

# Sperm retrieval, fertilization rates, and clinical outcomes of infertile men with Y chromosome microdeletion

## A retrospective cohort study

Jenna Baffa\*, Gilad Karavani\*, Bader Akroof, Mohamed S. Kattan, Susan Lau, Keith Jarvi

Division of Urology, Department of Surgery, Mount Sinai Hospital, University of Toronto, Toronto, ON, Canada

\*Equal contribution first authors

Cite as: Baff J, Karavani G, Akroof B, et al. Sperm retrieval, fertilization rates, and clinical outcomes of infertile men with Y chromosome microdeletion: A retrospective cohort study. *Can Urol Assoc J* 2025;19(4):116-22. <http://dx.doi.org/10.5489/cuaj.8879>

Published online December 9, 2024

### ABSTRACT

**INTRODUCTION:** We aimed to explore whether a Y chromosome microdeletion (YCM) confers adverse effects on surgical sperm retrieval potential and intracytoplasmic sperm injection (ICSI) outcomes in men with azoospermia and severe oligospermia.

**METHODS:** This was a retrospective cohort study that included infertile men with azoospermia or severe oligospermia who were evaluated for karyotype analysis and YCM testing at a university-affiliated hospital between 2010 and 2022. Outcomes of microdissection testicular sperm extraction (mTESE) for surgical sperm retrieval were compared between men diagnosed with YCM and the control group, in which no YCM was found. Additionally, patients from each group who underwent in vitro fertilization (IVF)-ICSI cycle using ejaculated sperm or surgically retrieved mature spermatozoa were compared regarding their IVF-ICSI cycle outcomes, fertilization rates, cleavage, and blastocyst formation, and clinical pregnancy rates.

**RESULTS:** A total of 116 azoospermic and oligospermic men who underwent YCM testing were included in the study: 19 with YCM and 97 without. Overall, nine mTESE procedures were performed for patients with YCM and 38 for men from the control group. There were no significant differences between the YCM and control groups in mature sperm retrieval rates (11.1% vs. 26.3%,  $p=0.663$ ), although a trend towards higher rates of elongated and round spermatids as the most mature germ cell was noted in the YCM group (66.7% vs. 28.9%,  $p=0.054$ ). Of the 13 men with mature sperm — either ejaculated or surgically retrieved (mTESE) — that had known ICSI cycle outcomes, three men had proven YCMs and 10 controls had no identified YCMs. Basic characteristics were similar between the groups, except for testosterone levels, which were higher in the YCM group ( $23.0 \pm 13.1$  vs.  $9.4 \pm 6.4$  nmol/L,  $p=0.027$ ). Fertilization rates and cleavage rates were similar between the YCM and control groups (42.3% vs. 49.7% and 42.3% vs. 39.3%,  $p=0.491$  and 0.774, respectively). Blastocyst formation rates, and pregnancy rates, while not statistically significant, showed a trend for favorable outcomes in the control group compared to the YCM group (24.1% vs. 7.7%, 72.7% vs. 20.0%,  $p=0.078$  and 0.106, respectively).

**CONCLUSIONS:** YCM does not affect sperm retrieval rates. Fertilization and cleavage rates are not impaired by microdeletions, while blastocyst formation rates and clinical pregnancy

rates per embryo transfer follow a non-significant trend for unfavorable outcomes in the YCM group. Clinical and embryonic development results should be interpreted with caution, as these groups are relatively small.

### INTRODUCTION

Infertility is defined as the inability to conceive after 12 months of unprotected intercourse.<sup>1</sup> Approximately 8–15% of reproductive-age couples will experience infertility, of which half will be attributed to male factor.<sup>2</sup> The majority of male factor infertility patients will present with suboptimal sperm concentration, more specifically, oligospermia (sperm concentration < 15 million/ml), reduced sperm motility, and in the minority of cases, azoospermia (complete absence of sperm in ejaculate).<sup>3</sup>

Azoospermia can be further classified into two categories: non-obstructive (NOA) and obstructive (OA). Within OA, spermatogenesis is not impaired; however, a post-testicular obstruction blocks sperm from transferring into the ejaculate.<sup>3</sup> In NOA, sperm production is reduced due to primary testicular failure, with various underlying etiologies.<sup>4</sup> NOA can be acquired, including cases of trauma, testicular torsion, varicocele, inflammation, drug use, and radiation.<sup>5</sup> NOA can also be congenital, including cryptorchidism or genetic abnormalities, such as Klinefelter syndrome (KS) and azoospermia factor (AZF) microdeletions.<sup>5</sup>

The Y chromosome, the smallest of the human genome, consists of a

## KEY MESSAGES

■ Y chromosome microdeletion does not affect surgical sperm retrieval rates in men with azoospermia.

■ In vitro fertilization-intracytoplasmic sperm injection (ICSI) outcomes are not impaired by Y chromosome microdeletion.

■ Y chromosome microdeletion testing should be offered to men with severe oligospermia and testicular failure, the results of which could be used in counseling infertile couples.

short arm (Yp) and a long arm (Yq).<sup>6</sup> At the distal-most aspects of the Y chromosome are pseudoautosomal regions (PAR), which participate in recombination with the X chromosome, flanking the euchromatic and heterochromatic non-recombinant regions.<sup>3,6,7</sup> The proximal aspect of Yq was initially thought to be non-functional; however, in 1976, researchers discovered deletions within this region led to a phenotype of azoospermia, therefore labeling it the azoospermia factor region.<sup>7</sup>

The AZF region is broken down into three clinically significant loci — AZFa, AZFb, and AZFc — each harboring numerous genes required for proper spermatogenesis. Further research on the structure of these regions identified amplicon sequences organized into palindromes, allowing susceptibility to non-allelic homologous recombination and deletions.<sup>7</sup> AZFa and AZFb, which are deleted in 0.5–4% and 1–5% of men with microdeletions, respectively, will result in complete loss of spermatogenesis and azoospermia, with poor prognosis for sperm retrieval via microdissection testicular sperm extraction (mTESE);<sup>8–10</sup> however, deletions of AZFc, with an incidence of 60–70% amongst men with YCM, holds the best prognosis for sperm retrieval and subsequent use of sperm in assisted reproductive technologies (ART).<sup>9,10</sup>

While it is well-established that an AZFc microdeletion will disrupt spermatogenesis, leading to either severe oligospermia or azoospermia, the quality of the sperm and resultant clinical outcomes remain controversial.<sup>9,10</sup> With the advent of intracytoplasmic sperm injection (ICSI), men with a YCM and suboptimal sperm concentration can father a biological child. Patients may undergo retrieval of sperm via mTESE, with reported retrieval rates between 60–75%, or produce via ejaculation.<sup>10</sup>

Several previous studies have reported that AZFc microdeletions do not affect ICSI outcomes when compared to patients with an intact Y chromosome.<sup>10–13</sup> In contrast, other reports have shown significant reductions in fertilization rate<sup>5,14–19</sup> and subsequent clinical outcomes, including blastocyst development, clinical pregnancy, and live birth rate.<sup>5,15,20–22</sup> Current understanding of the biological and clinical significance of YCM is limited. With controversial results reported across the literature, the true effect of YCM on ICSI outcomes and their biological mechanisms have yet to be elucidated.

In this retrospective cohort study, we investigated the effect of YCM on sperm retrieval success and subsequent clinical outcomes after ICSI treatment in patients with oligospermia and azoospermia.

## METHODS

## Patients

This was a retrospective cohort study that included azoospermic and oligospermic men who presented with infertility to Murray Koffler Urologic Center, Mount Sinai Hospital, Toronto, Canada. After semen analysis and a diagnosis of NOA or severe oligospermia (sperm concentration of <5 million/ml), karyotype analysis and YCM testing were performed on peripheral blood lymphocytes at North York General Hospital, Toronto, Canada, from years 2010–2022. The study group included men with proven AZF microdeletion (YCM group). Men with no identified YCM were allocated to the control group (Figure 1).

Surgical samples from patients undergoing mTESE were sent to various labs within the Toronto area and if mature sperm was found, it was used in an in vitro fertilization (IVF)-ICSI cycle. The control group was matched with the YCM group by female age and clinic at which the IVF-ICSI cycle was performed.

## Y chromosome microdeletion analysis

Polymerase chain reaction (PCR) amplification of sequence-tagged sites (STS) in AZFa, AZFb, and AZFc regions of the Y chromosome was performed. Data were analyzed to determine the presence or absence of an STS marker. All YCM tests were performed at North York General Hospital, Toronto, Canada.

## Outcome measures

Primary outcomes were sperm retrieval rate and fertilization rate per cycle. Secondary outcomes were cleavage rate, blastocyst formation rate, and clinical

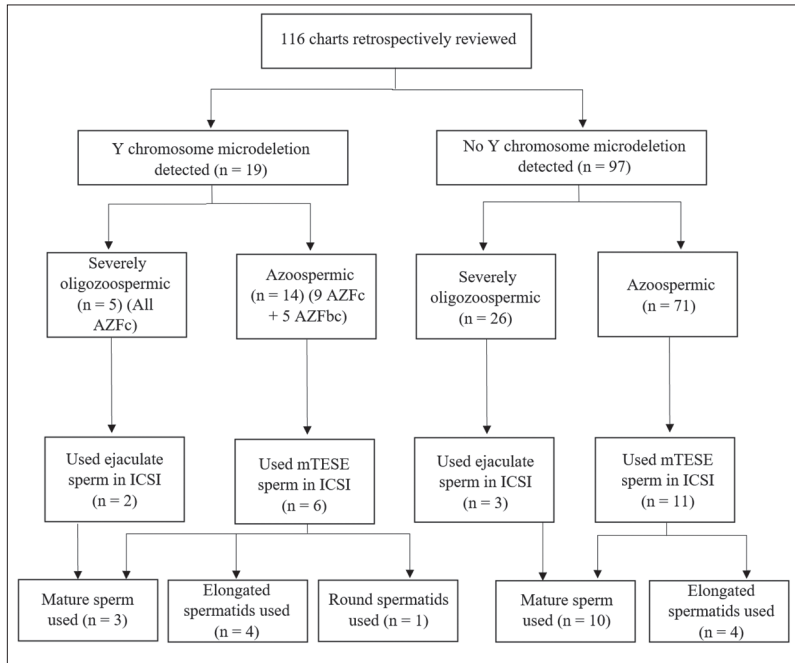


Figure 1. Study population flow chart. ICSI: intracytoplasmic sperm injection; mTESE: microdissection testicular sperm extraction.

**Table 1. Sperm retrieval rates among men who underwent microdissection testicular sperm extraction with and without YCM**

Variable	YCM group	Control group	p
Number of mTESEs	9	38	
Number of mTESEs resulting in elongated/round spermatids retrieval	6/9 (66.7%)	11/38 (28.9%)	0.054
Number of mTESEs resulting in mature sperm retrieval	1	10	
SRR - mature spermatozoa (%)	1/9 (11.1%)	10/38 (26.3%)	0.663

Categorical data are expressed as n/N (%) and compared between two groups by Chi-squared test or Fisher’s exact test. mTESE: microdissection testicular sperm extraction; SRR: sperm retrieval rate; YCM: Y chromosome microdeletion.

pregnancy rate per embryo transferred. The fertilization rate was calculated as the proportion of fertilized oocytes divided by the number of injected metaphase II (MII) (mature) oocytes. Cleavage rate was calculated as the proportion of cleaved zygotes divided by the number of mature oocytes. Blastocyst formation rate was calculated as the proportion of embryos developed into blastocyst stage at day 5–6, divided by the number of mature oocytes.

**Ethics**

Data collection (05-0161-E) and analysis (07-0032-E) were approved by the Research Ethics Board (REB) at Mount Sinai Hospital. All patients consented to having their medical information reviewed and records used in research.

**Statistical analysis**

Data are presented as mean ± standard deviation (SD) for continuous variables and proportion (%) for categorical variables. Student’s t-test was used for comparison of continuous variables between two groups. Chi-squared test or Fisher’s exact test (when expected frequency <5) were used for comparison of categorical variables between two groups. A p-value of <0.05 was considered statistically significant. All analyses were performed using GraphPad Prism (version 9).

**RESULTS**

YCM were detected in 19 of 116 patients (16.4%). Within the YCM group, 14 of 19 men had a complete AZFc microdeletion (73.7%) and five had complete AZFb+c microdeletions (26.3%). There were no reported patients with an AZFa microdeletion. Five YCM patients (all with AZFc YCM) had severe oligospermia and the remaining 14 were azoospermic. YCM was not identified in 97 patients. Twenty-six of 97 patients in the control group had severe oligospermia and 71 had azoospermia (Figure 1).

In the entire cohort, the sperm retrieval rates using mTESE were compared between the YCM and control groups (Table 1). Nine patients with YCM (an AZFc YCM was found in seven of them) underwent mTESE (three of the remaining five patients decided not to proceed with mTESE, one decided to use donor sperm, and one was lost to followup), of which one (11.1%) resulted in mature sperm being found after processing in the IVF laboratory, and in six cases, only elongated or round spermatids were isolated. Surgery was performed on two patients with an AZFb+c microdeletion where elongated spermatids were found after mTESE.

Thirty-eight patients from the control group underwent mTESE in our center. The remaining patients either chose not to attempt surgical sperm retrieval, opted to pursue treatment at a different center, or decided to use donor sperm. Background information on previous mTESE procedures was available for 16 patients in this group, of whom nine had undergone mTESE elsewhere before seeking another mTESE procedure at our clinic. Among the 38 mTESE procedures performed on men without YCM at our clinic, mature

sperm was successfully retrieved in 10 cases (26.3%), while immature sperm (elongated or round spermatids) was found in 11 cases (29.0%). This difference in sperm retrieval outcomes was not statistically significant ( $p=0.663$ ).

For the purpose of analysis of ART outcomes using ejaculated or surgically retrieved mature sperm in both groups, we excluded 16 men (out of 19) from the YCM group due to use of sperm donor ( $n=1$ ), no mature sperm found from mTESE ( $n=7$ ), mTESE not done ( $n=6$ ), or no associated IVF cycle information ( $n=2$ ).

Eighty-seven of 97 men from the control group were excluded from the ART outcomes analysis due to no sperm found after mTESE ( $n=28$ ), no mTESE done ( $n=31$ ), and no associated IVF cycle or unavailable information ( $n=28$ ).

Finally, three patients with a detected AZFc YCM and 10 patients without YCM, all of whom had successful sperm retrieval via mTESE or ejaculated sperm and had available ART cycle information, were included in the analysis of ICSI outcomes (Figure 1). Testicular (via mTESE) sperm was used in one out of three (the remaining two had ejaculated sperm) patients in the AZFc YCM group and in seven of 10 (the remaining three had ejaculated sperm) patients in the control group.

The baseline characteristics of the 13 men with known ART outcomes (three AZFc YCM and 10 controls) were all similar in both groups (Table 2), while testosterone level differed and was higher in the YCM group ( $23.0 \pm 13.1$  vs.  $9.4 \pm 6.4$  nmol/L,  $p=0.027$ ).

The general IVF-ICSI clinical outcomes of the YCM and control groups using either ejaculated or surgically retrieved mature sperm are shown in Table 3. The average number of oocytes retrieved, the oocyte maturation rate, and fertilization and cleavage rates were comparable between groups. The blastocyst formation did not significantly differ between the groups, although a trend towards poorer outcomes in the YCM group compared to the control group was noted (7.7% vs. 24.1%,  $p=0.078$ ), similar to pregnancy rates and live births rates (20.0% vs. 72.7%, 0% vs. 40.0%,  $p=0.106$  and 0.231, respectively). A total of five embryos were transferred in the YCM group (two blastocysts and three cleavage stage embryos at day 3), resulting in one pregnancy that ended in miscarriage. In contrast, 11 embryos were transferred in the control group and to date, four live births and one ongoing pregnancy have been recorded from female partners within the no YCM group.

**Table 2. Basic characteristics of patients with known In-vitro fertilization outcomes (n=13) with the use of mature (ejaculated or testicular) sperm for intracytoplasmic sperm injection**

Variable	YCM group	Control group	p
Number of patients	3	10*	
Female age	29.0±3.6	31.4±4.0	0.386
Male age	30.3±1.5	33.7±5.7	0.121
Duration of infertility (years)			
FSH (mIU/ml)	10.7±3.8	15.3±7.9	0.359
LH (mIU/ml)	6.0±1.2	9.0±4.3	0.265
Testosterone (nmol/L)	23.0±13.1	9.4±6.4	0.027
Use of testicular sperm for ICSI	1	3	
Use of ejaculated sperm for ICSI	2	7	

\*Out of the 13 non-YCM men with ejaculated ( $n=3$ ) and surgically retrieved testicular ( $n=10$ ) sperm, 3/10 men from the testicular sperm group were lost to followup. Continuous data are expressed as mean  $\pm$  SD and compared between two groups by Student's t-test. Categorical data are expressed as n/N (%) and compared between two groups by Chi-squared test or Fisher's exact test. FSH: follicle-stimulating hormone; ICSI: intracytoplasmic sperm injection; LH: luteinizing hormone; MT: Micro-TESE; YCM: Y chromosome microdeletion.

**Table 3. In vitro fertilization outcomes (n=13) with the use of mature (ejaculated or testicular) sperm for intracytoplasmic sperm injection**

Variable	YCM group	Control group	p
Number of patients	3	10*	
Number of oocytes retrieved	13.3±2.1	19.4±8.8	0.274
Number of mature oocytes	8.7±2.5	14.5±6.1	0.142
Overall number of mature oocytes	26	145	
Fertilization rate (%)	11/26 (42.3%)	72/145 (49.7%)	0.491
Cleavage stage rates (%)	11/26 (42.3%)	57/145 (39.3%)	0.774
Blastocyst rates (%)	2/26 (7.7%)	35/145 (24.1%)	0.078
Embryos transferred (n)	5**	11	
Pregnancy rates (%)	1/5 (20.0%)	8/11 (72.7%)	0.106
Live birth rates (%)	0/5	4/10 (40.0%***)	0.231

\*Out of the 13 non-YCM men with ejaculated ( $n=3$ ) and surgically retrieved testicular ( $n=10$ ) sperm, 3/10 men from the testicular sperm group were lost to followup. \*\*Two blastocysts and three cleavage stage day 3 embryos were transferred. \*\*\*One pregnancy was reported as ongoing. Continuous data are expressed as mean  $\pm$  SD and compared between two groups by Student's t-test. Categorical data are expressed as n/N (%) and compared between two groups by Chi-squared test or Fisher's exact test. YCM: Y chromosome microdeletion.

“ Our study demonstrated a non-significant trend of reduced blastocyst formation and clinical pregnancy per embryo transfer rates in men with an AZFc YCM. ”

## DISCUSSION

YCM accounts for approximately 7% of all genetic cases of male infertility, with YCM found in 9–16% of the subset of infertile men with NOA and 5–10% of those with severe oligospermia.<sup>3,14,23,24</sup> These reports are consistent with the prevalence of YCM within our study cohort of men with azoospermia and severe oligospermia.

In addition, the study results, showing a lack of difference in the sperm retrieval rates for men with and without YCM, are also consistent with previous literature.<sup>5,10</sup> In this study, 11.1% of YCM patients were able to achieve successful surgical retrieval of mature sperm. This contrasts with other reports of retrieval success in AZF-deleted men, which range from 64.2–78.9%.<sup>5,14,16,25</sup> The overall successful sperm retrieval rates we report are lower than previously reported in the literature (retrieval rates reported between 40–60%),<sup>3,5</sup> likely due to the fact that our center is a tertiary infertility clinic, with many of the patients having had previous unsuccessful sperm retrieval attempts.

We also analyzed the rates of retrieval of immature sperm. We reported that mature sperm were seen in only 23.4% of cases in the entire cohort, while the most mature germ cells comprise an additional 36.2% of cases. Because some clinics only use mature spermatozoa, while others may use elongated and round spermatids in ICSI cycles, it is important to understand the different types of sperm that can be retrieved surgically to better inform patients about the likelihood of retrieval success and subsequent possibilities. This knowledge helps guide patients through their treatment options and set realistic expectations.

The effect of microdeletions on ICSI outcomes remains controversial, with variable reports of effects on reproductive outcomes for men with a AZFc YCM.<sup>10</sup> A recent systematic review and meta-analysis of 34 studies between 1998 and 2018 showed significantly decreased fertilization, clinical pregnancy, and live birth rates in men with an AZFc YCM compared to men with an intact Y chromosome.<sup>26</sup> Our study found comparable fertilization and cleavage rates in patients with or without a microdeletion. While the fertilization rate reported here in microdeletated patients

is consistent with previous studies, the control group fertilization rate is quite low.<sup>11,14,15</sup>

Although most studies report decreased fertilization rates within AZFc YCM patients, the biologic mechanisms of this effect are largely unknown. It is widely accepted that the AZF region of the Y chromosome plays a significant quantitative role in spermatogenesis; however, deletions within this region may affect the ability of sperm to cause oocyte activation and subsequent fertilization.<sup>9,12,15,16</sup> The molecular mechanisms of AZFc microdeletions on fertilization capacity remain to be elucidated; however, studies are analyzing potential effects by observing male-to-female embryo ratios, hypothesizing that if AZFc microdeletions are the cause of decreased sperm quality, there would be reduced numbers of male embryos created.<sup>12,15,20</sup>

Our study demonstrated a non-significant trend of reduced blastocyst formation and clinical pregnancy per embryo transfer rates in men with an AZFc YCM. There exists only one study in which blastocyst formation rates were significantly reduced in AZFc microdeletion patients;<sup>27</sup> however, this was postulated to be the result of a significantly reduced cleavage rate. No previous studies report reduced clinical pregnancy rates per embryo transfer in patients with an AZFc YCM, but our reported rate of 20% is consistent with other IVF studies.<sup>11,12,14,18,20,21</sup> Clinical pregnancy rate per embryo transfer in other studies within non-microdeletated groups ranges from 23–56%.<sup>10-13,17,18,20,21</sup>

Sperm source has been postulated to effect ICSI success. Significant differences were not found when ejaculate and testicular sperm sources were compared to each other, implying sperm origin is not the driving factor behind reproductive outcomes.<sup>16</sup> As previous investigators have commonly concluded that the presence of a microdeletion is of higher importance than sperm source, our main analysis grouped patients who underwent mTESE and those who produced sperm via ejaculation. To further support this decision, a 2021 study of 656 patients performed a linear and logistic regression analysis between microdeletated and control groups by adjusting for use of testicular or ejaculated sperm and found the main proponent behind poor ICSI outcomes was the presence of a microdeletion rather than sperm source.<sup>15</sup>

This study reports ICSI success rates between AZFc YCM and non-microdeletated patients with the use of mature spermatozoa and adds to the scarce literature on this unique group of patients. As this was a retrospective study, with ICSI cycles performed at various clinics during a wide range of years, inter-embryologist

variation in sperm selection and ICSI technique was uncontrolled and is certainly a contributing factor to the SRR and fertilization success rates. Additional research involving larger sample sizes and the use of a single andrology laboratory to conduct testicular tissue examination is warranted.

In clinical settings, 80% of couples with AZFc microdeletions will choose IVF-ICSI over sperm donation, adoption, or no treatment.<sup>28</sup> It is, therefore, important to educate patients on the chances of successful sperm retrieval and the effects of microdeletions on subsequent clinical outcomes. It is also imperative to educate patients about the risk of transmitting the deletion to male embryos, with the possibility of future infertility. Some studies have suggested preimplantation genetic testing to select for female embryos, thereby avoiding the risk of transmitting the microdeletion to offspring;<sup>11,12</sup> however, while technically feasible, within Canada, sex selection for non-lethal conditions is considered unethical and impermissible.

Further studies are needed with increased sample size and inclusion of male offspring to determine ICSI prognosis. A critical area of future work will pertain to elucidating the molecular mechanisms behind AZFc YCM and potential oocyte activation.

### Limitations

There are limitations to our study that should be addressed. The first is the number of patients included did not reach the calculated sample size for a statistical power of 80%. Therefore, the possibility of type II error is high, meaning small differences between groups were likely not able to be detected and subtle disparities between cohorts might have gone undetected, potentially explaining the lack of significance in fertilization, cleavage, blastocyst formation, and clinical live birth rates.

The lack of available information on female fertility is a possible confounder. Numerous female factors are known to affect egg quality and quantity including age, body mass index, polycystic ovarian syndrome, premature ovarian failure, and endometriosis. In this study, only female age was available as an indicator of egg quality, and the potential of other conditions known to affect fertility could have impaired fertilization, cleavage, blastocyst formation, and clinical pregnancy rates.

### CONCLUSIONS

AZFc YCMs are found in approximately one of six men with severe oligospermia and azoospermia due to testicular failure. This study and previous reports suggest

that the presence of the AZFc YCM does not influence surgical sperm retrieval rates but may impair IVF-ICSI outcomes. YCM testing should be offered to men with severe oligospermia and testicular failure, the results of which could be used in counseling infertile couples.

**COMPETING INTERESTS:** Dr. Jarvi is a minority owner of FlowLabs Inc. The remaining authors do not report any competing personal or financial interests related to this work.

**ACKNOWLEDGEMENTS:** The authors would like to thank Dr. Jim Meriano, Dr. Scot Hamilton, Pat-Chronis-Brown, Dr. Crystal Chan, and Dr. Iryna Kuznyetsova, who kindly provided IVF outcomes from their respective clinics to make this study possible.

This paper has been peer reviewed.

### REFERENCES

1. World Health Organization. WHO Laboratory Manual for the Examination and Processing of Human Semen. 6th ed. Geneva: World Health Organization, 2021.
2. Witherspoon L, Dergham A, Flannigan R. Y-microdeletions: A review of the genetic basis for this common cause of male infertility. *Transl Androl Urol* 2021;10:1383-90. <https://doi.org/10.21037/tau-19-599>
3. Rabinowitz MJ, Huffman PJ, Haney NM, et al. Y-Chromosome microdeletions: A review of prevalence, screening, and clinical considerations. *Appl Clin Genet* 2021;14:51-9. <https://doi.org/10.2147/TACG.S267421>
4. Yuen W, Golin AP, Flannigan R, et al. Histology and sperm retrieval among men with Y chromosome microdeletions. *Transl Androl Urol* 2021;10:1442-56. <https://doi.org/10.21037/tau.2020.03.35>
5. Zhang HL, Zhao LM, Mao JM, et al. Sperm retrieval rates and clinical outcomes for patients with different causes of azoospermia who undergo microdissection testicular sperm extraction-intracytoplasmic sperm injection. *Asian J Androl* 2021;23:59. [https://doi.org/10.4103/aja.aja\\_12\\_20](https://doi.org/10.4103/aja.aja_12_20)
6. Foresta C, Moro E, Ferlin A. Y Chromosome microdeletions and alterations of spermatogenesis. *Endocr Rev* 2001;22:226-39. <https://doi.org/10.1210/edrv.22.2.0425>
7. Colaco S, Modi D. Genetics of the human Y chromosome and its association with male infertility. *Reprod Biol Endocrinol* 2018;16:14. <https://doi.org/10.1186/s12958-018-0330-5>
8. Carpinello OJ, Marinaro J, Hill MJ, et al. Karyotypic abnormalities and Y chromosome microdeletions: How do these impact in vitro fertilization outcomes, and how common are they in the modern in vitro fertilization practice? *F&S Reports* 2021;2:300-7. <https://doi.org/10.1016/j.xfre.2021.06.001>
9. Scovell JM, Ory J. Intracytoplasmic sperm injection outcomes are comparable in ejaculated sperm but poor in testicular sperm. But why? An opportunity to further understand the AZFc region. *Fertil Steril* 2021;116:66. <https://doi.org/10.1016/j.fertnstert.2021.05.075>
10. Choi JM, Chung P, Veeck L, et al. AZF microdeletions of the Y chromosome and in vitro fertilization outcome. *Fertil Steril* 2004;81:337-41. <https://doi.org/10.1016/j.fertnstert.2003.06.030>
11. Liu XY, Wang RX, Fu Y, et al. Outcomes of intracytoplasmic sperm injection in oligospermic men with Y chromosome AZFb or AZFc microdeletions. *Andrologia* 2017;49:e12602. <https://doi.org/10.1111/and.12602>
12. Liu X hong, Qiao J, Li R, et al. Y chromosome AZFc microdeletion may not affect the outcomes of ICSI for infertile males with fresh ejaculated sperm. *J Assist Reprod Genet* 2013;30:813-9. <https://doi.org/10.1007/s10815-013-0009-y>
13. Xi Q, Zhang Z, Wang R, et al. Obstetric and perinatal outcomes of intracytoplasmic sperm injection for infertile men with Y chromosome microdeletions. *Medicine* 2019;98:e17407. <https://doi.org/10.1097/MD.00000000000017407>
14. Yamaguchi K, Ishikawa T, Mizuta S, et al. Clinical outcomes of microdissection testicular sperm extraction and intracytoplasmic sperm injection in Japanese men with Y chromosome microdeletions. *Reprod Med Biol* 2020;19:158-63. <https://doi.org/10.1002/rmb2.12317>
15. Zhang L, Mao J Ming, Li M, et al. Poor intracytoplasmic sperm injection outcome in infertile males with azoospermia factor c microdeletions. *Fertil Steril* 2021;116:96-104. <https://doi.org/10.1016/j.fertnstert.2021.01.025>
16. Zhu YC, Wu TH, Li GG, et al. Decrease in fertilization and cleavage rates, but not in clinical outcomes for infertile men with AZF microdeletion of the Y chromosome. *Zygote* 2015;23:771-7. <https://doi.org/10.1017/S096719941400046X>

17. van Golde RJT. Decreased fertilization rate and embryo quality after ICSI in oligospermic men with microdeletions in the azoospermia factor c region of the Y chromosome. *Hum Reprod* 2001;16:289-92. <https://doi.org/10.1093/humrep/16.2.289>
18. Abur U, Gunes S, Asci R, et al. Chromosomal and Y-chromosome microdeletion analysis in 1,300 infertile males and the fertility outcome of patients with AZFc microdeletions. *Andrologia* 2019;51:e13402. <https://doi.org/10.1111/and.13402>
19. Zhu Y, Wu T, Li G, et al. The sperm quality and clinical outcomes were not affected by sY152 deletion in Y chromosome for oligospermia or azoospermia men after ICSI treatment. *Gene* 2015;573:233-8. <https://doi.org/10.1016/j.gene.2015.07.051>
20. Sasamine K, Mizuta S, Nishiyama R, et al. Fertilization and embryonic development of azoospermia with AZFc microdeletion. *Fertil Steril* 2015;104:e238. <https://doi.org/10.1016/j.fertnstert.2015.07.752>
21. Ishikawa T, Mizuta S, Yamaguchi K, et al. Sperm retrieval rates and clinical outcomes with testicular sperm extraction in relation to the etiology of azoospermia. *Fertil Steril* 2019;112:e288. <https://doi.org/10.1016/j.fertnstert.2019.07.847>
22. Yang X, Li T, Pan X. Analysis of embryo development and pregnancy outcome in patients with microdeletion of AZFC region on y chromosome after ICSI treatment. *Fertil Steril* 2021;116:e346. <https://doi.org/10.1016/j.fertnstert.2021.07.929>
23. Dutta S, Paladhi P, Pal S, et al. Prevalence of Y chromosome microdeletion in azoospermia factor subregions among infertile men from West Bengal, India. *Mol Genet Genomic Med* 2021;9:e1769. <https://doi.org/10.1002/mgg3.1769>
24. Yuen RKC, Merkoulouitch A, MacDonald JR, et al. Development of a high-resolution Y-chromosome microarray for improved male infertility diagnosis. *Fertil Steril* 2014;101:1079-85.e3. <https://doi.org/10.1016/j.fertnstert.2013.12.027>
25. Sabbaghian M, Mohseni Meybodi A, Rafeae A, et al. Sperm retrieval rate and reproductive outcome of infertile men with azoospermia factor c deletion. *Andrologia* 2018;50:e13052. <https://doi.org/10.1111/and.13052>
26. Golin AP, Yuen W, Flannigan R. The effects of Y chromosome microdeletions on in vitro fertilization outcomes, health abnormalities in offspring and recurrent pregnancy loss. *Transl Androl Urol* 2021;10:1457-66. <https://doi.org/10.21037/tau-19-672>
27. Punjani N, Flannigan R, Hart K, et al. Sperm retrieval rates and pregnancy outcomes in men with AZF deletions. *Fertil Steril* 2020;114:e374. <https://doi.org/10.1016/j.fertnstert.2020.08.1106>
28. Nap AW, Van Golde RJT, Tuerlings JHAM, et al. Reproductive decisions of men with microdeletions of the Y chromosome: The role of genetic counselling. *Hum Reprod* 1999;14:2166-9. <https://doi.org/10.1093/humrep/14.8.2166>

---

CORRESPONDENCE: Dr. Gilad Karavani, Division of Urology, Department of Surgery, Mount Sinai Hospital, University of Toronto, Toronto, ON, Canada; Giladk84@gmail.com