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Testis-sparing surgery and scrotal violation for testicular masses suspicious for malignancy: A systematic review and meta-analysis

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Abstract

Radical inguinal orchiectomy is the standard of care for men diagnosed with a testicular mass suspicious for germ cell tumor (TGCT). Non-traditional approaches to management, including testis-sparing surgery (TSS) and scrotal orchiectomy, occur in clinical practice. We systematically reviewed studies evaluating outcomes after TSS and scrotal violation for the management of a suspected TGCT. We used PubMed, Embase, and the Cochrane Central Register of Controlled Trials (January 1980–December 2018) to search for studies addressing morbidity and oncologic outcomes after TSS or scrotal violation for testicular masses concerning for TGCT. Paired reviewers independently screened abstracts for inclusion, sequentially extracted data, and assessed study quality. Twenty-one studies were included (10 TSS, 11 scrotal violation). Risk of local recurrence after TSS on meta-analysis was 7.5% after 3 to 5 years (absolute proportion reported in studies: 10.9%). Aggregated rates of positive margins (1.4%) and testicular atrophy (2.8%) across studies were low with 7.1% of patients requiring subsequent androgen therapy. Scrotal violation led to a higher aggregate risk of local recurrence compared to no scrotal violation (2.5% vs. 0.0%, $P < 0.001$) but did not appear to impact subsequent metastasis and survival in the short term (3–5 years). Most patients received adjuvant therapy after scrotal violation with 9.3% found to harbor residual primary tumor after scrotal scar excision. TSS carries a quantifiable risk of local recurrence after 3 to 5 years despite the majority receiving adjuvant radiation or chemotherapy. Scrotal violation carries a risk of local recurrence but does not appear to impact subsequent metastasis and survival in the short term.

Keywords: Testicular cancer; Germ cell tumor; Testis-sparing surgery; Scrotal violation; Systematic review

1. Introduction

Radical inguinal orchiectomy is the current standard of care for men diagnosed with a testicular mass suspicious for germ cell tumor (GCT) to optimize local control. However, patients with small (≤2 cm), nonpalpable masses may have benign histology in up to 80% of cases leading to increased interest in testis-sparing surgery (TSS) [1]. TSS is therefore considered for patients with a high likelihood of benign tumors, and examination of intraoperative frozen sections is performed leading to radical orchiectomy for testicular GCT (TGCT) and TSS for benign findings. TSS is additionally offered to men with suspicion of a TGCT with synchronous bilateral tumors, a metachronous contralateral tumor, or a solitary testis. In these cases, the testicle is spared despite the finding of malignant TGCT with the goal of preserving endocrine function. Outcomes for patients receiving TSS for malignancy is poorly understood with data largely limited to 1 report from the German Testicular Cancer Study Group until recent years [2–11].

Another nonstandard approach to TGCTs, orchiectomy in the setting of scrotal violation, has generally been avoided due to the concern of jeopardizing oncologic control. Scrotal violation can occur due to intentional transscrotal orchiectomy, biopsy of a testicular mass, or scrotal

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exploration leading to an incidental diagnosis. One prior review included data from studies ranging from the years 1914 to 1990 and found higher rates of local recurrence due to scrotal violation [12]. Interestingly, they noted 4 cases of local recurrence after high inguinal orchiectomy, but this finding is exceedingly rare in a nonviolated scrotum in the modern era with only 1 case report which was attributed to growing teratoma syndrome [13]. Despite concerns about oncologic control, some individuals have advocated for the adoption of trans-scrotal orchiectomy [14].

Therefore, we aimed to synthesize the studies evaluating oncologic outcomes after TSS and scrotal violation for testicular masses suspicious for TGCT. We aimed to quantify rates of local control and subsequent morbidity including adjuvant treatments received and metastasis.

2. Methods

The methods for this systematic review followed the Agency for Healthcare Research and Quality (AHRQ) Methods Guide for Effectiveness and Comparative Effectiveness Reviews [15]. Key Questions were defined by the American Urological Association (AUA) Guidelines Panel for Testicular Cancer. We used PubMed, Embase, and the Cochrane Central Register of Controlled Trials to search for studies from January 1980 to December 2018.

The Key Question related to orchiectomy specifically aimed to answer the following question: What is the effectiveness of radical orchiectomy (inguinal and trans-scrotal approaches) or testis-sparing/partial orchiectomy for men with an undiagnosed mass suspicious for testicular germ cell tumor?

2.1. Study selection

Study selection was based on predefined eligibility criteria within a PICOTS format for stage I and IIA/IIB TGCT (Supplemental Table 1). Two reviewers independently screened titles, abstracts, and full text for inclusion. Differences between investigators were resolved through consensus adjudication. We used DistillerSR (Evidence Partners, 2010) to manage the screening process. We further restricted this review to studies published since 1990 for TSS and since 1980 for scrotal violation to ensure older studies regarding scrotal violation were captured.

2.2. Data extraction and statistical methods

We created standardized forms for data extraction and pilot tested forms prior to data extraction. Reviewers extracted information on the general study characteristics, clinical data, and pathologic data including histology (seminoma, nonseminomatous GCT (NSGCT), and benign). Outcomes were abstracted for the population of patients at risk for each specific outcome. Outcomes for TSS included local recurrence, metastasis, all-cause mortality, positive margins (presence of GCT), testicular atrophy, and need for androgen therapy.

A meta-analysis was conducted for the outcome of local recurrence after TSS using random effects modeling. Freeman-Tukey double arcsine transformation was applied to stabilize variances for binomial data [16,17].

Outcomes for scrotal violation included local recurrence, metastasis, all-cause mortality, and residual tumor for patients undergoing scrotal scar excision. Data were also tabulated for patients undergoing inguinal orchiectomy without scrotal violation when reported in studies. The unadjusted proportion of patients experiencing local recurrence, metastasis, and all-cause mortality after scrotal violation and inguinal orchiectomy was pooled and compared by a Pearson chi-square test. Given the expected rate of 0% for local recurrence after inguinal orchiectomy, assessing relative risk was precluded. Analyses were conducted using STATA version 15.0 (STATA Corp, College Station, TX, 2017).

2.3. Risk of bias assessment and strength of the body of evidence

Two reviewers independently assessed the risk of bias in included studies. The Cochrane Risk Of Bias Assessment Tool for Non-Randomized Studies of Interventions (ACROBAT-NRSI) was used for cohort studies [18]. For noncomparative single-arm studies, we considered 3 items: design (specifying cohort inclusion for solitary, synchronous, or metachronous tumors for TSS or type of scrotal violation), consecutive enrollment, and objective measurement of outcome. If all 3 items were rated favorably, the study was considered high quality; if just 1 was unfavorable or unclear, the study was considered moderate quality. If 2 or 3 were unfavorable or unclear, the study was considered low quality. We graded strength of evidence on outcomes adapting the AUA's 3 predefined levels of strength of evidence.

3. Results

From 7,037 unique citations screened, 10 studies related to TSS and 11 studies related to scrotal violation met inclusion criteria with all classified as retrospective cohort studies (Fig. 1) [2−11,14,19−28].

3.1. Testis-sparing surgery

3.1.1. Study characteristics

Among TSS studies, 8 (80%) were from Europe [2−6,8,10,11] with mean age ranging from 27.6 to 40.0 years (Table 1) [2,4−6,8−10]. A total of 313 patients with 318 testicular masses were captured in TSS studies with 50% left-sided, 47.9% right-sided, and 2.1% bilateral tumors among studies reporting laterality (Supplemental Table 2) [2,3,5,9]. Among all studies, 28 (8.8%) patients had a normal contralateral testis, 114 (35.8%) had a metachronous tumor, 44 (13.8%) had a synchronous tumor, 14

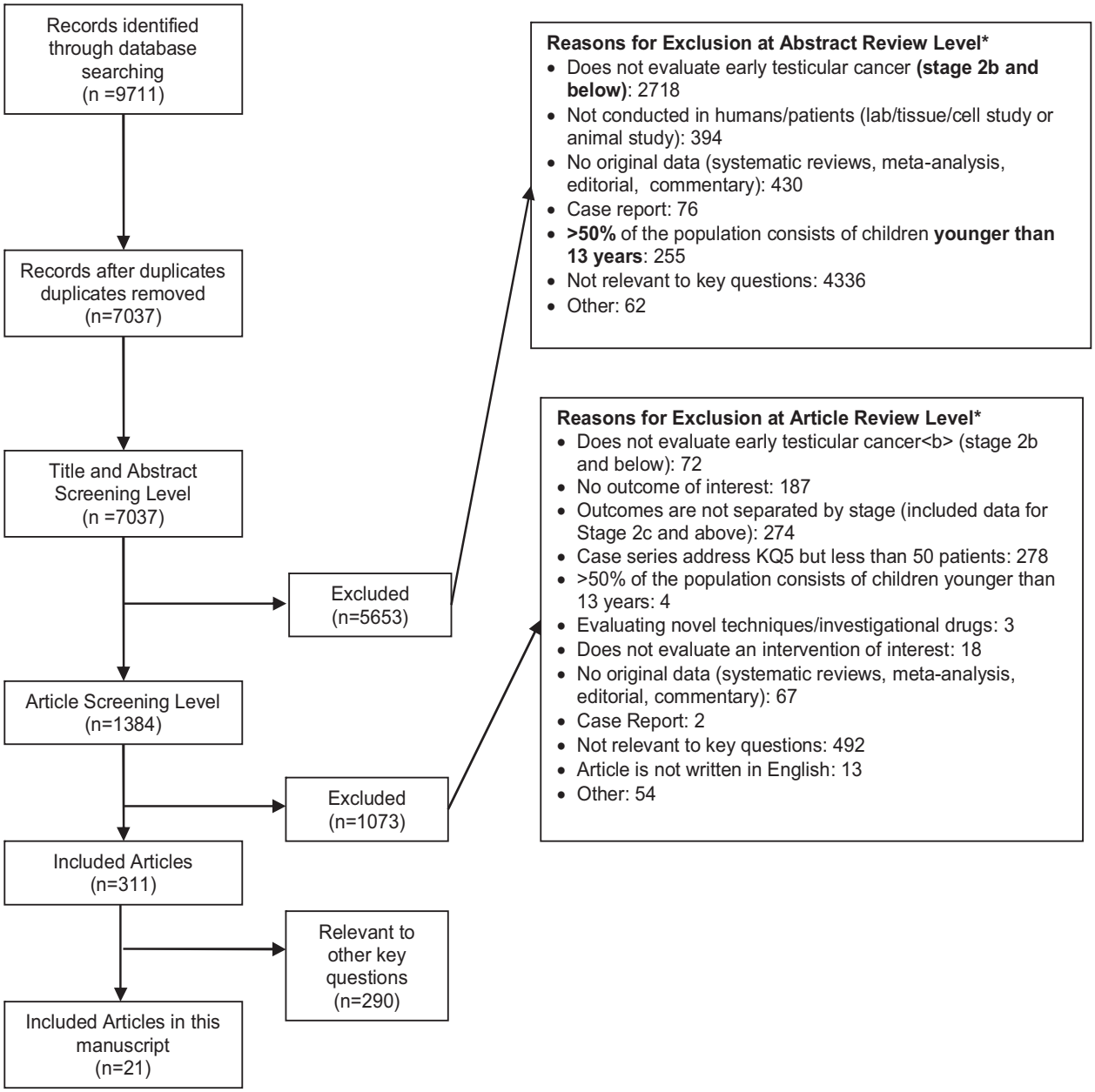

Fig. 1. Summary of the literature search.

(4.4%) had a tumor in a solitary testicle, and 118 (37.1%) were not specified (includes 3 bilateral). A total of 283 masses underwent TSS with mean tumor size ranging from 1.05 to 1.75 cm across studies [2,4,6,8–11]. One study included patients who had normal contralateral testicles [2]. Indication for TSS was variably reported. Seven studies reported clinical presentation diagnosis due to palpation in 99 (44%), ultrasound-only diagnosis in 31 (13.8%), infertility evaluation in 24 (10.7%), testicular pain in 20 (8.9%), hormonal evaluation in 10 (4.4%), and not specified in 41 (18.2%) [2–7,9].

Of the 283 masses receiving TSS, 77 (27.2%) tumors were benign on final pathology. Of the 206 (72.8%) malignant tumors, 18 (8.7%) were clinical stage II (Supplemental Table 3) [2–11]. Among the 5 studies reporting on consecutive patients receiving TSS, which included both malignant and benign tumors, there were 85 (53.1%) malignant and 75 (46.9%) benign lesions [2,3,5–7]. Of the 206 malignant masses undergoing TSS, 122 (59.2%) were seminoma, 82 (39.8%) NSGCT, 1 (0.5%) GCT not otherwise specified, and 1 (0.5%) with carcinoma in situ (CIS) only. A total of 91 (44.2%) received adjuvant local radiation while 41

Table 1
Study characteristics for included studies evaluating testis-sparing surgery for the treatment of testicular masses suspicious for testicular germ cell tumors.

Author, year	Continent	Country	Location	Years	Centers	*N*	Age (years)			
							Mean	Median	Range	SD
Bojanic, 2017 [2]	Europe	Serbia	Clinic of Urology, Clinical Center of Serbia	2010−2015	Single	28	35.3	-	23−50	7.3
Dell'Atti, 2016 [3]	Europe	Italy	Department of Urology, University Hospital St. Anna	2001−2010	Single	49	-	33	18−62	-
Bojanic, 2015 [4]	Europe	Serbia	Clinic of Urology, Clinical Center of Serbia	1996−2013	Single	24	29.0	-	16−54	8.6
Leonhartsberger, 2014 [5],[a]	Europe	Austria	Medical University Innsbruck	2003−2010	Single	65	38.9	-	20−69	-
Ferretti, 2014 [6]	Europe	France	Multiple Hospitals	1984−2013	Multiple	25	31.9	-	22−45	5.3
Lawrentschuk, 2011 [7]	North America	Canada	University of Toronto	1994−2009	Single	27	-	34		-
Heidenreich, 2001 [8]	Europe	Germany	German Testicular Cancer Study Group	1994−2000	Multiple	73	31.5	-	20−42	-
Kazem, 1999 [9]	North America	USA	Penn State Geisinger Medical Center	NR	Single	2	40.0	40	36−44	-
Weissbach, 1995 [10]	Europe	Germany	Krankenhaus Am Urban	NR	Single	14	27.6	26	20−39	6.0
Heidenreich, 1995 [11]	Europe	Germany	Eberhard-Karls University, Military Hospital Koblenz	1974−1991	Single	6	-	-	-	-

SD = standard deviation.
[a] Only 30 of the 65 patients had TSS while the remainder had radical orchiectomy.

(19.9%) received adjuvant chemotherapy. The dose of local radiation varied but was in the 16 to 20 Gy range.

3.1.2. Oncologic outcomes and harms

Median follow-up ranged from 36 to 91 months across studies (Table 2) [2−11]. Local recurrence was observed in 22 (10.9%) of 201 patients at risk corresponding to a rate of 7.5% (95% confidence interval (CI) 2.4%−14.4%) on meta-analysis (Fig. 2). For the 3 studies where no adjuvant local radiation was applied, local recurrence was observed in an aggregated 20.3% (14/69) [2−4]. Among remaining studies with variable use of adjuvant therapy, 6.1% (8/132) experienced local recurrence including 7 patients who had not received adjuvant local radiation and 1 with teratoma who had a positive surgical margin and did receive local radiation. For studies where subsets of patients could be identified, 9 (16.7%) of 54 with seminoma and 3 (8.1%) of 37 with NSGCT developed local recurrence [2,4−7,9−11]. Metastases and all-cause mortality were low at 3.0% (6/201) and 0.5% (1/201), respectively [2−11].

The rate of positive margins was low at 1.4% (2/138 from 7 studies; range 0%−10%). Notably, testicular atrophy was noted in 2.8% (8/282 from 11 studies; range 0%−14.3%) of patients with 7.1% (17/238 from 10 studies; range 0%−22.2%) requiring subsequent androgen therapy among at-risk patients [2−11]. Of 2 studies with patients requiring androgen therapy, 1 noted the indication to be hypogonadism [7], 1 did not specify an indication [8], and neither noted a predetermined threshold to begin therapy.

3.1.3. Risk of bias and strength of evidence

The risk of bias was assessed as moderate in 9 of the 10 studies. One was determined to have a high risk of bias because of lack of information about consecutive enrollment and objective outcome measurement [7]. Strength of evidence was assigned Grade C for low quality of evidence due to small sample sizes across studies with variable design and follow-up.

3.2. Scrotal violation

3.2.1. Study characteristics

For scrotal violation studies, 4 (36.4%) were from North America [14,21,25,28], 3 (27.3%) from Europe [20,26,27], and 3 (27.3%) from Asia [19,22,24] with a mean age ranging from 25.2 to 40.0 years (Table 3) [14,21,22,28]. A total of 1,862 patients with 1,863 tumors undergoing orchiectomy were identified among studies evaluating scrotal violation with 45.0% left-sided, 54.9% right-sided, and 0.1% bilateral for studies reporting complete laterality (Supplemental Table 4) [14,19−28]. For studies reporting data, 345 (28.1%) were seminoma and 882 (71.9%) were NSGCT. Clinical stage was reported for 1,575 patients as 1,153 (73.2%) Stage I, 331 (21.0%) Stage II (IIA or II unspecified), and 91 (5.8%) >Stage IIB. A total of 364 (19.5%)

Table 2
Outcomes for patients included in studies related to testis-sparing surgery for the treatment of testicular masses suspicious for testicular germ cell tumors.

Author	Follow-up (month)			Local recurrence			Metastasis			All-cause mortality			Positive margin			Atrophy			Androgen therapy		
	Median	Mean	Distribution value	At risk[a]	Events	(%)	At risk[a]	Events	(%)	At risk[a]	Events	(%)	At risk[a]	Events	(%)	At risk[a]	Events	(%)	At risk[a]	Events	(%)
Bojanic, 2017 [2] (GCT only)	45	40.9	SD : 20.5	9	1	11.1%	9	0	0.0%	9	0	0.0%	9	0	0.0%	27	0	0.0%	-	-	-
Dell'Atti, 2016 [3] (GCT only)	-	59.0	Range : 41−74	35	6	17.1%	35	0	0.0%	35	0	0.0%	-	-	-	49	0	0.0%	43	0	0.0%
Bojanic, 2015 [4] (GCT only)	51	-	Range : 7−178	25	7	28.0%	25	1	4.0%	25	0	0.0%	-	-	-	26	1	3.8%	24	0	0.0%
Leonhartsberger, 2014 [5] (GCT only)	50	-	Range : 3−107	8	0	0.0%	8	0	0.0%	8	0	0.0%	8	0	0.0%	33	0	0.0%	33	0	0.0%
Ferretti, 2014 [6] (GCT only—bilateral)	53	-	SEM: 13.1	7	1	14.3%	7	0	0.0%	7	0	0.0%	10	1	10.0%	11	1	9.1%	7	0	0.0%
Ferretti, 2014 [6] (GCT only—solitary)	36	-	SEM: 6.9	9	1	11.1%	9	0	0.0%	9	0	0.0%	10	0	0.0%	14	0	0.0%	12	0	0.0%
Lawrentschuk, 2011 [7] (GCT only)	68	-	Range : 0−169.2	14	2	14.3%	14	0	0.0%	14	0	0.0%	14	0	0.0%	27	0	0.0%	27	6	22.2%
Heidenreich, 2001 [8] (GCT only)	91	-	Range: 3−191	73	4	5.5%	73	3	4.1%	73	1	1.4%	73	1	1.4%	73	4	5.5%	72	11	15.3%
Kazem, 1999 [9] (GCT only)	36	-	-	2	0	0.0%	2	0	0.0%	2	0	0.0%	-	-	-	2	0	0.0%	2	0	0.0%
Weissbach, 1995 [10] (GCT only)	-	-	-	14	0	0.0%	14	2	14.3%	14	0	0.0%	14	0	0.0%	14	2	14.3%	12	0	0.0%
Heidenreich, 1995 [11] (GCT only)	43	-	-	5	0	0.0%	5	0	0.0%	5	0	0.0%	-	-	-	6	0	0.0%	6	0	0.0%

GCT = germ cell tumor; SD = standard deviation; SEM = standard error of the mean.

[a] Only patients with germ cell tumors included for local recurrence, metastasis, and overall survival (excluded patients receiving immediate radical or completion orchiectomy for reason other than local recurrence [e.g., atrophy]); positive surgical margin rate reported for all germ cell tumors including patients later receiving completion orchiectomy; all patients (malignant and benign) included for atrophy and need for postoperative androgen therapy as reported in study.

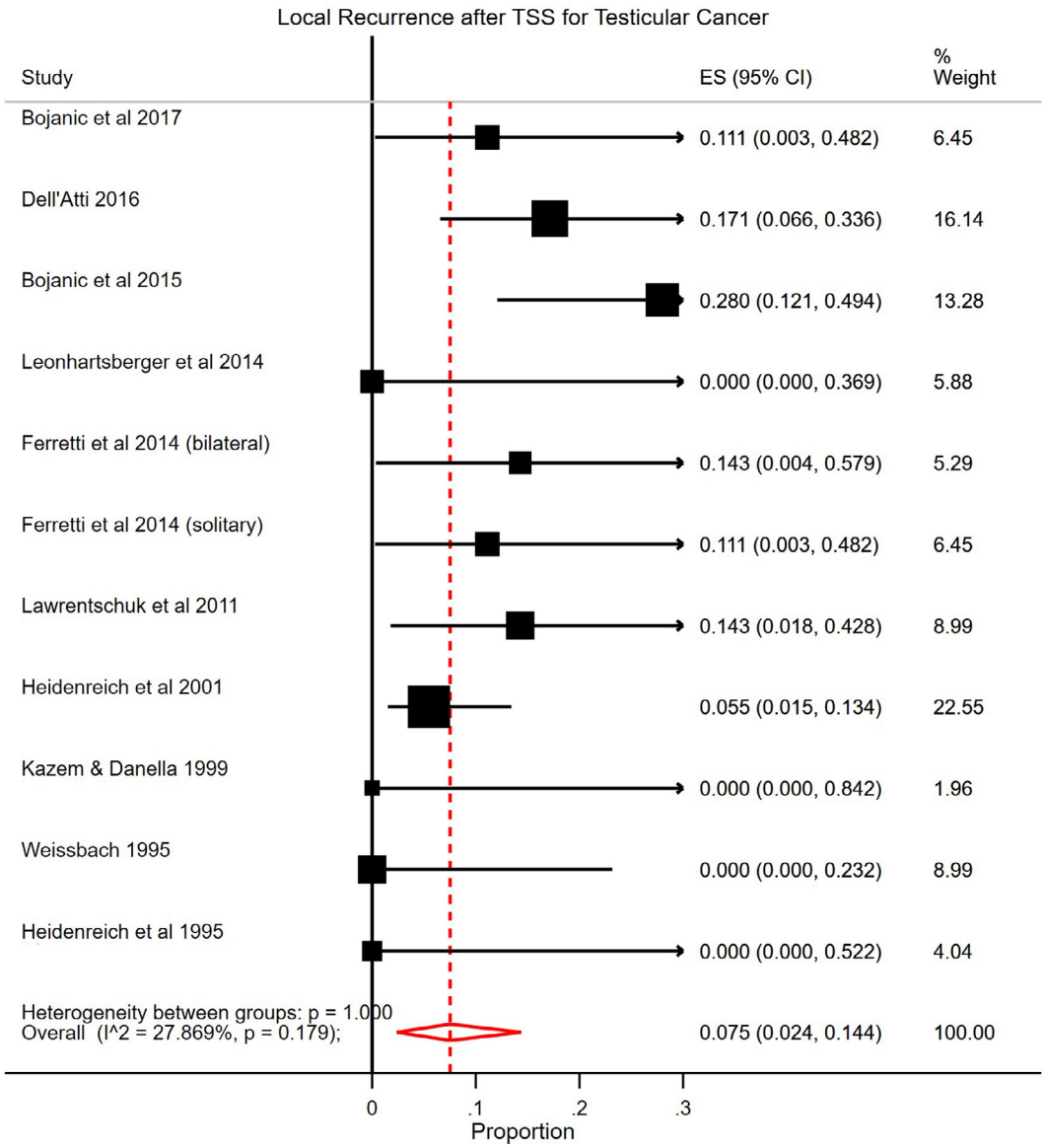

Fig. 2. Meta-analysis for the proportion of patients experiencing local recurrence after testis-sparing surgery for testicular germ cell tumors across studies included in the systematic review.

experienced scrotal violation due to trans-scrotal orchiectomy in 159 (43.7%), scrotal exploration in 72 (19.8%), prior testicular biopsy/aspiration only in 46 (12.6%), and other or unspecified violation in 87 (23.9%) (Supplemental Table 5). For patients with data on adjuvant treatment after scrotal violation, all 53 with seminoma received either local radiation (50) or scrotal scar excision (3) while 89 (65.4%) of 136 with NSCGT had scrotal scar excision. Some patients with NSGCT received radiation (2) or chemotherapy (per routine care).

3.2.2. *Oncologic outcomes*

Median follow-up ranged from 24 to 126 months (mean follow-up 25.0–174.0 months) between studies (Table 4). Local recurrence was observed in 8 (2.5%) of 315 patients who had scrotal violation compared to none (0.0%) undergoing inguinal orchiectomy without scrotal violation ($P < 0.001$) [14,19–23,25–28]. While 1 study [25] did not separately report outcomes for patients with seminoma and NSGCT, other studies demonstrated a local recurrence in 1 (1.9%) of 52 with seminoma and 7 (3.1%) of 229 with NSGCT [14,19–23,26–28]. A subset of studies reported the proportion of patients experiencing metastasis [14,19,24–28] and all-cause mortality [14,19,21,24]. The pooled unadjusted proportion of patients experiencing metastasis (16.6% vs. 18.1%, $P = 0.637$) and all-cause mortality (10.2% vs. 8.0%, $P = 0.547$) were similar for scrotal violation compared to no scrotal violation without the ability to differentiate seminoma and NSGCT. Notably, among studies evaluating scrotal excision specimens, 10 (9.3%) of 108 patients were found to have residual tumor [21,24,25,28].

Table 3
Study characteristics for included studies evaluating scrotal violation for the treatment of testicular masses suspicious for testicular germ cell tumors

Author, year	Continent	Country	Location	Years	Centers	Comparison group	*N*	Age (years)		
								Mean	Median	Range
Khader, 2012 [19]	Asia	Jordan	King Hussein Cancer Center	2003–2010	Single	Yes	74	-	34	15–71
Harding, 1995 [20]	Europe	UK	West of Scotland cancer registry	1975–1989	Multiple	Yes	442	-	28	14–68
Leibovitch,1995 [21]	North America	USA	Indiana University School of Medicine	1965–1993	Single	No	78	28.3	-	14–47
Arcadi, 1994 [14],[a]	North America	USA	Whittier College	1955–1991	Single	No	8	36.1	31	27–56
Stein, 1994 [22]	Asia	Israel	Northern Israel Oncology Center	1968–1988	Single	Yes	84	40.0	39	20–75
Lindeman,1991 [23]	Australia	Australia	Westmead Hospital	1980–1987	Single	Yes	73	-	37	21–67
Ozen, [24]	Asia	Turkey	University of Hacettepe	1978–1986	Single	Yes	105	-	-	-
Giguere, 1988 [25]	North America	US Army	Multiple Hospitals	1979–1985	Multiple	Yes	462	-	-	-
Kennedy, 1986 [26]	Europe	UK	Royal Marsden Hospital, London and Surrey	1979–1985	Single	Yes	210	-	-	-
Pizzocaro,1985 [27]	Europe	Italy	Istituto Nazionale per lo Studio e la Cura dei Tumori	1974–1981	Single	Yes	102	-	29	1.5–63
Boileau, 1984 [28]	North America	USA	M.D. Anderson Hospital and Tumor Institute	1977–1979	Single	Yes	224	25.2	-	-

SD = standard deviation.
[a] Malignant subset of tumors only; study also included 18 benign tumors.

3.2.3. Risk of bias and strength of evidence

The risk of bias was determined to be moderate in 7 studies [14,21,22,24,25,27,28] and high in 4 studies [19,20,23,26]. Most of the studies did not clearly describe the consecutive enrollment. Strength of evidence was assigned Grade C for low quality of evidence due to small sample sizes across studies with variable design and follow-up.

4. Discussion

We identified 21 studies evaluating the outcomes of TSS and scrotal violation for patients with testicular masses suspicious for TGCT. After a median of 3 to 5 years, the risk for local recurrence was found to be about 7.5% after TSS based on meta-analysis. Notably, the majority of patients received adjuvant treatment with radiation or chemotherapy, which may have lowered the rate of recurrence but potentially introduced variability between studies. Rates of positive margins (1.4%) and testicular atrophy (2.8%) were low with only 7.1% of patients requiring subsequent androgen therapy. For scrotal violation, the rate of local recurrence after 3 to 5 years was low but notably higher than high inguinal orchiectomy (2.5% vs. 0.0%, $P < 0.001$). There did not appear to be an impact on subsequent metastasis and survival in the short term. Nearly all patients with seminoma received adjuvant local radiation and two-thirds with NSGCT had scrotal scar excision. Adjuvant therapy appears important with 9.3% of excised scrotal scars found to harbor residual primary tumor.

No prior systematic review has assessed the effectiveness of TSS for TGCT with TSS largely reserved for benign tumors in clinical practice. Therefore, it is not surprising that 6 (60%) of the included studies were conducted between 2011 and 2017. Across studies including all-comers diagnosed with a testicular mass (benign and malignant masses) undergoing TSS, only 47% were found to be benign. The finding is notable because while 80% of asymptomatic masses diagnosed on ultrasound-only may be benign by prior estimates, the present review includes a population where diagnosis was due to palpation or testicular pain in 53% and infertility or hormonal evaluation in 15%, constituting a different underlying clinical presentation [1]. Furthermore, all instances of local recurrence in the literature were among patients who did not receive adjuvant local radiation and 1 case of a radio-resistant tumor (teratoma) with a positive surgical margin [8].

While most studies included patients with indications similar to the German Testicular Cancer Study Group cohort of synchronous bilateral tumors, a metachronous contralateral tumor, or a solitary testis, 1 study from Serbia reported on patients with a normal contralateral testis [2,8]. In the report from Serbia, 10 of 28 patients receiving TSS demonstrated a TGCT, with 1 proceeding immediately to radical orchiectomy, presumably due to patient preference after frozen section examination [2]. Only 1 of the 9

Table 4
Outcomes for patients in included studies evaluating scrotal violation for the treatment of testicular masses suspicious for testicular germ cell tumors.

Author, year	Group	Follow-up (month)				Scrotal violation			Inguinal orchiectomy			Scrotal violation			Inguinal orchiectomy			Scrotal violation			Inguinal orchiectomy			Scrotal violation		
						Local recurrence			Local recurrence			Metastasis			Metastasis			All-cause mortality			All-cause mortality			Residual tumor		
		Median	Mean	Distribution measure	Distribution value	At risk	Events	(%)	At risk	Events	(%)	At risk	Events	(%)	At risk	Events	(%)	At risk	Events	(%)	At risk	Events	(%)	At risk	Events	(%)
Harding, 1995 [20]	Scrotal violation	-	-	-	-	77	1	1.3%				-	-	-				-	-	-				-	-	-
Harding, 1995 [20]	Inguinal Orchiectomy	-	-	-	-				318	0	0.0%				-	-	-				-	-	-			
Leibovitch, 1995 [21]	Scrotal violation	33	-	Range	3–240	78	5	6.4%				-	-	-				78	4	5.1%				56	6	10.7%
Arcadi, 1994 [14]	Scrotal violation	126	174.0	Range	72–360	8	0	0.0%				8	1	12.5%				8	1	12.5%				-	-	-
Stein, 1994 [22]	Inguinal Orchiectomy	-	96.0	Range	7–241				74	0	0.0%				-	-	-				-	-	-			
Stein, 1994 [22]	Scrotal violation	-	97.0	Range	7–242	10	0	0.0%				-	-	-				-	-	-				-	-	-
Lindeman, 1991 [23]	Inguinal Orchiectomy	51	-	Range	15–109				65	0	0.0%				-	-	-				-	-	-			
Lindeman, 1991 [23]	Scrotal violation	51	-	Range	15–109	8	0	0.0%				-	-	-				-	-	-				-	-	-
Ozen, 1988 [24]	Inguinal Orchiectomy	-	25.0	Range	6–95				-	-	-				70	6	8.6%				70	10	14.3%			
Ozen, 1988 [24]	Scrotal violation	-	25.0	Range	6–95	-	-	-				35	5	14.3%				35	8	22.9%				21	2	9.5%
Giguere, 1988 [25]	Inguinal Orchiectomy	-	-	-	-				330	0	0.0%				330	69	20.9%				-	-	-			
Giguere, 1988 [25]	Scrotal violation	36	-	-	-	35	0	0.0%				35	8	22.9%				-	-	-				22	0	0.0%
Kennedy, 1986 [26]	Inguinal Orchiectomy	-	-	-	-				174	0	0.0%				174	34	19.5%				-	-	-			
Kennedy, 1986 [26]	Scrotal violation	34	37.1	SD/Range	18.1/9–86	36	0	0.0%				36	4	11.1%				-	-	-				-	-	-
Boileau, 1984 [28]	Inguinal Orchiectomy	-	-	-	-				192	0	0.0%				98	30	30.6%				-	-	-			
Boileau, 1984 [28]	Scrotal violation	-	-	-	-	32	1	3.1%				18	4	22.2%				-	-	-				9	2	22.2%
Pizzocaro, 1985 [27]	Inguinal Orchiectomy	-	60.0	-	-				78	0	0.0%				78	6	7.7%				-	-	-			
Pizzocaro, 1985 [27]	Scrotal violation	-	60.0	-	-	24	1	4.2%				24	5	20.8%				-	-	-				-	-	-
Khader, 2012 [19]	Inguinal Orchiectomy	-	33.0	Range	1–200				67	0	0.0%				67	3	4.5%				67	1	1.5%			
Khader, 2012 [19]	Scrotal violation	-	33.0	Range	1–200	7	0	0.0%				7	0					7	0	0.0%				-	-	-

remaining patients subsequently developed recurrence requiring radical orchiectomy after a median follow-up of 45 months in the cohort [2]. The use of TSS for patients with TGCT and a normal contralateral testis is controversial due to the lack of perceived benefit when compared to radical orchiectomy. AUA guidelines currently recommend 18 to 20 Gy adjuvant radiotherapy after TSS with findings of TGCT or GCNIS for patients prioritizing cancer risk reduction [29].

Although high inguinal orchiectomy has been the standard of care for more than 100 years, scrotal violation is still observed in clinical practice [12]. A prior review noted a rate of local recurrence of 2.9% after scrotal violation vs. 0.4% for inguinal orchiectomy based on older studies starting from 1914 [12]. Based on more recent studies, we observed a similar rate of local recurrence of 2.5% after scrotal violation with no cases of local recurrence after inguinal orchiectomy without scrotal violation. However, no included study in this systematic review demonstrated compromised outcomes for metastasis or survival due to scrotal violation [14,19–28]. Importantly, patients with seminoma generally received local radiation and two-thirds with NSGCT received scrotal scar excision with 9.3% harboring residual tumor. Therefore, the ability to determine the rate of local recurrence without adjuvant treatment is limited, and current guidelines suggest adjuvant treatment may rarely be considered in the form of radiotherapy or scrotal scar excision [29]. We agree close monitoring may be appropriate for most patients with shared decision-making utilized for use of local radiation for seminoma and scrotal scar excision for NSGCT. Additional data are needed on patients forgoing adjuvant treatment to make a stronger statement. Studies also noted that some patients received chemotherapy per routine clinical practice, but most did not quantify any data on the frequency or type of chemotherapy employed [20,21,23,24,28,30].

Limitations of this systematic review identified a number of research gaps. Studies on TSS included small samples sizes across studies, which made it difficult to evaluate predictors of local recurrence such as histology (seminoma vs. NSGCT) or clinical stage. Patients were also not stratified by the type of adjuvant treatment received, which may have affected outcomes or contributed to variation between studies. For studies on scrotal violation, the subset of patients with seminoma was small with almost all receiving local radiation. The uncertain indications for why some patients with NSGCT received scrotal scar excision while others did not, along with variation in use of chemotherapy, prevented assessment of the impact of adjuvant treatment for NSGCT. The systematic review did not have data available from each study to analyze individual patient data.

5. Conclusion

The systematic review quantified a risk of local recurrence after TSS of 7.5% after 3 to 5 years for patients diagnosed with small testicular GCTs with the majority receiving adjuvant radiation or chemotherapy. Rates of positive margins (1.4%) and testicular atrophy (2.8%) were low with 7.1% of patients requiring subsequent androgen therapy. Scrotal violation carries a low risk of local recurrence, which was higher than inguinal orchiectomy (2.5% vs. 0.0%, $P < 0.001$) but does not appear to impact subsequent metastasis and survival in the short term. Most patients received adjuvant therapy with 9.3% receiving scrotal scar excision found to harbor residual primary tumor. Additional research is needed with patients more clearly stratified by clinical stage, histology, and adjuvant treatment received.

Disclosures

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Supplementary materials

Supplementary material associated with this article can be found in the online version at https://doi.org/10.1016/j.urolonc.2020.02.023.

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