Successful cryptozoospermia management with multiple semen specimen collection

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Objective: To determine the prevalence of sperm suitable for intracytoplasmic sperm injection (ICSI) in fresh ejaculated semen samples provided by men scheduled for a microdissection testicular sperm extraction (mTESE) procedure. Secondary objectives included an evaluation of the effect of a short abstinence period on semen quality and ICSI outcomes for men with cryptozoospermia.
Design: Retrospective cohort study.
Setting: Academic medical center.
Patients: All men were scheduled to undergo a mTESE procedure by a single, high-volume surgeon at an academic center from September 1, 2015, to May 1, 2021.
Intervention: Presence of sperm suitable for ICSI in the ejaculate on the day of scheduled mTESE.
Main Outcome Measures: Prevalence of sperm suitable for ICSI in the ejaculate among previously diagnosed men with azoospermia. Secondary outcomes included changes in semen parameters, clinical pregnancy rate, and live birth rate.
Results: Of 727 planned mTESE procedures, 69 (9.5%) were canceled because sperm suitable for ICSI were identified in a fresh ejaculated sample produced on the day of scheduled surgery (typically one day before oocyte retrieval). Overall, 50 men (50/727, 6.9%) used these rare, ejaculated sperm for ICSI. Semen samples obtained with <24 hours of abstinence were more likely to have better motility than the sample initially provided on the day of the planned mTESE. The live birth rate per ICSI attempt using these rare, ejaculated sperm was 36% (19/53).
Conclusion: Providing a fresh ejaculated semen sample on the day of mTESE allows nearly 10% of men with azoospermia to avoid surgery with satisfactory ICSI outcomes. Providing multiple ejaculated samples over a short period of time does not adversely affect sperm concentration and may enhance sperm motility in men with cryptozoospermia. (Fertil Steril® 2023;120:996–1003. ©2023 by American Society for Reproductive Medicine.)
El resumen está disponible en Español al final del artículo.

Key Words: Abstinence, cryptozoospermia, infertility, semen, ART

Intracytoplasmic sperm injection (ICSI) has overcome many of the barriers traditionally associated with male infertility, including low numbers of sperm, impaired motility, and/or abnormal morphology (1, 2). It also allows surgically retrieved sperm to fertilize oocytes, thereby giving men with azoospermia the chance to conceive a biological child (2). Despite this technology, men with nonobstructive azoospermia (NOA) remain difficult to treat because of varying degrees of spermatogenic failure (3). Because of this variation, NOA has been increasingly recognized as a spectrum (3, 4). Included within this spectrum is cryptozoospermia (also known as virtual azoospermia), which is defined by the World Health Organization as the presence of rare sperm only after centrifugation of a semen sample (3, 5–8). Many of these men with cryptozoospermia are judged to have inadequate ejaculated sperm for ICSI and are recommended to undergo surgical sperm retrieval.

However, when rare, motile ejaculated sperm are identified, these sperm can be used for ICSI instead of testicular sperm, thus allowing men with cryptozoospermia to avoid surgery. Although surgical risks are generally limited, testicular sperm extraction can lead to inflammation, scarring, a transient decrease in spermatogenesis and serum testosterone levels, and (in very rare cases) permanent testicular devascularization (9, 10). Avoiding surgery also

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spares patients the risk of anesthesia and the cost of a surgical procedure, which may be substantial (11).

Despite these benefits, it is unclear how many men may be able to avoid surgery by providing an ejaculated semen sample before their scheduled procedure and whether ejaculated sperm offer the same ICSI outcomes as testicular sperm for men with cryptozoospermia (12, 13). Specifically, there is concern that these rare, ejaculated sperm may be exposed to oxidative stress in the genital tract and/or during processing, thus reducing sperm quality and ICSI outcomes (12, 13). Although early evidence suggests that a short abstinence interval improves ICSI outcomes in men with oligoasthenozoospermia, there is limited data on short abstinence intervals for men with cryptozoospermia (14).

To further answer these questions, we evaluated our practice of having men scheduled for microdissection testicular sperm extraction (mTESE) provide a fresh ejaculated semen sample on the day of their scheduled surgery, typically the day before oocyte retrieval. When motile sperm are found, they are counseled on the option of using this sperm for ICSI and deferring surgery. When they defer surgery, additional semen samples are requested on the day of oocyte retrieval, which is typically 24 hours after the planned mTESE. Our primary aim was to determine the prevalence of sperm in fresh ejaculated semen samples provided by men scheduled for an mTESE procedure. Secondary objectives included ICSI outcomes and the impact of a short (24 hours) or very short (several hours) abstinence interval on sperm parameters for these men with cryptozoospermia.

MATERIALS AND METHODS

Patients

Under an institutional review board (IRB)-approved protocol (Weill Cornell Medicine IRB 20-04021763), a retrospective review was performed of consecutive men scheduled to undergo mTESE by one high-volume surgeon from September 2015 to May 2021. Couples who had ICSI cycles canceled secondary to female factors or who electively canceled and/or rescheduled their ICSI cycles were excluded. We then identified those patients whose mTESE procedures were canceled because of rare sperm being identified in the ejaculate on the day of planned surgery. Men were excluded from further analysis when no ICSI cycles were performed or when frozen and/or donor sperm were used for ICSI. Men were included only when they had prior semen analyses demonstrating azoospermia and/or cryptozoospermia judged inadequate for ICSI. Inadequate sperm for ICSI was defined as no motile sperm or only rarely detected motile sperm identified in the ejaculated sample (estimated <10 motile sperm in the total semen sample). Given that these men had a history of inadequate motile ejaculated sperm to inject all oocytes, they were scheduled for mTESE.

Additional patient data obtained from electronic medical records for analysis included male and female age, body mass index (BMI, kg/m^2), race and ethnicity, baseline serum follicle stimulating hormone (FSH) levels (normal 1.5–12.3 mIU/mL), testis volume (as determined using physical examination), genetic data (both karyotype and Y-chromosome microdeletion test results), and ICSI cycle results. Intracytoplasmic sperm injection cycle results included the number of oocytes retrieved, the number of metaphase II oocytes, the number of 2 pronuclei zygotes, the number of cycles with embryo transfer (ET), the number of embryos transferred, the day of ET, the number of clinical pregnancies, and the number of live births.

The demographic details for men meeting inclusion criteria (i.e., mTESE canceled, ejaculated sperm suitable for ICSI identified and used in an ICSI cycle) were then compared with all men who underwent an mTESE procedure performed by the same, high-volume surgeon from November 1995 to August 2022.

Semen Specimen Collection and Processing

Semen samples were collected by masturbation after 3–5 days of abstinence, and samples were allowed to liquefy for at least 20 minutes at 37 °C before analysis (15). Sperm concentration and motility were assessed in a Makler counting chamber. Morphology was classified according to strict criteria by a trained embryologist (8).

When no sperm were identified on initial analysis, centrifugation at 1,500 to 3,000 x g was performed. Individual sperm were then counted using the entire surface of the chamber by placing 10 μL of the test sample on a glass slide with a cover slip. If no sperm were seen on the evaluation of the neat sample and 100 sperm or fewer were identified in the concentrated sample, then the patient was classified as having cryptozoospermia. Only men judged to have inadequate sperm to proceed with ICSI and scheduled for surgical sperm retrieval were included in this study.

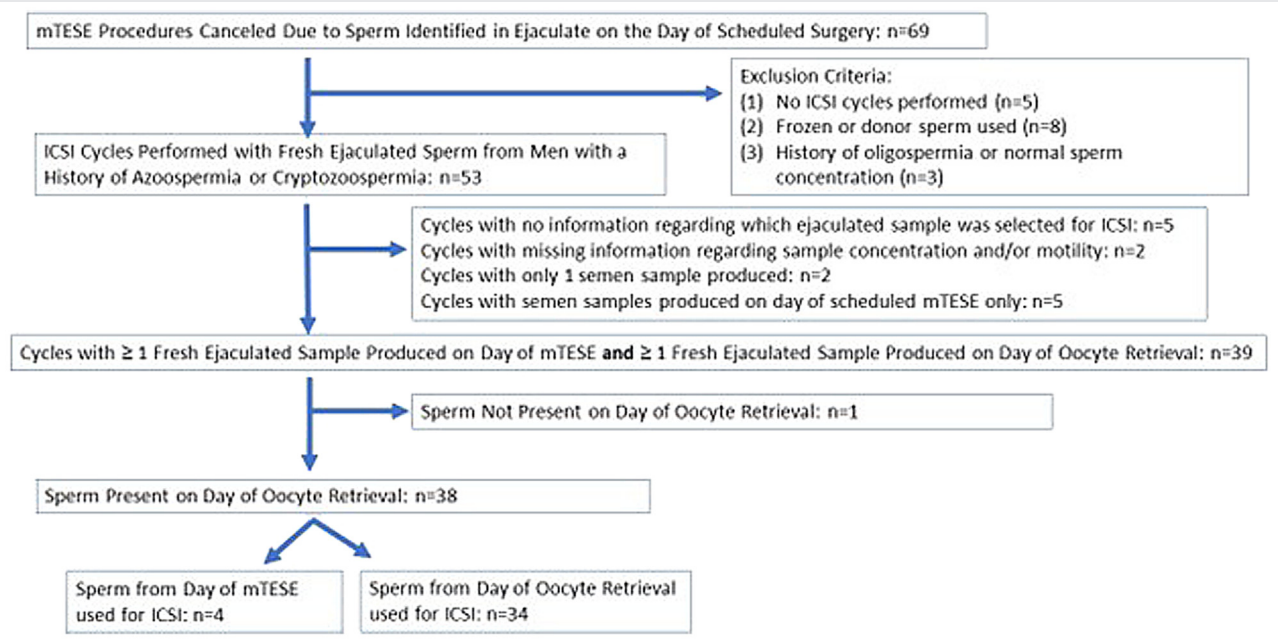
In cases of cryptozoospermia, an extensive search was performed to identify and isolate any injectable sperm, the details of which have been previously described (16). This process required 2–6 embryologists and at least 2 hours of searching (16). For sperm with poor or absent motility, the sperm suspension was exposed to 0.35 mM of pentoxifylline, and motility was reassessed.

When rare sperm were identified, the man was encouraged to provide additional semen samples on the day of oocyte retrieval. For those couples with oocyte retrieval and mTESE scheduled on the same day, the male partners were encouraged to provide multiple semen samples later that day. For most couples, however, oocyte retrieval was scheduled for 24 hours after the planned mTESE. In this case, the male partners were instructed to provide additional semen samples on the day after the planned mTESE for processing and evaluation.

Ovarian Stimulation and Oocyte Preparation

Oocyte retrieval was performed after stimulation with gonadotropins using previously established protocols (15–18). An ovulatory trigger (either human chorionic gonadotropin [hCG] and/or leuprolide acetate) was administered when ≥ 2 follicles were ≥ 17 mm in diameter. Oocyte retrieval was performed approximately 35–36 hours after administration of the ovulatory trigger.

FIGURE 1



Sperm selected for intracytoplasmic sperm injection.

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Microinjection Procedure and Embryological Evaluation

The details of the injection procedure have previously been described, as have the selection of the sperm and the immobilization-permeabilization method (15, 17). Oocytes were examined for fertilization 12–17 hours after the injection procedure. Embryos were cultured in a time-lapse incubator, with each embryo being monitored continuously. Embryo transfer was performed on days 3 or 5 after microinjection.

Pregnancy Assessment and Therapeutic Implantation Support

As previously described (16), starting on the day of oocyte retrieval, 16 mg methylprednisolone daily and 250 mg tetracycline every 6 hours were administered to the female partner for 4 days. Progesterone (25–50 mg per day intramuscularly or via vaginal administration) was started 1 day after oocyte retrieval and continued until the establishment of pregnancy. A serum β-hCG assay was performed 14 days after retrieval. Pregnancy was defined as biochemical when only a positive hCG was detected or clinical when at least one fetal heartbeat was visualized on ultrasound.

Statistical Analysis

Descriptive statistics were performed for all clinical variables. Continuous variables were reported as medians and interquartile ranges (IQRs), and categorical variables were reported as frequencies and proportions. Comparisons between samples produced after various abstinence intervals were performed using Wilcoxon matched-pairs signed rank tests.

Demographic details were compared between men meeting study inclusion criteria (n = 50) and all men who underwent mTESE at our center from November 1995 to August 2022 (n = 1,873) using Wilcoxon rank sum tests. Multivariable logistic regression was performed also to determine characteristics associated with having ejaculated sperm suitable for ICSI present on the day of mTESE. Variables included in the regression model included age ($<$40 years vs. $\geq$40 years), baseline FSH ($<$7.6 vs. $\geq$ 7.6 mIU/mL), and average testicular volume ($<$12 vs. $\geq$12 cc). Logistic regression analysis was performed using R statistical software (version 4.1.1., RStudio, Boston, MA); all other comparative analyses were performed using GraphPad Prism (version 9.5.1, San Diego, CA). For all analyses, statistical significance was considered at a P value of $<$.05.

Ethical Approval

This research protocol was approved by the Weill Cornell Medicine IRB (IRB 20-04021763).

RESULTS

Prevalence of Sperm in the Ejaculate Among Men Scheduled for mTESE

Of 727 mTESE procedures scheduled from September 2015 to May 2021, 69 (9.5%) were canceled because sperm were identified in the ejaculate on the day of surgery (Fig. 1). Of these,

TABLE 1

Descriptive characteristics of men who had microdissection testicular sperm extraction (mTESE) procedures canceled and subsequent intracytoplasmic sperm injection (ICSI) cycles performed using cryptozoospermic semen samples, vs. men who underwent mTESE procedures.

	Men with sperm present in ejaculate on the day of mTESE (mTESE canceled), and fresh, cryptozoospermic ejaculated sample used for ICSI (n = 50)	Men who underwent mTESE (n = 1,873)	*P* value[1]
Male age (y), median (IQR)	34 (31, 39)	34 (31, 39)	.7
Female partner age (y), median (IQR)	33 (29, 36.5)		
BMI (kg/m^2), median (IQR)	26.6 (23.4, 29.0)		
Race, n (%)			
- Other, or declined to state	27 (54%)		
- White	16 (32%)		
- Hispanic	3 (6%)		
- Asian	2 (4%)		
- African American	1 (2%)		
- Native Hawaiian	1 (2%)		
Baseline FSH (mIU/mL), median (IQR)	9 (5, 18)	20 (12, 30)	**<.001**
Left testis volume (cc), median (IQR)	14 (8, 16)	8 (4, 12)	**<.001**
Right testis volume (cc), median (IQR)	14 (10, 18)	8 (4, 14)	**<.001**
Average testis volume (cc), median (IQR)	14 (9, 18)	8 (4, 13)	**<.001**
Chromosomal data, n (%)			
- Normal (Normal Karyotype, No YCMD)	38 (76%)		
- AZFc YCMD	9 (18%)		
- Robertsonian translocation	2 (4%)		
- Isodicentric chromosome 22	1 (2%)		
Preoperative hormonal medications, n (%)			
- None	27 (54%)		
- Clomiphene citrate	16 (32%)		
- Anastrozole	7 (14%)		
Prior semen analyses, n (%)			
- Azoospermia	40 (80%)		
- Cryptozoospermia	10 (20%)		

Abbreviations: AZFc = azoospermia factor C; BMI = body mass index; FSH = serum follicle stimulating hormone; IQR = interquartile range; SD = standard deviation; YCMD = Y-chromosome microdeletion.
[1] = Wilcoxon rank sum test.

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53 men had a history of azoospermia (53/69, 76.8%), 13 had a history of cryptozoospermia (13/69, 18.8%), and 3 had a history of oligospermia, or a normal sperm concentration (3/69, 4.3%), but with a history of inadequate sperm for ICSI preoperatively. Overall, 50 men (50/727, 6.9%) used these rare, ejaculated sperm for ICSI.

Outcomes of ICSI Cycles Performed with Fresh Cryptozoospermic Semen Samples

After excluding cycles in which no ICSI was performed (n = 5), frozen or donor sperm were used (n = 8), or the male partner had a history of a normal sperm concentration or oligospermia (n = 3), 53 ICSI cycles were performed using rare, fresh, ejaculated motile sperm from 50 men with a history of azoospermia or cryptozoospermia. Most men had a normal karyotype and no Y-chromosome microdeletions (76%, 38/50) (Table 1). Of the remaining 12 men, 9 (18%) had an azoospermia factor c microdeletion, 2 (4%) had a Robertsonian translocation, and 1 (2%) had an isodicentric chromosome.

Of the 53 ICSI cycles, 44 resulted in ET (83%) (Table 2). The clinical pregnancy rate per ICSI attempt was 38% (20/53). The live birth rate (LBR) per ICSI attempt was 36% (19/53), and the LBR per ET was 43% (19/44).

Effect of Abstinence Interval on the Quality of Cryptozoospermic Samples

To assess the effect of a short abstinence interval on sperm quality, we performed a separate analysis of ICSI cycles in which ≥1 semen sample was produced on the day of scheduled mTESE and ≥1 semen sample was produced approximately 24 hours later on the day of oocyte retrieval (n = 39). For the men who provided samples on both the day of scheduled mTESE and the subsequent day of oocyte retrieval, sperm were again found 24 hours later over 97% of the time (97.4%, 38/39) (Fig. 1). Additionally, when sperm were found on the day of oocyte retrieval, they were selected for ICSI in nearly 90% of cycles (34/38) (Fig. 1).

To understand why sperm produced on the day of oocyte retrieval was more often chosen for ICSI, we examined the semen parameters of samples produced on the day of mTESE versus those produced 24 hours later, on the day of oocyte retrieval (Table 3). For this analysis, the mean values for sperm concentration, motility, and total motile sperm count (TMSC) were calculated and compared (Table 3). Most patients demonstrated an absolute higher mean motility (n = 25, 64%), concentration (n = 18, 46%), and TMSC (n = 18, 46%). However, there were no statistically significant differences (P>.05 for all).

TABLE 2

Outcomes of ICSI cycles performed with freshly ejaculated sperm from men scheduled to undergo mTESE.

ICSI cycles, n	53
Male age at cycle (y), median (IQR)	34 (31, 39)
Female age at cycle (y), median (IQR)	33 (29, 36.5)
Oocytes retrieved, n (median, IQR)	942 (16, 12–23)
MII oocytes retrieved, n (median, IQR)	734 (12, 8–20)
Fertilized oocytes (2PN), n (median, IQR)	413 (7, 3–12)
Fertilization rate (2PN/MII), % (n)	56% (413/734)
• Fertilization rate per cycle (%), median (IQR)	58% (34%–78%)
Number of cycles with embryo transfer, n (%)	44 (44/53, 83%)
Embryos transferred, n (median, IQR)	73 (2, 1–2)
• Day 3 transfer, n (%)	22 (50%)
• Day 5 transfer, n (%)	22 (50%)
Number of clinical pregnancy cycles, n	20
• Clinical pregnancy rate per cycle, % (n)	38% (20/53)
• Clinical pregnancy rate per ET, % (n)	45% (20/44)
Number of live birth cycles, n	19
• Live birth rate per cycle, % (n)	36% (19/53)
• Live birth rate per ET, % (n)	43% (19/44)
Number of cycles using sperm treated with pentoxifylline, n (%)	19 (36%)
• Number of cycles with embryo transfer, n (%)	15
• Number of clinical pregnancy cycles, n	8
• Clinical pregnancy rate per cycle, % (n)	42% (8/19)
• Number of live birth cycles, n	7
• Live birth rate per cycle, % (n)	37% (7/19)

Abbreviations: ET = embryo transfer; ICSI = intracytoplasmic sperm injection; IQR = interquartile range; MII = metaphase II; 2PN = 2 pronuclei zygotes; TESE = microdissection testicular sperm extraction.

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Knowing that embryologists typically select the best-looking sperm for ICSI, we identified and compared the sample(s) with the highest sperm concentration, motility, and TMSC produced on each day (Table 3). Overall, most patients demonstrated a positive absolute change in sperm motility (n = 27, 69%), concentration (n = 23, 59%), and TMSC (n = 23, 59%) on the day of oocyte retrieval. Motility was significantly higher in the samples obtained on the day of oocyte retrieval (median 50% vs. 33%, P=.0008). There were no statistically significant differences in sperm concentration or TMSC (P>.05 for both).

Finally, to assess the impact of a very short abstinence interval (hours), we identified cycles in which the male partner provided ≥2 semen samples on the day of oocyte retrieval (n = 34) (Table 3). Most patients demonstrated a positive absolute change in motility after this very short abstinence period (n = 19, 56%), and approximately one-third demonstrated an improvement in concentration (n = 12, 35%) and TMSC (n = 11, 32%). There were no statistically significant differences noted between the 2 samples (P>.05 for all).

Multivariable Logistic Regression: Predictors of Finding Ejaculated Sperm on Day of mTESE Usable for ICSI

To determine predictors of finding ejaculated sperm on the day of mTESE suitable for ICSI, the demographic details of the men who utilized ejaculated samples produced on the day of mTESE and/or the day of oocyte retrieval for ICSI (n = 50) were compared with those of all men who previously underwent mTESE at our center from November 1995 to August 2022 (n = 1,873). Characteristics evaluated included age, FSH (either <7.6 or ≥7.6 mIU/mL), and average testicular volume (either <12 or ≥12 cc). Overall, age was unrelated to the likelihood of finding usable sperm on the day of mTESE (odds ratio [OR] 0.89, 95% confidence [CI]: 0.41–1.73); however, FSH ≥7.6 mIU/mL was negatively associated with finding usable ejaculated sperm (OR 0.37, 95% CI: 0.20–0.70), and average testis volume ≥12 cc was positively associated with finding usable ejaculated sperm (OR 2.54, 95% CI 1.35–4.84) (Supplemental Table 1, available online).

DISCUSSION

In this study, we found that nearly 10% of men presenting for an mTESE procedure had adequate motile sperm present in the ejaculate to avoid this planned surgery. Although there is controversy in the literature regarding the utility of rare, ejaculated sperm for ICSI (12, 13), we found that the LBR per ICSI attempt was 36% for men with cryptozoospermia using freshly ejaculated sperm. This is higher than previous studies, including a recent meta-analysis of men with cryptozoospermia men that reported an LBR per ICSI cycle of 20.0% for ejaculated sperm and 28.8% for testicular sperm (13). Similarly, in a large study of 285 men with cryptozoospermia, the LBR per ET was reported to be 27.1% for couples using ejaculated sperm (n = 166) and 44.0% for those using testicular sperm (n = 56) (19). Although the results were not reported using an ICSI attempt and the investigators did not include an intention-to-treat analysis, comparatively, our findings suggest a higher LBR per ET (43% in our series) using rare ejaculated sperm vs. this prior report (19). Additionally, the clinical pregnancy rate per ICSI attempt using fresh, cryptozoospermic samples reported in this study (38%) is similar to the clinical pregnancy rate for cycles performed with fresh testicular sperm at our center (40.2%) (20). Overall, these results suggest that rare, ejaculated sperm can achieve acceptable ICSI outcomes and are a reasonable alternative to testicular sperm for men with cryptozoospermia.

We also found that over 97% of men with rare motile sperm in the ejaculate on the day of scheduled mTESE will again have sperm in the ejaculate 24 hours later. These samples produced with a short (approximately 24-hour) abstinence interval were often observed to be of higher quality and were subsequently selected for ICSI in nearly 90% of cycles. This further validates our practice of having men with cryptozoosperma provide multiple semen samples—both on

TABLE 3

Comparison of semen samples.

(A) Day of mTESE vs day of oocyte retrieval (n = 39 cycles)

Semen parameter	Day of mTESE	Day of oocyte retrieval	*P* value	Cycles with absolute improvement on the day of oocyte retrieval (n, %)
Mean motility (%), median (IQR)	33 (8; 50)	34 (13; 52)	.22	25 (64.1%)
Mean sperm concentration (sperm/mL), median (IQR)	1,300 (200; 200,000)	900 (400; 200,000)	.45	18 (46.2%)
Mean TMSC (sperm), median (IQR)	20 (6; 500)	30 (6; 200)	.95	18 (46.2%)

(B) Best semen parameters: day of mTESE vs day of oocyte retrieval (n = 39 cycles)

Semen parameter	Day of mTESE	Day of oocyte retrieval	*P* value	Cycles with absolute improvement on the day of oocyte retrieval (n, %)
Motility (%), median (IQR)	33 (9; 54)	50 (25; 66)	**.0008****	27 (69.2%)
Sperm concentration (sperm/mL), median (IQR)	1,300 (200; 200,000)	1,400 (600; 400,000)	.25	23 (58.9%)
TMSC (sperm), median (IQR)	20 (6; 200)	40 (9, 200)	.47	23 (58.9%)

(C) 1st vs 2nd sample produced on the day of oocyte retrieval (n = 34 cycles)

Semen parameter	1st Sample	2nd Sample	*P* value	Cycles with absolute improvement on 2nd sample (n, %)
Motility (%), median (IQR)	33 (11; 52)	28 (4; 53)	0.70	19 (55.9%)
Sperm concentration (sperm/mL), median (IQR)	1,000 (400; 4,000)	700 (400; 4,000)	0.34	12 (35.3%)
TMSC (million), median (IQR)	20 (8; 200)	20 (4; 60)	0.18	11 (32.4%)

Abbreviations: IQR = interquartile range; mTESE = microdissection testicular sperm extraction; TMSC = total motile sperm count.
**statistically significant ($P < .05$)

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the day of scheduled mTESE and on the day of oocyte retrieval—to obtain the best quality sperm for ICSI.

When evaluating the semen parameters of these consecutive samples, we found that there was higher sperm motility for samples obtained with a 24-hour abstinence interval or less. This is consistent with a recent meta-analysis that found that the highest overall mean sperm motility was observed with ≤1 day of abstinence (21). When comparing multiple samples produced within a very short (hours) abstinence period, however, we did not identify a statistically significant difference in sperm motility or any other semen parameters. This conflicts with other studies that have found significant improvements in sperm motility among men with severe oligoasthenozoospermia after an abstinence period of just 1–2 hours (14, 22, 23), as well as a recent meta-analysis that found that a ≤4-hour abstinence period is associated with significant improvements in sperm concentration, total motility, and progressive motility for men with abnormal semen parameters (24). However, it is important to consider that in our study population, the second semen sample produced on the day of oocyte retrieval had higher motility for over half of the patients and a higher sperm concentration for over one-third of patients. Although the mean values were not significantly different among the sequential samples, only limited numbers of sperm are needed for ICSI; therefore, obtaining additional motile sperm may be critical for success. Similarly, Barbagallo et al. (14) have previously reported that sperm obtained with a 1-hour abstinence period results in better reproductive outcomes for men with severe oligoasthenoteratozoospermia. Although we did not directly compare the ICSI outcomes of samples produced after a 1-hour abstinence period with the rest of the cohort, this is an opportunity for future study.

Finally, our multivariable logistic regression analysis suggests that men with a normal FSH (<7.6 mIU/mL) and normal average testis volume (≥12 cc) are more likely to have sperm present on the day of mTESE compared with those with abnormal findings. These results are similar to prior work that has reported that men with cryptozoospermia are more likely to have a larger testis volume and lower FSH than NOA men (25). Although additional analyses with other demographic characteristics could more clearly define which men are most likely to have sperm present in the ejaculate on the day of a scheduled mTESE, these findings are a helpful initial step and may be useful selection criteria for centers that cannot perform semen analysis on all men before a scheduled mTESE because of limited resources.

Although this study seems to support the message that "more samples = more sperm with higher motility available for ICSI," it does have several limitations. First, it is inherently limited by its retrospective nature. In addition, it was performed at a single, high-volume academic center, which has multiple, very skilled embryologists present on-site and therefore may not be applicable to all practice settings. Additionally, the nature of studying a population with cryptozoospermia limited our ability to perform additional tests such as DNA fragmentation testing, which may have offered insight into sperm quality and affected reproductive outcomes. Finally, we have not purposefully analyzed the various abstinence intervals that could be used for sperm collection in men with cryptozoospermia to identify the optimal abstinence period to provide the best sperm quality, nor have we directly compared our ICSI outcomes with a testicular sperm comparator group. This is an area of future study that is needed to optimize our management of men with cryptozoospermia.

CONCLUSIONS

The results in this manuscript document the benefit of providing a semen sample, even for men with documented azoospermia, before sperm retrieval surgery. In addition, this study is one of the first to evaluate the reproductive outcomes of men with cryptozoospermia who were requested to provide multiple ejaculated semen samples over a 24- to 36-hour period. Our initial findings suggest that men with cryptozoospermia should be counseled to provide multiple ejaculated semen samples before ICSI, as nearly all will have sperm present on subsequent samples, and this sperm is likely to have higher motility. Additional studies are needed to further delineate the optimal abstinence interval for this population with cryptozoospermia.

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Manejo exitoso de la criptozoospermia con recolección de varias muestras de semen

Objetivo: Determinar la prevalencia de muestras adecuadas de semen para inyección intracitoplasmática de espermatozoides (ICSI) en muestras de semen fresco eyaculado entregadas por varones programados para extracción de tejido testicular por microdisección (mTESE). Los objetivos secundarios incluyeron la evaluación de un corto periodo de abstinencia en la calidad del semen y los resultados de ICSI para varones con criptozoospermia.

Diseño: Estudio retrospectivo de cohortes.

Entorno: Centro médico académico.

Paciente(s): Todos los hombres programados a una mTESE por un único cirujano experimentado en un centro académico desde el 1 de septiembre de 2015 al 1 de mayo de 2021.

Intervención(es): Presencia de semen adecuado para ICSI en el eyaculado entre hombres previamente diagnosticados de azoospermia.

Medida(s) de Resultado(s) principal(es): Prevalencia de semen adecuado para ICSI en eyaculado de varones diagnosticados de azoospermia. Los objetivos secundarios incluyeron cambios en los parámetros seminales, tasa de gestación clínica, y tasa de nacido vivo.

Resultado(s): De las 727 mTESE planificadas, 69 (9.5%) fueron canceladas debido a una muestra adecuada de semen para ICSI en el eyaculado recogido el día de la cirugía programada (típicamente un día antes de la recuperación de ovocitos). En general, 50 varones (50/727, 6.9%) utilizaron estas excepcionales muestras para ICSI. Las muestras obtenidas con menos de 24 horas de abstinencia tuvieron más frecuentemente mejor movilidad que aquellas muestras recogidas inicialmente el día que se planificó la mTESE. La tasa de nacido vivo por intento de ICSI usando estas excepcionales muestras de eyaculado fue de 36% (19/53).

Conclusión: Entregar una muestra de semen eyaculado fresco el día de la mTESE permite que cerca de un 10% los varones con azoospermia eviten la cirugía con resultados satisfactorios de ICSI. Entregar múltiples muestras de eyaculado en un corto periodo de tiempo no afecta adversamente la concentración de semen y puede incrementar la movilidad en varones con criptozoospermia.