future studies that evaluate long-term child outcomes and include more about the male partner's characteristics, the specifics of the surgical technique used for acquisition, and the resultant embryo quality, may inform clinical practice and counseling.

Compliance with ethical standards

The Centers for Disease Control and Prevention institutional review board approved this study.

Conflict of interest The authors did not report any potential conflicts of interest. AM was supported by a research grant from the American Society for Reproductive Medicine.

Disclaimer The findings and conclusions in this report are those of the authors and do not necessarily represent the official position of the Centers for Disease Control and Prevention.

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