

## Testis-sparing Surgery for the Conservative Management of Small Testicular Masses: An Update

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**Abstract.** *Background: Malignant germ cell tumours represent the vast majority of palpable testicular masses, and radical orchiectomy is still considered the standard-of-care. Testis-sparing surgery (TSS) could be an alternative to radical orchiectomy in patients diagnosed with small testicular masses (STMs). The aim of this article was to review the current indications and the oncological and functional outcomes of TSS when performed for STMs. Materials and Methods: We performed a non-systematic review of literature using the Medline database, including a free-text protocol using the terms “testis sparing surgery”, “partial orchiectomy”, “testis tumour” and “sex cord tumour”. Only the articles reporting data on organ-sparing surgery for testicular neoplasms were evaluated. Results: No randomized controlled trials comparing TSS with radical orchiectomy have been reported. Indications for TSS are controversial, especially for patients with normal contra-lateral testis. For testicular masses of less than 2 cm, TSS seems to be the best treatment option. Frozen-section examination is an essential assessment at the time of TSS, and allows for discrimination of benign from malignant neoplasms. Intermediate- and long-term follow-up results showed no significant risk of local and distant recurrences in the main series reported in literature. Conclusion: According to currently available data, TSS is a safe and effective treatment for STMs in selected patients, and bypasses surgical overtreatment, without compromising oncological*

*and functional outcomes. Further studies are needed in order to confirm the oncological safety of this procedure.*

Testicular cancer accounts for about 1-1.5% of all male neoplasms and 5% of urological tumours, with an estimated incidence of 3-10 new cases occurring per 100,000 males/per year in Western countries (1). Malignant germ cell tumours represent the vast majority of palpable, symptomatic testicular masses, and radical orchiectomy is still considered the standard-of-care for the surgical management of these lesions (2). In patients with bilateral testicular malignancies or congenital monorchidism, definitive treatment by orchiectomy is associated with androgen deficiency and infertility, and detrimental functional effects have been widely documented (3). Interestingly, potential late-appearing negative hormonal and reproductive consequences have been described, even at long-term follow-up after unilateral orchiectomy (4, 5). The recent, widespread use of high-frequency ultrasonography has led to an increasing number of incidentally detected small testicular masses (STMs), defined as non-palpable, less than 25 mm in diameter, intrascrotal masses (6). Since most STMs are benign (7), and considering the negative endocrine and exocrine consequences related to the loss of testicular parenchyma (8, 9), the complete orchiectomy can be considered too “costly” from a hormonal and reproductive point of view. Therefore, the 2011 (EAU) Guidelines consider organ-sparing surgery as an alternative to radical orchiectomy, only for patients with synchronous bilateral testicular tumours, metachronous contralateral tumours, or with a lesion in solitary testis with normal preoperative testosterone levels, provided that the tumour volume is <30% of testicular volume and surgical rules are respected (2).

The aim of the present article was to review the current indications for testis-sparing surgery (TSS), and evaluate the oncological and functional results of patients who had undergone organ-sparing surgery for STMs.

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## Patients and Methods

We performed a non-systematic review of literature using the Medline database, including only a free-text protocol using the terms "testis-sparing surgery", "partial orchiectomy", "testis tumour" and "sex cord tumour" across the title and abstract fields of the records. The following limits were used: English language; humans; male; adults. Two Authors (G.G. and E.B.) separately reviewed all the retrieved abstracts and selected the articles reporting data about organ-sparing surgery for testicular or sex cord neoplasms. During a second step analysis, we carefully examined the corresponding full-length articles, and any discrepancy regarding inclusion was resolved by open discussion. Other significant studies cited in the reference lists of the selected articles were also evaluated.

## Results

*Indications for TSS.* The indications for TSS as conservative treatment of testicular malignancies are still controversial, especially for patients with normal contralateral testis. However, organ-sparing surgery is gaining increasing interest in the urological community as a viable alternative to radical orchiectomy in many cases. According to the German Cancer Study Group indications, TSS can be considered only for selected patients with malignant tumours in solitary testis or bilateral tumor with a lesion diameter of the lesion <2 cm and no invasion of the rete testis, with normal preoperative serum (LH) levels (10). In all these cases, the enucleation of the mass must be accompanied by multiple biopsies of the surrounding tissue and adjuvant radiotherapy must be considered for seminomas. Moreover, the 2011 update of the EAU Guidelines consider organ-sparing surgery as an alternative surgical management only for patients with synchronous bilateral testicular tumours, metachronous contralateral tumours, or for lesions in patients with solitary testis and normal preoperative testosterone levels, provided that tumour volume is less than 30% the testicular volume and surgical rules are respected (2). Extensive experience with TSS has already been described for the treatment of benign tumours (11), and the application of testicular ultrasound (US) and intraoperative frozen-section analysis examination (FSE) can allow the operator to determine with certainty the benign nature of the testicular mass, with a possibility of recurrence of virtually zero (12-17). The diameter of the mass seems to be one of the most important parameters for the indication of elective TSS; several studies demonstrated that in the case of non-palpable, asymptomatic masses with a diameter of less than 2 cm, TSS can be the best management (18-22), as the prevalence of benign histology is approximately 80% (23). Moreover, TSS has gained particular acceptance in paediatric surgery due to the higher incidence of benign neoplasms; in addition, this approach has a special role in young children as it reduces the late-onset hypogonadism and has important physiological and cosmetic advantages (24-26).

*Operative technique.* The operative technique was firstly described by Stoll and collaborators in 1986, performing the enucleation of a non-palpable Leydig cell tumor with intraoperative US (27). Hopps and Goldstein improved the technique with the introduction of US-guided needle localization and microsurgical exploration, with the aim of improving detection and completeness of the excision of the mass (22). More recently, Hallak and collaborators introduced the use of an operating microscope, which allows the surgeon to perform precise microdissection of the tumour and sperm extraction in case of azoospermia (28). In every described technique, the procedure starts with the exploration of the testis through an inguinal access, in order to be able to convert the operation to radical orchiectomy if necessary. The spermatic cord is isolated and clamped by a tourniquet or a soft vascular clamp; this procedure should prevent dissemination or seeding of the neoplasm during its excision and should be performed at the beginning of the procedure or immediately before enucleation of the mass in order to reduce the time of warm ischaemia (10). Some authors proposed enucleating the tumour without clamping the spermatic cord, with the aim of preserving vascularisation of the testis (29). Thereafter, the testis is externalized through the same inguinal access and located in a separate operative field to avoid contamination or dissemination of the neoplasm in the case of malignant tumour. The mass is usually identified by straight palpation of the testis or with intraoperative US, usually guided by a needle (18, 21). The gubernaculum testis is either clamped or sectioned. Cold ischaemia for better preservation of the gonad is still controversial and some even consider this approach harmful (29). After the enucleation of the mass, with or without a margin of normal-appearing parenchyma, FSE is performed. Some suggest performing multiple biopsies of the surrounding tissue after the enucleation, which could be analysed at the same time as FSE (30). US can be used after excision to assess the completeness of tumour removal. Some consider the removal of the vascular clamp only after the completion of the FSE; conversely, other surgeons suggest limiting ischaemia only at the moment of the excision of the tumor, thus limiting potential damage to the healthy testicular parenchyma (18). Lastly, in the case of negative FSE findings, the albuginea is sutured and the testis is returned to its original position; in the opposite case, a traditional radical orchiectomy is performed in order to ensure for the best oncological result.

*The role of the FSE.* After an initial scepticism about the reliability of a precise analysis (31), FSE has gained increasing credibility among the scientific community, thanks to the standardization of handling and processing of the specimens (32). At the time of TSS, FSE represents an essential point, especially because FSE has proven to be a safe and accurate method to identify testicular tumours, with

an high accuracy in discerning benign from malignant neoplasms (31-36). A non-conclusive diagnosis at FSE seems to be very rare (22, 37). The main limit of FSE may be the experience of pathologist, who should at least be dedicated to urological pathology and should have wide experience with testicular tumours.

#### *Histological patterns and oncological outcomes after TSS.*

To the best of our knowledge, there are no randomized controlled trials comparing TSS with radical orchiectomy, and only retrospective studies and case reports are currently available in literature. It has been reported that 90% of palpable testicular lesions or tumors more than 2 cm are malignant, while STMs prove to be benign in 80% of cases (3, 6). In detail, the rate of benign findings ranges from 60% to 77% for tumors smaller than 20 mm, and increases up to 80% for lesions under 5 mm (38-41). Table I reports histological patterns and oncological results of the reported series. De Stefani *et al.* reported 91% of benign lesions in a cohort of 23 patients with STMs treated with TSS. FSE revealed two (9%) malignant lesions confirmed at final pathology, which demonstrated typical seminomas in both cases (21). These two patients underwent radical orchiectomy. The mean follow-up was 35±25 months, with all patients being free of disease (21). In another large series, Steiner *et al* reported results of 18 STMs treated with TSS in patients with normal contralateral testis (6). Interestingly, all the lesions were benign at final histological examination, and no local recurrences had been detected at a mean follow-up of 35.7 months after organ-sparing surgery. In a paper published in 2003 by Carmignani and collaborators, 7 out of 10 patients with small non-palpable testicular lesions underwent conservative surgery after negative FSE (7). Radical orchiectomy was performed in the remaining three patients after the histological diagnosis of adenomatoid tumor with multifocal abscesses in one case and Leydig cell tumour with positive margins at FSE in two cases. Definitive histological analysis confirmed multifocal, diffused Leydig cell tumor. No local recurrence was detected at a mean follow-up of nine months (7). More recently, a series of 23 cases of Leydig cell tumours with a median dimension of 11.4 mm was reported (14). In one patient FSE revealed a large B-cell lymphoma, but the patient was conservatively treated with TSS. After a follow-up of 47 months, the authors did not report any local recurrence. Moreover, we recently reported histological and oncological outcomes of 15 consecutive patients treated with surgical exploration with TSS intent for STMs (18). The final pathological report showed there to be 13 benign lesions and two malignancies: a pure seminoma in one case and a low-grade paratesticular fibromyxoid liposarcoma in the other. The latter was not detected by FSE as the diagnosis can be inconclusive (42), and radical orchiectomy was performed subsequently after

the final pathological report. We did not find local recurrence after a median follow-up of 19.6 months (18). In the reported series by Shilo *et al.*, 16 patients underwent surgical exploration with TSS intent (20). FSE correctly revealed benign findings in all 11 patients (69%) who underwent TSS. The malignant lesions were described as seminoma in three cases, teratoma in one and embryonal carcinoma in one; these five patients underwent definitive radical orchiectomy. After a mean follow-up of 48 months, all patients were alive and free of disease (20). The data from these retrospective series and case reports, with medium- and long-term follow-up, confirm that STMs are benign in the majority of cases, and TSS could be a safe and effective option for selected patients, and would avoid surgical overtreatment without compromising the oncological outcomes. The rate of local recurrences after TSS is quite low, especially in highly selected cases with adequate FSE.

#### *Functional outcomes after TSS.*

After unilateral orchiectomy, the remaining testicle was traditionally considered sufficient to compensate for the loss of testicular parenchyma and, therefore, to maintain normal hormonal and reproductive functions. However, recent studies have revealed that even the loss of one testis is significantly associated with important alterations of fertility, long-term exocrine and endocrine deficit, and severe sexual and psychosocial implications (4, 5, 8, 9). It has been demonstrated that even in the absence of adjuvant therapy, radical orchiectomy is associated with a significant decrease in spermatogenesis (5), even being associated with azoospermia in a non-negligible proportion of patients (43). Epidemiological, clinical and histological evidence supports the association between impaired spermatogenesis and testicular cancer, especially for germ cell tumours (44), probably because of the gene-related association between gonadal dysgenesis and testicular tumours. After long-term follow-up from unilateral radical orchiectomy, evidence suggests that serum testosterone is significantly reduced compared to levels in the general population, and this condition can evolve into severe late-onset hypogonadism in young patients (5). Moreover, even if sexual function can generally be considered normal, the loss of one testis is frequently accompanied by an alteration of the male body image (45, 46). The side-effects of radical orchiectomy can be partially avoided by the preservation of testicular parenchyma allowed by TSS, which can also be performed in the presence of malignant tumour in young but very selected patients. If TSS is performed with the aim of preserving fertility, it is important to reduce the warm ischaemia time to under 30 min in order to avoid irreversible damage to the tissues (3, 47), and to postpone adjuvant radiotherapy in the case of testicular intraepithelial neoplasia, in association with a close follow-up (3).

Table I. Histological and oncological results of series reported up to September 2013.

Authors reference	Period	Patients (no.)	Mean age (years) ±SD (range)	Markers dimension (mm)	Mean US	FSE	Surgery	Histology	Local recurrence (no.)	Follow-up (Months) ±SD (range)
De Stefani <i>et al.</i> (21)	2004-2011	23	30±11.1	Normal	14±5.2	21 Benign 2 Malignant	21 TSS 2 RO	5 Leydig cell tumor 4 Epidermoid cyst 2 Seminomas 3 Scarring (flogosis) 2 Mature teratoma 2 Normal seminal tissue 1 Mesothelioma 1 Sertoli cell tumor 1 Hemorrhagic necrosis 1 Simple cyst 1 Congenital cyst	1 (after TSS)	35±15
Steiner <i>et al.</i> (6)	1994-2002	18	29.9 (0.4-58)	Normal	11.5 (3-24)	18 Benign	18 TSS	10 Leydig cell tumor 2 Sertoli cell tumor 3 Epidermoid cyst 2 Fibrotic pseudotumor 1 Adenomatoid tumor	0	35.7 (12-91)
Carmignani <i>et al.</i> (7)	2000-2002	10	41 (5-76)	5> hCG 4> αFP	1.14 (0.5-3.1)	8 Benign 2 Benign/R1	7 TSS 3 RO	3 Fibrosis 2 Infraction 2 Leydig cell tumor (R1) 1 Leydig cell hyperplasia 1 Mesothelial hyperplasia 1 Adenomatoid tumor with multifocal abscesses	0	9 (1-19)
Carmignani <i>et al.</i> (14)	1987-2006 (2 monorchid)	23	35 (5-61)	High FSH and LH in 4 patients	11.4 (5-31)	22 Benign 1 Malignant	22 TSS 2 retro-peritoneal lymph node dissections (in case of NSCGT)	20 Leydig cell tumor 1 non-malignant stromal tumor 1 Large B-cell lymphoma	0	47 (3-230)
Gentile <i>et al.</i> (18)	2009-2012	15	44.4±18.7	Normal	0.95±0.44	13 Benign 1 Malignant	13 TSS 2 RO	5 Leydig cell tumor 2 Flogosis 1 Epidermoid cyst 1 Sertoli cell tumor 1 Adenomatoid tumor 1 Seminoma 1 Fibromyxoid 1 Liposarcoma 1 Dermoid cyst 1 Abscesses 1 Hematoma	0	19.6±11.1
Shilo <i>et al.</i> (20)	1994-2009	16	32.3±12.3	Normal	16.4±5.9 (pathological size)	11 Benign 5 Malignant	11 TSS 5 RO	4 Leydig cell tumor 2 Epidermoid cyst 3 Seminoma 1 Adenomatoid tumor 1 Sertoli cell tumor 1 Teratoma 1 Embryonal carcinoma 1 Cyst 1 Focal fibrosis	2 Small paratesticular haematomas	48 (30-68)

TSS: Testis-sparing surgery; RO: radical orchiectomy; NSGCT: non-seminomatous germ cell tumors.

## Conclusion

A TSS approach for small testicular lesions allows as much healthy parenchyma to be preserved as possible, but should be performed only in selected cases and at experienced centres. This surgical approach is safe and feasible, and allows optimal oncological and functional results in most cases. When planning TSS, the FSE is of paramount importance in the histological evaluation and surgical decision-making. Notably, all the specimens should be sent to a dedicated and experienced uro-pathologist, in order to maximize the accuracy of the histological diagnosis. The oncological risks for the patients are minimal if the correct steps of the procedure are performed. Intermediate and long-term follow-up showed no significant risk of local and distant recurrences in the main series reported in the literature, and aesthetical and functional (endocrine and reproductive) outcomes are optimal and promising. TSS should be considered a promising approach for the conservative management of STMs found to be benign at FSE, and could be an alternative, organ-preserving treatment for small malignant lesions in highly selected imperative or elective cases. In order to assess and confirm the oncological safety of TSS, and to expand its indications, further prospective, multicentre studies or randomized controlled trials are needed.

## Conflicts of Interest

None.

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