arTs Università degli Studi di Trieste
Archivio della ricerca – postprint

Testis Sparing Surgery of Small Testicular Masses: Retrospective Analysis of a Multicenter Cohort

Giorgio Gentile,* Michele Rizzo, Lorenzo Bianchi, Marco Falcone, Donato Dente, Mario Cilletti, Alessandro Franceschelli, Valerio Vagnoni, Marco Garofalo, Riccardo Schiavina, Eugenio Brunocilla, Francesco Claps, Giovanni Liguori, Carlo Trombetta, Massimiliano Timpano, Luigi Rolle, Angelo Porreca, Costantino Leonardo, Cosimo De Nunzio, Fulvio Colombo and Giorgio Franco

From the Andrology Unit, University Hospital S. Orsola-Malpighi (GG, AF, VV, FC) and Department of Urology, University of Bologna (LB, MG, RS, EB), Bologna and Departments of Urology, University of Trieste, Hospital of Cattinara (MR, FC, GL, CT), Trieste, University of Turin, Hospital Molinette (MF, MT, LR), Abano Terme Hospital, Abano Terme (DD, AP), Padua and Sapienza University of Rome (MC, CL, CDN, GF), Rome, Italy

Abbreviations and Acronyms

FSE = frozen section examination
ITGCNU = intratubular germ cell neoplasia, unspecified type
RO = radical orchiectomy
STM = small testicular mass
TSS = testis sparing surgery
US = ultrasound

Accepted for publication September 17, 2019.
No direct or indirect commercial, personal, academic, political, religious or ethical incentive is associated with publishing this article.
The corresponding author certifies that, when applicable, a statement(s) has been included in the manuscript documenting institutional review board, ethics committee or ethical review board study approval; principles of Helsinki Declaration were followed in lieu of formal ethics committee approval; institutional animal care and use committee approval; all human subjects provided written informed consent with guarantees of confidentiality; IRB approved protocol number; animal approved project number.
* Correspondence: Andrology Unit, University Hospital S. Orsola-Malpighi, Bologna, Italy (e-mail: dr.giorgio.gentile@gmail.com).

Purpose: We evaluated possible factors predicting testicular cancer in patients undergoing testis sparing surgery.

Materials and Methods: We retrospectively analyzed the records of all patients who underwent testis sparing surgery for a small testicular mass at a total of 5 centers. All patients with 1 solitary lesion 2 cm or less on preoperative ultrasound were enrolled in the study. Testis sparing surgery consisted of tumor enucleation for frozen section examination. Immediate radical orchiectomy was performed in all cases of malignancy at frozen section examination but otherwise the testes were spared. Univariate and multivariate analysis were performed and ROC curves were produced to evaluate preoperative factors predicting testicular cancer.

Results: Overall 147 patients were included in the study. No patient had elevated serum tumor markers. Overall 21 of the 147 men (14%) presented with testicular cancer. On multivariate analysis the preoperative ultrasound diameter of the lesion was a predictor of malignancy (OR 6.62, 95% CI 2.26–19.39, p=0.01). On ROC analysis lesion diameter had an AUC of 0.75 (95% CI 0.63–0.86, p=0.01) to predict testicular cancer. At the best cutoff of 0.85 the diameter of the lesion had 81% sensitivity, 58% specificity, 24% positive predictive value and 95% negative predictive value.

Conclusions: Our study confirms that small testicular masses are often benign and do not always require radical orchiectomy. Preoperative ultrasound can assess lesion size and the smaller the nodule, the less likely that it is malignant. Therefore, we suggest a stepwise approach to small testicular masses, including tumorectomy, frozen section examination and radical orchiectomy or testis sparing surgery according to frozen section examination results.

Key Words: testis, orchiectomy, neoplasms, ultrasonography, organ sparing treatments

TESTICULAR cancer represents between 1% and 1.5% of male neoplasms and 5% of all urological tumors.[1–3] RO is the standard treatment in patients with clear features of malignancy and a normal contralateral testis. In patients with controversial findings intraoperative FSE of the enucleated mass is recommended and should guide treatment.[4]

The evolution and widespread use of US imaging has led to an increased

incidental diagnosis of STMs, including benign ones, which are diagnosed more and more often at FSE.[5,6] Previous studies suggested that asymptomatic, nonpalpable testicular lesions smaller than 2 cm can be benign in up to 80% of cases.[7–10] Unfortunately, no imaging techniques can clearly define the benign or malignant nature of these lesions and histological evaluation is still needed.[4]

Given the high incidence of benign tumors, straightforward orchiectomy of STMs exposes many young men to an unnecessary procedure with its related side effects.[10,11] To date organ sparing management has proved to be technically feasible, enabling preservation of a considerable amount of testis parenchyma.[9,12–14] Despite that, TSS is not yet standard management of STMs and it is often offered only at select centers or reserved for patients with an abnormal contralateral testis.[15] Therefore, it is a priority to identify a strategy of STM management which is able to treat malignant lesions safely while reducing the considerable risk of overtreatment.

The aim of this study was to evaluate possible predictors of testicular cancer in patients undergoing TSS and propose an updated treatment strategy for STMs

PATIENTS AND METHODS

After receiving study approval from the ethical committee of Sapienza University of Rome as well as Internal Review Board approval (IRB No. 4882) we retrospectively analyzed the records of all patients treated with TSS of STMs at a total of 5 Italian centers between January 2013 and December 2016. The study was performed according to the principles of the Helsinki Declaration.

Patients with a solitary lesion with a diameter of 2 cm or less at preoperative US were enrolled in the study. Exclusion criteria were a testicular mass greater than 2 cm, multiple lesions or a solitary testis. All medical records were analyzed and data were recorded, including patient age at surgery, clinical presentation, preoperative US dimensions, tumor markers (α-fetoprotein, β-human chorionic gonadotropin and/or lactate dehydrogenase), intraoperative dimensions, ischemia time and surgical pathology findings. All surgical specimens were reviewed by an expert uropathologist. Staging was performed according to the TNM 2009 classification. All patients were followed according to the EAU (European Association of Urology) guideline recommendations.[4]

Surgical Technique

TSS consists of surgical inguinal exploration, testicular exteriorization and identification of masses by palpation or intraoperative US. Spermatic cord clamping, albuginea incision and tumor enucleation were then performed for FSE (figs. 1 and 2). Multiple biopsies were also obtained of the surrounding parenchyma. When a malignant tumor was diagnosed on FSE, immediate orchiectomy was performed. In cases of benign or nontumor lesions the testis was repaired and repositioned in the scrotum.

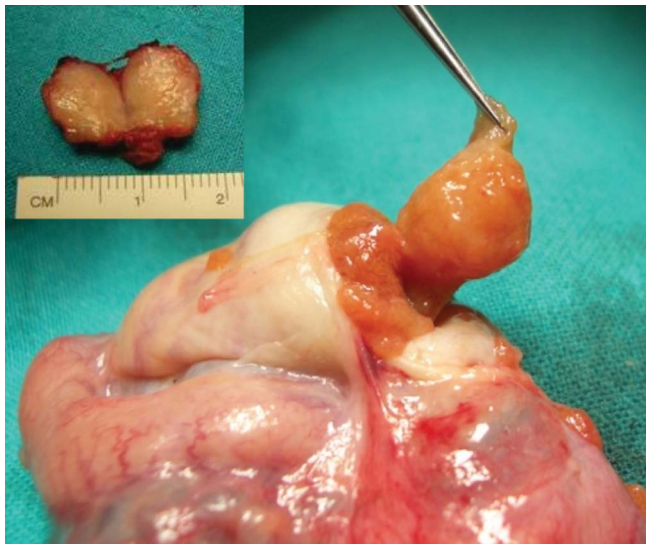

Figure 1. Testicular tumorectomy of seminoma

Statistical Analysis

Statistical analysis was done with IBM® SPSS® 25. Continuous variables are presented as the median and IQR, and were compared by the independent Student t-test and the Mann-Whitney U test, and the Kruskal-Wallis 1-way test based on a normal and not normal distribution, respectively. Variable distribution normality was tested by the Kolmogorov-Smirnov test. Categorical variables were tested with the chi-square test.

Using multiple logistic regression with the enter method the statistically significant variables as assessed on univariate analysis were entered and investigated as cancer predictors. ROC curves were produced to evaluate the AUC and the diagnostic performance of the model as well as all significant variables included in multivariate analysis to predict testicular cancer. The best cutoff value was obtained by ROC analysis, and sensitivity, specificity, and negative and positive predictive values were then calculated. Data are presented as the mean ± SD or the median and IQR with $\alpha=5\%$ considered statistically significant.

RESULTS

Overall 147 patients were included in study. Table 1 lists the general characteristics of the cohort. Of 56 patients with pain or a lump 20 presented with palpable lesions and 36 presented with pain. In 36 patients US was performed for infertility evaluation. Of 55 patients with an incidental US diagnosis 35 (63%) underwent scrotal US as suggested by a general practitioner apparently without any specific clinical reason and 20 (37%) underwent scrotal US based on the patient decision. All patients presented with negative tumor markers, that is markers in the normal range.

Overall 21 of these 147 patients (14%) presented with testicular cancer. All cases were classified as classic seminoma pT1 (stage I). In patients with

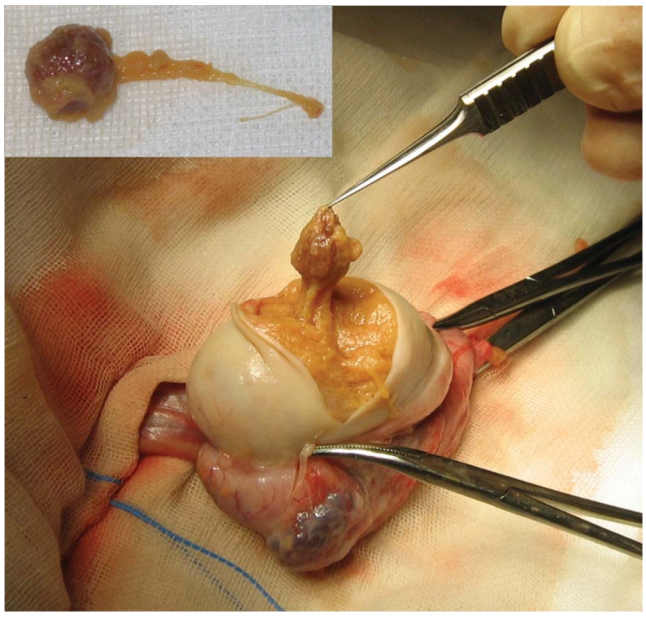

Figure 2. Testicular tumorectomy of Leydig cell tumor

cancer lesions had a larger diameter on preoperative US or pathological evaluation than in patients with benign lesions. No difference was recorded in patient age between the groups. A significant difference in clinical presentation was observed in patients with vs without cancer (table 1). Overall 85 patients presented with an US lesion less than 1 cm, of whom only 6 (7%) presented with testis cancer. In this group 4 patients were referred for infertility and 2 were referred for a palpable lesion.

On multivariate analysis only the preoperative US diameter of the lesion was a predictor of malignancy (table 2). The risk of finding a malignant lesion increased sevenfold per mm. On ROC analysis the preoperative US size of the lesion showed an AUC of 0.75 (95% CI 0.63–0.86, p=0.01) to predict testicular cancer (fig. 3). Including the other possible variables in the multivariable model did not increase the AUC of the US lesion (data not shown).

At the best cutoff of 0.85 cm the lesion diameter had 81% sensitivity, 58% specificity, 24% positive predictive value and 95% negative predictive value.

FSE findings were confirmed by the final pathology result in 146 cases (99.3%). However, in 1 case FSE revealed a Leydig cell tumor while the final pathology examination showed a Leydig-Sertoli cell tumor. Final pathology findings of nonmalignant lesion included a benign tumor in 108 cases (74.3%), including Leydig cell tumors in 54, Leydig cell hyperplasia in 28, a dermoid cyst in 11, a Sertoli cell tumor in 6, an adenomatoid tumor of the tunica vaginalis in 3, a Sertoli-Leydig cell tumor in 2, an epidermoid cyst in 2, mucinous cystadenoma in 1 and vascular hyperplastic lesions in 1 (table 3). Finally, in 18 of the 147 cases (12%) no tumor was found and there was normal parenchyma in 3, testicular atrophy in 2, an inflammatory mass in 8, hematomas in 2 and an abscess in 3.

In 17 cases (11.9%) multiple biopsies of the surrounding parenchyma diagnosed ITGCNU. Of these cases 15 (88.2%) were associated with seminoma, 1 (5.9%) was associated with a Leydig cell tumor and 1 (5.9%) was associated with an adenomatoid tumor. RO was performed when ITGCNU was associated with seminoma. In the other 2 cases ITGCNU was associated with benign tumors. Those 2 patients elected testis sparing and close US followup was performed.

No postoperative complications were detected. No patient underwent adjuvant treatment after RO and none experienced recurrence or contralateral metachronous seminoma at a median followup of 24 months. During followup no significant change was observed in the postoperative fertility workup in the benign groups. Particularly only 2 of the 36 patients referred for infertility presented with testicular cancer and underwent RO. Those 2 men elected not to continue with fertility screening after surgery.

DISCUSSION

According to the EAU guidelines TSS can be considered a viable alternative to RO in cases of synchronous bilateral testis cancer, metachronous

Table 1. *Cohort population general characteristics*

	Overall	No Ca	Ca	p Value
No. pts (%)	147	126 (86)	21 (14)	—
Mean ± SD age/median (IQR)	35 ± 11/33 (28–41)	35 ± 1/34 (28–42)	33 ± 7/32 (28–40)	0.364
No. clinical presentation (%):				0.034
Pain or lump	56 (38)	50 (89)	6 (11)	
Infertility	36 (24.5)	34 (94.4)	2 (5.6)	
Incidental	55 (37.5)	42 (76.4)	13 (23.6)	
Mean ± SD cm preop US size/median (IQR)	0.87 ± 0.44/0.8 (0.5–1.2)	0.84 ± 0.42/0.80 (0.50–1.20)	1.37 ± 0.71/1.2 (0.90–1.75)	0.001
Mean ± SD mins operative time/median (IQR)	94 ± 35/90 (70–111)	94 ± 36/90 (70–116)	95 ± 27/98 (69–116)	0.652
Mean ± SD mins ischemia time/median (IQR)	15.9 ± 2.5/16 (15–18)	16 ± 2.1/16 (15–18)	15 ± 2.9/16 (14–17)	0.090
Mean ± SD cm pathological size/median (IQR)	0.92 ± 0.52/0.8 (0.5–1.2)	0.87 ± 0.44/0.80 (0.5–1.12)	1.23 ± 0.80/1.20 (0.55–1.80)	0.033
Mean ± SD mos followup/median (IQR)	26 ± 15/24 (16–32)	26 ± 15/24 (16–32)	26 ± 18/24 (12–32)	0.772

Table 2. *Cancer detection binary logistic regression analysis*

	OR (95% CI)	p Value
Age	0.97 (0.92–1.03)	0.290
Clinical presentation:		
Pain or lump	Referent	
Infertility	0.98 (0.17–5.66)	0.980
Incidental	2.52 (0.81–7.88)	0.111
Preop US size (mm)	6.62 (2.26–19.39)	0.001

contralateral tumors or in a solitary testis with normal preoperative serum hormone levels when tumor volume is less than approximately 30% of testicular volume.[4] The amount of preserved testicular parenchyma and the preoperative serum concentrations of luteinizing hormone and testosterone particularly enable the decision to follow such an approach. Furthermore, for bilateral testicular tumors it was recommended to perform RO of the testis with the largest mass and TSS of the contralateral testis.[16]

Currently it is a widespread consensus that masses less than 2 cm on preoperative US are frequently found to be a benign neoplasm or a nontumorous lesion on final pathology findings.[6,17] Therefore, many groups have proposed TSS associated with FSE as a viable alternative to RO to treat STMs.[18] However, to our knowledge there is currently no unique definition of a STM with a maximum lesion diameter varying between 1 and 2.5 cm according to different investigators.[6,18–22]

In our study we enrolled 147 patients with a solitary lesion 2 cm or less as the largest diameter on preoperative US. Only the preoperative US diameter of the lesion was a predictor of malignancy. The risk of a malignant lesion increased sevenfold per mm. At the best cutoff of 0.85 the diameter of the lesion had 81% sensitivity, 58% specificity, 24% positive predictive value and 95% negative predictive value. Nevertheless, given the sensitivity of FSE, in 99.3% of cases the FSE findings were confirmed by the final pathology results, approximately supporting the sensitivity reported in other large series.[18,23] In our opinion TSS could also be offered as the first choice therapy of STMs greater than 0.85 cm with the option of surgical conversion to RO if malignancy is suspected on FSE.

It must be underlined that all patients enrolled in our study were treated for testicular pathology at a regional referral center. This probably confirms that FSE sensitivity depends on pathologist experience.[7] A STM was identified at surgery in 57% of cases by straight palpation while in 42% intraoperative US was needed but we found no difference in warm ischemia time or procedure duration.[14,24] In our study 85 of the 147 patients (57%) presented with a US lesion less than 1 cm, including 6 who presented with testis cancer.

To date our study has confirmed that the probability of testis cancer in a patient with a small testicular lesion (less than 1 cm) on US is less than 10%. However, the small number of events did not allow for a definitive conclusion or deeper analysis. Further studies should be done to evaluate whether US followup in these patients could further discriminate benign vs malignant lesions according to the speed of growth of the small mass detected on US.[4,7,9,15]

At the final pathology examination a surprisingly elevated number of Leydig cell tumors were found (54 of 147 cases or 36.7%). Despite what other groups have suggested,[25,26] in our series Leydig cell tumors and Leydig cell hyperplasia in a total of 23 cases did not appear to be more significantly associated with infertility than the other tumors. There was no case of recurrence or metastasis, confirming the safety of TSS to treat Leydig cell tumors, as stated in another study with longer followup.[25]

In our series we found 6 cases of Sertoli cell tumor, an uncommon neoplasm. Conservative management is rarely reported for this type of tumor.[8]

ITGCNU was associated with seminoma in 88.2% of patients. In these cases RO was performed, resulting in all cases of a finding of pure seminoma stage I-pT1 at final pathology. However, we also found ITGCNU in 2 patients with a benign neoplasm and the testis was spared according to patient choice, notwithstanding the 50% reported risk of cancer during the next 5 years.[12,26–28] Adjuvant therapy[12] was not performed in these 2 patients because of a desire to procreate, supported

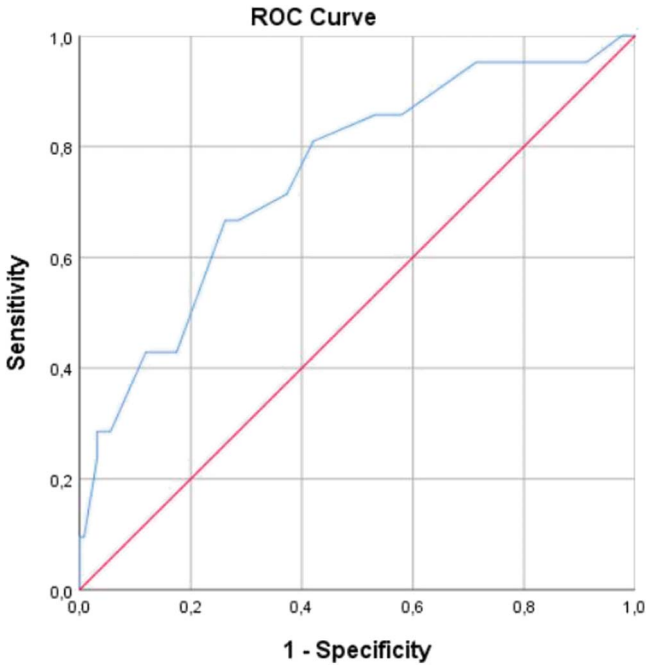

Figure 3. ROC analysis of testis cancer detection according to preoperative ultrasound size.

Table 3. *Nonmalignant lesion pathology report*

	No. Pts (%)
Overall	147
Benign tumor:	108 (74.3)
Leydig cell tumor	54 (50)
Leydig cell hyperplasia	28 (26)
Dermoid cyst	11 (10.2)
Sertoli cell tumor	6 (5.6)
Tunica vaginalis adenomatoid tumor	3 (2.8)
Sertoli-Leydig cell tumor	2 (1.8)
Epidermoid cyst	2 (1.8)
Mucinous cystadenoma	1 (0.9)
Vascular hyperplastic lesion	1 (0.9)
Benign lesion:	18 (12)
Normal testicular parenchyma	3 (16.6)
Testicular atrophy	2 (11.2)
Testicular inflammatory infiltrates	8 (44.4)
Hematoma	2 (11.2)
Abscess	3 (16.6)

by the possibility of delaying radiant treatment.[4] In the 2 patients testis cancer had not developed by 24 and 77 months of followup, respectively.

Considering the study population, final pathology findings in 12.2% of cases revealed no neoplasm while a benign neoplasm was found in 73.5% and a malignant tumor was found in 14.3%. RO was performed only in those cases. Currently all patients are followed and no metastasis or recurrence was reported, confirming the encouraging results in the literature of the oncologic safety of TSS as STM treatment.[7–10,18,20,21]

This study has some limitations. It is a retrospective study and there was a lack of preoperative and postoperative data on the patient hormonal and seminal profile because of the difficulty in collecting information due to the multicenter design of the study. Considering the retrospective nature of the study, we could not also exclude that patients classified with incidental disease and who showed the highest incidence of testicular cancer reported some discomfort or pain which was not recorded in our files.

There was also a lack of centralizing the pathological reports, which were not reviewed by a single pathologist but rather analyzed at each center by a dedicated uropathologist. In our series we also report a median of 16 minutes of ischemia time, which is not always reproducible at all centers and could be also related to the fact that all centers were referral centers for infertility and testis surgery, and a dedicated uropathologist was located on the same level as the operating room. We also acknowledge that sperm cord clamping and multiple biopsies are not always necessary and could induce unnecessary damage to Leydig cells. However, for the sake of homogeneity we included in the analysis only patients who underwent the same surgical technique, including sperm cord clamping and multiple biopsies, at a total of 5 centers.

Furthermore, followup duration appeared to be relatively short, considering that Leydig cell tumor metastasis has been described up to 8 years after RO.[29] We also had no data on previous imaging, considering that all of our study population was undergoing the first observation at each institution and no data on previous possible US examinations were available or reported by patients.

Finally, our study mostly focused on the management of testicular benign lesions, considering that only 14% of analyzed lesions were malignant. Our experience does not impact the possible management of small testicular cancer in a solitary testis or in patients with a normal contralateral testis. However, all patients in our series presented with a STM (less than 2 cm), which could have potentially been malignant unless FSE or definitive pathology had demonstrated the benign nature of the lesion. Further studies should overcome our limitations and better investigate the role of testis sparing surgery in the management of testicular cancer.

CONCLUSIONS

Our multicenter study confirms that STMs (less than 20 mm) are often benign and do not always require RO. Preoperative US can accurately assess lesion size and the smaller the lesion, the less likely that it will be malignant. Therefore, the described stepwise approach to small testicular nodules, which includes tumorectomy, FSE and orchiectomy or testis sparing according to FSE results, might represent optimal treatment in the presence of STMs. This strategy allows for safe management of malignant lesions, avoiding unnecessary sacrifice of the testis in patients with benign lesions, which may lead to malpractice issues. Therefore, we believe that TSS of STMs should be warranted and further investigated for wider adoption in the current treatment of testicular tumors.

REFERENCES

1. La Vecchia C, Bosetti C, Lucchini F et al: Cancer mortality in Europe, 2000-2004, and an overview of trends since 1995. Ann Oncol 2010; **21:** 1323.
2. Curado MP, Edwards B, Shin R et al: Cancer Incidence in Five Continents, Volume IX. IARC Scientific Publication No. 160. Geneva, Switzerland: World Health Organization 2007.
3. Engholm G, Ferlay J, Christensen N et al: NORDCAN—a Nordic tool for cancer information, planning, quality control and research. Acta Oncol 2010; **49:** 725.

4. Albers P, Albrecht W, Algaba F et al: Guidelines on testicular cancer: 2015 update. Eur Urol 2015; **68:** 1054.

5. Tokuc R, Sakr W, Pontes JE et al: Accuracy of frozen section examination of testicular tumors. Urology 1992; **40:** 512.

6. Carmignani L, Gadda F, Gazzano G et al: High incidence of benign testicular neoplasms diagnosed by ultrasound. J Urol 2003; **170:** 1783.

7. Brunocilla E, Gentile G, Schiavina R et al: Testis-sparing surgery for the conservative management of small testicular masses: an update. Anticancer Res 2013; **33:** 5205.

8. Gentile G, Brunocilla E, Franceschelli A et al: Can testis-sparing surgery for small testicular masses be considered a valid alternative to radical orchiectomy? A prospective single-center study. Clin Genitourin Cancer 2013; **11:** 522.

9. Giannarini G, Dieckmann KP, Albers P et al: Organ-sparing surgery for adult testicular tumors: a systematic review of the literature. Eur Urol 2010; **57:** 780.

10. Borghesi M, Brunocilla E, Schiavina R et al: Role of testis sparing surgery in the conservative management of small testicular masses: oncological and functional perspectives. Actas Urol Esp 2015; **39:** 57.

11. Nord C, Bjøro T, Ellingsen D et al: Gonadal hormones in long-term survivors 10 years after treatment for unilateral testicular cancer. Eur Urol 2003; **44:** 322.

12. Heidenreich A, Bonfig R, Derschum W et al: A conservative approach to bilateral testicular germ cell tumors. J Urol 1995; **153:** 10.

13. Hopps CV and Goldstein M: Ultrasound guided needle localization and microsurgical exploration for incidental nonpalpable testicular tumors J Urol 2002; **168:** 1084.

14. Hallak G, Cocuzza M, Sarkis AS et al: Organ-sparing microsurgical resection of incidental testicular tumors plus microdissection for sperm extraction and cryopreservation in azoospermic patients: surgical aspects and technical refinements. Urology 2009; **73:** 887.

15. Paffenholz P, Held L, Loosen SH et al: Testis sparing surgery for benign testicular masses: diagnostics and therapeutic approaches. J Urol 2018; **200:** 353.

16. Ferretti L, Sargos P, Gross-Goupil M et al: Testicular-sparing surgery for bilateral or monorchide testicular tumors: a multicenter study of long-term oncological and functional results. BJU Int 2014; **114:** 860.

17. Tuygun C, Ozturk U, Goktug HN et al: Evaluation of frozen section results in patients who have suspected testicular masses: a preliminary report. Urol J 2014; **11:** 1253.

18. Matei DV, Vartolomei MD, Renne G et al: Reliability of frozen section examination in a large cohort of testicular masses: what did we learn? Clin Genitourin Cancer 2017; **15:** e689.

19. Connolly SS, D'Arcy FT, Bredin HC et al: Value of frozen section analysis with suspected testicular malignancy. Urology 2006; **67:** 162.

20. Steiner H, Höltl L, Maneschg C et al: Frozen section analysis guided organ-sparing approach in testicular tumors: technique, feasibility, and long-term results. Urology 2003; **62:** 508.

21. Bozzini G, Picozzi S, Gadda F et al: Long-term follow-up using testicle-sparing surgery for Leydig cell tumor. Clin Genitourin Cancer. 2013; **11:** 321.

22. Keske M, Canda AE, Yalcin S et al: Is testis-sparing surgery safe in small testicular masses? Results of a multicentre study. Can Urol Assoc J 2017; **11:** E100.

23. Elert A, Olbert P, Hegele A et al: Accuracy of frozen section examination of testicular tumor of uncertain origin. Eur Urol 2002; **41:** 290.

24. Dell'Atti L: Efficacy of ultrasound-guided testicle-sparing surgery for small testicular masses. J Ultrasound 2016; **19:** 29.

25. Giannarini G, Mogorovich A, Menchini Fabris F et al: Long-term followup after elective testis sparing surgery for Leydig cell tumors. J Urol 2007; **178:** 872.

26. Ehrlich Y, Konichezky M, Yossepowitch O et al: Multifocality in testicular germ cell tumors. J Urol 2009; **181:** 1114.

27. Favilla V, Russo GI, Spitaleri F et al: Prevalence of intratubular germ cell neoplasia and multifocality in testicular germ cell tumors $\leq$ 2 cm: relationship with other pathological features. Clin Genitourin Cancer 2015; **13:** e31.

28. Hoei-Hansen CE, Rajpert-De Meyts E, Daugaard G et al: Carcinoma in situ testis, the progenitor of testicular germ cell tumors: a clinical review. Ann Oncol 2005; **16:** 863.

29. Grem JL, Robins HI, Wilson KS et al: Metastatic Leydig cell tumor of the testis: report of 3 cases and review of the literature. Cancer 1986; **58:** 2116.

The growing use of scrotal US as part of the infertility workup and as an adjunct to physical examination has led to the increased detection of STMs. While to our knowledge the best practice management in these cases remains elusive, the current series adjoining previous studies reiterates the benign nature of many of these smaller tumors. The ability of tumor size on preoperative US to predict malignancy in this setting was good but far from great (AUC 0.75). With this in mind it remains reasonable to consider partial orchiectomy and frozen section analysis as the best means to rule out malignancy.

However, established guidelines recommend TSS in unique circumstances of bilateral synchronous tumors or a tumor in a solitary testis not comprising more than 30% of total testis volume (reference 4 in article). Thus, if partial orchiectomy is offered to men with a contralateral healthy testis for diagnostic purposes only (ie radical orchiectomy would be done inevitably if malignancy is detected on frozen section analysis), its clear advantage over strict surveillance and surgical intervention upon an increase in tumor size must be evident. With the latter approach the risk of stage progression in men who in fact harbor a small germ cell tumor appears negligible.[1]

In my experience the oncologic safety of carefully observing STMs using serial US in patients with adequate compliance is equally effective, obviating the potential deleterious impact of surgery on fertility and endocrine testicular function without compromising long-term outcomes.

Ofer Yossepowitch
Department of Urology
Tel Aviv Sourasky Medical Center
Tel Aviv, Israel

REFERENCE

1. Bieniek JM, Juvet T, Margolis M et al: Prevalence and management of incidental small testicular masses discovered on ultrasonographic evaluation of male infertility. J Urol 2018; **199:** 481.

REPLY BY AUTHORS

We agree that the ideal strategy in patients with a STM would be to follow them with periodic US and perform surgery only in those who show significant growth during followup. This is our actual policy in masses less than 5 mm in diameter. In this group few patients required surgical exploration during followup. It is likely that in cases of such small lesions strict surveillance may not change the progression of germinal tumors, as reported by Bieniek et al, who noted a mean lesion diameter of 4.14 ± 2.0 mm (reference 1 in Editorial Comment).

However, sparse data are available in the literature on the natural history of larger masses when left untreated. Our study shows that even larger lesions up to 20 mm in diameter may be benign, indicating that strict surveillance might be justified even for masses larger than 5 mm. Our experience also demonstrates that with increasing lesion size the risk of cancer significantly increases 7 times per mm. This information could be used to better counsel patients about the risk of harboring testicular cancer and eventually better support a followup strategy in patients with a STM.

We believe that 2 research lines which might help us in the near future are 1) study of the individual lesion growth rate, which could differentiate benign from malignant lesions, and 2) new imaging diagnostic tests such as contrast enhanced US[1] or testicular magnetic resonance imaging, which might improve the diagnostic performance of scrotal US.

REFERENCE

1. Isidori AM, Pozza C, Gianfrilli D et al: Differential diagnosis of nonpalpable testicular lesions: qualitative and quantitative contrast-enhanced US of benign and malignant testicular tumors. Radiology 2014; **273:** 606.