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ORIGINAL PAPER

Semen parameters in testicular tumor patients before orchiectomy: What is the impact of testicular tumor stage and histology?

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Summary ***Purpose: To evaluate the influence of testicular cancer histology and stage on sperm parameters in cryopreserved samples collected prior to orchiectomy.***

Materials and methods: We conducted a retrospective analysis of tumor histology, stage and sperm parameters of patients who underwent pre-orchiectomy sperm cryopreservation for testicular cancer between March 2010 and March 2023. The World Health Organization (WHO) 2010 sperm reference values were used to identify patients with subnormal semen parameters and to further categorize patients by sperm alteration. Localized disease was classified as Stage I, while metastatic disease encompassed Stages II and III. Continuous variables were compared using t-test or Mann Whitney U test, and categorical variables using Chi-square and Fisher´s exact test.

Results: A total of 64 patients was identified, 48 (75%) classified as stage I and 16 (25%) classified as stage II/III. No difference was found in semen parameters between patients with seminoma and patients with non-seminoma germ cell tumor (NSGCT). Patients with stage II/III disease had significantly lower percentages of progressive motility (36% vs 53%, p = 0.021) and total motility (60% vs 69%, p = 0.015) than stage I patients.

When categorizing by sperm alterations according to WHO 2010 reference values, patients with stage II/III disease had significantly higher proportions of asthenozoospermia (38% vs 15%, p = 0.048) and teratozoospermia (63% vs 31%, p = 0.027) than stage I patients. Elevated tumor markers were not associated with sperm abnormalities.

Conclusions: Patients with metastatic testicular cancer present with worse sperm quality than patients with localized disease. Sperm cryopreservation should be offered to all patients with testicular cancer, and especially emphasized in patients with metastatic disease.

KEY WORDS: *Testicular cancer; Male infertility; Cryopreservation; Sperm parameters; Orchiectomy.*

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INTRODUCTION

Testicular cancer (TCa) is the most common malignant tumor in young adult men aged 15-40 years, and accounts for about 1% of all neoplasms in men (1). The incidence of TCa has been steadily increasing in recent years, predominantly in developed countries (2, 3).Despite having high cure and long-term survival rates, the fertility burden on survivors is still a major concern. Studies have demonstrated a reduction in semen parameters, notably pre-orchiectomy sperm concentration and total sperm count, as well as a decrease in fertility among patients with TCa compared to their healthy counterparts (4).

Moreover, patients with TCa often need additional treatments which further impair spermatogenesis and fertility. Despite advancements in these treatments, the gonadotoxic effects of chemotherapy and radiation, coupled with the potential for impaired ejaculation and subsequent infertility following *retroperitoneal lymph node dissection* (RPLND), contribute to a consistent decrease in fertility among males undergoing additional therapy post-orchiectomy (5).

In that regard, there is a need for literature investigating the potential role of TCa stage in the fertility potential of these patients. The aim of our study was to evaluate the impact of TCa stage and histology on preorchiectomy semen parameters, as a surrogate for fertility. We also analyzed the role of elevated tumor markers on sperm abnormalities.

MATERIALS AND METHODS

Patient selection

We retrospectively collected data on all patients who consecutively received radical orchiectomy for presumed TCa and who underwent semen cryopreservation before orchiectomy, between March 2010 and March 2023. We excluded patients with bilateral tumors, patients without *germ cell tumor* (GCT) on final pathology, patients who did not undergo semen cryopreservation and patients who underwent cryopreservation after orchiectomy.

The study was approved by the Ethical Committee of our center.

Variables

Our database included data regarding age at diagnosis, *body mass index* (BMI), tumor size, tumor histology, clinical stage, serum tumor markers, namely *alpha-fetoprotein* (α-FP), beta subunit of *human chorionic gonadotropin* (β-hCG) and *lactate dehydrogenase* (LDH), and semen

parameters. Serum tumor markers were considered elevated if they were above the upper normal limit provided by the laboratory (α-FP 0-7 μg/L, β-hCG 0-2 U/L, LDH 135-225 U/L). Semen parameters reviewed included patient´s semen volume, sperm concentration, progressive motility, total motility and morphology. The *World Health Organization* (WHO) 2010 sperm reference values (6) were used to identify patients with subnormal semen parameters and to further categorize patients by sperm alteration (oligozoospermia was defined as < 15 million spermatozoa/mL, asthenozoospermia as < 32% progressive motile spermatozoa and teratozoospermia as < 4% normal forms). Stage I disease was considered localized disease, whereas Stage II/III disease was considered metastatic disease.

Statistical analysis

Continuous variables with normal distribution are presented as mean ± standard deviation and compared by Student´s t-test, while continuous variables with non-normal distribution are presented as medians accompanied by *interquartile ranges* (IQRs) and compared by the Mann-Whitney-U test. Categorical variables are presented as proportions, and comparisons of two categorical variables are performed with the Pearson's Chi-square test and Fisher exact test. A multivariate regression analysis was performed. Statistical analyses were conducted using SPSS Statistics version 27. All tests were two-sided, and statistical significance was set at $p < 0.05$.

Results

A total of 123 patients were diagnosed with TCa at our institution in the studied timeframe. A total of 64 patients (52%) were included (patients who underwent semen cryopreservation before orchiectomy). Of these, 48 patients (75%) classified as stage I and 16 patients (25%) classified as stage II/III. According to histology, 33 patients (52%) were seminoma and 31 patients (48%) were non-seminoma GCT (NSGCT). Baseline characteristics are presented in Table 1. Age, BMI and tumor size were similar between groups. There was a significantly bigger proportion of NSGCT in stage II/III patients as compared to patients in the stage I group (75% *vs* 40%, p = 0.014).

A comparison of sperm parameters between both groups according to histology (seminoma vs NSGCT) is presented in Table 2. All semen parameters were similar between groups, and therefore no difference was observed between patients with seminoma and patients with NSGCT.

A comparison of sperm parameters between both groups according to stage (stage I *vs* stage II/III) is presented in Table 3. In general, all sperm parameters where lower in the stage II/III patients. Stage II/III patients had significantly lower percentage of progressive motility (35.51% in stage II/III *vs* 53.00% in stage I, p = 0.021) and significantly lower percentage of total motility (59.95% in stage II/III *vs* 69.10% in stage I, p = 0.015). Additionally, there was a trend towards lower progressive motility and lower total motility (as absolute numbers) in stage II/III patients, as well as a tendency to a lesser percentage of morphologically normal spermatozoids in this group.

Sperm parameters were further categorized according to the WHO 2010 sperm reference values, and the groups according to stage (I vs II/III) were compared. The results are presented in Table 3. Stage II/III patients had a significantly higher proportion of asthenozoospermia (38% in stage II/III *vs* 15% in stage I, p = 0.048) and a significantly higher proportion of teratozoospermia (63% in stage II/III *vs* 31% in stage I, p = 0.027). Despite not reaching statistical significance, patients in stage II/III

Table 1.
Baseline characteristics of the patients.

	Stage I (n = 48)	Stage II/III (n = 16)	P
Age	31.00 ± 5.88	30.69 ± 12.34	0.923
BMI	24.84 ± 4.33	26.67 ± 4.03	0.506
Tumor size	38.85 ± 21.59	42.88 ± 23.07	0.528
Histology			
Seminoma	29 (60%)	4 (25%)	0.014
NSCGT	19 (40%)	12 (75%)	

BMI: body mass index; NSGCT: non-seminoma germ cell tumor.

Table 2.
Comparison of preorchiectomy sperm parameters according to tumor histology.

	Total (n = 64)	Seminoma (n = 33)	NSGCT (n = 31)	p
Semen volume (mL)	2.95 ± 1.60	3.09 ± 1.56	2.79 ± 1.66	0.468
Sperm concentration (millions/mL)	31.50 (10.48-70.00)	37.00 (15.50-84.50)	28.00 (9.00-66.00)	0.330
Progressive motility (millions/mL)	19.21 (3.98-39.31)	22.08 (4.11-42.88)	11.50 (3.38-33.53)	0.295
Progressive motility (%)	48.63 ± 22.20	50.61 ± 23.36	46.52 ± 21.07	0.465
Total motility (millions/mL)	21.83 (6.35-51.32)	26.91 (7.00-54.20)	16.40 (5.75-43.20)	0.347
Total motility (%)	65.55 (52.45-77.75)	67.00 (52.95-79.80)	64.50 (52.30-74.50)	0.444
Normal morphology (millions/mL)	1.56 (0.29-4.83)	1.70 (0.52-5.51)	1.55 (0.26-4.20)	0.493
Normal morphology (%)	4.00 (2.25-7.00)	5.00 (3.00-7.00)	4.00 (2.00-8.00)	0.866

NSGCT: non-seminoma germ cell tumor.

Table 3.
Comparison of preorchiectomy sperm parameters according to tumor stage.

	Total (n = 64)	Stage I (n = 48)	Stage II/III (n = 16)	p
Semen volume (mL)	2.95 ± 1.60	3.01 ± 1.71	2.75 ± 1.28	0.578
Sperm concentration (millions/mL)	31.50 (10.48-70.00)	33.50 (15.25-73.00)	23.00 (0.03-47.00)	0.129
Progressive motility (millions/mL)	19.21 (3.98-39.31)	20.79 (5.33-42.48)	9.65 (0.01-30.84)	0.077
Progressive motility (%)	48.63 ± 22.20	53.00 ± 19.29	35.51 ± 25.67	0.021
Total motility (millions/mL)	21.83 (6.35-51.32)	24.43 (8.37-54.06)	12.45 (0.01-36.32)	0.088
Total motility (%)	65.55 (52.45-77.75)	69.10 (55.43-79.25)	59.95 (5.00-66.68)	0.015
Normal morphology (millions/mL)	1.56 (0.29-4.83)	1.63 (0.50-5.40)	0.80 (0.01-4.15)	0.195
Normal morphology (%)	4.00 (2.25-7.00)	5.00 (3.00-7.00)	3.00 (0.00-7.50)	0.102

Table 4.
Comparison of categories of preorchiectomy sperm alterations according to the WHO 2010 sperm reference values and to tumor stage.

	Stage I (n = 48)	Stage II/III (n = 16)	P
Oligozoospermia (< 15 millions/mL) n (%)	11 (23%)	7 (44%)	0.108
Asthenozoospermia (< 32% progressive motility) n (%)	7 (15%)	6 (38%)	0.048
Teratozoospermia (< 4% normal forms) n (%)	15 (31%)	10 (63%)	0.027
Azoospermia (complete absence of spermatozoa)	2 (4%)	1 (6%)	1.000
Any abnormality n (%)	21 (44%)	10 (63%)	0.194

Table 5.
Multivariate regression analysis for the role of elevated tumor markers as predictors of any abnormality in sperm parameters in patients with testicular cancer.

Covariate	OR	95% CI	P
Elevated α-FP	2.859	0.693, 11.787	0.146
Elevated β-hCG	0.486	0.125, 1.890	0.297
Elevated LDH	2.748	0.895, 8.436	0.097

CI: confidence interval; OR: odds ratio.

group also had higher percentage of oligozoospermia (44% in stage II/III *vs* 23% in stage I, p = 0.108). The proportion of patients with azoospermia was similar between groups.
On multivariate regression analysis, elevated tumor markers (AFP, β-hCG and LDH) were not associated with abnormalities in sperm parameters (Table 5).
Three patients (5%) used their cryopreserved semen for *assisted reproduction techniques* (ART); two patients had a seminoma and one patient had a NSGCT. Two patients had stage I disease and one patient had stage II/III disease. Non-cryopreserved paternity data was unavailable.

Discussion

Testicular cancer can play a major role in infertility. Analysis of cryopreservation data demonstrates that normal sperm quality is observed in less than half of men with TCa before treatment, and 10-35% suffer from infertility. Fertility may be impacted by TCa through a multitude of axis, including intrinsic infertility associated with the testicular dysgenesis syndrome, the testicular tumor local effect, and systemic effects of hormones secreted by the tumor (7). There is a paucity of literature on the impact of tumor stage and histology in sperm outcomes of patients with TCa, with a previous study failing to demonstrate any relation between these factors (8). To the best of our knowledge, this is the largest series on the impact of tumor stage and histology on sperm quality. In our study, we demonstrated that patients with metastatic disease (stage II/III) have worse sperm parameters than patients with localized disease (stage I), namely lower progressive and total motility and a higher proportion of asthenozoospermia and teratozoospermia. Tumor histology showed no influence on sperm parameters in individuals with TCa and elevated tumor markers were not associated with sperm abnormalities.
TCa can have local adverse effects on spermatogenesis through local growth of the testicular tumor. The occurrence of spermatogenesis defects is most prominent in the vicinity of malignant tumors (9), a trend not observed in benign tumors (10). Larger tumor size is correlated with lower levels of spermatogenesis in the ipsilateral testis (11). In fact, testicular tumors > 4 cm exhibit a significant decrease in spermatogenesis compared to tumors < 4 cm (12). TCa can also exert deleterious effects on sperm quality through secreted hormones. Elevated serum levels of α-FP or β-hCG can disrupt the physiologic feedback mechanism of the *hypothalamic-pituitary-gonadal* (HPG) axis, which directly regulates testicular function, and hence spermatogenesis (13). Disruptions in the levels of *luteinizing hormone* (LH), *follicle-stimulating hormone* (FSH), and testosterone are associated with spermatogenesis and a reduction in sperm concentration (5). It has also been demonstrated that any kind of cancer, including TCa, may lead to worse sperm quality, with sperm parameters below the WHO reference values; causative factors have been hypothesized to be a rise in pro-inflammatory circulating cytokines and interleukins (14). Moreover, testicular cancer is associated with elevated oxidative stress and DNA fragmentation, both potentially contributing to decreased fertility (15, 16). Despite these detrimental effects of testicular tumor on sperm quality, orchiectomy does not result in improvement of spermatogenesis; instead, it further deteriorates sperm quality. *Petersen et al.* (17) demonstrated a reduction in sperm concentration, total sperm count and serum inhibin B levels in patients who underwent radical orchiectomy for TCa, as well as de novo azoospermia in 9% of patients. A more recent multicenter study evaluating pre and post orchiectomy semen samples concluded that sperm concentration significantly decreased after orchiectomy (18). These studies highlight the importance of cryopreservation, which should ideally be done before orchiectomy, since there is currently no evidence that expedited radical orchiectomy translates into oncological benefit (19). Furthermore, in this setting we might find patients who are amenable to surgical *testicular sperm extraction* (TESE) at the time of orchiectomy (onco-TESE) (7).
Patients with TCa may be subject to additional treatments other than radical orchiectomy, and these treatments may further impair the fertility of these patients.
Chemotherapy in TCa is dependent on platinum-based agents (cisplatin and carboplatin), which may be combined with other agents, such as bleomycin and etoposide (7). By penetrating the testis blood barrier and targeting actively dividing cells, chemotherapy significantly impairs spermatogenesis, resulting in oligozoospermia and azoospermia. There is a well-established correlation between the failure to conceive and the cumulative dose of chemotherapy (20, 21). In a study of 1191 TCa survivors, higher doses of chemotherapy translated into a significant impairment of spermatogenesis, resulting in only 29% of patients being normozoospermic after 11

years of follow-up (22). There is potential for recovery of spermatogenesis, in a time-dependent manner, with 48% and 80% of patients with normal pretreatment sperm concentrations recovering spermatogenesis by 2 and 5 years, respectively (23). Radiation therapy is another modality for treatment of TCa. It may be applied to retroperitoneal metastases, in which case the testes are exposed to scatter radiation only, generally at low doses which protect fertility, or directly to the testes, in case of germ cell neoplasia in situ; in the latter case, with radiation doses of 16-20 Gy frequently used, there are high rates of irreversible azoospermia (5). Finally, RPLND is another modality of additional treatment in TCa. RPLND might cause retrograde ejaculation or anejaculation due to damage of lumbar plexus and splenic nerves, which renders the patients infertile. Despite the very high rates of ejaculatory function preservation with modern nerve sparing techniques, fibrosis might still make this technique difficult, resulting in substantial rates of anejaculation (7). Our study concluded that patients with metastatic disease (stage II/III) have significantly worse semen parameters than patients with localized disease (stage I); these findings underscore the need for cryopreservation especially in metastatic patients, and a greater emphasis should be placed on cryopreservation in this subset of patients, given that treatment of these patients with one or more of these modalities of adjuvant treatment is generally the rule.

Only a few studies have evaluated the potential role of histology and stage on sperm quality (8, 24, 25). *Fraietta et al.* (24) reviewed the data of 100 patients with TCa and analyzed the patients' sperm quality according to histologic type (seminoma *vs* NSGCT) and concluded that patients with seminoma had a higher number of motile and morphologically normal spermatozoids than those with NSGCT. A more recent study by *Badia et al.* (8) concluded that histology did not influence semen parameters, as these were similar between patients with seminoma and NSGCT. This aligns with the results of our study, where we showcased that patients with distinct histology exhibited comparable semen parameters. As for the role of stage, *Halstuch et al.* (25) demonstrated that severe oligozoospermia (< 5 million/mL) was more common in metastatic than non-metastatic NSGCT. The same conclusion could not be drawn for patients with seminoma. *Badia et al.* (8) also evaluated the role of stage on semen parameters, and again concluded that semen parameters were similar in TCa patients with localized and metastatic disease. These results are conflicting with the results of our study. We did demonstrate differences between different stages, with metastatic disease showing less progressive and total motility and a higher proportion of asthenozoospermia and teratozoospermia, and this was demonstrated for patients with stage II/III irrespective of histology. Rates of oligozoospermia were, however, similar between groups, despite a tendency towards less oligozoospermia in localized disease. Moreover, despite the previously noted effect of secreted hormones, we did not demonstrate and association between elevated tumor markers and sperm abnormalities. We hypothesize that it is the systemic inflammatory process of metastatic testicular cancer, rather than the hormonal burden of elevated tumor markers, that might be responsible for a detrimental effect on spermatogenesis.

Semen cryopreservation should be discussed and offered to all patients with TCa, ideally before orchiectomy to maximize chances of fertility, and if not done before orchiectomy should be pursued prior to chemotherapy or radiation therapy (26). Despite these recommendations, only 24-30% of TCa patients undergo sperm cryopreservation (24, 27-29). In our study, 64 patients (52%) out of 123 patients diagnosed with TCa underwent semen cryopreservation before orchiectomy, with an additional 12 (10%) patients undergoing semen cryopreservation after orchiectomy and before adjuvant treatments, which translated into a total sperm cryopreservation rate of 62%. The timing of cryopreservation is of importance, as noted by the work of *Rives et al.* (18), in which they demonstrated that mean sperm concentration before orchiectomy was significantly higher than after surgery ($32x10^6$/mL *vs* $24x10^6$/mL). Moreover, as previously noted, semen cryopreservation before orchiectomy has the potential for selection of patients for onco-TESE, which is another advantage (7). It is also worth noting that despite advancements in ART in the last years, sperm cryopreservation remains the most cost-effective strategy for fertility preservation (30).

Therefore, it is the authors' opinion that semen cryopreservation should be offered in every patient with TCa, if possible before orchiectomy, and in light of the results of our study a heightened emphasis should be placed on patients with metastatic disease, as these display overall worse sperm quality and will most probably be subject to additional treatments.

Our study has several limitations that deserve acknowledgment. The main shortcomings come from its retrospective nature. We could only analyze the information on the medical records, and as a consequence the success rate of pregnancies from cryopreserved sperm samples could not be evaluated. Furthermore, we used decreased semen parameters as a surrogate for decreased fertility, even though a direct relationship between the two hasn't been established. Additionally, despite our institution being a high-volume referral center for TCa, the relatively short sample size of 64 patients may limit statistical power. In that sense, further studies, preferably prospective and multicenter, are needed in the future to support our findings.

Conclusions

Testicular cancer has the potential for infertility. Patients with metastatic testicular cancer (stage II/III) have worse sperm quality, namely less progressive and total motility of spermatozoids and a bigger proportion of asthenozoospermia and teratozoospermia than patients with localized testicular cancer (stage I). Histology appears to play no major role in sperm quality and elevated tumor markers were not shown to be associated with sperm abnormalities. Sperm cryopreservation should be offered to all patients with testicular cancer, ideally before orchiectomy, and this should be further emphasized in patients with metastatic disease. Further studies are recommended to validate these findings.

References

1. Park JS, Kim J, Elghiaty A, Ham WS. Recent global trends in testicular cancer incidence and mortality. Medicine. 2018; 97:e12390.

2. Nigam M, Aschebrook-Kilfoy B, Shikanov S, Eggener S. Increasing incidence of testicular cancer in the United States and Europe between 1992 and 2009. World J Urol. 2015; 33:623-31.

3. Gurney JK, Florio AA, Znaor A, et al. International Trends in the Incidence of Testicular Cancer: Lessons from 35 Years and 41 Countries. Eur Urol. 2019; 76:615-23.

4. Djaladat H, Burner E, Parikh PM, et al. The Association Between Testis Cancer and Semen Abnormalities Before Orchiectomy: A Systematic Review. J Adolesc Young Adult Oncol. 2014; 3:153-9.

5. Parekh N V, Lundy SD, Vij SC. Fertility considerations in men with testicular cancer. Transl Androl Urol. 2020; 9(Suppl 1):S14-23.

6. Cooper TG, Noonan E, von Eckardstein S, et al. World Health Organization reference values for human semen characteristics. Hum Reprod Update. 2010; 16:231-45.

7. Moody JA, Ahmed K, Yap T, et al. Fertility managment in testicular cancer: the need to establish a standardized and evidence-based patient-centric pathway. BJU Int. 2019; 123:160-72.

8. Badia RR, Patel A, Chertack N, et al. Impact of testicular cancer stage on semen parameters in patients before orchiectomy. Urol Oncol. 2023; 41:151.e11-151.e15.

9. Ho GT, Gardner H, DeWolf WC, et al. Influence of testicular carcinoma on ipsilateral spermatogenesis. J Urol. 1992; 148:821-5.

10. Ho GT, Gardner H, Mostofi K, et al. The effect of testicular nongerm cell tumors on local spermatogenesis. Fertil Steril. 1994; 62:162-6.

11. Choy JT, Wiser HJ, Bell SW, et al. Predictors of spermatogenesis in orchiectomy specimens. Urology. 2013; 81:288-92.

12. Shoshany O, Shtabholtz Y, Schreter E, et al. Predictors of spermatogenesis in radical orchiectomy specimen and potential implications for patients with testicular cancer. Fertil Steril. 2016; 106:70-4.

13. Coward RM, Kovac JR, Smith RP, Lipshultz LI. Fertility Preservation in Young Men Treated for Malignancies: Options for Precancer Treatment. Sex Med Rev. 2013; 1:123-34.

14. Peluso G, Tisato V, Singh AV, et al. Semen Cryopreservation to Expand Male Fertility in Cancer Patients: Intracase Evaluation of Semen Quality. J Pers Med. 2023; 13:1654.

15. Said TM, Tellez S, Evenson DP, Del Valle AP. Assessment of sperm quality, DNA integrity and cryopreservation protocols in men diagnosed with testicular and systemic malignancies. Andrologia. 2009; 41:377-82.

16. Kumar K, Lewis S, Vinci S, et al. Evaluation of sperm DNA quality in men presenting with testicular cancer and lymphoma using alkaline and neutral Comet assays. Andrology. 2018; 6:230-5.

17. Petersen PM, Skakkebaek NE, Rørth M, Giwercman A. Semen quality and reproductive hormones before and after orchiectomy in men with testicular cancer. J Urol. 1999; 161:822-6.

18. Rives N, Perdrix A, Hennebicq S, et al. The semen quality of 1158 men with testicular cancer at the time of cryopreservation: results of the French National CECOS Network. J Androl. 2012; 33:1394-401.

19. Emmanuel A, Kanthabalan A, Alexander C, et al. Expedited Radical Orchidectomy for Testicular Cancer: Compromising Fertility Outcomes Without Oncological Benefit? Eur Urol. 2021; 80:766-7.

20. Puscheck E, Philip PA, Jeyendran RS. Male fertility preservation and cancer treatment. Cancer Treat Rev. 2004; 30:173-80.

21. Brydøy M, Fosså SD, Klepp O, et al. Paternity following treatment for testicular cancer. J Natl Cancer Inst. 2005; 97:1580-8.

22. Brydøy M, Fosså SD, Klepp O, et al. Sperm counts and endocrinological markers of spermatogenesis in long-term survivors of testicular cancer. Br J Cancer. 2012; 107:1833-9.

23. Lampe H, Horwich A, Norman A, et al. Fertility after chemotherapy for testicular germ cell cancers. J Clin Oncol. 1997; 15:239-45.

24. Fraietta R, Spaine DM, Bertolla RP, et al. Individual and seminal characteristics of patients with testicular germ cell tumors. Fertil Steril. 2010; 94:2107-12.

25. Halstuch D, Shtabholtz Y, Neufeld S, et al. The absence of spermatogenesis in radical orchiectomy specimen is associated with advanced-stage nonseminomatous testicular cancer. Urol Oncol. 2021; 39:838.e15-838.e20.

26. Patrikidou A, Cazzaniga W, Berney D, et al. European Association of Urology Guidelines on Testicular Cancer: 2023 Update. Eur Urol. 2023; 84:289-301.

27. Ping P, Gu BH, Li P, et al. Fertility outcome of patients with testicular tumor: before and after treatment. Asian J Androl. 2014; 16:107-11.

28. Sonnenburg DW, Brames MJ, Case-Eads S, Einhorn LH. Utilization of sperm banking and barriers to its use in testicular cancer patients. Support Care Cancer. 2015; 23:2763-8.

29. Magelssen H, Haugen TB, von Düring V, et al. Twenty years experience with semen cryopreservation in testicular cancer patients: who needs it? Eur Urol. 2005; 48:779-85.

30. Gilbert K, Nangia AK, Dupree JM, et al. Fertility preservation for men with testicular cancer: Is sperm cryopreservation cost effective in the era of assisted reproductive technology? Urol Oncol. 2018; 36:92.e1-92.e9.

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