Asian Journal of Andrology (2014) 16, (107–111)

www.asiaandro.com; www.ajandrology.com

Open Access

ORIGINAL ARTICLE

Male Fertility

Fertility outcome of patients with testicular tumor: before and after treatment

Ping Ping[1], Ben-Hong Gu[2], Peng Li[1,3], Yi-Ran Huang[1], Zheng Li[1,3]

Testicular cancer (TC) is the most curable type of cancer, with a survival rate of more than 95%. Oncologists are faced with the challenge that gonadotoxic cancer treatments can compromise future fertility, either temporarily or permanently. Our aim was to investigate the long-term effects of TC treatments on male fertility and on the offspring of patients who had received these treatments. Between January 1996 and December 2010, 125 eligible patients, ranging from 18 to 54 years (median age 36.3 ± 15.7), with unilateral TC underwent surgery, chemotherapy or radiotherapy at our center. Some of these patients had their semen samples cryopreserved in the Shanghai Human Sperm Bank. The clinical data were evaluated, and questionnaire and telephone follow-up surveys were given to all patients. The data were analyzed to determine the patients' fertility status pre- and posttreatment. Of the 125 eligible patients, 93.6% (117/125) were accessible and were evaluated. Among 81 men who were married before diagnosis, 21 had conceived successfully before diagnosis and six reported azoospermia. Posttreatment conception was attempted by 73 men; of these, 16 conceived naturally and 19 conceived by artificial reproductive techniques, resulting in 37 healthy babies with no congenital malformations. Of the patients who had not conceived before treatment, 21.9% (21/96) banked their sperm and 23.8% of these patients (5/21) subsequently used the banked sperm. Retroperitoneal lymph node dissection, chemotherapy and radiotherapy were the most highly correlated with lack of conception post-TC treatment. Sperm banking should be recommended to TC patients with the desire for biological conception. There is no evidence to suggest that TC treatments are associated with birth defects or childhood malignancies.

Asian Journal of Andrology (2014) **16,** (107–111); doi: 10.4103/1008-682X.122194; published online: 16 December 2013

Keywords: chemotherapy; fertility; radiotherapy; sperm bank; testicular cancer

INTRODUCTION

Testicular cancer (TC) is the most common and treatable cancer affecting men of reproductive age. It accounts for 1% of all cancers in men, but 60% of all cancers in young males 15–35 years of age.[1] Successful treatment approaches have resulted in longer life expectancy of TC survivors.[2] Over the last several decades, survival rates for TC have steadily increased with a 10-year survival rate over 95%.[3] Since many young patients have not yet attempted to conceive at diagnosis, fertility is certainly a main concern of survivors after treatment.

The most frequently used treatment for TC is a combination of orchiectomy (surgical removal of the affected testis), and either radiotherapy or platinum-based chemotherapy. Chemotherapeutic regimens including alkylating agents and radiation treatments directed to the gonads are particularly gonadotoxic.[4] Negative side effects of treatment include impaired spermatogenesis, resulting in azoospermia or oligozoospermia.[5] Additionally, DNA damage in sperm is significantly higher in posttreatment TC patients compared to that of normal volunteers.[6]

In many TC patients, sperm quality is already abnormal and may even lack viable spermatozoa at the time of diagnosis.[7] Cytotoxic therapy influences spermatogenesis at least temporarily and in some cases permanently, and the degree of spermatogenesis impairment depends on the combination of drugs used and the cumulative dose.[8] Alkylating agents, such as cyclophosphamide and procarbazine, are the most detrimental to germ cells.[9] Radiation therapy, especially whole-body irradiation, is also associated with the risk of permanent sterility.[10]

Since spermatozoa may carry damaged DNA even long after treatment has finished, the concern remains that cancer survivors may transmit a defective genome to their offspring.[11] Prior studies assessing fertility after TC treatment have reported some impairment, but few have reported fertility preservation and its use or TC posttreatment follow-up of patients' offspring. Most studies have evaluated European and American populations, but there is a lack of published data regarding fertility of TC patients among the Chinese population. As TC varies in its incidence among different ethnic groups, fertility in Asian populations may vary due to factors concerning culture and treatment modalities; the health of children born after TC treatment has not been comprehensively addressed. Thus, the aim of the present study was to explore fertility status, strategies of fertility preservation and the general health of biological children of TC survivors after cancer therapies in a Chinese population.

[1]Department of Urology, Shanghai Human Sperm Bank, Shanghai Institute of Andrology, Ren Ji Hospital, School of Medicine, Shanghai Jiao Tong University, Shanghai, China; [2]Department of Surgery, Shanghai Pudong District Traditional Chinese Medicine Hospital, Shanghai, China and [3]Shanghai Key Laboratory for Assisted Reproduction and Reproductive Genetics, Shanghai, China.
Correspondence: Dr. Z Li (lizhengboshi@163.com)
Received: 07-05-2013; Revised: 05-07-2013; Accepted: 26-09-2013

PATIENTS AND METHODS

Study population

This was a retrospective study of patients treated for TC in the Department of Urology, Ren Ji Hospital, School of Medicine, Shanghai Jiao Tong University with approval from the hospital ethics committee. Between January 1996 and December 2010, 149 unilateral TC patients were referred to our department for treatment. Exclusion criteria included mental retardation, age younger than 18 years or older than 60 years and recurrent cancer in the other testicle. There were totally 125 qualified patients who participated in the survey, consisting of a mailed questionnaire and telephone follow-up. The patients' information and treatment history were traced from the hospital case notes. General data such as age, marital and fertile status were reviewed. The clinical pathologic information such as tumor size, histopathologic diagnosis, stage of cancer and treatment details were obtained.

Cancer therapy groups

The subjects were stratified into four groups for analysis, according to the type of treatment received: (i) surgery only, including radical orchiectomy, orchidectomy, partial orchiectomy and radical orchiectomy combined with retroperitoneal lymph node dissection; (ii) surgery combined with chemotherapy only; (iii) surgery combined with radiotherapy; (iv) surgery combined with chemotherapy and radiotherapy. The distribution of these groups is as the following: the number of patients of seminoma is 49.6% (58/117), lymphoma 12.0% (14/117), Leydig cell tumor 7.7% (9/117), dysembryoma 6.8% (8/117), mixed germ cell tumors 6.0% (7/117), embryoma 5.1% (6/117), dermoid cyst 3.4% (4/117), liposarcoma 2.6%(3/117), adenomatoid tumor 2.6% (3/117), leiomyoma1 0.7% (2/117), papillary stromal tumor 1.7% (2/117) and yolk sac tumor 0.9% (1/117).

Data collection questionnaire

In December 2011, participants with available contact information were mailed a standard, self-administered questionnaire to assess fertility (**Table 1**). A total of 125 letters were distributed with a completed questionnaire response rate of 74.4% (93/125). The remaining 32 patients were followed-up with a telephone interview, which was consistent with the questionnaire. The questionnaire was broken down into four parts concerning fertility pre- or posttreatment. In part one, respondents were asked if they had tried to conceive, whether they were successful in conception and if they had any children pre-treatment. In part two, participants were asked if they had difficulty conceiving, any known causes of infertility, semen parameters and the method of conception pre- or posttreatment. In part three, patients were asked to describe their knowledge of sperm banking, cryopreservation and its usage. In part four, patients answered questions concerning the health status of their offspring.

Table 1: Content of the questionnaire on fertility status section

1. Have you tried to father children before testicular cancer treatment?
   - □ Never, (*the reason* is that _____)
   - □ Yes, I succeed. Number of children _____
   - □ No, I did not success
   - (*the reason:* □ unknown □ poor semen parameters □ female factors □ others _____)
   - □ If you have semen analysis pretreatment, the sperm concentration is _____ million per ml
2. Have you tried to have children after testicular cancer treatment?
   - □ Never, (*the reason* is that _____)
   - □ Yes, I succeed
   - Number of children _____
   - The modalities of fertility □ conceive naturally □ conceive by AIH □ conceive by IVF
   - □ conceive by ICSI
   - □ No, I did not success
   - (*the reason*: □ unknown □ poor semen parameters □ female factors □ others _____)
   - □ If you have semen analysis post-treatment, the sperm concentration is _____ million per ml
3. Have you cryopreserved semen?
   - □ No, (*the reason* is that □ I have children. □ I did not want to have a child. □ I have no knowledge of sperm cryopreservation □ azoospermia or extremely severe oligoasthenozoospermia □ others)
   - □ Yes, (*the reason* is that □ I have children, still want to conceive in the future. □ I have no children yet. □ others)
4. If you cryopreserved the sperm, what's your sperm banking time?
   - □ I cryopreserved semen before all treatments
   - □ I cryopreserved semen during the interval between the surgery and chemotherapy or radiotherapy
   - □ I cryopreserved semen after all treatments.
     - Times of pregnancy □ None □ _____ time(s)
     - Number of children □ None □ _____
     - Abortion □ None □ _____ time(s)

Congenital malformations of children

□ None, healthy □ born with malformations, in detail _____)

AIH: artificial insemination by husband; ICSI: intracytoplasmic sperm injection; IVF: *In vitro* fertilization.

RESULTS

Characteristics and TC treatment of the study population

Of the 125 invited patients, medical records and follow up data were accessible and complete in 93.6% (117/125 participants). The median age at diagnosis was 36.3 ± 15.7 years (ranging from 18 to 54 years). The median interval between treatment and survey completion was 10.2 years (ranging from 1 to 15 years). Among 117 patients, 86 underwent radical orchiectomy (remove a testicle and the full spermatic cord through an incision in the inguinal region), 23 underwent orchiectomy (remove testis only) and eight patients had organ-preserving orchiectomy with indications of asymptomatic, non-palpable, small-volume masses (maximum size of the lesion is <2 cm). After orchiectomy, 11 participants underwent radical orchiectomy combined with retroperitoneal lymph node dissection. Thirty-five patients had postoperative chemotherapy of cisplatin-based standard chemotherapy regimens, consisting mainly of two to four cycles of cisplatin, bleomycin or etoposide. Twenty-eight patients had radiotherapy (para-aortic and ipsilateral iliac irradiation of 25–35 Gy), and seven received combined radiochemotherapy. The demographic information, pre- and posttreatment semen parameter and fertility outcomes available for each treatment group were summarized in **Table 2**.

Conception rates and health of offspring

Of the 117 assessable patients, 69 of 81 married men reported that they had attempted to conceive before diagnosis, and 30.4% (21/69) had succeeded in fathering children. Of the men who had not conceived, 31.2% patients (15/48) reported oligoasthenozoospermia and 12.5% (6/48) reported azoospermia according to their semen analysis reports. After treatment, 73 patients tried to conceive and 35 were successful. Among men who successfully conceived, 21.9% (16/73) conceived naturally and 26.0% (19/73) achieved conception by assisted reproductive techniques (ART) either through *in vitro* fertilization or

Table 2: Demographic and fertility characteristics of different treatment group

	Surgery+ surveillance	*Surgery+ RPLND*	*Surgery+ chemotherapy*	*Surgery+ radiotherapy*	*Surgery+ Chermotherapy+ radiotherapy*
Total number	36	11	35	28	7
Average age (year)	33.6±15.1	38.1±13.2	35.3±17.4	37.3±16.5	30.3±12.4
Pretreatment sperm concentration (million per ml)	18.1±5.2	12.2±3.5	15.0±4.1	14.8±2.4	5.3±1.6
Posttreatment sperm concentration (million per ml)	10.7±3.4	7.5±2.5	3.4±1.1	1.3±0.4	0-1/HP
Post-diagnosis live birth	12	4	10	9	2

RPLND: retroperitoneal lymph node dissection.

intracytoplasmic sperm injection treatment using fresh semen (11/19) or through the use of cryopreserved semen (8/19). Successful post-diagnosis conception resulted in 37 healthy babies and four abortions during the first trimester of pregnancy. Among the four abortions, three cases were unexplained early spontaneous abortions and one case was induced abortion due to early embryo development ceasing. No congenital malformations or childhood malignancies were found among babies born posttreatment in the cohort.

Semen cryopreservation

Of all 96 patients who did not conceive a child before treatment, 21.9% (21/96) banked their semen. Of that subgroup, 23.8% (5/21) chose to cryostore their semen samples prior to all treatment for ART treatment because of the increased risk of posttreatment oligoasthenozoospermia or azoospermia from high-dose chemotherapy or radiotherapy. The other 16 men banked their semen during the interval between the surgery and chemotherapy or radiotherapy. The mean semen concentration pre-freeze was $11.2 \times 10^6\,ml^{-1}$ (range from 3.5 to $46.2 \times 10^6\,ml^{-1}$) and mean progressive motility rate was 23.7% (range from 9.5% to 52.3%) according to the data of Shanghai Human Sperm Bank. All of the above patients who banked their semen followed the instructions of a medical professional. The failure to bank sperm from participants was attributed to: (i) the lack of available information given to patients regarding sperm banking or (ii) the semen quality pre- or post-freeze. If semen quality was poor and no motile sperm were detected, then cryopreservation was deemed unnecessary (**Figure 1**).

DISCUSSION

Negative effects of TC treatment on spermatogenesis

Since TC is the most common cancer affecting men of reproductive age and has a high cure rate of over 90%, fertility is one of the main concerns of survivors. TC therapy can result in subfertility or sterility due to gonad removal or permanent damage to germ cells from adjuvant therapy. Spermatogenesis damage after TC treatment largely depends on the type of therapy and gonadal function pretreatment. In our study, only 21.9% of couples who attempted pregnancy after TC treatment were successful. The results were similar to a Norwegian population-based study that observed a 30% decrease in fertility in TC survivors compared with the fertility of the normal population.[12] In this study, some patients presented with poor semen quality even before TC treatment. Colpi *et al.*[13] also reported that only 37% of men with TC presented with normal semen characteristics, based on WHO criteria. The lowest fertility rates have been observed among TC patients who were treated with chemotherapy followed by radical orchiectomy and retroperitoneal lymph node dissection. Retroperitoneal lymph node dissection in men with TC can cause infertility due to ejaculatory dysfunction resulting from the pelvic plexus.[14]

Patients may also be rendered oligospermic or azoospermic due to gonadotoxic agents, which directly damage proliferating cells. Indeed, early differentiating sperm cells are exquisitely sensitive to these agents. Cytostatic chemotherapy, which targets cells outside the G0 phase, mainly destroys rapidly proliferating spermatogonias. Alkylating agents, including cisplatin, are widely used for TC and increase the risk of azoospermia. A linear relationship has been reported between increasing cumulative alkylating agent dosage and the inability to conceive.[13] Furthermore, sperm concentration and motility were dramatically decreased in TC patients 6–18 months after chemotherapy compared to community volunteers. Significant sperm DNA damage and low DNA compaction remained as long as 24 months posttreatment.[15]

Radiation therapy negatively affects spermatogenesis, either transiently or permanently by directly inducing DNA damage.[16] The germinal epithelia of the testis are very sensitive to the detrimental effects of radiotherapy irrespective of the patient's pubertal status at the time of treatment. In most males, radiation doses as low as 0.1−1.2 Gy can impair spermatogenesis, with doses above 4 Gy causing permanent azoospermia.[17] Very low fertility rates have been observed in patients who were treated with radiotherapy in the pelvic region. However, the deleterious effects of radiation therapy on gonadal function can vary based on total dosage, source of radiation, gonadal protection, scatter radiation and individual susceptibility.[13]

Sperm cryopreservation and its use

As radiation and chemotherapy can significantly compromise the DNA integrity and quality of sperm after treatment,[18] semen cryopreservation before treatment should be recommended for most patients.[19] However, TC itself may influence spermatogenesis as 43.8% (21/48) of patients in this study reported oligozoospermia or azoospermia prior to treatment. In this study, only 21.9% of TC patients having no children before treatment cryopreserved semen samples over the past 15 years, indicating that only a minority of patients asked for sperm banking.

The huge discrepancy between the number of patients with TC who choose to use sperm banking and those who do not may lie in the following reasons: (i) lower level of awareness by the medical team or the patient in regards to the need to bank sperm or a general knowledge of ART, (ii) limited time between diagnosis and treatment, as treatment is usually initiated as soon as possible and (iii) poor semen quality leading to immotile sperm after cryopreservation, or failure of ejaculation due to high levels of anxiety or weakness. Based on the questionnaire and survey results of this study, a lack of awareness seems to be the driving reason for poor participation in sperm banking.

Awareness of established fertility preservation techniques and assisted reproductive technologies is essential to ensure appropriate counseling of young cancer patients who wish to choose biological parenthood in the future. In this study, the use rate of cryopreserved sperm was higher than in other reports (21.9% *vs* < 10%, respectively).[20]

These low rates of banked sperm may be explained by either the decision by patients to stop having more children or fertility recovery. As fertility was recovered in some patients, a fresh semen sample may be preferred over cryopreserved semen samples to reduce poor post-thaw semen quality when necessary for use in ART.

Cryopreserved sperm may be used for intrauterine insemination and/or *in vitro* fertilization with intracytoplasmic sperm injection, although the freeze-thawing process used for cryopreservation can cause damage, resulting in impaired sperm motility. Indeed, successful cryopreservation of sperm employed in intrauterine insemination that results in pregnancy remains very low.[21] With advances in ART, particularly intracytoplasmic sperm injection, the problems of low sperm numbers and poor motility may be circumvented.[22] For example, if the patient is sufficiently mature both physically and emotionally, production of semen by masturbation is feasible in most cases and alternative methods, such as electroejaculation or penile vibration under anesthesia, may also be considered in patients having difficulty producing semen by masturbation.

Recovery of spermatogenesis following cancer treatment

Many men are rendered azoospermic following radiation or chemotherapy for TC. However, after completion of chemotherapy, partial recovery of spermatogenesis may occur within 2 years and may continue to improve thereafter.[23,24] The timing of the recovery and the sperm quality is often variable. A number of factors, including treatment regimen, pretreatment fertility potential and type of TC may influence the recovery time and sperm quality.[25] Among TC survivors, some are successful in achieving biological conception, although many have more difficulty compared to the general population or those in active surveillance.[26] The mean time from TC diagnosis to the birth of the first child posttreatment is about 7 years, from 5% to 22% of couples attempting to conceive with ART.[27]

Birth defects of offspring born post-treatment

A concern of many cancer patients is whether offspring exposed to cytotoxic agents or radiotherapy have an increased risk of birth defects. There is no data to suggest that children born to TC patients post-chemotherapy have an increased risk.[28] Previous research has shown a decrease in the number and motility of sperm and an increase in abnormal sperm morphology after treatment.[29,30] Reports on the chromatin quality of surviving sperm are conflicting.[31,32] Animal studies indicate that the coadministration of bleomycin, etoposide and *cis*-platinum in the rat resulted in elevated early postnatal mortality among progeny sired by males exposed to BEP (bleomycin, etoposide and cisplatin).[33] Increased frequency of sperm aneuploidy has also been reported after the initiation of chemotherapy and may persist up to 18 months or longer.[11] Thus, the impact of treatment on progeny safety has become increasingly important. An assessment of sperm DNA integrity in cancer patients before and after treatment showed that the DNA fragmentation index decreased significantly following various anti-cancer treatments.[34] While the clinical impact of such effects in humans is still under investigation, men are advised to wait 12−24 months after the completion of therapy before pursuing fertility treatments.

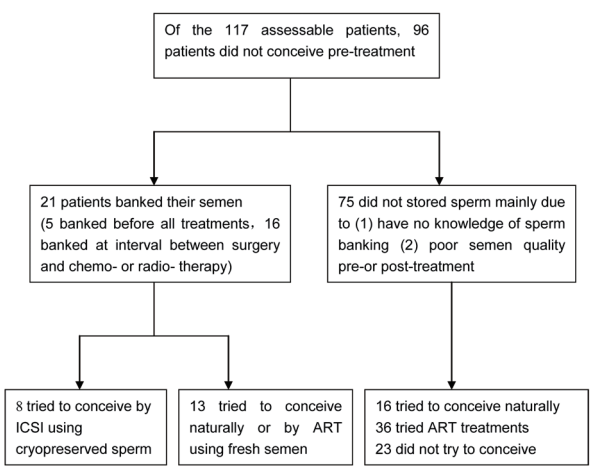

Figure 1: Patients concerning sperm cryopreservation.

CONCLUSIONS

The results of this study have clinical implications. First, chemotherapy, radiotherapy, orchiectomy and cancer itself all have negative effects on spermatogenesis. Among them, high-dose chemotherapy and radiotherapy may result in a permanent decrease in spermatogenesis. Therefore, it is crucial to offer sperm preservation prior to the start of therapy in men diagnosed with TC. The results of this study indicate that conception was possible for 48% (35/73) of men after TC treatment using natural and artificial means even with limitations in semen quality or quantity, and no birth defects or childhood malignancies were reported. Only 21.6% of men surveyed chose to use sperm banking prior to TC therapy, perhaps reflecting a need to educate both TC patients and medical practitioners about sperm cryopreservation.

AUTHOR CONTRIBUTIONS

PP and BHG contributed equally to the design of the research, the analysis and interpretation of the data, and the drafting of the manuscript. PL was responsible for the data analysis. YRH participated in collection of clinical data. ZL is the principal investigator, supervised the project, and revised this manuscript. All authors read and approved the final manuscript.

COMPETING INTERESTS

The authors declare that they have no competing interests.

ACKNOWLEDGMENTS

The authors thank the staff of Shanghai Human Sperm Bank for collecting data of patients who have semen sample cryopreserved. The research was supported by the following grants: National Basic Research Program of China (No. 2011CB944504), the Science and Technology Commission of Shanghai Municipality (No. 10JC1409900), Project supported by the Shanghai Key Laboratory for Assisted Reproduction and Reproductive Genetics (No. 12DZ2260600), Scientific Development Foundation of Shanghai Population and Family Planning Commission (No. 2012JG07), Key Clinical Program of the Ministry of Health of China and Pudong New Area sanitary system key disciplinary group project (No. PWZxkq2010-03).

REFERENCES

1 McGlynn KA, Devesa SS, Sigurdson AJ, Brown LM, Tsao L, *et al*. Trends in the incidence of testicular germ cell tumors in the United States. *Cancer* 2003; 91: 63–70.
2 Schagen SB, Boogerd W, Muller MJ, Huinink WT, Moonen L, *et al*. Cognitive complaints and cognitive impairment following BEP chemotherapy in patients with testicular cancer. *Acta Oncol* 2008; 47: 63–70.
3 Verdecchia A, Francisci S, Brenner H, Gatta G, Micheli A, *et al*. EUROCARE-4 Working Group. Recent cancer survival in Europe: a 2000–02 period analysis of EUROCARE-4 data. *Lancet Oncol* 2007; 8: 784–96.
4 Shetty G, Meistrich ML. Hormonal approaches to preservation and restoration of male fertility after cancer treatment. *J Natl Cancer Inst Monogr* 2005; 33: 36–9.

5 Huyghe E, Matsuda T, Daudin M, Chevreau C, Bachaud JM, *et al*. Fertility after testicular cancer treatments: results of a large multicenter study. *Cancer* 2004; 100: 732–7.
6 Kim C, McGlynn KA, McCorkle R, Zheng T, Erickson RL, *et al*. Fertility among testicular cancer survivors: a case-control study in the U.S. *J Cancer Surviv* 2010; 4: 266–73.
7 Fraietta R, Spaine DM, Bertolla RP, Ortiz V, Cedenho AP. Individual and seminal characteristics of patients with testicular germ cell tumors. *Fertil Steril* 2010; 94: 2107–12.
8 O'Flaherty C, Hales BF, Chan P, Robaire B. Impact of chemotherapeutics and advanced testicular cancer or Hodgkin lymphoma on sperm deoxyribonucleic acid integrity. *Fertil Steril* 2010; 94: 1374–9.
9 Brennemann W, Stoffel-Wagner B, Helmers A, Mezger J, Jäger N, *et al*. Gonadal function of patients treated with cisplatin based chemotherapy for germ cell cancer. *J Urol* 1997; 158: 844–50.
10 Magelssen H, Brydøy M, Fosså SD. The effects of cancer and cancer treatments on male reproductive function. *Nat Clin Pract Urol* 2006; 3: 312–22.
11 De Mas P, Daudin M, Vincent MC, Bourrouillou G, Calvas P, *et al*. Increased aneuploidy in spermatozoa from testicular tumour patients after chemotherapy with cisplatin, etoposide and bleomycin. *Hum Reprod* 2001; 16: 1204–8.
12 Howell S, Shalet S. Gonadal damage from chemotherapy and radiotherapy. Endocrinol Metab Clin North Am. 1998; 27: 927-43.
13 Colpi GM, Contalbi GF, Nerva F, Sagone P, Piediferro G. Testicular function following chemo-radiotherapy. *Eur J Obstet Gynecol Reprod Biol* 2004; 113: S2–6.
14 Beck SD, Bey AL, Bihrle R, Foster RS. Ejaculatory status and fertility rates after primary retroperitoneal lymph node dissection. *J Urol* 2010; 184: 2078–80.
15 Howell SJ, Shalet SM. Spermatogenesis after cancer treatment: damage and recovery. *J Nat Cancer Inst Monogr* 2005; 34: 12–7.
16 O'Flaherty CM,'Chan PT, hHales BF, aRobaire B. Sperm chromatin structure components are differentially repaired in cancer survivors. *J Androl* 2012; 33: 629–36.
17 Shalet SM, Tsatsoulis A, Whitehead E, Read G. Vulnerability of the human leydig cell to radiation damage is dependent upon age. *J Endocrinol* 1989; 120: 161–5.
18 Stahl O, Eberhard J, Cavallin-Stahl E, Jepson K, Friberg B, *et al*. Sperm DNA integrity in cancer patients: the effect of disease and treatment. *Int J Androl* 2009; 32: 695–703.
19 Trottmann M, Becker AJ, Stadler T, Straub J, Soljanik I, *et al*. Semen quality in men with malignant diseases before and after therapy and the role of cryopreservation. *Eur Urol* 2007; 52: 355–67.
20 Girasole CR, Cookson MS, Smith JA Jr, Ivey BS, Roth BJ, *et al*. Sperm banking: use and outcomes in patients treated for testicular cancer. *BJU Int* 2007; 99: 33–6.
21 Scammell GE, White N, Stedronska J, Hendry WF, Edmonds DK, *et al*. Cryopreservation of semen in men with testicular tumour or Hodgkin's disease: results of artificial insemination of their partners. *Lancet* 1985; 2: 31–2.
22 Ragni G, Somigliana E, Restelli L, Salvi R, Arnoldi M, *et al*. Sperm banking and rate of assisted reproduction treatment: insights from a 15-year cryopreservation program for male cancer patients. *Cancer* 2003; 97: 1624–9.
23 Spermon JR, Kiemeney LA, Meuleman EJ, Ramos L, Wetzels AM, *et al*. Fertility in men with testicular germ cell tumors. *Fertil Steril* 2003; 79: 1543–9.
24 Skinner R, Wallace WH, Levitt G. Long-term follow-up of children treated for cancer: why is it necessary, by whom, where and how? *Arch Dis Child* 2007; 92: 257–60.
25 Matos E, Skrbinc B, Zakotnik B. Fertility in patients treated for testicular cancer. *J Cancer Surviv* 2010; 4: 274–8.
26 Brydoy M, Fossa SD, Klepp O, Bremnes RM, Wist EA, *et al*. Paternity following treatment for testicular cancer. *J Natl Cancer Inst* 2005; 97: 1580–8.
27 Magelssen H, Haugen TB, von During V, Melve KK, Sandstad B, *et al*. Twenty years experience with semen cryopreservation in testicular cancer patients: who needs it? *Eur Urol* 2005; 48: 779–85.
28 Hawkins MM. Pregnancy outcome and offspring after childhood cancer. *BMJ* 1994; 309: 1034.
29 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.
30 Gandini L, Sgrò P, Lombardo F, Paoli D, Culasso F, *et al*. Effect of chemo- or radiotherapy on sperm parameters of testicular cancer patients. *Hum Reprod* 2006; 21: 2882–9.
31 Spermon JR, Ramos L, Wetzels AM, Sweep CG, Braat DD, *et al*. Sperm integrity pre- and post-chemotherapy in men with testicular germ cell cancer. *Hum Reprod* 2006; 21: 1781–6.
32 Stahl O, Eberhard J, Jepson K, Spano M, Cwikiel M, *et al*. The impact of testicular carcinoma and its treatment on sperm DNA integrity. *Cancer* 2004; 100: 1137–44.
33 Bieber AM, Marcon L, Hales BF, Robaire B. Effects of chemotherapeutic agents for testicular cancer on the male rat reproductive system, spermatozoa, and fertility. *J Androl* 2006; 27: 189–200.
34 Smit M, van Casteren NJ, Wildhagen MF, Romijn JC, Dohle GR. Sperm DNA integrity in cancer patients before and after cytotoxic treatment. *Hum Reprod* 2010; 25: 1877–83.

How to cite this article: Ping P, Gu BH, Li P, Huang YR, Li Z. Fertility outcome of patients with testicular tumor: Before and after treatment. *Asian J Androl* 2013 Dce 16. doi: 10.4103/1008-682X.122194. [Epub ahead of print]