



Testis-sparing Surgery in the Treatment of the Normal Contralateral Testicle: A Prospective Multicenter Bench Study Following Radical Orchiectomy

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Abstract

Objective: Testicular tumors can be seen bilaterally in 2-3% of cases as synchronous or metachronous. The long cancer-specific survival in early-stage testicular cancer requires consideration for fertility and quality of life issues because of organ loss in these patients. In the present case series, the surgical outcome and histopathological features of testis-sparing surgery were evaluated using bench work after a standard radical orchiectomy in testicular tumor patients with normal contralateral testis.

Materials and Methods: Patients with a testicular mass confirmed by ultrasonography and/or magnetic resonance imaging and normal contralateral testis were included in the study. All patients underwent standard radical orchiectomy. Partial orchiectomy was performed on a separate operating table (bench) following radical orchiectomy. After visual evaluation of the removed tumor mass, seven biopsies were taken from the tumor bed for frozen section examination (FSE). If a residual tumor was found in the tumor bed because of FSE, parenchymal resection was performed until a negative margin was achieved. The patients' age, tumor marker levels, tumor type, tumor diameter, rete testis invasion, epididymis and spermatic cord invasion, necrosis, and presence of lymphatic-vascular invasion were recorded.

Results: Sixteen patients were included in the study. The mean age of the patients was 31.6±11.6 years. The mean tumor diameter was 26.9±15.3 mm, and the mean tumor-testicular-volume ratio was 33.2±24.9 percentage. The surgical margin was positive in 12.5% (n=2/16) patients in the FSE. In these two patients, the tumor-testicular volume ratio was above 50%, the tumor diameter was greater than 50 mm, and necrosis and invasion of the tunica albuginea were observed in the final histopathology. The tumor histopathology of patients was pure seminoma, non-seminomatous germ cell tumors, mixed germ cell tumor, sex cord stromal tumor, and fibrosis in 50% (n=8/16), 12.5% (n=2/16), 25% (n=4/16) 6.5% (n=1/16) and 6.5% (n=1/16) of the cases, respectively. Histopathological examination revealed 37.5% (n=6/16) intratubular germ cell neoplasia in the adjacent testicular tissue.

Conclusion: Our experience in the present case series shows that testis-sparing surgery is technically straightforward. Surgical margin positivity can be detected in patients with a large tumor or a high tumor-testicular-volume ratio. FSE is useful for detecting surgical margin positivity.

Keywords: Organ-sparing surgery, testicular cancer, partial orchiectomy

Cite this article as: Özkan TA, Özen A, Kabay Ş, Can C, Eruyar AT, Açıklın M, Eskiçorapçı S, Turkish Urooncology Association, Kidney and Testicular Cancers Study Group, Türkeri L. Testis-sparing Surgery in the Treatment of the Normal Contralateral Testicle: A Prospective Multicenter Bench Study Following Radical Orchiectomy. Bull Urooncol 2023;22(3):89-93.

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Received: 06.02.2022 **Accepted:** 20.06.2022



Introduction

Testicular tumors are one of the most common malignant tumors that appear in the young age group. Testicular tumors can be bilaterally seen in 2-3% of cases as synchronous or metachronous (1). Currently, the standard treatment for a testicular mass with a suspicion of malignancy is radical orchiectomy.

Urologists are well aware of the complications caused by organ loss because of other urologic tumor treatments. For example, organ-sparing surgery has claimed its place as a standard practice in urological practice in kidney tumors. The long cancer-specific survival in early-stage testicular cancer requires special consideration for the consequences of organ loss in these patients. The problems caused by testicular loss are not limited to infertility. These may include cosmetic deficiency, erectile dysfunction, loss of muscle strength, and psychological problems due to testosterone deficiency. Therefore, organ-sparing surgery in testicular tumors should be considered, although testis-sparing surgery is recommended only for selected patients treated by clinicians and facilities with experience in this approach (2).

Thus, in the presence of solitary testis or bilateral synchronous testis cancer, testis-sparing surgery may be performed to prevent problems associated with fertility and adverse effects on testosterone hormonal imbalance (3,4).

Usually, small testicular masses are deemed suitable for organ preservation, which may provide a foundation for this particular approach. Small masses are thought to be less capable of invasion and migration. They may be either benign or early lesions during malignancy (3). Nevertheless, there has not been enough experience with testis-sparing surgery to recommend it in an individual with a normal contralateral testis until now, nor is there enough prospective literature data to support this approach in such patients. At present, there is no clear recommendation for testis-sparing surgery in the European Urology guidelines.

Data obtained from the results of retrospective studies showed that testis-sparing surgery may be an alternative in carefully selected cases (5). In the present case series, the surgical outcome and histopathological features of testis-sparing surgery were evaluated with bench work mimicking the in situ surgical procedure after a standard radical orchiectomy in testicular tumor patients with normal contralateral testis.

Materials and Methods

This study was planned and conducted by the Turkish Urooncology Association, Kidney and the Testicular Cancers study group. The patients with a testicular mass confirmed by ultrasonography and/or magnetic resonance imaging with normal contralateral testis were included in the study.

“Bench” Procedure

All patients underwent standard radical orchiectomy. The specimen was immediately placed in ice water and monitored by a 15-19 °C heat probe on a separate operating table (bench). After the procedure, partial orchiectomy was initiated. Localization of the tumor was defined by palpation or, in small nonpalpable tumors by intraoperative ultrasonography. The

mass location was evaluated, and the tunica albuginea was opened. The tumor and its surrounding fibrous pseudocapsule were resected along with approximately 3 mm of healthy-appearing testicular tissue. After visual evaluation of the removed tumor mass, seven biopsies were taken from the tumor bed two anterior, two posterior, one medial, one lateral, and one central and sent for frozen section examination (FSE). If a residual tumor was found in the tumor bed because of FSE, parenchymal resection was performed until a negative margin was achieved. Following the bench procedure, the tunica albuginea was closed with a 5/0 monofilament polycaprone suture. The remaining surgical specimens were fixed in 10% buffered formalin and sent for histopathological examination.

For pathological examination, serial sections were taken at 5 mm intervals from the testicular tumor and remaining testicular tissue that underwent partial orchiectomy on the bench, and macroscopic examination was performed. The rete testis was sampled in a separate cassette. Tissue samples were fixed in 10% buffered formalin, and 5-micron-thick sections were taken, stained with hematoxylin-eosin, and evaluated under a microscope. The tumor type, tumor diameter, rete testis invasion, epididymis and spermatic cord invasion, necrosis, and lymphatic-vascular invasion were recorded. Intratubular germ cell neoplasia (ITGCN) was evaluated by applying placental alkaline phosphatase for immunohistochemical evaluation of sections close to the tumor and rete testis samples.

Ethics committee approval of the study was received from Osmangazi University on June 26, 2013 in a letter numbered 80558721/213. Informed consent was obtained from all participants.

Statistical Analysis

Study data were collected and managed using research Electronic Data Capture) tools hosted at the Urologic Cancer Database - Testis, Turkish Urooncology Association (UroCaD-T) (6,7). REDCap is a secure, web-based software platform designed to support data capture for research studies, providing 1) an intuitive interface for validated data capture; 2) audit trails for tracking data manipulation and export procedures; 3) automated export procedures for seamless data downloads to common statistical packages; and 4) procedures for data integration and interoperability with external sources.

Results

Sixteen patients from three centers were included in the study. The mean age of the patients was 31.6±11.6 years. The median AFP was 2.84 ng/mL (range 1-897.8), beta hCG 1.28 range 0-100.7 mU/L. The mean LDH was 216.6±100.7 U/L. The mean tumor diameter was 26.9±15.3 mm, and the mean tumor/testicular-volume ratio was 33.2±24.9 percentage (Table 1). Intraoperative ultrasonography was not required for tumor localization in any of the patients.

After partial orchiectomy on the bench, the surgical margin was positive in 12.5% (n=2/16) patients in the FSE. A negative surgical margin was obtained by widening the margin of the partial orchiectomy. In these two patients with positive surgical margins, the tumor-testicular volume ratio was above 50%, the

Table 1. Demographic, laboratory and pathological data of the patients included in the study

Nr.	Age	AFP	bHCG	LDH	TTV (%)	FSE-SM	Tumor type	Tumor diameter (mm)	Tunica albuginea inv.	Tunica vaginalis inv.	Rete testis inv.	Necrosis	LVI	ITGCN	Multifocality
1	34.8	5.8	2	243	50	Positive	Seminoma	50	Yes	No	No	Yes	No	No	No
2	38.9	2.52	1.28	195	30	Negative	Seminoma	37	No	No	No	Yes	No	No	No
3	37.9	2.84	1.2	133	6	Negative	Seminoma	40	No	No	No	No	No	No	No
4	31.5	49.8	20.1	139	25	Negative	Mixt Germ Cell Tumor	30	No	No	No	No	No	No	No
5	62	5.2	2	191	25	Negative	Benign	14	-	-	-	-	-	-	-
6	35.4	5.0	0.1	368	26	Negative	Mixt Germ Cell Tumor	13	No	No	No	Yes	No	No	No
7	16.5	*	*	*	11	Negative	Mixt Germ Cell Tumor	27	No	No	No	Yes	No	Yes	No
8	17.7	897.8	47.71	205	26	Negative	Mixt Germ Cell Tumor	25	No	No	No	Yes	Yes	Yes	No
9	37.1	1.11	0.1	345	15	Negative	Seminoma	10	No	No	No	No	No	Yes	No
10	32	2.59	0.1	362	30	Negative	Seminoma	20	Yes	No	Yes	No	No	Yes	No
11	22.8	192.4	<0.01	38.4	20	Negative	NSGCN	10	No	No	No	No	No	Yes	No
12	20.9	1.3	2	153	57	Negative	Seminoma	30	No	No	Yes	No	Yes	No	No
13	43.5	3.7	21.20	252	95	Negative	NSGCN	55	Yes	No	Yes	Yes	Yes	No	No
14	35.3	1.2	100.7	139	20	Negative	Seminoma	20	Yes	No	No	Yes	No	No	No
15	16.6	1.08	1.00	138	2	Negative	Leydig Cell	4.5	No	No	No	No	No	No	No
16	24.8	1.00	1.00	348	80	Positive	Seminoma	65	Yes	Yes	No	Yes	No	Yes	Yes

AFP: Alpha-fetoprotein, bHCG: Beta-Human chorionic gonadotropin, LDH: Lactate dehydrogenase, TTV: Tumor-testis volume ratio, FSE-SM: Frozen section examination-surgical margin, LVI: Lymphovascular invasion, ITGCN: Intratubular germ cell neoplasms, NSGCN: Non-seminomatous germ cell neoplasia, *missing due to recording error

tumor diameter was greater than 50 mm, and necrosis and invasion of the tunica albuginea were observed in the final histopathology. In one of these two patients, ITGCN and multifocal millimetric tumor nodules with no preoperative imaging findings were detected in the remaining testicular tissue. Both of these patients' final histopathological examinations were reported as seminoma.

The tumor histopathology rates of patients' pure seminoma, non-seminomatous germ cell tumors, mixed germ cell tumor, sex cord stromal tumor, and fibrosis were 50% (n=8/16), 12.5% (n=2/16), 25% (n=4/16) 6.5% (n=1/16) and 6.5% (n=1/16), respectively. Histopathological examination revealed 37.5% (n=6/16) ITGCN in the adjacent testicular tissue.

Discussion

Leaving aside the oncological consequences, testicular cancer patients are exposed to the adverse functional effects of radical orchiectomy because of its long survival time. Psychological/cosmetic problems that may arise following orchiectomy can be prevented primarily with a testicular prosthesis. However, the management of the effects of infertility and hypogonadism, especially those caused by bilateral synchronous or metachronal tumor conditions, may be more difficult (2). In theory, testis-sparing surgery appears ideal for the management of these unfavorable effects. Furthermore, at least some of these masses may be benign in relation to their size (8). Nevertheless, the fear of compromising oncological control in a patient with a normal contralateral testis seems to be an obstacle to the widespread adaptation of testis-sparing surgery. Thus, organ-sparing surgery in testicular cancer is currently recommended only in selected patients with bilateral synchronous and metachronous tumors and intraoperative FSE (3).

Intraoperative FSE evaluation has high sensitivity for the differentiation of malignancies and correlates well with the final histopathology. Therefore, FSE can also be used during testis-sparing surgery for malignant/benign discrimination, especially in small, nonpalpable, and/or multiple testicular masses (9). In this case series, FSE was used only for surgical margin control. A positive surgical margin was detected in two patients in whom both had a tumor size over 50 mm with a tumor/testicular-volume ratio more than 50%. These findings suggest that adverse pathological features, such as mass size, invasion of the tunica albuginea, and ITGCN, may be associated with positive surgical margins in the two patients with germ cell tumors. In cases where testis-sparing surgery is planned for imperative indications such as a solitary testis, in the presence of masses with tumor size over 50 mm or with a high tumor-testicular volume ratio, FSE may be useful for preventing a final positive surgical margin.

For treating germ cell tumors, testis-sparing surgery is recommended for tumors 25 mm in the presence of synchronous bilateral tumors or metachronous

contralateral tumors (10). With the selection of small-sized tumors, surgical margin positivity can be avoided. Moreover, the remaining testicular volume will be greater, and better functional outcomes may be achieved in terms of fertility and hormonal activity.

It is important to determine the location of the mass using pre-operative imaging. This allows the surgeon to access the tumor with less tissue trauma. However, testicular tumors can be easily located with palpation because of the prominent capsule and testicular tissue features, such as the softness and elasticity of the seminiferous tubules. Because of these tissue properties, the localization and surgical margins of the mass can be easily determined after incision of the tunica albuginea without the need for intraoperative imaging. Enucleation is possible when the tumor must be completely separated from the surrounding tissue. Therefore, it can be performed relatively easily compared with the surgical technique used in the partial surgery of other urological cancers.

There may be multifocality in testicular tumors (11,12). If a radiological diagnosis has not been made, we may not be able to pathologically detect the multifocal testicular tumor (13).

In this case series, pathologically detected multifocal tumors were observed without a radiological finding. Ultrasonographic archive images of this case were re-evaluated without any change in the radiological conclusion. The reason for this may be the images chosen by the radiologist for archiving, the small size of the mass, or the radiological echogenicity characteristics. Whatever the reason, it should not be forgotten that, while rare, such a situation may occur and can be a source of recurrence and progression.

Although testicular tumors can be surgically removed, the size of the mass, fixation of the tunica albuginea, or unfavorable location of the mass may adversely affect the remaining functional testicular tissue. In the resection of these masses, FSE should be used for testis-sparing surgery and for oncological control, and the amount of remaining functional tissue should be considered. The fact that it is possible to perform this surgical procedure does not allow us to abandon the basic oncological principles.

Study Limitations

This study has some limitations. First it is a patient series with a limited number of cases. Because of the nature of the bench study, there is a lack of information about the changes that may occur in sertoli and leading cells due to ischemia, and no further follow-up was possible for that testis. In addition, pre-operative and postoperative hormonal functional evaluation of patients in this setting would not reflect the contribution of the preserved testicular tissue.

Conclusion

Our experience in the present case series indicates the technical feasibility of testis-sparing surgery as a straightforward procedure, especially in small testicular tumors. Testis-sparing surgery may prove to be a valuable technique, especially in benign masses, to prevent long-term negative results.

Surgical margin positivity can be detected in patients with a large tumor or a high tumor-testicular-volume ratio. FSE is useful for detecting surgical margin positivity. Further studies may focus on the effect of unfavorable histopathological findings, such as the invasion of the tunica albuginea, ITGCN, and necrosis, on surgical margin positivity. Further studies would help to identify factors that may determine the best candidate for testis-sparing surgery, including oncological risk, fertility outcomes, and hormonal functions.

Acknowledgements

Publication: Urological Surgery Congress, 2018 Antalya.

Contribution: There is not any contributors who may not be listed as authors.

Conflict of Interest: No conflict of interest was declared by the authors.

Financial Disclosure: The authors declared that this study received no financial support.

Ethics

Ethics Committee Approval: Ethics committee approval of the study was received from Osmangazi University on June 26, 2013 in a letter numbered 80558721/213.

Informed Consent: Informed consent was obtained from all participants.

Peer-review: Externally peer-reviewed.

Authorship Contributions

Surgical and Medical Practices: T.A.Ö., A.Ö., C.C., A.T.E., M.A., Concept: Ş.K., S.E., L.T., Design: Ş.K., S.E., L.T., Data Collection or Processing: T.A.Ö., A.Ö., C.C., Analysis or Interpretation: T.A.Ö., A.Ö., Literature Search: T.A.Ö., A.Ö., C.C., Writing: T.A.Ö., A.Ö.

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