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The habits of European urologists in the field of cryopreservation before the urological cancers treatment

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Abstract

Introduction: Treatments against urogenital cancers frequently have fertility side-effects. The strategy to preserve fertility after oncologic treatments is still a matter of debate with a lack of evidence and international guidelines. The aim of this study is to investigate fertility preservation practices before urogenital cancer treatments and to compare national habits.

Material and methods: An online anonymous survey was submitted from January to June 2021 to six European urological societies. The 31-items questionnaire included questions about demography, habits of evaluation, and management of fertility preservation in case of urogenital cancer treatments.

Results: Two hundred twenty-eight urologists from six urological societies in five different countries (Belgium, The Netherlands, Luxembourg, France, Finland) filled out the survey.

Three quarter (74%; $n = 166$) usually propose a cryopreservation before orchidectomy.

In case of oligo/azoo-spermia, the technique performed for the sperm extraction during orchidectomy varies among the sample: 70.5% ($n = 160$) of the responders do not perform a Testicular Sperm Extraction (TESE) nor a Percutaneous Epididymal Sperm Aspiration (PESA).

The cryopreservation for prostate cancer treatments is never proposed in 48.17% ($n = 105$) of responders but conversely it is always proposed in 5.05% ($n = 11$).

The cryopreservation before bladder cancer treatments is not commonly proposed (67.5%, $n = 154$).

Conclusion: Our study showed variable country specific tendencies in terms of fertility preservation in the period of treatment of urological cancers. These differences seem to be related to national guidelines recommendations. Standardization of international guidelines is urgently needed in the field of fertility for urological cancer patients.

KEYWORDS
bladder cancer, male fertility, prostate cancer, testicular cancer

1 | INTRODUCTION

In the past few decades, therapeutic advances have improved the long-term survival and prognoses of patients with urogenital cancers.[1] Multimodal cancer treatments are frequently aggressive, and side-effects can include infertility. Several treatments can adversely affect spermatogenesis such as radiotherapy or chemotherapy[1] and some surgical procedures, like retroperitoneal lymphadenectomy, can impair ejaculation.[2]

It is not always possible to predict the treatment toxicity due to the patient susceptibility, patient baseline fertility situation, drug characteristics—gonadotoxic effects and type of malignancy.[1] Some patients will become definitively azoospermic or, conversely, will recover partially or totally their spermatogenesis after the treatment.[3]

For these reasons, the Ethics Committee of American Society for Reproductive Medicine and the American Society of Clinical Oncology have recognized the importance to discuss with patients the potential effect of cancer treatments on fertility, to present options for fertility preservation and to address for fertility preservation.[4,5] This is of particular interest for young patients who have not had paternity projects yet and in particular considering that testicular cancer (TC) is the most frequent cancer in young men (incidence between 15–35 years) who have often long-term survival expectation.[6,7] The European Association of Urology (EAU) recommends cryopreservation for TC and suggests to propose semen preservation and fertility assessment, but no recommendation is given for bladder or prostate cancer.[8]

Currently, the only way to efficiently preserve the reproductive potential in adult or adolescent male patients remains sperm cryopreservation. Various assisted reproductive techniques are available. The insemination is possible but in vitro fertilization or intracytoplasmic sperm injection can be preferred due to possible reduction in sperm mobility after freeze-thawing. It is a quiet simple and effective way of preserving fertility potential even in oncologic patients with poor semen characteristics.

We performed a European study about daily oncological practice and fertility management during oncologic treatment. The aim was to assess the information rates and the implementation of cryopreservation before urogenital cancer management (testicular, bladder, prostate) by urologists.

2 | MATERIAL AND METHODS

From January to June 2021, we offered to participate in an online anonymous survey to different European urological societies from 12 countries: Ireland, United Kingdom, Sweden, Finland, Denmark, The Netherlands, Belgium, France, Spain, Portugal, Italy, Germany. Six scientific societies accepted to submit the survey to their members by e-mail: The Société Belge d'Urologie (SBU), Belgische Vereniging voor Urologen (BVU), the Association Française d'Urologie (AFU), the Société d'Andrologie de Langue Française (SALF), The Nederlandse Vereniging voor Urologie (NVU), and the Finnish Urological Society (FUS).

The 31-items questionnaire included seven demographic questions about urologists: country, region, age, status, gender, sub-specialty, and type of center. There were five questions about cryopreservation and

vasectomy. There were five questions about cryopreservation during vasectomy reversal. It included 14 questions about urogenital cancers (testicular, prostate, and bladder cancer) and fertility preservation: number of each cancer, proposition of cryopreservation before management, timing of the cryopreservation for TC, reason of the timing (Table 1). The section concerning cryopreservation and vasectomy or vaso-vasostomy was discussed in a previous article.[9]

2.1 | Statistical analysis

Statistical analyses were performed using SPSS software version 25 (SPSS Corp., Somers, New York). The p-value < 0.05 was considered statistically significant. Binary variables were expressed as count and proportion. Comparison of parameters between countries were made using the Pearson's chi-squared test, Fisher's exact test, and binomial test when possible. Comparison between urologists with or without andrological training was made using only Pearson's chi-squared test.

3 | RESULTS

3.1 | Population

Two hundred and twenty-eight urologists from five countries responded to the survey: France (58.3%; $n = 133$), Belgium (29.4%; $n = 67$), The Netherlands (6.6%; $n = 15$), Luxembourg (3%; $n = 7$), and Finland (2.6%; $n = 6$). The median age of the population was 47 years (28 – 86). More than 80% were men (83.5%; $n = 193$). Fifteen percent ($n = 35$) worked in a University Hospital, 34% in a public center ($n = 79$) and 48% in a private center ($n = 111$). Fourteen percent were specialized in andrology ($n = 32$: 22 from France, 5 from Belgium and 5 from The Netherlands).

3.1.1 | Testicular cancer

Orchidectomy, in average, is performed in 5.1 cases per year, (interval from 0 to 40 per year) by urologists. A large majority (96.5%; $n = 223$) of urologists is in favor of cryopreservation in the context of TC. Three quarter (74%; $n = 166$) usually propose a cryopreservation before orchidectomy. The justification is in 55% ($n = 124$) the better quality of sperm before orchidectomy, in 58% the guideline recommendations ($n = 96$) and in 31% ($n = 51$) the risk of chemotherapy toxicity. A quarter (26%; $n = 58$) would propose a cryopreservation before chemotherapy but the majority (66%; $n = 38$) only after the orchidectomy because of the short period of time between the diagnosis and the operation; 45% ($n = 26$) because of the sperm banking delay problems, 38% ($n = 22$) because of the chemotherapy toxicity of and 10% ($n = 6$) thinks that sperm quality will be better after orchidectomy.

A cryopreservation is proposed more often before orchidectomy if the urologist is focused on andrology ($p = 0.021$) or on oncologic urology ($p = 0.029$) and if the clinician is younger than 50 years old ($p = 0.0167$).

A cryopreservation is proposed more often after orchidectomy in Belgium (57.6%; $n = 38$) or Luxemburg (50%; $n = 3$) than in France (11.5%; $n = 15$), Finland (16.7%; $n = 1$) or in The Netherlands (6.7%; $n = 1$) ($p < 0.001$) (Table 2). There was no statistical difference according to the number of orchidectomy/year between countries (Table 2).

France (59%) and The Netherlands (67%) justify the cryopreservation by following the guidelines compared to the other three countries (Belgium 23.9%; Luxembourg 28.6%; Finland 33.3%) ($p < 0.001$) (Table 2).

The delay to access the fertility preservation does not explain the cryopreservation after orchidectomy for andrologists (0%) but well for 15% ($n = 29$) of non-andrologists ($p = 0.19$). The accessibility to the fertility center is the explanation in 23.8% of Belgian urologists, 28.6% in Luxembourg, and 8.5% in France but not in The Netherlands (0%) and Finland (0%) ($p = 0.007$) (Table 2).

The sperm quality is considered as better quality after the orchidectomy for 7.5% ($n = 5$) of the Belgian responders, 1.77% ($n = 1$) in France and 0% in other countries (no significative difference; $p = 0.075$). For this variable 50% of uro-oncologists were represented but no andrologists. Half of the responders think that the quality of sperm is better before orchidectomy (44.9%; $n = 101$) without significant difference for andrologists (56.2%; $p = 0.16$) or uro-oncologists (42.5%; $p = 0.6$). Urologists from France and The Netherlands think significantly more that the sperm quality is better before orchidectomy than after in comparison with the three other countries ($p = 0.0055$).

Postponing the orchidectomy for a week could be harmful on an oncological point of view for 23.3% of the responders and significantly more for oncologist (36.3%; $n = 29$, $p = 0.0006$) but significantly less in France (12.8%; $n = 17$) than in other European countries ($p = 0.0002$)

In case of oligo/azoo-spermia, the technique performed for the sperm extraction during orchidectomy varies among the sample: 70.5% ($n = 160$) of the responders do not perform a Testicular Sperm Extraction (TESE) nor a Percutaneous Epididymal Sperm Aspiration (PESA), 17.2% ($n = 39$) perform only a TESE and 12.3% ($n = 28$) a TESE and PESA. There is a significant difference between urologists without andrology practice and andrologists who practice much more a TESE extraction during the orchidectomy : 12.8% versus 43.8% ($p < 0.0001$) (Table 2). No difference was found between the two populations for TESE with PESA (12.3% for urologists and 12.5% for andrologists) (Table 2). The results show that the combination TESE + PESA is much more used in The Netherlands (40%, $n = 6$) and France than in other countries. Three countries performed only TESE (Finland 33.3%, Luxembourg 28.6%, and Belgium 26.9%). Cryopreservation practice varies between countries ($p = 0.003$).

TESE or combination of TESE + PESA are significatively more implemented when the number of orchidectomy/year is > 10: 17.1% versus 60% and 11.1% versus 40%, respectively ($p = 0.0073$).

When an extraction is done, it can be done in both testicles, in the tumor-bearing testis or in the contralateral one. Among urologists who perform this technique (51%, $n = 116$), 19% prefer to do it in the

TABLE 1 Online survey questionnaire.

Cryopreservation at the time of urogenital cancers, vasectomy and vasectomy reversal	
Epidemioly	
Where do you practice urology?	Country
What is your status?	Urologist, Andrologist, other
What is your specialty?	General urology, Onco-urology, Functional urology, Andrology, Pediatric urology, endourology, other
How old are you?	Age
What gender?	Man, Woman
In what type of center do you practice urology?	University Center, Public peripheral center, Private peripheral center
Oncology	
Approximately how many oncologic orchidectomy do you perform per year?	Number/year
Do you perform cryopreservation for TC?	Yes/No
When do you perform cryopreservation for TC?	Before orchidectomy; after orchidectomy and before chemotherapy; at the start of chemotherapy; after chemotherapy; other
Why do you perform cryopreservation at this specific moment?	- Because it is recommended by the guidelines - Because I think that orchidectomy is more urgent than the fertility - By habits - Because of the delay to get access to fertility preservation - Because I think that quality of sperm will be better AFTER orchidectomy - Because I think that quality of sperm is better BEFORE orchidectomy - Because I think that chemotherapy is NOT TOXIC for fertility - Because I think that chemotherapy is TOXIC for fertility - Other
What is the most urgent for you?	Orchidectomy, Fertility preservation
Do you think that postponing the orchiectomy for a week to perform cryopreservation could be harmful from an oncological point of view?	Yes/No
In case of oligo/azoo-spermia, which technique do you use for sperm extraction during orchidectomy?	- No extraction - Testicular Sperm Extraction (TESE) - TESE + Percutaneous Epididymal Sperm Aspiration (PESA) - Other
In which testis do you perform sperm extraction?	- Both - In contra-lateral testis only - In the tumor-bearing testicle only
About how many significant prostate cancers do you diagnose per year?	Number/year
Do you discuss cryopreservation with your patient with significant prostate cancer?	- Always - Rarely, only if it is a patient < 50 years old - Rarely, only if it is a patient < 55 years old - Never
What proportion of your patients benefit from cryopreservation before prostate cancer treatment?	0%; 1%–10%; 10%–20%; 20%–30%; other
About how many muscle invasive bladder cancers do you diagnose per year?	Number/year
Do you discuss cryopreservation with your patient with muscle invasive bladder cancer?	- Always - Rarely, only if it is a patient < 50 years old - Rarely, only if it is a patient < 55 years old - Never
What proportion of your patients benefit from cryopreservation for bladder cancer before treatment?	0%; 1%–10%; 10%–20%; 20%–30%; other
Vasectomy/Vaso-vasostomy: The section concerning cryopreservation and vasectomy or vasovasostomy was discussed in a previous article (9).	

TABLE 2 Study results.

	Cryopreservation before orchidectomy (*n*)	Cryopreservation after orchidectomy (*n*)	p-value	Odds ratio
<50 years old	102	26	0.0167	/
>50 years old	33	15		
No andrology practice	137	55	0.021	0.258 (0.08–0.88)
Andrology practice	29	3		
No oncological practice	115	31	0.029	1.96 (1.06–3.62)
Oncological practice	51	27		
Belgium	28	38	<0.001	/
Luxembourg	3	3		
France	116	15		
Finland	5	1		
The Netherlands	14	1		
	Timing of cryo not according to the guidelines (n)	**Timing of cryo according to the guidelines (n)**	***p*-Value**	**Odds ratio**
Belgium	51	16	<0.001	/
Luxembourg	5	2		
France	53	76		
Finland	4	2		
The Netherlands	5	10		
	Delay to access to fertility preservation is not an obstacle (n)	**Delay to access to fertility preservation is an obstacle (n)**	**p-value**	**Odds ratio**
No andrology practice	164	29	0.019	0
Andrology practice	32	0		
Belgium	51	16	0.007	/
Luxembourg	5	2		
France	119	11		
Finland	6	0		
The Netherlands	15	0		
	Sperm better before orchidectomy (*n*)	**Sperm NOT better before orchidectomy (*n*)**	***p*-Value**	**Odds ratio**
No andrology practice	110	83	0.16	1.7 (0.8–3.6)
Andrology practice	14	18		
No oncological practice	78	67	0.6	0.86 (0.5–1.5)
Oncological practice	46	34		
Belgium	44	23		/
Luxembourg	5	2		
France	62	68		
Finland	5	1		
The Netherlands	8	7		
	Postponing orchidectomy is not harmful (*n*)	**Postponing orchidectomy is harmful (*n*)**	***p*-Value**	**Odds ratio**
No oncological practice	124	24	0.0008	2.94 (1.56–5.52)
Oncological practice	51	29		
Belgium	43	24	0.0002	/

(Continues)

TABLE 2 (Continued)

	Postponing orchidectomy is not harmful (*n*)	Postponing orchidectomy is harmful (*n*)	*p*-Value	Odds ratio
Luxembourg	5	2		
France	116	17		
Finland	4	2		
The Netherlands	7	8		

	No extraction (*n*)	TESE (*n*)	TESE + PESA (*n*)	*p*-Value	Odds ratio
No andrological practice	146	25	24	<0.0001	/
Andrological practice	14	14	4		
Belgium	42	18	7	0.003	/
Luxembourg	5	2	0		
France	103	14	15		
Finland	4	2	0		
The Netherlands	6	3	6		
⩽10 orchidec/year	143	34	22	0.0073	/
>10 orchidec/year	0	3	2		

	No sperm extraction (*n*)	Contro-lateral testis extraction (*n*)	Both testis extraction (*n*)	Tumor-bearing extraction (*n*)	*p*-Value	Odds ratio
Belgium	22	28	8	9	0.0266	/
Luxembourg	4	2	0	1		
France	74	31	19	9		
Finland	4	2	0	0		
The Netherlands	8	1	3	3		

tumor bearing testis, 55.1% in the contralateral one, and 25.9% in both testicles. There is a significant difference between andrologists who perform more bilateral extraction (43.5% vs. 21.5%) or more tumor-bearing extraction (21.7% vs. 18.3%) and less contralateral extraction only (34.8% vs. 60.2%) ($p = 0.0028$). There was no statistically significant difference considering oncological sub-specialties. There was a difference among countries with more contralateral extraction rates in Belgium and tumor-bearing extraction rates in The Netherlands ($p = 0.0266$) (Table 2).

3.1.2 | Prostate cancer

The cryopreservation for prostate cancer treatments is never proposed in 48.17% ($n = 105$) of responders but conversely it is always proposed in 5.05% ($n = 11$). It is only proposed for patients < 50 years old in 29.82% ($n = 65$) or proposed for patients < 55 years old in 16.97% ($n = 37$). There is no difference between andrologists or oncological specialists but there are different practices among countries ($p = 0.0346$). The French specialists propose significantly more cryopreservation before prostate cancer treatments: 30.1% ($n = 40$) for patients < 50 years old, 24.1% ($n = 32$) for patients < 55 years old and 3% ($n = 4$) for every patient respectively. The second country for cryopreservation proposal is The Netherlands (46.7%, $n = 7$), then Belgium (43.3%, $n = 29$) Finland (33.33, $n = 2$), and Luxembourg (28.6%, $n = 2$). The proportion of patients that will benefit from cryopreservation before treatment is evaluated as 0% for the majority of the responders (75.4%, $n = 172$), around 1%–10% of the patients in 22.8% of the responders ($n = 52$) and 10%–20% of the patients in 1.3% ($n = 3$). The evaluation of the cryopreservation's proportion is not influenced by andrological or oncological practice in each country.

3.2 | Bladder cancer

The cryopreservation before bladder cancer treatments is commonly not proposed (67.5%, $n = 154$). A quarter propose a preservation for patients < 50 years old (29%, $n = 66$), 1.3% for patients < 55 years old ($n = 3$) and 2.2% for every patient ($n = 5$). The andrologists have significantly more cryopreservation discussions (50% versus 29.6%). The proportion of cryopreservation in this setting represents 1%–10% of patients in 9.8% of the responders ($n = 22$) and 10%–20% of the patients in 1% ($n = 2$), respectively. The proportion of cryopreservation is significatively more important for andrologists

than urologists: 22% versus 7.8% and 3.1% versus 0.5%, respectively ($p = 0.015$).

4 | DISCUSSION

The TC, although representing only 1% of all cancers, is the most common cancer in men of reproductive age. With a 10-year survival rate of 98% for non-metastatic forms (73% at 5 years), fertility preservation and management is a major issue.[8]

The issue of sperm cryopreservation in case of testicular neoplasia seems to be well acquired in our sample but the timing of sperm banking and the technique seems less well defined. A quarter of responders perform the preservation after the orchidectomy. The explanation is the orchidectomy's urgency, especially for onco-urologists. There is no precise time limit in the international guidelines for testicular surgery as long as the time to orchidectomy remains reasonable.[8] However, there is an important focus on fertility preservation.[8,10,11] The urologists from France and The Netherlands propose more cryopreservation before orchidectomy. Those results could be related to an easier accessibility to cryopreservation centers in those countries, like the "Centre de conservation des oeufs et du sperme" (CECOS) in France.[12] The justification for sperm banking before the orchidectomy is also more framed by the guidelines follow up in those two countries.[13,14]

The risk factors of TC are: cryptorchidism, hypospadias, decreased spermatogenesis, and sub-fertility or infertility, familial history of TC among first-degree relatives, and the presence of contralateral tumor.[8] TC is 20 times more frequent in infertile men.[15] Only 50% of patients coming for sperm cryopreservation in the context of TC have a normal sperm concentration.[16] A cryopreservation before orchidectomy is a real opportunity to analyze patient semen quality and identify azoospermia or severe oligo-zoospermia.[11,17] It may be beneficial to address patients for fertility preservation earlier in the course of TC treatments to propose per-operative TESE or PESA if a severe spermatogenesis impairment is funded. A pre-operative fertility conservation could also offset the risk of the non-functioning remaining testicle.[8,17]

About 10% of the specialists think that the sperm quality will improve after orchidectomy however it is debated. The semen concentration can decrease after orchidectomy, considering however the lack of evidence, and the contralateral testicle remaining non-functional.[18] On the other hand, TC specific factors induce worsening of semen quality and the orchidectomy might lift off these local and general disturbances. Sperm recovery to an improved spermatogenesis needs about 2–3 years. Knowing the peak of incidence of TC in the third decade of life for non-seminoma (NSGCT) and mixed germ cell tumor (GCT), and the fourth decade for pure seminoma (ST), this period of time, without any certainty of recovery, could be detrimental to procreation projects. Given the advances in treatment, more patients with urogenital cancer are surviving and looking to return to the normal life. Fertility preservation plays an important role for the quality of life.[19] Orchidectomy is the best moment to collect sperm via TESE or PESA in case of azoospermia or oligoasthenozoospermia.[20] Unfortunately, 70% of the responders do not perform this extraction. The sperm extraction is more implemented in France, The Netherlands, by andrologists and by urologists performing more than 10 orchidectomy per year. The specialists who are specialized in TC care and fertility are obviously more concerned about the cryopreservation. Once again, French and Dutch urologists seem to be also more familiar with this intraoperative procedure as explicitly stated in their national guidelines and less precisely in the European guidelines.[7,13,14] The very important reason to perform a PESA in combination with the TESE is the epididymal sperm even if only 12.3% of the responders perform the two procedures. The spermatozoa acquire their fertilizing ability and forward mobility properties during epididymal transit.[21]

The interactions between infertility and TC are complex. The testicular dysgenesis syndrome is a pre-existing risk factor for TC, there is a local effect of the tumor and additional adverse effects such as stress and depression.[22] The testicular tumor will have both a local effect on spermatogenesis with greater disturbances in the tissues in contact with the tumor but may also cause a disturbance of spermatogenesis in the contralateral testicles in the case of a large tumor.[2] The mechanisms of action involved are the hormonal secretion by the tumor of beta-human chorionic gonadotropin (β-HCG) and alpha-fetoprotein (α-FP) causing an increase in intra-testicular estradiol or the disturbance of the hypothalamo–hypophyseal axis.[18] The tumor can also induce the development of anti-sperm antibodies.[18] Our general results show a preference for the tumor contralateral testis sperm extraction, but the TC does not have only a local effect but well a contralateral testis disturbance and general effect. Due to this justification, it could be preferable to start with a tumor-bearing TESE and/or PESA at a distance from the tumor and complete with a contralateral testis extraction if the taken samples are insufficient. This approach is preferred by the andrologists responders and Dutch urologists. Those results can be influenced by the low rate of urologists with training in andrology or in oncofertility (mean of five orchidectomies per year).

The complementary treatments for TC are chemotherapy (mainly bleomycin, etoposide, vinblastine) and retroperitoneal lymph node dissection (RPLND) or radiotherapy.[8] The platinum salts cross the blood–testicular barrier to actively target dividing cells, with a significant effect on spermatogenesis (oligo—azoospermia).[19] In the majority of cases, a recovery of spermatogenesis within 2 years is observed and can be complete with recovery of mean semen parameters after a certain time from the end of the treatment.[13,23] The RPLND can affect the ejaculation and cause retrograde ejaculation or anejaculation even with a nerve sparing approach (15%).[13] The radiation therapy will primarily target the retroperitoneal lymph nodes. Testicular radiation is the main cause of testicular insufficiency. The effect is dose dependent with permanent azoospermia at 16–18 Gray and Leydig cell failure at > 20 Gray.[8] In the absence of pre-orchidectomy conservation, it is essential to offer a sperm banking after orchidectomy and before complementary treatments.

The vast majority of responders does not talk about sperm cryopreservation for prostate or bladder cancer patients older than 55 years old. Practitioners are more likely to discuss fertility before prostate cancer or bladder cancer management if the patient is younger than

55 years old (47% for prostate and 30% for bladder cancer). Delayed parenthood is constantly increasing worldwide due to various socio-economic factors.[24] The median men's age at the birth of their first child is around 31 years old in Luxemburg and The Netherlands. This age is around 28 years old in Finland, France, and Belgium. Five percent of men have children after the age of 45 years old.[25] The cryopreservation proportion is low among prostate and bladder cancer patients (1%–10% of the patients). It is certainly due to the age of these cancers' incidence. The demography evolution could justify a preventive approach and an information about fertility preservation for younger patient. Once again, the most sensitive countries to the issue seem to be French, Dutch urologist, or andrologists.

To extrapolate the data results in other countries, we need study less unbalanced towards Belgium and French responders and responders from other European countries.

5 | CONCLUSION

Our study showed variable country specific tendencies in terms of fertility preservation in the period of treatment of urological cancers. These differences seem to be related to national guidelines and recommendations. International guidelines are urgently needed in the field of fertility for urological cancer patients. It is of utmost importance to study the potential benefit of semen preservation before orchidectomy for future fertility of TC patients.

CONFLICT OF INTEREST STATEMENT

The authors declare no conflict of interest.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available on request from the corresponding author. The data are not publicly available due to privacy or ethical restrictions.

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REFERENCES

1. Trottmann M, Becker AJ, Stadler T, et al. Semen quality in men with malignant diseases before and after therapy and the role of cryopreservation. *Eur Urol*. 2007;52(2):355-367.
2. Matos E, Skrbinc B, Zakotnik B. Fertility in patients treated for testicular cancer. *J Cancer Surviv*. 2010;4(3):274-278.
3. Suzuki K, Yumura Y, Ogawa T, Saito K, Kinoshita Y, Noguchi K. Regeneration of spermatogenesis after testicular cancer chemotherapy. *Urol Int*. 2013;91(4):445-450.
4. Ferrari S, Paffoni A, Filippi F, Busnelli A, Vegetti W, Somigliana E. Sperm cryopreservation and reproductive outcome in male cancer patients: a systematic review. *Reprod Biomed Online*. 2016;33(1):29-38.
5. Loren AW, Mangu PB, Beck LN, et al. Fertility preservation for patients with cancer: American Society of Clinical Oncology clinical practice guideline update. *J Clin Oncol*. 2013;31(19):2500-2510.
6. Ferrari S, Paffoni A, Reschini M, et al. Variables affecting long-term usage rate of sperm samples cryopreserved for fertility preservation in cancer patients. *Andrology*. 2021;9(1):204-211.
7. Laguna MP, Pizzocaro G, Klepp O, Algaba F, Kisbenedek L, Leiva O. EAU guidelines on testicular cancer. *Eur Urol*. 2001;40(2):102-110.
8. Patrikidou A, Cazzaniga W, Berney D, et al. European Association of Urology Guidelines on Testicular Cancer: 2023 Update. *Eur Urol*. 2023;84(3):289-301. doi:10.1016/j.eururo.2023.04.010
9. Degraeve A, Roumeguere T, Tilmans G, et al. Société Belge d'Urologie (SBU), the Belgische Vereniging voor Urologen (BVU), the Association Française d'Urologie (AFU), the Nederlandse Vereniging voor Urologie (NVU), the Société d'Andrologie de Langue Française (SALF), the Finnish Urological Society (FUS). European countries have different rates of sperm cryopreservation before vasectomy and at the time of reversal. *Andrology*. 2022;10(7):1286-1291. doi:10.1111/andr.13182
10. Emmanuel A, Kanthabalan A, Alexander C, et al. Expedited radical orchidectomy for testicular cancer: compromising fertility outcomes without oncological benefit? *Eur Urol*. 2021;80(6):766-767.
11. Ferlin A, Calogero AE, Krausz C, et al. Management of male factor infertility: position statement from the Italian Society of Andrology and Sexual Medicine (SIAMS): endorsing organization: Italian Society of Embryology, Reproduction, and Research (SIERR). *J Endocrinol Invest*. 2022;45(5):1085-1113.
12. Walschaerts M, Bujan L, Chouquet C, Rossi V, Juillard JC, Thonneau P. Sperm cryopreservation incidence in men with testicular cancer: towards a stabilization in testicular cancer incidence? Results from the CECOS network. *Basic Clin Androl*. 2018;28:11.
13. Murez T, Fléchon A, Branger N, et al. French AFU Cancer Committee Guidelines—Update 2022–2024: testicular germ cell cancer. *Prog Urol*. 2022;32(15):1066-1101.
14. Nederlandse Vereniging voor Urologie. Kwaliteitsnormen testiscarcinoom. Versie 3. 2017. https://www.nvu.nl/kwaliteitsbeleid/kwaliteitsnormen/
15. Walsh TJ, Croughan MS, Schembri M, Chan JM, Turek PJ. Increased risk of testicular germ cell cancer among infertile men. *Arch Intern Med*. 2009;169(4):351-356.
16. 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(6):1394-1401.
17. Jacobsen KD, Fosså SD, Bjøro TP, Aass N, Heilo A, Stenwig AE. Gonadal function and fertility in patients with bilateral testicular germ cell malignancy. *Eur Urol*. 2002;42(3):229-238. discussion 37–8.
18. Ostrowski KA, Walsh TJ. Infertility with testicular cancer. *Urol Clin North Am*. 2015;42(3):409-420.
19. Moody JA, Ahmed K, Yap T, Minhas S, Shabbir M. Fertility managment in testicular cancer: the need to establish a standardized and evidence-based patient-centric pathway. *BJU Int*. 2019;123(1):160-172.
20. Blecher GA, Chung E, Katz D, Kim SHK, Bailie J. Onco-Testicular Sperm Extraction (oncoTESE): a contemporary concept review and report of Australian sperm retrieval rates and fertility outcomes. *Urology*. 2022;160:109-116.
21. Sullivan R, Mieusset R. The human epididymis: its function in sperm maturation. *Hum Reprod Update*. 2016;22(5):574-587.
22. Záková J, Lousová E, Ventruba P, et al. Sperm cryopreservation before testicular cancer treatment and its subsequent utilization for the treatment of infertility. *Sci World J*. 2014;2014:575978.
23. Drechsel KCE, Pilon MCF, Stoutjesdijk F, et al. Reproductive ability in survivors of childhood, adolescent, and young adult Hodgkin lymphoma: a review. *Hum Reprod Update*. 2023;29(4):486-517.

24. Zacchini F, Sampino S, Ziętek M, Chan A. Delayed parenthood and its influence on offspring health: what have we learned from the mouse model†. *Biol Reprod*. 2022;106(1):58-65.
25. Statbel La Belgique en chiffres. Une mere a en moyenne 31 ans à la naissance de son enfant. 2021.

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