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ORIGINAL ARTICLE

Are ultrasonographic measurements a reliable parameter to choose non-palpable testicular masses amenable to treatment with sparing surgery?

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Summary

Purpose: *To analyze the dimensional characteristics between non-palpable testicular masses detected during ultrasonographic (US) study and their postoperative dimensions reported in definitive histological diagnosis, and evaluate if the sonographic measurements may be a relevant parameter to improve the identification of testicular lesions amenable to treatment with testicular-sparing surgery (TSS).*

Methods: *A total of 77 patients who underwent radical orchiectomy or TSS for non-palpable testicular masses suspected for malignant neoplasms were included into this study. Preoperative US studies were also carried out in all patients to evaluate the diameter, volume and sonographic characteristics of the testicular lesions and the contralateral testes. All patients underwent inguinal orchiectomy or testicular exploration (for masses ≤1.5 cm) through an inguinal approach.*

Results: *The mean age at the time of diagnosis was 36.5 years. The predominant finding was a hypoechoic mass (71.4%). The vast majority of all malignant masses appeared markedly hypoechoic (89.8%); moreover, this differed significantly from benign lesions (39.3%, p<0.001). Calcified lesions were significantly associated with benign tumors (77.8%, p<0.002). The mean maximum lesion diameter of the affected testicle determined by preoperative US study was 14.1 mm (range 7-21). The mean maximum lesion determined postoperatively by pathology was 13.4 mm (range 5-20). Tumor lesions estimated by US study were more accurate in benign tumors, but the results were not statistically significant (p=0.323).*

Conclusions: *We demonstrated that the sonographic diameter of the testicular lesions seems to be one of the most important parameter for the indication of an elective TSS and US is an accurate method for detecting and measuring these lesions.*

Key words: *measurements, orchiectomy, testicular cancer, testicular-sparing surgery, size, ultrasound*

Introduction

In general, most testicular tumors show a non-palpable lesion and are malignant in 80-90% of the cases [1]. With the use of scrotal ultrasography in the evaluation of urologic diseases such as infertility, orchitis or trauma, the rate of incidentally detected nonpalpable testicular masses is increasing [2]. An US study seems to have good sensitivity but scarce specificity [3]. The definitive diagnosis of a testicular tumor can only be obtained through inguinal orchiectomy and subsequent histological examination. Radical orchiectomy has been the standard treatment approach for malignant testicular masses for several decades [4]. However, TSS is now a well-known and increasingly accepted surgical technique for small testicular suspicious masses as well as for lesions in solitary testis and bilateral testicular masses even if they are thought to be malignant [4,5]. Recent

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reports observed that the management option for small testicular masses include certain characteristics such as the dimensions of lesions (≤1.5 cm) that appear to be an interesting parameter to consider and to assess the safety of TSS [6,7].

The aim of this study was to analyze the dimensional characteristics between the testicular masses detected during US study and their postoperative dimensions reported in the definitive histological diagnosis, and to evaluate if the sonographic measurements may be a relevant parameter to improve identification of testicular lesions amenable to treatment with TSS.

Methods

This retrospective study was conducted in two academic referral centres between June 2006 and December 2016. A total of 77 patients who underwent radical orchiectomy or TSS for non-palpable testicular masses suspected for malignant neoplasms, were included into the study. Preoperative serum tumor marker levels including α-fetoprotein (AFP), β human chorionic gonadotropin (βhCG) and lactate dehydrogenase (LDH) were measured in all patients. For standardization of the clinical data, patients with a history of traumatic scrotal injury, abnormal blood levels of sex hormones, palpable testicular masses and incomplete clinical data were excluded from our study. Preoperative US studies were also carried out in all patients to evaluate the diameter, volume and sonographic characteristics of the testicular lesions and the contralateral testes. US study was performed using a machine equipped with a 7-12 MHz multi-frequency linear probe by two experienced sonographers who had been performing US studies on patients with testicular diseases for more 15 years (LD, AG). To avoid distortion of testicular shape, the scanning was performed carefully by using light pressure, with the patients lying in supine position. Gray-scale images of the testes were obtained in transverse and longitudinal planes. Testicular lesions were examined in at least two planes in the long and transverse axis and calculated using the size (maximum diameter) of the masses. All patients underwent inguinal orchiectomy or testicular exploration (for masses ≤1.5 cm) through an inguinal approach under spinal anesthesia. After exteriorization of the testis through inguinal access, the lesions were identified with intraoperative US. The spermatic cord was clamped temporarily to occlude spermatic vessels. The masses were excised leaving 2 to 3 mm borders of normal-appearing tissue around the lesion, and immediately sent to the pathologist for frozen section examination (FSE). If a malignant germ cell tumor was found in the presence of a normal contralateral testis, radical orchiectomy was performed, but if the result of FSE was benign, organ-sparing surgery was done. Immediately after the excision of the mass and the closure of the tunica albuginea, the clamp of the spermatic cord was removed. All testicular masses were submitted to definitive histological examination including immunohistochemistry and were reviewed by a dedicated uro-pathologist. In gray-scale US, seminomas are more likely to be hypoechoic, heterogeneous, associated with calcified patterns in normal testicular parenchyma and can have a lobulated or multinodular configuration than non-seminoma tumors.

Statistics

Descriptive statistics for variables with a normal distribution, non-normal distribution, and categorical variables were evaluated using means and standard deviations or medians and interquartile ranges, according to their distribution. The association between US dimensions and postoperative dimensions reported by pathologists were evaluated using the Student's t-test or the Mann-Whitney U test, depending or their distribution. Statistical analyses were performed using SPSS 23 for PC (IBM Corp. Armonk, NY). A p value <0.05 was considered to indicate statistical significance.

Results

The patient and lesion characteristics including US features and pathologic evaluation of the 77 patients are summarized in Table 1. The mean

Table 1. Distribution of clinical characteristics in 77 patients affected by non-palpable testicular lesions

Characteristics	*n (%)*
Age (years), median (range)	36.5 (22-74)
21-30	21 (27.3)
31-40	28 (36.3)
41-50	14 (18.2)
51-60	9 (11.7)
61-70	3 (3.9)
71-80	2 (2.6)
Indication for sonography	
Scrotal pain	32 (41.5)
Scrotal mass	13 (16.9)
Infertility	26 (33.8)
Atrophy of testis	6 (7.8)
Location	
Right	31 (40.3)
Left	44 (57.1)
Right and Left	2 (2.6)
Echogenicity of lesions	
Hypoechoic	55 (71.4)
Heterogeneous	9 (11.7)
Calcified	13 (16.9)
Ultrasound results size (mm), median (range)	14.1 (7-21)
Pathologic results size (mm), median (range)	13.4 (5-20)
Surgery	
Orchiectomy	40 (52)
Testicular sparing	37 (48)
Follow-up (months), median (range)	27.8 (6-48)

Table 2. Distribution of malignancy in sonographic findings

Histology	*Malignant (n=49)*	*Benign (n=28)*	*p value*
Sonographic findings, n (%)			
Hypoechoic	44 (89.8)	11 (39.3)	< 0.001
Heterogeneous	3 (6.1)	10 (35.7)	< 0.001
Calcified	2 (4.1)	7 (25)	< 0.002

Table 3. Pathologic results of patients who underwent surgery

Pathology	*n (%)*
Orchiectomy: Malignant lesions	
Seminoma	17 (22.1)
Non-seminoma	8 (10.4)
Lymphoma	2 (2.6)
Orchiectomy: Benign lesions	
Leydig cell tumor	4 (5.2)
Epidermoid cyst	1 (1.3)
Hamartoma	1 (1.3)
Chronic inflammation	2 (2.6)
Fibrosis	5 (6.5)
Testicular sparing surgery: Malignant lesions	
Seminoma	16 (20.8)
Non-seminoma	6 (7.8)
Testicular sparing surgery: Benign lesions	
Epidermoid cyst	3 (3.9)
Fibrosis	7 (9.1)
Granulomatous orchitis	2 (2.6)
Leydig cell tumor	3 (3.9)

age at the time of diagnosis was 36.5 years (range, 22-74). Patients in the third decade (28/77; 36.3%) were affected predominantly. In our study, scrotal pain was the first most common indication for US study in patients with incidentally discovered non-palpable testicular lesions (32/77; 41.5%), followed by infertility (26/77; 33.8%), scrotal mass such as hydrocele, epididymis cyst and/or varicocele (13/77; 16.9%), and atrophy of the testis (6/77; 7.8%). Of the 77 patients studied, 75 had bilateral testes, one had only the right testis and one had only the left testis. The US findings showed a variety of lesions with different approaches including hypoechoic, homogeneous, heterogeneous, and calcified lesions. The predominant finding was a hypoechoic mass (55/77; 71.4%). The vast majority of all malignant masses appeared markedly hypoechoic (44/49; 89.8%); moreover, this differed significantly from benign lesions (11/28; 39.3%, p<0.001). Calcified lesions were significantly associated with benign histology (9/7; 77.8%, p<0.002) (Table 2).

Of all 37 patients in whom TSS was accomplished, 15 had benign and 22 had malignant lesions according to FSE. Permanent pathologic sections confirmed frozen section results in all cases (100% accuracy) and surgical margins were negative in all cases. In the 15 patients with benign lesions, the final pathologic evaluation revealed epidermoid cyst in 3 patients, fibrosis in 7, granulomatous orchitis in 2 and Leydig cell tumor in 3 patients (Table 3).

TSS was performed with no significant intra-postoperative complications and all patients were discharged within two days after surgery. After a mean follow-up of 27.8 months (range 6-48) all patients were free of disease on the basis of clinical examination and imaging studies.

The retrospective nature of this study gave no possibility to assess the hormonal status after surgery. The mean maximum lesion diameter of the affected testicle determined by US study preoperatively was 14.1 mm (range, 7-21) and the controlateral testicle was sonographically normal in all cases. The mean postoperative maximum lesion determined by the pathologist was 13.4 mm (range, 5-20). Tumor lesions estimated by US study were more accurate in benign tumors, but the results were not statistically significant (p=0.323).

Discussion

The incidental findings of sonographic testicular lesions in young adults represent a clinical and legal problem [8]. Although US can identify these lesions, it is not always possible to use imaging to determine whether they are inflammatory or neoplastic and benign or malignant [9]. In the past, all intratesticular lesions were theoretically treated with radical orchiectomy; however, to date, a TSS is supported especially for bilateral and/or multiple lesions or in monorchid patients [7]. The advantages of TSS comprise the improvement of the patient's overall quality of life, endocrine function, fertility, and the avoidance of the negative cosmetic effects of radical orchiectomy [6,7]. However, the indications for TSS as conservative treatment of testicular cancer are still controversial, especially

for patients with normal contralateral testis [10]. 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 <1.5 cm and no invasion of the rete testis. In all these patients, the enucleation of the lesion must be accompanied by multiple biopsies of the surrounding tissue and adjuvant radiotherapy must be considered for seminomas [11]. The diameter of the lesions seems to be one of the most important parameter for the indication of elective TSS. There is only scant published data on the correlation between sonographic findings and the histological size of testicular tumors [1,7,12]. If the size was cited in order to justify a TSS, it was without correlating to the preoperative sonographic findings [13]. Tumor size is an important predictor of malignant disease. However, there is no definitive diameter cut-off for this discrimination, a diameter not bigger than 20 or 25 mm is used as a cut-off in most series [14]. Carmignani et al. have underlined the relationship between lesion diameters and the presence of germ cell tumors, showing that lesions of 16-32 mm have a high relative risk for malignancy [15]. Shtricker et al. reported that an US measurement of malignant testicular lesions underestimates the size in 25% of the patients. Therefore, this evaluation can have a serious impact on the decision of TSS [16]. According to the authors' opinion, a reason for underestimation might be that US only shows the central body of the malignancy and cannot show the peripheral layers that are of clinical significance. The results of our study indicate that a quantitative estimation of tumor diameter by US is an accurate method of measuring tumor size. However, the estimation of tumor size is of little value in predicting the presence of malignancy in masses greater than 10 mm. Germ cell tumors are the most significant condition potentially observed during scrotal US and US characteristics of these tumors are typically hypoechoic and have an overall homogeneous appearance [17]. However, contrast-enhanced US has recently drawn the interest in the medical community for improving the diagnostic accuracy in testicular lesions [18]. Isidori and colleagues showed in a large prospective study of 115 patients with nonpalpable testicuar masses that a contrast-enhanced US study had a high accuracy in the diagnosis of small testicular lesions (area under ROC curve performance: 0.927; 95% confidence interval: 0.872, 0.981) [19]. Finally, our study along with previously published series, suggested that benign testicular tumors are common among small testicular masses and TSS is a safe and effective treatment with excellent outcomes and without significant complications [20].

The limitations of the present study are evident. The retrospective nature of our study may result in unrecognized biases. First, according to the predefined criteria, we exluded all palpable lesions. Second, the study was performed for a period of 10 years, during which it is plausible that changes in US technology may have changed the features of small testicular lesions. Third, our data must be validated with future multicenter studies before any broad generalizations are made. However, these disadvantages are partly outweighed by a median follow-up of 28 months.

Conclusions

The results of this study confirm the favourable data in the literature, indicating that US constitutes an excellent diagnostic method with 100% sensitivity in the diagnosis of testicular masses. The hypoechoic pattern and size greater than 10 mm were risk factors of malignancy. Moreover, we demonstrated that the diameter of the lesions seems to be one of the most important parameters for the indication of an elective TSS and US is an accurate method for detecting and measuring testicular lesions. Long-term follow-up and multicentre studies are necessary to confitm these results and suggest that TSS does not compromise the oncological efficacy in the treatment of these tumours.

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Conflict of interests

The authors declare no conflict of interests.

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