Radical and testis-sparing surgery for primary testicular tumors: A single-center experience

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Abstract. The aim of the present study was to assess the oncological and functional outcomes of testis-sparing surgery (TSS) for testicular tumors compared with radical orchiectomy (RO) in a single center. A retrospective comparative cohort study was conducted in Changzheng Hospital. Patients were identified using the hospital information system from January 1999 to December 2016, collecting all of the data regarding clinical, treatment and prognostic profiles. Patient follow-up was also executed to obtain information on patients' survival status, serum markers profiles, disease progression, androgen substitution requirement and paternity status. In total 158 patients were enrolled into the cohort study, including 23 TSS cases. The TSS procedure was primarily conducted in younger patients (average age, 31.9 vs. 47.7 years) or those with smaller tumors (average tumor diameter, 26.0 vs. 51.5 mm). The overall survival and recurrence free survival revealed no differences in the two groups, suggesting similar oncolcical outcomes. Kaplan-Maier analysis demonstrated a higher cumulative paternity rate in the TSS group than in RO group, indicating a possible advantage of preserving patients' fertility in TSS over RO. TSS with proper adjuvant therapies proved to be a promising alternative in the avoidance of emasculation, infertility, life-long androgen substitution and other psychosexual difficulties, as the oncological outcomes were not inferior to RO in the selected cases. However, further investigation is required in order to assess its oncological and functional values.

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Introduction

Although diverse in morphological and clinical manifestations, neoplasms of the testicles account for a notable proportion of all male urogenital tumors. They had a relatively rare overall occurrence, with a peak prevalence rate during the second and third decades of life, being the most popular solid tumor in men of this age (1). According to the American Cancer Society statistics, in 2015 approximately 8,430 new cases of testicular cancer were diagnosed and more than 380 patients succumbed of the disease in the US (2). Similarly in China these figures were estimated to be 4,000 and 1,000, respectively in the year 2015 (3). With the development of cisplatin-based chemotherapy and the integration of surgery, testicular tumors, especially germ cell tumors (GCTs), have been considered a curable disease, the 5-year relative survival rate of which has notably increased from 83 to 97% in the past 4 decades (2). However, there are certain pathological patterns in which the treatment options are unclear and remain a clinical challenge. Testis-sparing surgery (TSS), commonly known as partial orchiectomy in recent years has emerged as promising treatment option especially in selective patients including bilateral lesions, monorchide tumors and those facing psychological stress or with paternity demand.

Traditionally TSS was a controversial surgical modality, carried out only in selected cases including bilateral organ-confined small lesions, tumors in a solitary testis with sufficient androgen production, or suspected benign tumors when serum tumor markers are normal (4) with no significant role in GCT patients. It was only by recent studies that showed equivalent oncological outcomes for organ-sparing surgery when compared with radical orchiectomy (RO) in elective groups. Also the functional issues and quality of life pertaining to treatment also seemed to be promising (5). However, comparative studies between TSS and traditionally applied RO are still limited both in quantity and in perspective view. Here we reviewed retrospectively our series of cases undergoing organ-sparing surgery for testicular tumors, and share our experiences in patient selection, surgical technics, and clinical difficulties we faced.

Subjects and methods

The retrospective cohort. The present study performed a retrospective comparative study only; all TSS and RO procedures

were conducted previously. Ethical approval was obtained from the Institutional Review Board of Second Military Medical University (Shanghai, China) and all participants provided written informed consent during the follow-up procedures. The present study retrospectively retrieved patients' information from the hospital information system (HIS) database of Changzheng Hospital from January 1999 to December 2016. The diagnoses in the HIS system were made and compiled according to the ICD-9 categories. During data retrieving, the ambiguous matching strategy was used to maximize the valid cases. All secondary tumors, such as those with metastasis and lymphoma testicular infiltration, were excluded from the study. The cohorts were determined according to surgical procedure, viz. RO group and TSS group, in order to better assess and compare the clinical and prognostic features for each surgical group.

Evaluation of clinical characteristics. After admission detail history taking and physical examinations were done and marital status as well as prior paternity was inquired in every patient. The patients usually presented with a chief complaint of palpable, painless mass within the scrotum, only few patients had discernable inguinal lymph nodes during physical examination. Scrotal ultrasound is the most widely used screening method for discrimination of testis tumors with extratesticular or epididymis lesions. Contrast enhanced pelvic CT and MRI scanning are two major diagnostic tools used before surgery. These two imaging techniques are more helpful to suggest the tumors' malignant nature and at the same time help assess the local and retroperitoneal lymph nodes as well as metastasis status.

When surgery is considered, both ultrasound and CT/MRI should be referred by the surgeons, for they act complementary roles in pre-operative assessments. The Doppler ultrasonography is helpful in the evaluation of the tumors' blood supply. Ultrasound may tend to overestimate the size of the tumors and underestimate the residual testis parenchyma (6), therefore a more precise portrait of the tumor should be obtained by CT/MRI to determine whether a partial orchiectomy is feasible or not.

Serum testosterone level (T), serum α-fetoprotein (AFP), human chorionic gonadotrophin (hCG) and lactate dehydrogenase (LDH) levels were also evaluated before surgery. Chest X-ray is essential to rule out the possible metastatic foci and complete the accurate staging in all clinically suspected cases, because testicular cancers are prone to metastasis especially to the lungs. Chest CT scan is also recommended if clinically indicated.

Intraoperative frozen-section examination (FSE) was sent when the surgeon encountered ambiguous consideration of whether the tumor was malignant or benign. However, definitive pathological diagnosis was determined by final pathological analysis (FPA). After TSS, tumor bed biopsy is mandatory to exclude positive margins and intratubular germ cell neoplasia (ITGCN), 6-point systemic biopsy is especially recommended in order to obtain higher positive rate. Normal parenchyma biopsy was not performed, because it is usually hard to define between tumor bed and normal parenchyma, since the cutting edge was supposed to be overriding the margin of the tumor. Therefore, the parenchyma biopsy is not emphasized in our practice.

Protocol of primary and adjuvant treatment. Surgery is the mainstay treatment for testicular tumors and RO is the surgery of choice in majority of the cases. TSS is recommended when: i) The tumor size is small enough to leave sufficient normal testicular parenchyma; ii) preoperative imaging suggestive of benign lesions; iii) monorchide or bilateral tumor patients who may be virtually castrated if RO is implemented; and iv) patients have strong psychological and social demand to preserve the organ, or fear of infertility and life-long androgen deficiency and substitution.

Adjuvant treatment, including chemotherapy, radiotherapy, and retroperitoneal lymph nodes dissection (RPLND), were to be done according to the instruction of the NCCN guideline for testicular cancer (version 1.2014).

Protocol of follow-up. Once surgical procedure was determined, follow-up sessions were also initiated simultaneously. Endpoint information (disease relapse, survival status, postoperative paternity) were obtained mainly by telephone, mail, e-mail and instant messaging (IM) tools (WeChat® and Fetion®). Medical imaging and serum tumor markers were acquired during outpatient department (OPD) visits. Measurement of serum tumor markers and endocrine status indices were implemented, including serum AFP, LDH, HCG and testosterone levels during the follow-up period. Childbearing and need for androgen substitution therapy after surgery were also inquired and recorded. Deaths due to disease and postoperative paternity by natural conception were considered as primary endpoints and disease relapse as secondary endpoint during follow-up.

Statistical analysis. The baseline of all the patients was described by a cross-sectional survey. The patients were subdivided into the RO and TSS groups. The differences in rates were tested using Chi-square or Fisher's exact probability test. The differences in quantitative values were tested using Student's t-test, after statistical tests confirmed samples' normal distribution and homogeneity of variance. When taking postoperative paternity, disease relapse and disease related deaths to be follow-up endpoints, survival analysis was applied using product limit method. Kaplan-Meier curves were plotted with log-rank test to estimate the difference between the two groups. All statistical analyses were applied using Stata® software (version 11.0 Special Edition; StataCorp LLC, College Station, TX, USA). Kaplan-Maier analysis plots were drawn using GraphPad Prism® 5 (version 5.01; GraphPad Software, Inc., La Jolla, CA, USA).

Results

Demographic and clinical features of the patients. A total of 158 patients were enrolled in this retrospective study. The enrollment procedure is shown in Fig. 1. Among these 158 patients only 125 completed the follow-up. Follow-up periods range from 8 to 214 months, with a median follow-up of 78 months. The average course of disease was 33.2 months (31.2 and 45 months in RO group and TSS group, respectively, no significant difference). The average age at diagnosis is 45.4 s (median age 44). The average age in TSS group (29.3 s, standard deviation 13.0) were younger compared to

Table I. Demographic and clinical features of patients.

Feature	Overall	RO	TSS
Patients, n	158	135	23
Course of disease, months (±SD)	33.2 (±83.2)	31.2 (±80.4)	45 (±99.3)
Average age of diagnosis (±SD)[a]			
Median age	45.0 (±17.9)	47.7 (±17.3)	29.3 (±13.0)
Average age	44	47	25
Left/Right, n	70/79	61/68	9/11
Bilateral tumors, n	9	6	3
Monorchide tumors, n	6	4	2
Clinical manifestations			
Local pain	37 (23.4%)	33 (24.4%)	4 (17.4%)
Fever	5 (3.2%)	5 (3.7%)	0 (0%)
Scrotum enlargement[b]	79 (50.0%)	77 (57.0%)	2 (8.7%)
Non-palpable disease	20 (12.7%)	15 (11.1%)	5 (21.7%)
Tumor diameter, mm (±SD)[c]	47.2 (±25.3)	51.5 (±24.4)	21.7 (±11.4)
Simultaneous hydrocele			
Unilateral	12	11	1
Bilateral	4	3	1
Overall	16	14	2
Tumor cyst degeneration	10	7	3
Previous or current cryptorchidism	18	16	2
Follow-up period, months (±SD)			
Average follow-up	82.3 (±48.9)	86.2 (±48.2)	59.2 (±43.3)
Median follow-up	78 (8-214)	85 (8-214)	44.5 (9-133)
Loss to follow-up rate (number of dropout)	20.9% (33)	20.7% (28)	21.7% (5)

[a]P<0.0001, Student's t-test; [b]P<0.0001, Pearson's Chi-square test; [c]P<0.0001, Student's t-test. RO, radical orchiectomy; TSS, testis-sparing surgery; SD, standard deviation.

RO group (47.7 s, standard deviation 17.3, P<0.0001), which showed the TSS procedure is in favor of younger patients. Here we noticed the imbalance between the two comparative cohorts, the reason may due to: i) The significance of TSS in the treatment of testicular tumors had just been recognized since a few decades ago; and ii) the selection of TSS candidates has an intrinsic bias towards younger patients with imperative functional demands. No positive surgical margin was reported and no ITGCN was detected during intraoperative biopsy and final pathology analysis in all 23 patients who underwent TSS.

We also carefully recorded patients' chief complaints, tumor size and other related clinical parameters. During the course of the disease we were surprised to note that local pain and fever, which were considered as a hallmark to suggest a non-tumorous lesion such as acute infection or torsion, occurred more than expected in our patients. This indicates that differential diagnosis based on symptoms and signs may not be quite reliable. Besides that, as is shown in the table, the average tumor size is much smaller in TSS group than in RO group, with only a few cases of scrotum enlargement observed in TSS than in RO group (Table I).
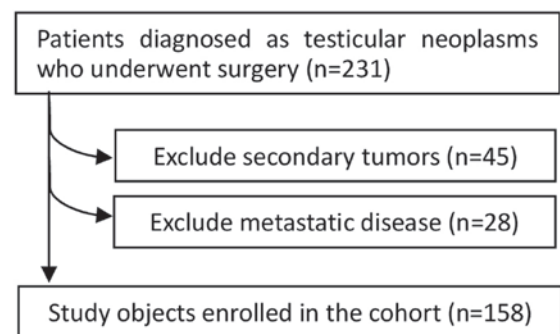

Figure 1. Schematic of the process by which patients were enrolled to the present study.

After the tumors resection, the specimens were sent to the hospital's pathology department to obtain a final pathological diagnosis (Table II). GCTs were the most commonly seen pathological type (accounts for 81.6% of all patients). The ratio was 86.7% in RO group and only 52.2% in TSS group, which reflected a current prudence of doctors when considered TSS for possible malignant cases. Among the 28 benign

Table II. Pathological types of tumors.

Histopathological types	Overall	RO	TSS
GCT[a]	129	117	12
Seminoma	66	61	5
NSGCT	63	56	7
Embryonal carcinoma	13	12	1
Yolk sac tumor	3	3	0
Mature teratoma	5	3	2
Dermoid cyst	3	3	0
Immature teratoma	2	2	0
Teratoma with malignant areas	5	5	0
Mixed forms	32	28	4
Adenoma of collecting ducts and rete	4	4	0
Paratesticular sarcoma	1	1	0
Adenomatoid tumor	4	3	1
Sex cord-gonadal stromal tumors	6	4	2
Leydig cell tumor	3	1	2
Sertoli cell tumor	3	3	0
Inflammatory granuloma	5	4	1
Epidermal cyst	8	2	6
Vascular anomaly	1	0	1
Sum	158	135	23

[a]P<0.0001, Pearson's Chi-square test. GCT, germ cell tumor; NSGCT, non-seminoma GCT; RO, radical orchiectomy; TSS, testis-sparing surgery.

lesions, 5 of them were mature teratomas, 3 dermoid cysts, 3 Leydig cell tumors, 3 Sertoli cell tumors, 5 inflammatory granulomas, 8 epidermal cysts and 1 vascular anomaly. Leydig cell tumor is a rare kind of testicular tumor rises from sex cord-gonadal stroma. These patients came to consultation because of gynecomastia. In the 3 Sertoli cell tumor cases, 1 were Peutz-Jeghers syndrome patient transferred from the department of gastroenterology, 1 with gynecomastia and 1 detected by self-palpation.

Oncological and functional outcome in bilateral and monorchide tumors. It was estimated that bilateral testicular tumors, both synchronous and metachronous, accounts only less than 5% of all testicular tumors. But when considering solitary testicular tumors together, the treatment-related definitive castration and the ensuing problems in fertility and virilization is not rare (7-9). Here we listed the characteristics and clinical turnover of a selected subgroup: Patients with bilateral tumors or solitary testicle tumors (Tables III and IV). It may be noticed in the table that only 2 of 6 monorchide tumor patients and 3 of 9 bilateral tumor patients received partial orchiectomy, the proportion of which was supposed to be higher. The main reasons for not choosing TSS were i) preoperative hypogonadism; ii) fear of disease relapse; and iii) not in urgent need of future paternity. The average age of the 10 patients undergoing RO (59.3 s) was significantly older than those who had testis-sparing surgeries (32.8 s). Three of the five TSS patients were

stage IA diseases, whereas in RO group only 1 patient was stage IA disease. All patients who underwent TSS were recommended for external irradiation of the remaining testis to eradicate the possible undetected ITGCN. However, the youngster (case no. 6, Table III) who refused this suggestion developed disease relapse after 12 months' follow-up, and RO was done after careful evaluation. In patients who were planning to father a child, sperm cryopreservation was performed for future use. The postoperative paternity status (by natural conception rather than use of cryopreserved sperm) was also recorded.

Oncological and functional outcome in TSS for unilateral malignant tumors. Although currently not recommended, in selected cases of unilateral GCTs depending on tumor size and other clinical conditions, TSS is considered as treatment of choice. Here we summarized patients who had undergone TSS with a pathological diagnosis of GCTs. The reason for choosing TSS instead of standard RO were: i) Cannot accept the loss of genital organ; ii) resent of possible hypogonadism as well as life-long androgen substitution; and iii) early clinical staging and tumor size small enough to allow a TSS procedure. Of the 7 unilateral GCT patients who had TSS, 5 cases were seminomas, 1 mature teratoma and 1 mixed forms GCT. They were all staged IA phase of disease according to AJCC's TNMS staging system. All, except the mature teratoma patient, were recommended for adjuvant radiotherapy after surgery, including 1 seminoma patient who had adjuvant radiotherapy

Table III. Characteristics and clinical turnover of bilateral and solitary testis tumors.

No.	Diagnosis	Surgical procedure	Age (years)	Reason of monorchide/ Chief complaints for consultation	Histological types	AJCC's TNMS staging	Adjuvant treatment	Turnover/Follow up (months)	Subsequent treatment following relapse
1	Monorchide	RO	37	Previous cryptorchidism	Seminoma	pT2N0M0S0/IB	Surveillance	-/182	-
2	Monorchide	RO	58	Prior history of GCT	Seminoma	pT2N0M0S0/IB	Surveillance	-/139	-
3	Monorchide	TSS	11	Prior history of parotitis, right testicle atrophy	Mature teratoma	pT1N0M0S0/IA	RT, total dose 20Gy in 10 days	-/117	-
4	Monorchide	RO	25	Previous cryptorchidism	Seminoma	pT2N1M0S0/IIA	BEP 3 cycles	-/70	-
5	Monorchide	RO	57	Previous cryptorchidism	Seminoma	pT2N1M0S0/IIA	EP 4 cycles	-/51	-
6	Monorchide	TSS	19	Previous cryptorchidism	Mixed forms GCT	pT1N0M0S0/IA	Surveillance	Local relapse/12	RO, EP 4 cycles
7	Bilateral	RO	59	Scrotum enlargement and palpable masses	Seminoma	pT2N1M0S0/IIA	RT/BEP 3 cycles	-/99	-
8	Bilateral	TSS	65	Palpable masses	Mixed forms GCT	pT2N1M0S0/IIA	RPLND/EP 4 cycles	-/92	-
9	Bilateral	RO	65	Scrotum enlargement and palpable masses	Yolk sac tumor	pT2N1M0S1/IIA	EP 4 cycles	Metastasis/86	RT, EP 4 cycles
10	Bilateral	TSS	34	Scrotum enlargement and palpable masses	Mixed forms GCT	pT1N0M0S0/IA	RPLND/RT, total dose 20Gy in 10 days	-/76	-
11	Bilateral	RO	72	Scrotum enlargement	Mixed forms GCT	pT1N1M0S0/IIA	BEP 3 cycles	Metastasis/4; Died/12	EP 2 cycles
12	Bilateral	RO	76	Scrotum enlargement	Immature teratoma	pT1N0M0S0/IA	Surveillance	Loss to follow up	-
13	Bilateral	RO	66	Palpable masses	Mixed forms GCT	pT2N0M0S0/IB	BEP 2 cycles	-/20	
14	Bilateral	RO	78	Palpable masses	Seminoma	pT1N0M0S0/IA	Surveillance	-/19	
15	Bilateral	TSS	35	Scrotum enlargement and palpable masses	Embryonal carcinoma	pT2N0M0S1/IS	BEP 3 cycles	-/12	

RPLND, retroperitoneal lymph node dissection; RT, radio therapy; BEP, bleomycin, etoposide and cisplatin; EP, etoposide and cisplatin; RO, radical orchiectomy; TSS, testis-sparing surgery; GCT, germ cell tumors; AJCC, American Joint Committee on Cancer; TNMS, tumor-node-metastasis staging.

Table IV. Functional and paternity results of bilateral and solitary testis tumors.

No.	Diagnosis	Surgical procedure	Age (years)	Marital/Paternity status (no. of children)	Preoperative sperm cryopreservation	Postoperative paternity by natural conception	Postoperative serum androgen level	Postoperative hormone substitution
1	Monorchide	RO	37	Unmarried/-	No	- (Unmarried)	Low	Yes
2	Monorchide	RO	58	Married/2	No	-	NA	No
3	Monorchide	TSS	11	Unmarried/-	No	- (Unmarried)	Normal	No
4	Monorchide	RO	25	Married/-	Yes	-	Low	Yes
5	Monorchide	RO	57	Married/-	No	-	NA	No
6	Monorchide	TSS	19	Unmarried/-	Yes	-(Unmarried)	Low	Yes
7	Bilateral	RO	59	Married/1	No	-	NA	No
8	Bilateral	TSS	65	Married/1	No	-	NA	No
9	Bilateral	RO	65	Married/1	No	-	NA	No
10	Bilateral	TSS	34	Married/1	No	-	Normal	No
11	Bilateral	RO	72	Married/2	No	-	NA	No
12	Bilateral	RO	76	Married/2	No	Loss to follow up	-	-
13	Bilateral	RO	66	Married/1	No	-	Low	Yes
14	Bilateral	RO	78	Married/2	No	-	NA	No
15	Bilateral	TSS	35	Married/-	Yes	-	Normal	No

NA, not available/not reported; RO, radical orchiectomy; TSS, testis-sparing surgery.

after successful child bearing. 4 of the 7 patients completed the follow-up process, and none of them had postoperative hypogonadism or needed androgen replacement therapy. No disease recurrence and cancer related deaths were observed during the follow-up.

Postoperative paternity, tumor relapse and survival. Kaplan-Maier plots based on product-limit method were applied in this section of analysis. We first observed postoperative paternity status. A cumulative hazard curve was plotted to show the postoperative paternity by natural conception rather than use of cryopreserved sperm. As is shown in Fig. 2, the cumulative paternity rate in TSS group is significantly higher than in RO group (log-rank test, P=0.0051). Kaplan-Maier analyses for disease relapse and cancer related deaths (Figs. 3 and 4) showed no significant difference between RO and TSS groups.

Discussion

The improvement in disease control of testicular tumors and the increase in therapy related long-term survival has enabled us to focus more on treatment-related side effects and preservation of quality of life. The germinal epithelium is exquisitely sensitive to platin-based chemotherapy and radiotherapy, which provides the opportunity to concentrate our research from life-saving procedure to function-saving novel therapies. In testicular tumor patients, impaired reproductive function (such as oligospermia and azoospermia) is not only the reason for seeking medical consultation (10), but also the undesirable treatment consequence related especially to RO (11), which is even more troublesome. Hypogonadism in testicular cancer survivors is a major concern for both patients and surgeons.

However, when considering the pros and cons of the testis-sparing surgery, the notorious nature of testicular cancers' fast growth and progression has always casted a shadow over the procedure's optimistic perspective. For many years discretion and conservatism had been the keynote of testicular cancer treatment. Despite the deleterious effect of radio-therapy or chemotherapy on both fertility and virility, radical measures including 'desperation surgery (salvage surgery)' and high-dose chemotherapy were thought to be beneficial for testicular cancer patients (12,13). Moreover, because of the organ's small size, acquisition of both a tumor-free surgical margin and well preserved normal parenchyma will be a great challenge. Finally, adjuvant radiotherapy and chemotherapy following TSS not only exhibit their toxic effect within therapeutic doses, but also may induce secondary malignant neoplasms (SMNs). Thus striking a balance between the merits and demerits of this controversial procedure is easier than a dilemma.

In our study, we illustrated the feasibility of the surgical procedure and the unique advantage that TSS possesses. One of the many advantages is the good potential of preserving fertility. The cumulative paternity rate shown in our results also supported the benefits of TSS, although this result has to be considered with caution of some inevitable biases. The postoperative child-bearing is a complex course which may be influenced by many confounders. The desire of paternity may vary depending on one's previous paternity status and social-economical ability. The surgical history on genital organ is an unfavorable factor to a youngster seeking to get married which apparently cannot be conclusively related to infertility. Contraceptive measures may also significantly influence the postoperative paternity rate, thus impairing the estimation of postoperative fertility preservation. Besides, the child birth in

Table V. Oncological and functional outcome in unilateral GCTs undergoing TSS.

No.	Age (years)	Side	Histological types	Tumor size (mm)	AJCC's TNMS staging	Adjuvant treatment	Turnover/Follow-up time (months)	Postoperative paternity by natural conception	Postoperative androgen level/substitution
1	22	Right	Seminoma	20	pT1N0M0S0/IA	RT, AS	Loss to follow up	-	-
2	47	Right	Seminoma	25	pT1N0M0S0/IA	RT, AS	-/133	No	Normal hormone level/No substitution
3	12	Right	Seminoma	7	pT1N0M0S0/IA	RT, AS	-/119	No	Normal hormone level/No substitution
4	43	Right	Mature teratoma	20	pT1N0M0S0/IA	AS	Loss to follow up	-	-
5	30	Right	Mixed form GCT	10	pT1N0M0S0/IA	RT, nerve-sparing RPLND, AS	-/74	No	Normal hormone level/No substitution
6	22	Left	Seminoma	18	pT1N0M0S0/IA	AS, RT recommended	-/39	Yes/24	Normal hormone level/No substitution
7	39	Left	Seminoma	23	pT1N0M0S0/IA	RT, AS	Loss to follow up	-	-

RT, radiotherapy; AS, active surveillance; RPLND, retroperitoneal lymph node dissection; RO, radical orchiectomy; TSS, testis-sparing surgery; GCT, germ cell tumors; AJCC, American Joint Committee on Cancer; TNMS, tumor-node-metastasis staging.
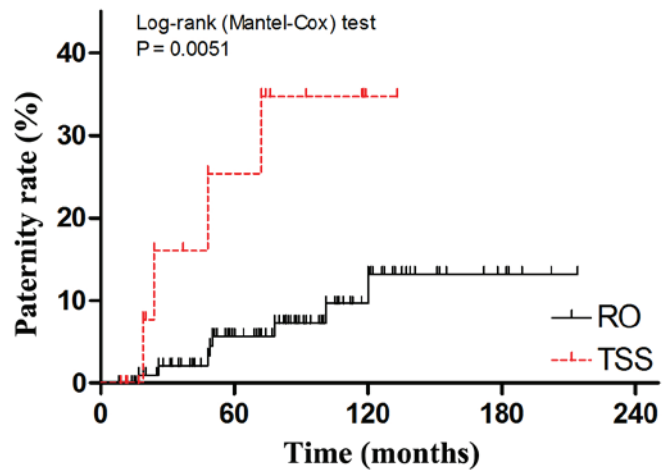

Figure 2. Kaplan-Meier analysis of postoperative paternity rate by natural conception. RO, radical orchiectomy; TSS, testis-sparing surgery.
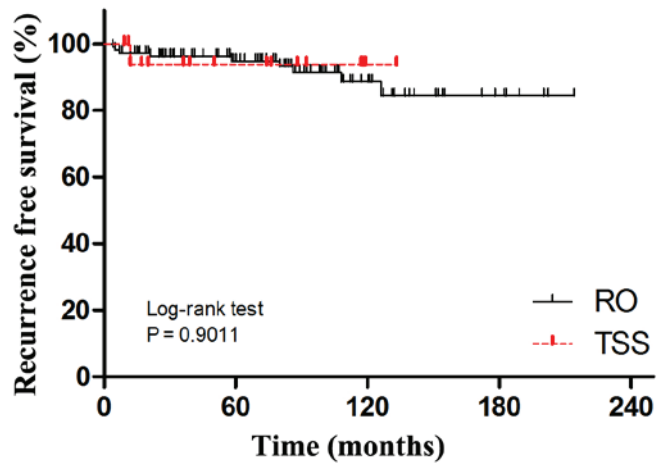

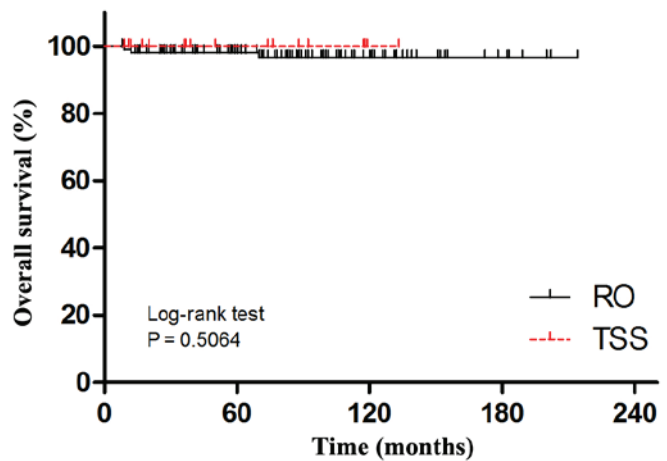Figure 3. Kaplan-Meier analysis of disease relapses. RO, radical orchiectomy; TSS, testis-sparing surgery.

Figure 4. Kaplan-Meier analysis of disease-associated mortalities. RO, radical orchiectomy; TSS, testis-sparing surgery.

China has always been regulated by laws and policies to avoid overpopulation, which may also impact the result. It is worthwhile to note that the post-TSS patients were advised to

father a child prior to radiotherapy as soon as possible to avoid possible reproductive toxicity (14). But even if conditions do not permit, TSS allows a short window period to recover from such harmful exposure (15-18). This is beneficial especially to those who do not have access to sperm cryopreservation or artificial insemination technology.

Another advantage of TSS compared with RO is the potential of preserving patients' virility. Hypogonadism occurred in approximately 10-20% of patients who underwent RO (19). The TSS procedure allows preservation of an essential amount of Leydig cells for normal endocrine functioning. It has already been well accepted that the TSS procedure with a good preservation of normal testicular parenchyma is particularly important in monorchide and bilateral testicular tumor patients. In our study, hypogonadism did not occur in post-TSS patients, which also supported this point of view.

TSS has already been accepted as a treatment modality for bilateral and monorchide tumors with normal preoperative testosterone levels. But elective TSS is currently still not advised in patients with a normal contralateral testis. However, RO survivors are at high risk of contralateral relapse when compared to average population, thus leaving with fewer therapeutic options. Besides, previous observation overestimated the proportion of malignant cases in all testicular tumors, while recent studies have proved a much lower constituent ratio (20). When considering children and adolescent patients, the registry-based epidemiology studies formerly conducted had conspicuous bias. The inaccurate assessment of pathological types and their degree of malignancy in children and adolescent patients' would definitely impact the therapeutic strategy as well as the functional outcome (21,22). It is reasonable to infer that previous treatment modality of testicular tumors should not be extrapolated precipitately to current status, especially in youngsters and other possible long-survivors who are more concerned about better quality-of-life (21). Therefore, recent studies on testicular cancer have emerged with promising results. Galosi *et al* (23) applied a 'diagnostic-therapeutic pathway' in small, non-palpable single testis lesions to minimize the overtreatment in benign tumors. Ye *et al* (24) retrospectively reviewed the trend of TSS for pediatric testicular tumors in South China, and advocated the potential benefits of this procedure. Keske *et al* (25) showed a significant decrease in neighboring testis ITGCN but increase in multifocality, hence advised caution and safety rim of normal tissue within the resection margin. Bojanic *et al* (26) even made a big step forward by evaluating the feasibility of TSS in GCTs alone. With a median follow-up time of 45 months, only 1 out of 9 GCT patients developed local recurrence after 39 months. None of the studies above had set definite criterion excluding TSS for malignant patients such as GCTs, but the results were still far from conclusive. In our study GCT patients underwent successful TSS and were observed with satisfactory outcomes. By extending the inclusion criteria of TSS we hope these results will provide supporting evidences to TSS procedure in oncological and functional efficacy.

Still there are some limitations within our study. Except the above-mentioned imbalance between the two comparative cohorts, the follow-up of functional results has not always been executed in a consistent manner. Some of the laboratory tests and radiological examinations were not listed as routine re-examination items since the introduction of TSS procedure in our department. It was only after around the year 2010 that we gradually established a set of follow-up protocols, including history taking, physical examination, medical image and laboratory tests. Also we noticed a very low detection rate of ITGCN, which is a considerable discrepancy between our result and previous reports. Analysis and retrospection were performed, and the following reasons had been summed up to be responsible for the unreasonable results: i) Small sample size (23 TSS cases, only 12 of them were GCTs) resulted in the lack of statistical power; ii) selection bias during the initial phase of the conduction of TSS (we usually preferred small, confined lesions which were easier to perform the surgery); and iii) the biopsy of tumor bed in the first few cases were performed in a more or less careless style, though (i.e., 1 point random biopsy and 2 points). A better-defined follow-up and biopsy protocol would be mandatory in the future to achieve better study results.

In summary, we believe TSS may be a suitable option for patients subgroup including: patients who are undecided or planning to father children in the near future, especially when they have hesitation in sperm cryopreservation/insist on natural insemination; patients who cannot accept loss of testis or the possibility of life-long androgen substitution. Once the tumor volume allows an organ-sparing attempt, especially if a benign tumor is assumed on preoperative examinations, TSS should be offered to patients as a potential option against the traditionally practiced RO.

Availability of data and materials

The datasets generated and/or analyzed during the current study are not publicly available due to individual privacy and ethical considerations. However, a minimal amount of the dataset used during the current study is available from the corresponding author on reasonable request.

Authors' contributions

FX, JZS, JKW and LHW designed the present study. FX and JZS performed statistical analysis and wrote the manuscript. JKW and LHW reviewed and edited the manuscript. YSL performed statistical analysis and reviewed the manuscript. YL, TL and JW executed the follow-up procedures. All authors read and approved the manuscript.

Ethics approval and consent to participate

Ethical approval was obtained from the Institutional Review Board of Second Military Medical University (Shanghai, China). Written informed consent was obtained from all participants.

Patient consent for publication

Not applicable.

Competing interests

The authors declare that they have no competing interests.

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