REVIEW PAPER

UROLOGICAL ONCOLOGY

Feasibility of active surveillance in small testicular mass: a mini review

Grzegorz Niemczyk[1,2], Łukasz Zapała[2], Tomasz Borkowski[2], Waldemar Szabłoński[2], Piotr Radziszewski[2], Agnieszka Cudnoch-Jędrzejewska[1]

[1]*Department of Experimental and Clinical Physiology, Laboratory of Centre for Preclinical Research, Medical University of Warsaw, Warsaw, Poland*
[2]*Department of Urology, Medical University of Warsaw, Warsaw, Poland*

Citation: Niemczyk G, Zapała Ł, Borkowski T, Szabłoński W, Radziszewski P, Cudnoch-Jędrzejewska A. Feasibility of active surveillance in small testicular mass: a mini review. Cent European J Urol. 2021; 74: 10-13.

Article history
Submitted: Sept. 21, 2020
Accepted: Jan. 7. 2021
Published online: Feb. 4, 2021

Corresponding author
Grzegorz Niemczyk
Medical University of Warsaw
Department of Experimental and Clinical Physiology
3c Pawińskiego Street
02-106 Warsaw, Poland
phone: +48 22 599 0708
gniemcz@hotmail.com

Introduction Widespread use of scrotal ultrasonography has led to the detection of incidental, non-palpable small testicular masses (STMs). Historically, all intratesticular masses were treated radically, however more conservative strategies are now being applied with growing evidence that up to 80% of STMs are benign lesions. Testis-sparing surgery is deemed a gold standard in STMs. However, the high probability of the benign nature of STMs and the excellent cure rate of localized testicular cancer has led to emerging attempts to use an active surveillance (AS) strategy for selected groups of patients.

Material and methods We conducted a non-systematic review of the literature in the PubMed and Embase databases for articles associated with AS strategy in STMs.

Results The main inclusion criteria for AS in patients with STMs were lack of risk factors of testicular cancer, no features of disseminated disease, negative tumor markers, non-palpable lesion that did not exceed 10 mm. Mean follow-up time of AS across the studies ranged from 9.6 to 29.6 months. Surveillance protocols were based on regular physical examination, scrotal ultrasonography and measurement of tumor markers. The change rate to active treatment ranged from 0% to 8% without reported deterioration of oncological outcomes. Patients have proceeded to surgical treatment based on their preference, lesion growth, change in echogenicity, tumor marker growth and the need for testicular exploration for other reasons.

Conclusions Active surveillance is a reasonable conservative strategy in the management of STMs in selected groups of patients with minimal risk of deteriorating impact on oncological outcomes.

Key Words: small testicular mass ‹› active surveillance ‹› testicular cancer ‹› oncology ‹› testis

INTRODUCTION

Widespread use of scrotal ultrasonography (US) due to infertility, testicular pain, and trauma has led to the detection of incidental, non-palpable small testicular masses (STM) [1]. Although there is no formal definition, most authors define STM for cases when the diameter does not exceed either 20 mm or 25 mm [2, 3].

The majority of palpable testicular masses (i.e., 90–95%) are malignant neoplasms and, historically, it was believed that this also applies to those discovered incidentally and therefore they were treated by radical orchidectomy [4]. However, recent data shows that up to 80% of STMs are benign lesions [3]. Consequently, the old dogma that every testicular mass should be considered a malignant tumor and treated radically is no longer valid [2]. Based on those assumptions, more conservative treatments have been applied. Testis-sparing surgery (TSS) has been proven to have excellent outcomes in selected groups of patients [2]. However, apart from obvious perioperative risk, there are data indicating that TSS puts some patients at the risk of developing de novo hypogonadism [5].

Taking together the high risk of the benign nature of STM and the risk associated with testicular surgery has led to emerging attempts to use an active surveillance (AS) strategy in a selected group of patients. In this review, up-to-date knowledge about the feasibility of AS in the management of STM is presented and summarized.

Evidence acquisition

A non-systematic search of the literature in the PubMed and Embase databases using the term 'small testicular mass' was undertaken. The list of references in the selected studies were manually searched and relevant studies were identified and also included in the review.

Evidence synthesis

The database search identified 922 articles and the manual search in the list of references of those articles identified an additional two articles. Finally, five studies met the eligibility criteria and were selected for further analysis [1, 6–9]. All of these studies were retrospective analyses of case series.

Clinical criteria for inclusion and exclusion from active surveillance

All lesions selected for AS were non-palpable and incidentally found during US studies. Patients were referred to US mostly due to infertility, but in some cases also due to testicular pain and swelling. The most important inclusion criteria are listed in Table 1. Across all included studies, negative tumor markers were usually obligatory. Patients with previous cryptorchidism, a history of testicular germ cell tumor (TGCT), or disseminated malignancy were excluded from AS [6, 8].

Scrotal ultrasonography criteria for inclusion and exclusion from active surveillance

Maximum lesion diameter did not exceed 10 mm. All studies included hypoechoic lesions for AS. Some studies also included hyperechoic and anechoic lesions [8, 9], whereas for other studies those features were exclusion criteria [7]. In two studies, vascularized lesions were also included for AS [7, 9], however coexisting microlithiasis was an exclusion criteria [7, 8].

Follow-up

Mean follow-up time across the studies ranged from 9.6 to 29.6 months (Table 1). Surveillance protocols differed slightly between the studies, but they were mainly based on regular physical examination, scrotal US and measurement of tumor markers. Check-ups were most abundant in the first year, with intervals of 3 months, starting 1–3 months after diagnosis. The change rate to active treatment ranged from 0% to 8%. Criteria were patient preference, lesion growth or change in echogenicity, tumor marker growth, and the need for testicular exploration for other reasons (e.g., sperm extraction).

DISCUSSION

On the basis of the studies reviewed, AS may be considered a feasible strategy in the management of STMs in selected groups of patients. The quantity of evidence presented in the above studies is low, but it is worth noting that the relative rarity of STMs

Table 1. *Characteristics of included studies*

	Patients	Referral to US	Tumor size (mean if available)	US features	Mean follow-up	Patients lost to AS (%)
Sheynkin et al. (2004)	1	Infertility	Not specified	Not specified	24 months	0 (0%)
Connolly et al. (2006)	12	Infertility, testicular pain or swelling	<10 mm (4.9 mm)	Hypoechoic, hyperechoic and anechoic	29.6 months	1 (8%)
Eifler et al. (2007)	10	Infertility	<5 mm	Hypoechoic and hyperechoic, heterogeneous Hypoechoic/ normal vascularity	9.6 months	0 (0%)
Benelli et al. (2017)	4	Infertility, testicular pain	<10 mm (6.1 mm)	Hypoechoic and anechoic Avascular	16 months	0 (0%)
Bieniek et al. (2018)	104	Infertility	<10 mm (4.14 mm)	Hypoechoic With and without vascularity	15.6 months	2 (2%)

US – scrotal ultrasonography; AS – active surveillance

make it difficult to carry out well-designed prospective trials.

Ideally, patients included in an active surveillance strategy should not have risk factors of testicular cancer as a previous history of TGCT or cryptorchidism. The cumulative risk of developing metachronous contralateral TGCT is up to 5% and the relative risk compared with the general population may be as high as 32% [10]. Similarly, a history of cryptorchidism increases the risk of TGCT by 1.6 to 7.5 times [11]. Therefore, any patient with STM and a history of TGCT or cryptorchidism should be excluded from AS. The size of testicular mass is a strong predictor of malignancy and can be used as a strong determinant in patient selection for AS [12]. All of the above studies included patients with a lesion diameter less than 10 mm. This is reasonable as the risk of malignancy may be as low as 6% at this cut-off point [12]. On the other hand, the risk of malignancy is increased to over 90% in lesions with a diameter more than 20 mm [2]. Gentile et al. performed an ROC analysis and found that a diameter of 8.5 mm has an 81% sensitivity, but only a 58% specificity in diagnosing malignancy. Importantly, the authors included in their analysis a wide range of patients who were referred for US due to testicular pain, lump, and infertility. Therefore, the results can be applied not only to non-palpable lesions. Interestingly, in a logistic regression model, only the preoperative diameter of the lesion and not the clinical presentation was a predictor of malignancy [13]. Alternatively, it is possible to determine lesion size by its volume [14]. Paffenholz et al. measured testicular mass volume and found that a volume of 2.8 cm^3 leads to a diagnosis of malignant tumor with an 83% sensitivity and an 89% specificity. No imaging modality can distinguish between benign and malignant lesions. Ultrasonographic features such as echogenicity or vascularity of the lesion may not have any impact on its histologic type. Although some authors included only hypoechoic lesions for AS, Shtricker at al. did not find a difference in echogenicity between benign and malignant lesions [15]. Eifler et al. found in their series that all of the hyperechoic and heterogenous lesions were scar tissues or benign lesions [9]. Similarly, the presence of vascularity in the lesion should not be considered unequivocally as malignancy. In the study by Bieniek et al., 70% of the benign testicular masses treated with TSS were vascularized [7]. Esen et al. analyzed the pathology results of hypervascularized testicular masses, postoperatively [16]. In subanalysis, four out of seven subcentimeter masses were found to be benign as well as seven out of thirteen non-palpable masses.

Multiparametric US is a promising tool that combines contrast-enhanced US (CEUS) and elastography. It improves the differential diagnosis between benign and malignant tumors. Particular patterns of vascularization and time-intensity curves after microbubble contrast injection at CEUS and increased stiffness at elastography support the diagnosis of malignancy [17]. Similarly, magnetic resonance imaging may also help in diagnosis [18]. The isointensity of the features of lesions on T1W and low ADC values are more distinctive for malignancy, however, there are inconsistencies among the studies reviewed [18].

In two studies, patients who switch from AS to active treatment had a delay for TGCT diagnosis of between 5.5 to 10 months [7, 8]. The cure rate for clinically localized TGCT is close to 99% [19], therefore the close monitoring of STMs and selecting an appropriate time to commence active treatment should not significantly impact oncological outcomes. Follow-up is a critical issue for patients on AS, however there is no established universal strategy. It should be based at least on regular physical examination, scrotal US and measurement of tumor markers every 3 months in the first year. It is supposed that TGCT should double its diameter within a period of 3 months [20]. Consequently, STMs that are supposed to be benign have a much slower growth rate. Bieniek et al. found that the interval growth of surveilled STMs, that behave clinically and radiologically in a benign manner, was 0.03 ±1.33 mm at mean follow-up of 1.3 years [7]. They suggested that the maximum growth rate of the lesion to keep the patient on AS was 1 mm per year. Patients with TGCT, who were initially on AS and proceeded to surgical treatment, have not been reported to have any recurrence at follow-up.

CONCLUSIONS

Active surveillance is a reasonable conservative strategy in the management of STMs with a minimal risk of deteriorating impact on oncological outcomes. Based on the current literature, it can be offered to selected patients with small (less than 10 mm) non-palpable lesions and negative tumor markers. Patients should be closely surveilled and in the case of lesion growth, palpable lesion or positive tumor markers, the physician should immediately make a decision to proceed to surgical treatment.

CONFLICTS OF INTEREST

The authors declare no conflicts of interest.

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