Prospective Investigation on the Paternity Intention and Affecting Factors in 84 Post-treatment Testicular Cancer Patients

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Purpose: to investigate the factors affecting post-treatment paternity intention in patients followed up after the diagnosis of testicular cancer and to make recommendations for the early postoperative period based on the identified factors.

Materials and Methods: This prospective descriptive study included a total of 185 patients who presented to our outpatient clinic between February 2000 and July 2020 who had radical orchiectomy due to suspected testicular cancer based on physical examination and other assessments. Contact information was found for 88 of 185 patients, and accordingly, the patients were reached by one-to-one phone calls. Upon literature review, a questionnaire consisting of 10 previously validated items was developed by the researchers. The patients were compared by separating them into two groups composed of patients with (Group 1) and without (Group 2) paternity intention.

Results: A total of 84 patients participated in the study, and the participation rate was 95.5%. It was found that 19 of 32 (38%) patients with paternity intention already had children. Only 21 (40%) of 52 patients without paternity intention were married. The mean age was 26.65 (18–39) years in Group 1, while it was 28.73 (19–45) years in Group 2. Tumor volume and serum tumor markers were higher in Group 2 than in Group 1. Parameters such as testicular side in which the tumor was located, smoking status, undescended testis history, and postsurgical chemotherapy history were not statistically significant difference between the two groups.

Conclusion: The major findings included that the young aged, unmarried, and serious testicular cancer (Tumor volume and serum tumor markers were higher) can be affecting factors for testicular cancer patients' paternity intention. Early psychological counseling about paternity may be useful for testicular cancer patients.

Keywords: cancer; fatherhood; infertility; testis; testicular cancer

INTRODUCTION

Testicular cancer is the most prevalent type of cancer in men aged 15–44 years in developed countries.(1) Low birth weight and a history of undescended testis are established etiological factors of testicular cancer along with sociocultural factors, including ethnicity, environmental exposure, family history, and inguinal hernia.[2,3] Testicular cancer is often detected at a young age, and there is a high treatment success rate, thanks to early diagnosis.[4]

In patients with testicular cancer, fertility remains an important problem.[3,5-7] The post-treatment infertility rate is as high as 30%.[8] Factors that affect semen parameters include patient's age, tumor type, treatment regimen, chemotherapy, radiotherapy, and retroperitoneal lymph node dissection.[9-13] Sperm cryopreservation is routinely recommended to patients prior to the surgery due to the risk of organic-induced infertility.[14]

Diagnosis and treatment of testicular cancer may impair the quality of life (QoL) of patients and create psychological stress along with infertility.[15] However, the paternity intention, which is considered secondary to cancer, is not adequately questioned, and thus, patients cannot be provided with routine psychosocial support in this regard. A study found that 51% of patients diagnosed with testicular cancer had paternity intentions for the future, while 49% did not.[16] There are insufficient studies on paternity intention in patients with testicular cancer although many studies in the relevant literature have focused on organic-induced infertility based on semen analysis.[17-20]

The present study intended to investigate the factors affecting post-treatment paternity intention in patients followed up after the diagnosis of testicular cancer and to make recommendations for the early postoperative period based on the identified factors.

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Table 1. Baseline characteristics of enrolled patients

Variable		Group 1	Group 2	*P*-value
Age (year)(IQR)		26.65 (9,25)	28.73 (10,5)	.199
Education status	Under high school	18.8%	26.9%	.006*
	High school and above	81.2%	73.1%	
Smoking status	Smoker	12	15	.410
	Non smoker	20	37	
Tumour Volume (cc)		37.5 (26,25)	43.1 (31,5)	.478
AFP (ng/mL)		221 (215,7)	1455 (312,75)	.418
β-HCG (mlU/mL)		99 (25,23)	3144 (44,05)	.677
LDH (U/L)		371(198,5)	541(278)	.078

Abbreviations: IQR, Interquartile Range; cc, Cubic Centimeter; ng/mL, nanogram / milliliter; mlU/mL, mililiter unit/mililiter; U/L, unit/liter.

MATERIALS AND METHODS

Study Design

This prospective descriptive study was approved by the local Ethics Committee and was conducted pursuant to the principles of the World Medical Association Declaration of Helsinki's Ethical Principles for Medical Research Involving Human Subjects (HBAEK:20/415).

Participants

The study included patients who presented to our outpatient clinic between February 2000 and July 2020 with complaints of testicular swelling or mass and for whom a radical orchiectomy decision was made due to suspected testicular cancer based on physical examination and other assessments. Patients who were not diagnosed with testicular cancer upon the pathology results were excluded from the study. A total of 185 patients meeting the criteria were included in the study. Contact information was found for 88 of 185 patients, and accordingly, the patients were reached by one-to-one phone calls. All the patients confirmed that their partner was not infertile. Only one patient declined to participate in the study. The interview could not be realized with one of the patients, because of death. In addition, two patients were excluded due to bilateral orchiectomy. The remaining 84 patients with testicular cancer were included in the study.

Data Collection

Upon literature review, a questionnaire consisting of 10 previously validated items was developed by the researchers. Study data were collected over the phone based on the patients' responses for the questionnaire items, including the education status, comorbid diseases, smoking status, additional treatment status after the surgery, number of children, follow-up periods, paternity status, treatment choices for infertility, and if any of their male children were diagnosed with undescended testis.

Upon collection of the data, the participants were classified into two groups composed of patients with (Group 1) and without (Group 2) paternity intention. Patients with paternity intention were further divided into two subgroups based on having (Group 1a) and not having (Group 1b) children. Patients without paternity intention were also divided into two subgroups as married (Group 2a) and not married (Group 2b).

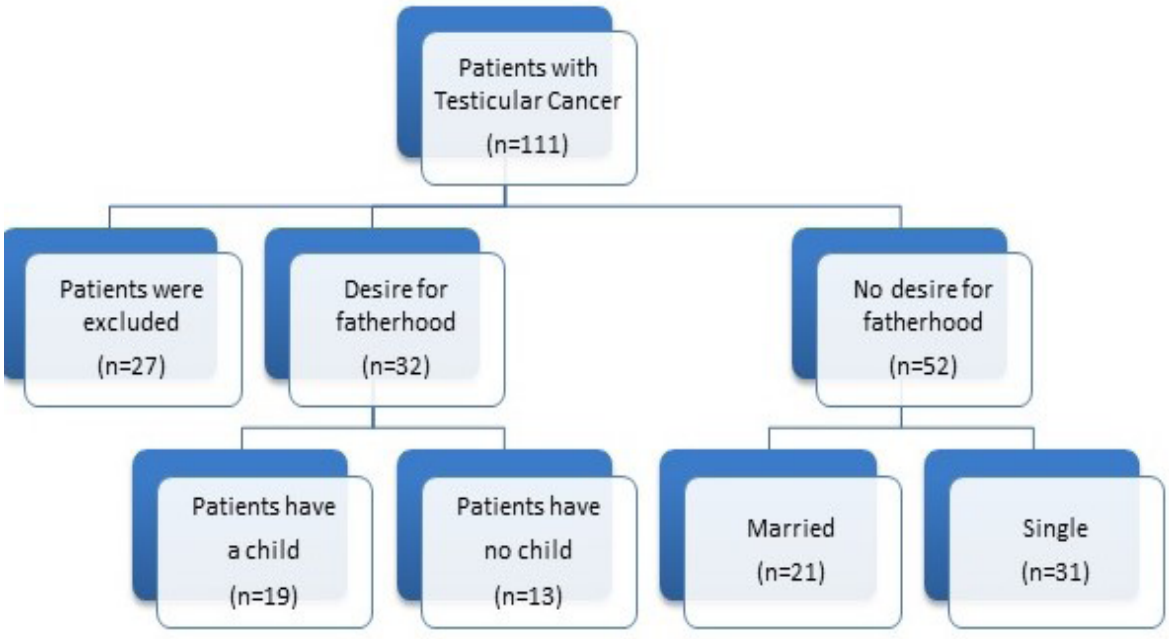

Figure 1. Flow Chart for patients' enrollment

Table 2. Statistical comparison of the factors in the questionnaire that affect paternity desire in both groups.

Variable		Group 1	Group 2	*P*-value
Testicular side	Right	16	29	.607
	Left	16	23	
Smoking status	(-)	20	37	.410
	(+)	12	15	
Undescended testis	(-)	27	47	.495
	(+)	5	5	
Chemotherapy	(-)	10	12	.408
	(+)	22	40	
Retroperitoneal LN	(-)	15	26	.781
	(+)	17	26	
Thorax LN	(-)	27	45	.761
	(+)	5	7	
Retro + Torax LN	(-)	27	45	.761
	(+)	5	7	

Abbreviations: LN, lymph node.
Chi-square test was used. $p < .05$ was accepted as the degree of significance. (n = 84)

Statistical Analysis

SPSS for Windows version 22.00 was used for the statistical analyses. Shapiro–Wilk test and Q-Q plot were used to determine normal data distribution. All the variables were non-normally distributed. Quantitative variables were expressed as median (interquartile range). Qualitative variables were expressed as frequency and percentage, and a Chi-square test was applied and no expected cell count was less than 1 and at most 20% of expected cell counts were less than 5. Mann–Whitney's U-test was used to evaluate all the non-normally distributed variables. A *p* value of <.05 was considered statistically significant in all analyses.

RESULTS

In this study, 88 patients were contacted over phone. A total of 84 patients participated in the study, and the participation rate was 95.5%. It was found that 19 of 32 (38%) patients with paternity intention already had children. Only 21 (40%) of 52 patients without paternity intention were married. The data are presented in the flowchart (**Figure 1**).

The patients were compared by separating them into two groups composed of patients with (Group 1) and without (Group 2) paternity intention. The mean age was 26.65 (18–39) years in Group 1, while it was 28.73 (19–45) years in Group 2. In Groups 1 and 2, the rates of high school and higher education were 81.2% and 73.1%, respectively, and it was higher in the group with paternity intention than in the group without such an intention ($P = .006$). While 37.5% of the patients in Group 1 were smokers, this rate was 28.8% in Group 2. An investigation of history of undescended testis and smoking data indicated that there was no statistically significant difference between the two groups ($P = .409$ and $P = .41$, respectively). Tumor volume and serum tumor markers were higher in Group 2 than in Group 1, but the difference was not statistically significant (**Table 1**).

Parameters such as testicular side in which the tumor was located, smoking status, undescended testis history, and postsurgical chemotherapy history were not statistically significant difference between the two groups. In addition, there was no effect of lymph node positivity in retroperitoneal, thorax, or both regions on the paternity intention in terms of the presence of lymph nodes (**Table 2**).

A comparison of the subgroups with and without children in Group 1 indicated that the use of food supplements was similar in both subgroups. However, the patients not having children applied to assisted reproductive techniques significantly more often than the other subgroup ($P = .006$) (**Table 3**).

While the mean time from treatment to paternity intention was 23 months (IQR:36) in the subgroup with children, this duration was 29 months (IQR:48) in the subgroup without children. Furthermore, pregnancy was achieved after an average of 7.6 months of unprotected sexual intercourse. The postoperative follow-up periods of the patients were 65.4 (IQR:64,4) and 72.6 (IQR:67,6) months in Groups 1 and 2, respectively, and there was no significant difference between the two groups ($P = .467$).

An investigation of the patients' pathology specimens showed that 7 patients out of 32 with paternity intention were diagnosed with seminoma and 25 with non-seminoma testicular cancer. On the other hand, 18 patients out of 52 without paternity intention were diagnosed with seminoma and 34 with non-seminoma testicular cancer. The pathology results did not have any effect on the paternity intention upon comparative analysis between the two groups ($P = .215$).

DISCUSSION

Testicular cancer generally occurs during the peak reproductive years of men, which coincides with career and family planning. The paternity intention and the success of fertilization in disease management vary depending on the administered treatments and the psychosocial effects of the disease. In the present study, 38.09% (n = 32) of the patients who were followed up after testicular cancer diagnosis stated their paternity intention following the diagnosis. Similarly, in a study by Spermon et al., paternity intention was stated by 43% of the subjects[13], whereas Uçar et al. reported the rate as 30%.[12] It is noteworthy that although the rates of paternity intention are at comparable levels, they tend to be below 50%. The young age of the population and the possible low level of marriage may account for these rates.[21] However, a study conducted in Norway published results inconsistent with the aforementioned reasoning. The likelihood of marriage among men diagnosed with cancer was 5% higher than that in men without cancer diagnosis (OR = 1.05, %95 CI: 1.01–1.11). According to the above study, the rates were significantly higher, especially after testicular cancer (OR = 1.11). Marriage after cancer diagnosis is more common today than it used to be, and there are minor general differences in the marriage rates of cured individuals compared to the population not diagnosed with cancer. Nevertheless, testicular cancer in men is associated with increased marriage rates.[22]

According to a study conducted in Turkey, 82.5% of patients diagnosed with cancer obtain information about their disease from a doctor. Moreover, 45.8% of the patients stated that communication with healthcare professionals was partially sufficient, 35.0% as insufficient, and 19.2% as sufficient. Additionally, 63.3% of the patients requested better communication with their

Table 3. The effect of using assisted reproductive techniques and supplementary food on having a child in those with a desire for paternity

Variable		Group 1a	Group 1b	*P*-value
Supplementary food	(-)	18	10	.135
	(+)	1	3	
Assisted reproductive techniques	(-)	15	4	.006*
	(+)	4	9	

Crosstab analysis was used. $p < .05$ was accepted as the degree of significance. (n = 32)

doctor. While 65.8% of the patients expected emotional support, 75% wanted to learn about the effects of the disease on their psychological state.[23] Another study found a high level of psychological morbidity in both patients and their relatives, even 5 years after diagnosis, despite an excellent prognosis in patients with testicular cancer.[24] It is advisable to start educational activities about the disease immediately after the diagnosis of testicular cancer, especially in case of patients with low educational status. At this point, patient associations can play an active role as regards psychosocial support for the disease. Recently, the web-based Kanker Nazorg Wijzer (Guidelines for Post-Cancer Care) was developed in the Netherlands to provide cancer survivors with psychosocial and lifestyle support. Although such a support is not available for patients with testicular cancer, it can be used to that end in the future.[25]

Although there is no clear correlation between testicular cancer treatment and biochemical hypogonadism, it may be suggested that sexual aversion and dysfunction may be substantially associated with psychological factors, including testicular cosmetic deficiency due to orchiectomy, chronic pain, or anxiety, fear, and mood disorders caused by cancer diagnosis.[26,27] In addition, major surgical interventions such as retroperitoneal lymph node dissection, which can lead to ejaculation and/or orgasm disorders in patients with testicular cancer, may give rise to such problems.[28] Physical and psychological changes in these patients also adversely affect their perspectives on business and general life and career decisions.[25] Although not addressed during the telephonic interviews with the patients, these unexpected changes may be effective in paternity intention. Education is another possible factor that decides the paternity intention in patients with testicular cancer.[30] The intention to have a child was higher in patients with testicular cancer with a higher educational status. The higher values of both tumor volume and tumor markers in Group 2 patients with a lower high school or higher education level may be associated with presenting late to a physician. The high success rate in testicular cancer is associated with early diagnosis. As the diagnosis period is delayed, the requirement for additional treatments increases. Gonadotoxic treatments lead to an overall reduction in male fertility by 30%, and there is currently no method available to predict which patients would become azoospermic following the treatment. The possible size difference in the palpable mass as a result of late diagnosis may also explain the lower paternity intention compared to the other group because of the fact that the patients are psychosocially more affected. Along with paternity intention, patients with larger, more invasive tumors are at risk for infertility due to local tumor effects.[29] The effects of late diagnosis in this patient group should be evaluated in further detail as regards both the paternity intention and infertility.

Chemotherapeutic agents constitute another aspect in the treatment of testicular tumor, which should be considered carefully in terms of both their effects and side effects. In the present study, there was no effect of adjuvant chemotherapy following orchiectomy on paternity intention, which was consistent with the relevant literature.[30] The patients became fathers after an average of 30 months after treatment in the present study, while the European Society of Medical Oncology recommends postponing pregnancy for at least 12 months after chemotherapy to avoid teratogenic effects.[31,32] Uçak et al. suggested in their study that this period was 3 years[30], whereas Spermon et al. reported that the patients became fathers within 1 year after the treatment.[33] Although the results are heterogeneous, it is noteworthy that the patients complied with the recommendations.

It is important to know how sociocultural differences in sexuality, masculinity, and fertility affect the survivors to better understand the impact of testicular cancer on the QoL. Although QoL distinctively deteriorates at diagnosis and throughout the treatment, it later returns to normal levels defined by matched controls. Nevertheless, there are several chronic conditions associated with the diagnosis and treatment of testicular cancer that plague the survivors and affect their QoL, including anxiety, sexuality, and fertility. Even if these issues have no impact on QoL measurements, they have an impact on QoL.[21]

As expected, the rate of use of supplemental food and assisted reproductive techniques was higher in patients with testicular cancer who had paternity intention but did not have a child when compared with the other group. This information reflects the desire of patients with testicular cancer who have fertility problems to access supportive treatments in case of a paternity intention. Therefore, the first problem to be addressed is the elimination of negative thoughts that psychosocially lead to paternity desire. Early introduction of supportive treatments against misconceptions should be discussed frequently by urologic oncologists and andrologists. A review published in 2019 reported that clear guidelines on fertility counseling for patients with cancer in the context of fertility preservation, which removes ambiguity as regards who conducts the counseling, what the counseling covers, and what level of psychosocial support can be most effective, might be helpful.[21] Early assessment of this patient group by psychiatrists and/or clinical psychologists through a multidisciplinary approach might be the “next step” in the management of patients with testicular cancer.

This study suffers from the following limitations. Although more patients could have been included in our retrospective archive-based study, the number of partic-

ipants was lower than anticipated because of the fact that there were patients whose data could not be accessed. Furthermore, the contact information of certain patients had changed. Owing to the COVID-19 pandemic, face-to-face interviews aimed to inform patients about paternity in psychosocial terms could not be conducted during the diagnosis and treatment. Another important point is that collecting patients' answers through phone call might be interfered by subjective thoughts of the authors. In addition, the lack of an age-matched control group can be considered as one of the limitations of the present study.

CONCLUSIONS

While studies in the relevant literature on testicular cancer and fertility have often focused on semen parameters, low educational status was found to be a factor that might negatively affect the paternity intentions in our study. Psychosocial counseling, which can be commenced immediately after the diagnosis, can play an important role in this regard and cover many factors that may negatively affect the QoL and the paternity intention. Early diagnosis should be reinforced by early psychological counseling.

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CONFLICT OF INTEREST

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