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Fertility Outcomes After a Single-Dose (AUC 7) Adjuvant Carboplatin Therapy for Stage I Testicular Seminoma: A Real-Life Observation

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Abstract

Background: Testicular seminoma is a highly curable cancer that often affects young men at the prime of their reproductive years. Since 2005, a single dose of carboplatin has been widely used as an adjuvant treatment for stage I seminoma. While this approach is effective, its impact on long-term fertility has remained uncertain. **Methods:** We conducted a real-world, retrospective analysis of men treated with one dose of adjuvant carboplatin for stage I seminoma between 2005 and 2024. Out of 59 initially screened patients, 18 met the inclusion criteria while 41 were excluded based on predefined eligibility criteria. We focused on the subset who later tried to conceive, using structured phone interviews to collect fertility outcomes. **Results:** Five patients attempted to have children after treatment, and all succeeded naturally. Interestingly, all had cryopreserved sperm before chemotherapy, but none ended up needing it. Most had minimal side effects, and none experienced serious complications or cancer recurrence. Even patients with abnormal pre-treatment semen analysis were able to father children. **Conclusion:** These real-life findings offer reassuring news: a single dose of carboplatin appears not to harm fertility in men treated for stage I seminoma. While sperm banking remains a safe backup, it may not be necessary for everyone. This study highlights the importance of personalized counseling and supports the continued use of single-dose carboplatin as a fertility-friendly treatment option. Larger studies are still needed to confirm these outcomes and better guide decision-making for patients and clinicians alike.

Keywords

Seminoma, Fertility, Carboplatin, Gonadal Toxicity

1. Introduction

Testicular cancer, although rare, is a highly treatable and often curable condition that primarily affects young men between the ages of 18 and 35 years, making early detection and awareness essential for optimal outcomes. Seminoma is the epitome of a highly treatable neoplastic malignancy. Approximately 80% of patients presenting with seminomatous germ cell tumors are diagnosed with stage I disease and substantial improvements in cancer treatment have resulted in longer survival and increased quality of life in this patient population [1]. Management options for these stage I patients include adjuvant radiotherapy or adjuvant chemotherapy, and even active surveillance. This latter option remains attractive for compliant men interested in avoiding immediate adjuvant therapy. Regarding chemotherapy, a single cycle of dose carboplatin AUC = 7 has been considered the best option for adjuvant treatment of stage I seminoma following orchiectomy since 2005 [2].

A main concern of adjuvant chemotherapy remains the long-term potential toxicities which can vary from nausea, emesis and gastrointestinal upset to more severe complications such as bone marrow suppression, renal toxicity and neurotoxicity [3]. Additionally, infertility and gonadal dysfunction continue to be recognized as adverse effects of chemotherapy particularly for seminomatous germ cell tumors [4]. Approximately 50% of patients with unilateral testicular cancer will have impaired spermatogenesis even prior to therapy, a percentage that can be further exacerbated by adjuvant chemotherapy [5]. Indeed, postoperative fertility is a major concern for young patients undergoing cancer treatment. The added gonadal toxicity of chemotherapy should be explained in detail prior to obtaining informed consent and sperm cryopreservation is therefore often discussed with patients undergoing stage I testicular seminoma treatment [6] [7].

Chemotherapy-related gonadal toxicity was extensively studied in the literature after standard germ cell tumor chemotherapy such as BEP (Bleomycin, etoposide and cisplatin) or EP (etoposide-cisplatin): Cisplatin is known to significantly affect fertility, as it can damage the cells in the testicles that support and produce sperm. This often leads to a reduced sperm count or even temporary absence of sperm, though many men see recovery within a couple of years. It can also affect testosterone production, but that's less common and usually seen in those receiving higher doses or who are older. Etoposide also impacts fertility, though to a lesser extent. It mainly targets the cells that divide to form sperm, sometimes causing a temporary drop in sperm count. However, when given in high cumulative doses, it may lead to lasting infertility. On the other hand, bleomycin doesn't seem to directly harm reproductive function, and there's very little evidence of it affecting either sperm production or hormone levels [6] [7]. However, spermatic toxicity following a single cycle of carboplatin-based adjuvant chemotherapy has not been clearly defined in the literature yet. This study seeks to assess the real-world clinical fertility outcomes after one cycle of carboplatin in this specific patient population.

2. Materials & Methods

2.1. Participants

After Institutional Review Board approval, we conducted a retrospective analysis of prospectively maintained data from our institution's electronic medical records (EMR). We included all adult patients with a confirmed diagnosis of stage I seminomatous testicular cancer from January 2005 to December 2024. Patients who were treated with BEP or RT, who underwent active surveillance or those treated with more than one dose of carboplatin were excluded from the final analysis. Only patients with a confirmed diagnosis who were treated with a single dose of carboplatin were included in our study. Furthermore, patients were also excluded from the analysis if they were younger than 18 years old, were lost to follow-up, refused to participate and/or give informed consent, or had missing data that precluded review. After selection of our final cohort, a precise and well-designed telephone script/questionnaire was used to contact the patients and obtain clinical information. The questionnaire was filled out by the authors of this manuscript, on behalf of the senior author (JK.).

Given our primary objective focusing on fertility outcomes after chemotherapy, we analyzed the outcomes of patients who attempted to conceive after treatment.

Preoperative baseline demographics, clinical, laboratory values, and semen analysis results were collected from the EMR/filled by the questionnaire at the time of diagnosis with stage I seminoma testicular cancer when available in our database. Initial tumor markers and tumor diameters were also reported. Data regarding surgical and medical management for all patients were also collected which included: age at orchidectomy, side of orchidectomy, dosage of carboplatin, interval between orchidectomy and carboplatin administration and potential toxicity to carboplatin. The sperm cryopreservation and its usage for conceiving are also noted. Baseline demographic and treatment characteristics were collected and reported for the overall cohort. Lastly, for patients who attempted to conceive after therapy completion, we described long-term outcomes in terms of fertility. Data were summarized using frequencies and percentages for categorical variables and means with Standard Deviations (SD) for continuous variables.

2.2. Stage I Seminoma Definition

According to the American Joint Committee on Cancer (AJCC) 8th edition TNM staging system, stage I seminoma is defined as a pure seminoma confined to the testis without evidence of metastasis. These tumors can also be further subdivided into stage IA (tumor limited to the testis and epididymis without lymphovascular invasion, and tumor size < 3 cm) and stage IB (tumor limited to the testis and epididymis with lymphovascular invasion or tumor size ≥ 3 cm) [8].

2.3. Endpoints

Our main objective is to report the short and long-term fertility after a single dose of adjuvant carboplatin for patients with confirmed stage I seminoma testicular cancer. Next to clinical outcome the usage of preserved sperm and number of children after therapy are also assessed.

3. Results

A total of 59 adult patients diagnosed with stage I seminomatous testicular cancer were identified in our database from 2005 through 2024. Of these, 29 patients were excluded for either receiving adjuvant BEP or RT (n = 15), active surveillance (n = 7), or being treated with 2 or more doses of carboplatin (n = 7). A total of 30 patients were eligible for inclusion after receiving a single dose of adjuvant carboplatin. However, an additional 12 patients were excluded due to lack of sufficient follow-up data (n = 8) or for refusing to participate in the study (n = 4). In our final cohort, 18 patients were included with a mean age of 40 ± 9 years (**Figure 1**).

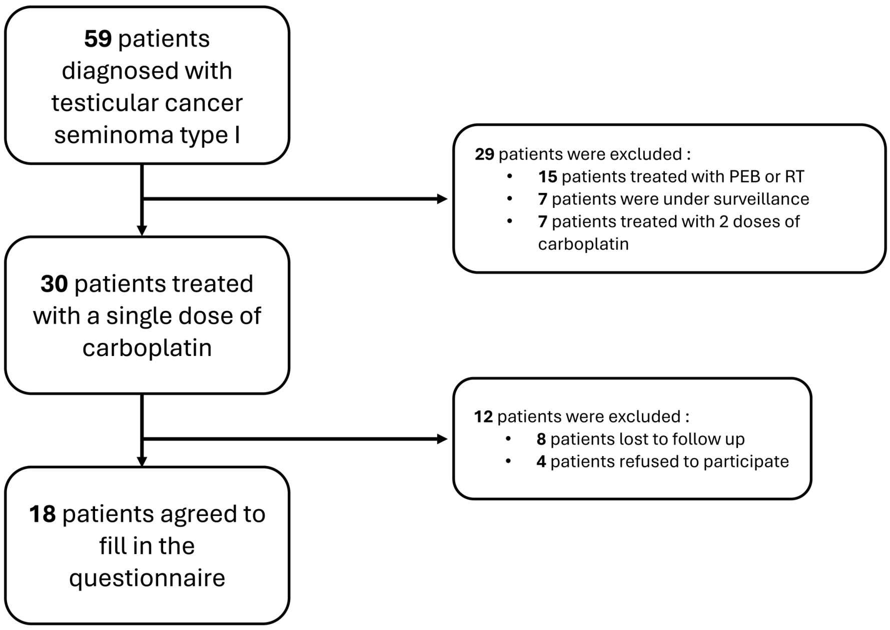

Figure 1. Patient flowchart.

Overall, 14 patients (77.8%) were married prior to diagnosis with 9 (50%) already having children. Only 3 (16.7%) patients had a positive history of cryptorchidism in early childhood. The mean age at diagnosis was 34.3 ± 8.8 years. Tumor markers (B-hCG) were positive for 4 (22.2%) patients and the mean tumor diameter at diagnosis was 4.7 ± 3.3 cm. Five patients attempted to conceive after treatment while 13 did not. Among these 5 patients, one has already had one child before the diagnosis.

In terms of surgical and medical management, there was an interval of 0.8 ± 0.5 months between orchiectomy and adjuvant chemotherapy. The mean dosage of carboplatin administered varied between 800 and 1200 mg total with a mean of 885 ± 123.3 mg. Thirteen patients (72.2%) experienced side effects related to carboplatin; however, these toxicities were successfully managed at home such as nausea, vomiting, and fatigue. In our patient population, we did not report any major toxicity occurrence (**Table 1**).

Table 1. Baseline characteristics, treatment details, and outcomes of the patient cohort.

	Total
N	18
Baseline characteristics and diagnosis parameters	
Current age (mean, SD)	40 (9)
Marital status (Married, %)	14 (77.8)
History of cryptorchidism (Y, %)	3 (16.7)
Children before diagnosis (Y, %)	9 (50)
Age at diagnosis (mean, SD)	34.3 (8.8)
Initial tumor marker (Y, %)	4 (22.2)
Tumor diameter (mean, SD)	4.7 (3.3)
Surgical and medical treatment characteristics	
Side of orchidectomy	9L/9R
Age at carboplatin (mean, SD)	35 (9)
Dosage carboplatin, mg (mean, SD)	885 (123.3)
Interval orchidectomy—carboplatin (months, mean, SD)	0.8 (0.5)
Toxicity to carboplatin (Y, %)	13 (72.2)
Cryopreservation (Y, %)	11 (61.1)
Current tumor status (cancer free %)	18 (100)

Regarding the 5 patients who attempted to conceive after receiving a single dose of adjuvant carboplatin treatment, all of them (n = 5) but only 1 (20%) had children prior to diagnosis. Three patients underwent semen analysis prior to treatment which was abnormal for 2 patients (66.7%) showing asthenospermia for patient 1 and oligospermia for patient 4 (**Table 2**). Initial tumor markers were negative for all 5 patients and the tumor diameter ranged from 2 to 5.5 cm. Similar to the overall cohort, these patients were treated with a single dose of adjuvant carboplatin shortly after orchidectomy with an interval ranging from 0.1 to 1 months at most. Carboplatin dose varied between patients with patient 1 receiving the lowest dose of 800 mg and patient 5 receiving 1000 mg. Patients 1, 2 and 5 experienced carboplatin-related toxicities such as diarrhea, fatigue and emesis. Lastly, all 5 patients (100%) underwent cryopreservation prior to treatment.

Table 2. Baseline characteristics and diagnosis parameters of the patients who attempted to conceive.

Patient	Current Age (years)	Marital Status	History of cryptorchidism (Y/N)	Semen analysis abnormality prior to carboplatin	Children before diagnosis (Y/N)	Age at diagnosis (years)	Initial tumor marker	Tumor diameter (cm)
1	41	Married	N	Y—Asthenospermia	N	40	N	2
2	33	Married	N	N/A	N	28	N	4.7
3	34	Married	N	N/A	N	28	N	4.5
4	28	Married	N	Y—Oligospermia	N	17	N	5.5
5	40	Married	N	N	Y	36	N	4.2

In our cohort, we did not report any cases of cancer recurrence after single sided orchidectomy with adjuvant carboplatin. Indeed, all 18 patients (100%) remained cancer free at the longest follow-up from 2 to 10 years. Regarding fertility outcomes, all the 5 patients who attempted to conceive were able to have children successfully (Table 3). Interestingly, all these 5 patients reported that they did not need to use the cryopreserved sperm to have children as they all had at least 1 child with patient 5 having 2 children after therapy completion (Table 3).

Table 3. Long-term outcomes (cancer recurrence and fertility) in the patients who attempted to conceive.

Patient	Current tumor status (Cancer free)	Attempts at conception after therapy	Usage of preserved sperm	Number of children after diagnosis
1	Y	Y	N	1
2	Y	Y	N	1
3	Y	Y	N	1
4	Y	Y	N	1
5	Y	Y	N	2

4. Discussion

Our study sheds light on the fertility outcomes of young men undergoing a single adjuvant dose of carboplatin treatment for stage I testicular seminoma. It represents a unique and pioneering contribution to the field, as it provides real-world insights by addressing a critical gap in the literature.

Drawing on nearly 20 years of real-world data in our institution (2005-2024), our study offers a thorough and in-depth analysis. By addressing the fertility outcomes, we almost affirm that a single dose of carboplatin, next to its therapeutic efficacy, could not affect long term fertility, supporting its use as a safe and reliable adjuvant treatment.

From a clinical standpoint, single-dose carboplatin should remain the preferred adjuvant therapy for stage I seminoma [9], as our results showed a disease-free survival of 100% with complete remission, minimal and benign long-term toxicities and a preserved fertility potential. While sperm cryopreservation remains a viable option; however, it may not be required for all patients, as all our 5 patients maintain normal fertility following treatment. It is essential to provide routine post-treatment fertility counseling, incorporating discussions on sperm banking, particularly for individuals with pre-existing sperm abnormalities [10] [11]. Avoiding unnecessary sperm banking not only spares patients the emotional and logistical burden but also helps sidestep potential ethical concerns related to long-term storage and disposal [12]. A more personalized approach to fertility counseling can ensure that decisions align with each patient's individual needs and circumstances.

Our study has several limitations that should be addressed in future research. The small sample size, with only 5 patients attempting conception, weakens the statistical power of the fertility conclusions, and a potential selection bias exists, as patients who chose to conceive may have better baseline fertility [13].

Time-to-conception data were not systematically collected for all patients, which limits understanding of the true impact of treatment on fertility. While all patients who attempted conception successfully fathered children naturally, the duration required to achieve pregnancy was not uniformly recorded. Consequently, it is unclear whether conception occurred within the expected timeframe for the general population or if treatment may have caused subtle delays in fertility. This information is particularly important because even if natural conception is ultimately successful, prolonged time-to-conception can have physical, emotional, and psychological implications for patients and their partners. Collecting detailed time-to-conception data in future studies would allow a more precise assessment of reproductive outcomes and help clarify whether single-dose carboplatin is truly "fertility-friendly" in both qualitative and quantitative terms.

Additionally, the lack of objective post-treatment semen analysis leaves uncertainty about changes in sperm quality, despite all 5 patients conceiving naturally. The retrospective design, relying on previous medical records and patient-reported outcomes through questionnaires, introduces the possibility of recall bias, as many patients were not comfortable discussing fertility issues, which may have led to inaccuracies in recalling fertility struggles or conception timelines [14]. Furthermore, the absence of genetic or hormonal data, such as serum testosterone levels, FSH, LH, and inhibin B, limits understanding of gonadal function recovery. To improve the impact of findings, larger multicenter studies with long-term follow-up and comprehensive hormonal and semen analysis are needed [15].

Future research should focus on several key areas. First, large-scale, prospective fertility studies are needed, including multicenter trials with pre- and post-treatment sperm analysis to track sperm recovery over time. These studies should also evaluate time-to-conception and potential miscarriages, which were not captured in this study. Additionally, long-term endocrine and hormonal monitoring should be incorporated, to evaluate the risk of late-onset hypogonadism in long-term survivors. Potential comparative studies between carboplatin and active surveillance may also determine if single-dose carboplatin affects fertility more than no treatment, potentially providing stronger evidence for personalized treatment decisions based on fertility concerns. Moreover, studies focusing on the quality of life and psychological impact on patients are essential, including assessments of sexual function, anxiety about infertility, and overall well-being post-treatment. Finally, it would be interesting to comprehend how carboplatin affects infertility at the molecular and cellular level in the gonads in future studies.

5. Conclusion

This study provides reassuring real-world data suggesting that single-dose carboplatin for stage I seminoma is not associated with a major impairment of fertility in our cohort. All patients who attempted conception were able to father children naturally, without significant toxicity or cancer recurrence. Nevertheless, given the very small number of patients (n = 5) attempting conception, these results must be interpreted with caution. Sperm banking should therefore remain a standard component of pre-treatment counseling, allowing patients to preserve reproductive options and make fully informed decisions prior to therapy. This study also provides valuable real-world evidence that a single-dose carboplatin treatment does not significantly impair fertility in stage I seminoma patients. A larger-scale multi-center retrospective study is certainly needed to accurately validate these findings.

Ethics Approval and Consent to Participate

The Ethics Committee of Hotel Dieu de France Hospital (CEHDF): This study was conducted in accordance with the Declaration of Helsinki and approved by the Institutional Review Board of CEHDF "comité d'éthique d'Hotel Dieu de France" (approval number: 2383).

Ethics Statement

Human **Ethics and Consent to Participate Declarations: Not Applicable.**

Oral informed consent was obtained from all participants prior to the interviews, which were conducted via telephone by personnel from our institution. Participants were informed about the study purpose, confidentiality, and their right to withdraw at any time without consequence.

Availability of Data and Materials

All data generated or analysed during this study are included in this published article.

Authors' Contribution

T. Z.: Conceived and designed the study, collected and analyzed data, interpreted results, and wrote the manuscript. Y. G.: Contributed to data collection, prepared the figures and tables, participated in contacting patients, and took part in writing the manuscript. R. G.: Participated in data collection, contacted patients, and took part in writing the manuscript. R. Z.: Assisted in data collection and contacted patients. N. D.: Reviewed and edited the manuscript and conducted the systematic literature review. J. K.: Provided critical review and performed the final data analysis.

Data Availability Statement

All data generated or analyzed during this study are included in this published article. No additional datasets were generated or used. Further details are available from the corresponding author upon reasonable request.

Conflicts of Interest

All authors read and approved the final manuscript; there was no conflict of interest.

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Abbreviations

BEP = Bleomycin, Etoposide and Cisplatin

EP = Etoposide Cisplatin

EMR = Electronic Medical Records

RT = Radiation Therapy

AJCC = American Joint Committee on Cancer