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Original Article

Association Between Testicular Microlithiasis and Ultrasound-based Testicular Volume in Pediatric Population

Pediatrik Popülasyonda Testiküler Mikrolitiazis ve Ultrason ile Ölçülen Testiküler Volüm Arasındaki İlişki

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ABSTRACT

Objective: A potential relationship between testicular microlithiasis (TM) and testicular atrophy in childhood might increase the risk of testicular malignancy and infertility in adulthood. The present study aimed to determine the effect of the presence of TM on testicular volume by comparing the ultrasound-based testicular volumes between boys with TM and controls.

Method: A total of 140 boys (mean ± standard deviation, 9.86 years ± 5.44 years; age range, 0-18 years) with two descended testes were classified into a study group of 70 patients with TM (TM group) and an age-matched control group of 70 boys without TM (non-TM group). The TM group was subdivided based on the number of microliths in one transducer field as 'mild TM' (5-20 microliths) and 'severe TM' (>20 microliths). The ultrasound-based testicular volume (mL) was estimated by the Lambert equation as 0.71× length × width × depth.

Results: The average testicular volume in the TM group was 1.44 (0.70-4.68) mL and 3.09 (0.84-14.65) mL in the non-TM group. A lower testicular volume was observed in patients with TM, however, this difference was not significant (p=0.096). The average testicular volumes in patients with 'severe TM' and 'mild TM' were not significantly different (p=0.106). A lower testicular volume was found in older boys (≥15 years) with 'severe TM'.

Conclusion: We found no significant association in the testicular volume between boys with TM and controls, however, a lower testicular volume was observed in boys with TM. Thus, a close clinical follow-up might be considered in these patients.

Keywords: Testicular microlithiasis, testicular volume, ultrasonography

ÖZ

Amaç: Çocukluk çağında testiküler mikrolitiazis (TM) ile testiküler atrofi arasındaki potansiyel bir ilişki, yetişkin döneminde testis malignitesi ve infertilite riskini artırabilir. Bu çalışma, TM'li erkek çocuklar ve kontroller arasında ultrason ile ölçülen testiküler volümlerini karşılaştırarak TM varlığının testis hacmi üzerindeki etkisini belirlemeyi amaçladı.

Yöntem: Çalışmamıza bilateral skrotal yerleşimli testisi olan toplam 140 erkek çocuk (ortalama ± standart sapma, 9,86 yıl ± 5,44 yıl; yaş aralığı, 0-18 yıl) dahil edildi. Çocuklar TM'li 70 hastadan oluşan bir çalışma grubu (TM grubu) ve aynı yaştaki TM'si olmayan 70 erkek çocuktan oluşan bir kontrol grubu (TM olmayan grup) olarak sınıflandırıldı. TM grubu, bir prob alanındaki mikrolit sayısına göre 'hafif TM' (5-20 mikrolit) ve 'şiddetli TM' (>20 mikrolit) olarak iki subgruplara ayrıldı. Testiküler volümü (mL), Lambert denklemi ile (0,71x uzunluk x genişlik x derinlik) hesaplandı.

Bulgular: Ortalama testis hacmi TM grubunda 1,44 (0,70-4,68) ml ve TM olmayan grubunda 3,09 (0,84-14,65) mL idi. TM'li hastalarda daha düşük testis hacmi gözlendi, ancak bu fark anlamlı değildi (p=0,096). 'Şiddetli TM' ve 'hafif TM' hastalarında ortalama testis hacimleri anlamlı olarak farklı değildi (p=0,106). 'Şiddetli TM' olan büyük erkek çocuklarda (≥15 yaş) daha düşük testis hacmi bulundu.

Sonuç: TM'li erkek çocuklar ve kontroller arasında testis hacminde anlamlı bir ilişki bulamadık, ancak TM'li erkek çocuklarda testis hacmi daha düşüktü. Bu nedenle bu hastaların yakın klinik takibi gerekebilir.

Anahtar kelimeler: Testiküler mikrolitiyazis, testis hacmi, ultrasonografi

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INTRODUCTION

Testicular microlithiasis (TM) is characterized by the presence of five or more microcalcifications in a single view of a testicular ultrasound [1]. TM is asymptomatic and commonly found incidentally on imaging [1,2]. The prevalence of TM is reported in the literature to range from 1.6% to 5.3% with a higher prevalence among children with testicular atrophy, undescended testis, genetic diseases (Down syndrome, Klinefelter syndrome), history of orchiopexy, and personal or family history of testicular germ cell tumor [3-5]. Several studies have also reported an association between TM and primary testicular neoplasia in the pediatric population [3]. According to the pediatric urology guideline of the European Association of Urology, self-examination of the testis is recommended on a monthly basis in boys with associated risk factors from puberty onwards. However, close clinical follow-up could be considered, if TM is still existing during the transition to adulthood [1]. In a 5-year follow-up study of 63 adults with TM by DeCastro et al. [6], only one patient had developed a testicular mixed germ cell tumor. As a result, a self-examination of the testicles was purposed for asymptomatic individuals with TM [6].

Testicular volume has been examined in children with undescended testis, varicocele, hydrocele, and Down syndrome [7-12], however, to date, the testicular volume in pediatric TM was reported in only one study with a small sample size (n=23) [13]. Our study reports the effect of the presence of TM on testicle volume in subjects from the newborn period up to 18 years of age.

Since a potential relationship between testicular atrophy and TM in childhood might increase the risk of testicular malignancy and infertility in adulthood, here we aimed to compare the ultrasound-based testicular volume between controls and boys with TM.

MATERIALS and METHODS

Ethical Statement

This comparative and cross-sectional study conformed to the Declaration of Helsinki and was approved by the University of Health Sciences Turkey, İzmir Dr Behçet Uz Pediatric Diseases and Surgery Training and Research Hospital Clinical Research Ethics Committee (approval number: 2021/16-06, date: 21.10.2021).

Study Design

Between November 2018 and June 2021, a total of 232 patients underwent ultrasound examination of testes in the Department of Radiology. Patients with testicular torsion (n=4); orchitis (n=16); testicular trauma (n=3); testicular mass (n=1); cryptorchidism (n=46); previous scrotal surgery (n=12); chromosomal anomalies (n=3); congenital adrenal hyperplasia (n=0); and age over 18 years (n=0) were excuded from the analysis.

The diagnosis of classic TM was established on the following ultrasonographic criteria: Five or more non-shadowing hyperechogenic foci in one testis or in one transducer field, microlith size between 1 and 3 mm, uniform distribution, and preserved testicular shape. Boys with less than 5 microliths in a single view (n=7) [14], unilateral TM (n=0), and abnormal biomarker levels (α-fetoprotein and β-human chorionic gonadotrophin) (n=0) were excluded from the study. Finally, a study group of 70 patients with two descended testes with TM (TM group) and an age-matched control group of 70 boys with two descended testes without TM (non-TM group) were enrolled. The TM group was divided into two subgroups based on the number of microliths in one transducer field: 'mild TM' (5-20 microliths) and 'severe TM' (>20 microliths) (Figure 1). The patients with

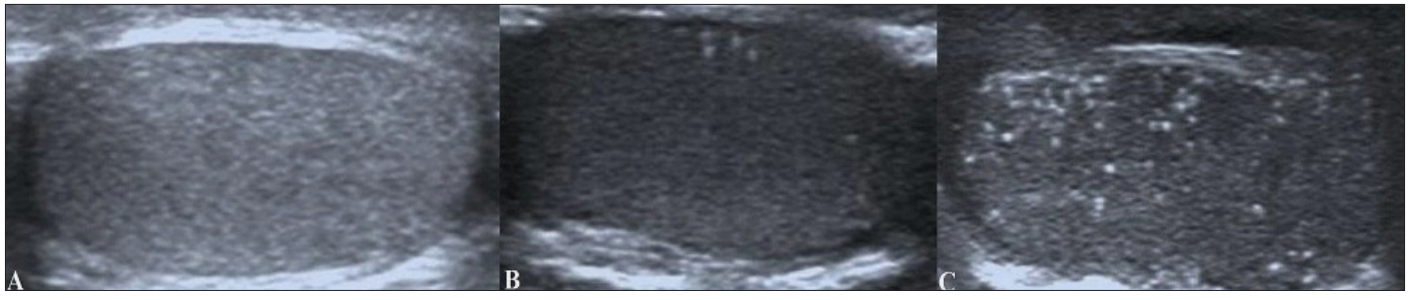

Figure 1. Sagittal ultrasound images of the testis (A) without testicular microlithiasis (non-TM group); (B) with 5-20 microliths in one transducer field (mild TM group); and (C) >20 microliths in one transducer field (severe TM group)

TM: Testicular microlithiasis

TM had normal levels of serum α-fetoprotein (α-FP) and β-human chorionic gonadotrophin (β-hCG).

The scrotal ultrasound scans were carried out by a single board-certified radiologist on an ultrasound machine (Aplio 500, Toshiba Medical System, Otawara, Japan) with a 5-12 MHz linear transducer. The ultrasound images were examined in two planes (transverse and sagittal). The maximum length (L) and width (W) of each testis were measured on a sagittal view and the maximum depth (D) was obtained from the transverse plane. The testicular volume (mL) was estimated by the Lambert equation as 0.71×L×W×D [15]. The testicular atrophy index (TAI) was calculated to evaluate the effect of the presence of TM on testicle volume by the following formula: TAI = (non-TM average testicle volume-TM average testicle volume)/non-TM average testicle volume x100 and expressed as a percentage [16].

Testicular atrophy was defined as a more than 50% reduction in the testicle volume compared to the normal testis (TAI >50%).

Statistical Analysis

The distribution of the numeric variables was skewed based on a Kolmogorov-Smirnov test ($p<0.05$). Qualitative variables were reported as percentages and numeric variables were presented as median [interquartile range (IQR) 25-75]. Non-normally distributed data were log-transformed before regression analysis or the Mann-Whitney U test was used to compare the differences between groups. Spearman's correlation coefficients were used for correlations.

Analyses were conducted using SPSS statistical software (version 20, SPSS Inc., Chicago, IL, USA). Statistical significance was considered as a p-value of <0.05.

RESULTS

Study Population

The mean age (±SD) of the boys was 9.86 years (±5.44) and ranged from 0 to 18 years. The study and age-matched control groups were classified into five age groups: group 1 (0-2 years; n=7); group 2 (3-6 years; n=16); group 3 (7-10 years; n=12); group 4 (11-14 years; n=16); and group 5 (15-18 years; n=19). The TM group comprised 44 patients with mild TM (mean age 9.64±4.87 years) and 26 patients with severe TM (mean age 10.23±6.39 years).

Testicular Volume Measurement

In patients with TM, the median IQR volume of the right and left testis were 1.50 (0.74-4.62) and 1.48 (0.77-4.94) mL, respectively. The median IQR volume of the right and left testis in boys without evidence of TM were 3.04 (0.82-14.76) and 2.01 (0.81-14.55) mL, respectively. The average testicular volume in the TM group was 1.44 (0.70-4.68) mL and 3.09 (0.84-14.65) mL in the non-TM group.

The right, left and average testicular volume increased significantly with increasing age and this was not dependent on the presence of TM (r=0.821, r=0.781, and r=0.827, respectively; $p<0.0001$ for all). The age-specific distribution and comparison of the right, left, and average testicular volume in the TM and non-TM groups are presented in Table 1. In the age-specific comparison, significantly lower testicular volumes were found in boys above 11 years with TM compared to those without TM ($p<0.01$ for all). However, there was no statistically significant association between the overall right, left, and average testicular volume in boys with TM compared to those without TM ($p=0.074$, $p=0.091$, $p=0.096$; respectively). Although it was statistically insignificant, a trend towards lower testicular volume was observed in patients with TM (Figure 2).

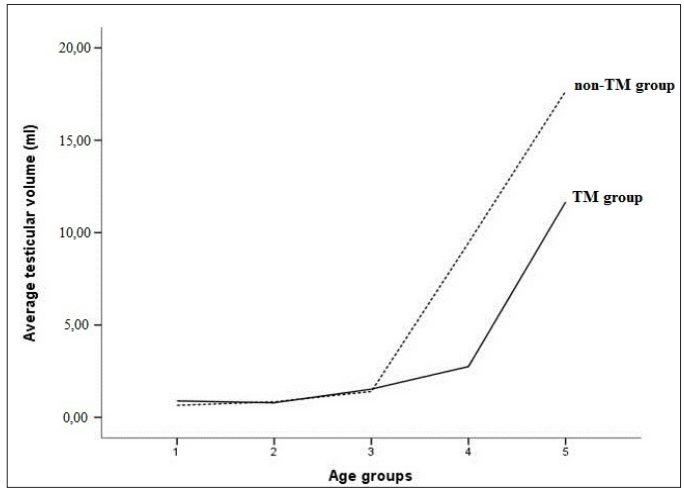

Figure 2. Comparison of the testicular volume (mL) between boys with testicular microlithiasis (TM group) and without testicular microlithiasis (non-TM group) among different age groups [Group 1 (0-2 years), Group 2 (3-6 years), Group 3 (7-10 years), Group 4 (11-14 years), Group 5 (15-18 years)]

TM: Testicular microlithiasis

Table 1. Ultrasound-based testicular volume in the TM and non-TM groups according to age groups

Age groups (years)	TM group			non-TM group			p-value
	Right testicular volume (mL)	Left testicular volume (mL)	Average testicular volume (mL)	Right testicular volume (mL)	Left testicular volume (mL)	Average testicular volume (mL)	
0-2	0.86 (0.63-1.51)	0.83 (0.43-1.30)	0.85 (0.43-1.43)	0.63 (0.52-0.65)	0.61 (0.45-0.76)	0.63 (0.48-0.70)	p^a =0.084 p^b=0.406 p=0.180
3-6	0.65 (0.46-1.04)	0.80 (0.61-0.99)	0.70 (0.59-1.14)	0.62 (0.46-1.02)	0.82 (0.64-0.95)	0.73 (0.58-0.98)	p^a=0.910 p^b=0.651 p=0.940
7-10	0.87 (0.42-1.56)	1.26 (0.47-1.80)	1.06 (0.47-1.66)	1.08 (0.86-1.23)	1.13 (0.84-1.40)	1.04 (0.92-1.27)	p^a=0.386 p^b=0.817 p=0.729
11-14	2.22 (1.24-3.83)	2.26 (1.18-4.86)	2.26 (1.32-4.38)	8.99 (6.24-12.02)	6.69 (4.53-12.07)	8.19 (5.54-11.60)	p^a<0.0001 p^b=0.002 p<0.0001
15-18	12.33 (4.41-18.61)	12.52 (4.24-18.18)	12.43 (4.28-17.32)	18.32 (14.84-19.7)	17.06 (14.44-20.3)	16.92 (14.49-20.01)	p^a=0.014 p^b=0.010 p=0.014
0-18	1.50 (0.74-4.62)	1.48 (0.77-4.94)	1.44 (0.70-4.68)	3.04 (0.82-14.76)	2.01 (0.81-14.55)	3.09 (0.84-14.65)	p^a=0.074 p^b=0.091 p=0.096

TM: Testicular microlithiasis; Data are expressed as median [interquartile range (IQR) 25-75]; p-values for comparing testicular volume between the TM and non-TM groups; p^a-values for comparing the right testicular volume; p^b-values for comparing the left testicular volume; p-values for comparing the average testicular volume; p-values were obtained using the Mann-Whitney U test; p-value <0.05 was considered significant

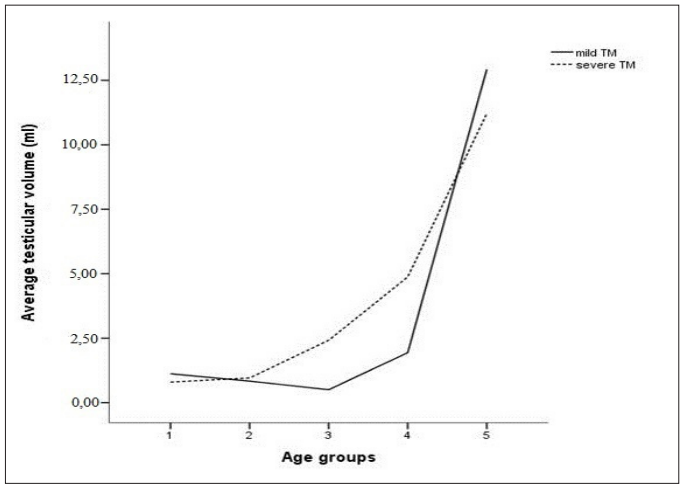

Figure 3. Comparison of the average testicular volume (mL) between boys with 'mild' testicular microlithiasis ('mild TM') and 'severe' testicular microlithiasis ('severe TM') among different age groups [Group 1 (0-2 years), Group 2 (3-6 years), Group 3 (7-10 years), Group 4 (11-14 years), Group 5 (15-18 years)]

TM: Testicular microlithiasis

The median values for the overall right, left, and average testicular volume in patients with 'severe TM' (2.90, 3.12, and 3.01 mL; respectively) and 'mild TM' (1.35, 1.33, and 1.35 mL; respectively) were not significantly different (p=0.072, p=0.148, p=0.106; respectively). The age-specific distribution and comparison of the right, left, and average testicular volume in the 'mild TM' and 'severe TM' groups are presented in Table 2. Significantly lower testicular volumes were found in 11-14-y-old boys with 'mild TM' than in those with 'severe TM' (p≤0.003). Although insignificant, the right, left and average testicular volumes were lower in older boys (≥15 years) with 'severe TM' compared to those with 'mild TM' (p=0.652, p=0.334, p=0.485; respectively). The overall right, left, and average testicular volumes in patients with 'severe TM' and non-TM groups were not significantly different (p=0.270, p=0.217, p=0.238; respectively). The distribution of the testicular volume measurements in boys with 'mild TM' and 'severe TM' according to age groups is summarized in Figures 3 and 4.

Table 2. Ultrasound-based testicular volume in the 'mild TM' and 'severe TM' groups according to age groups

Age groups (years)	'Mild TM' group			'Severe TM' group			p-value
	Right testicular volume (mL)	Left testicular volume (mL)	Average testicular volume (mL)	Right testicular volume (mL)	Left testicular volume (mL)	Average testicular volume (mL)	
0-2	1.07 (0.56-1.55)	0.87 (0.35-1.36)	0.96 (0.48-1.44)	0.86 (0.74-1.25)	0.83 (0.63-1.11)	0.85 (0.69-1.18)	p^a=0.500 p^b=0.811 p=0.646
3-6	0.55 (0.37-1.00)	0.79 (0.51-0.87)	0.63 (0.53-0.83)	0.99 (0.65-1.07)	0.87 (0.69-1.46)	0.94 (0.69-1.23)	p^a=0.211 p^b=0.152 p=0.141
7-10	0.73 (0.43-1.43)	1.16 (0.48-1.75)	1.04 (0.48-1.52)	1.50 (0.25-1.68)	1.55 (0.99-1.72)	1.53 (0.18-1.65)	p^a=0.215 p^b=0.456 p=0.296
11-14	1.76 (0.99-2.58)	1.83 (1.07-2.60)	1.70 (1.08-2.32)	4.70 (3.40-5.84)	5.26 (3.72-6.33)	5.00 (3.56-6.06)	p^a=0.001 p^b=0.003 p=0.002
15-18	16.30 (6.92-18.16)	13.88 (8.50-18.92)	15.28 (7.71-18.41)	8.84 (3.78-18.84)	8.90 (3.85-15.60)	8.87 (3.84-17.46)	p^a=0.652 p^b=0.334 p=0.485
0-18	1.35 (0.60-3.58)	1.33 (0.63-3.55)	1.35 (0.62-3.60)	2.90 (0.96-6.08)	3.12 (0.83-5.86)	3.01 (0.86-5.85)	p^a=0.072 p^b=0.148 p=0.106

TM: Testicular microlithiasis; 'mild TM' (5-20 microliths in one transducer field); 'severe TM' (>20 microliths in one transducer field). Data are expressed as median [interquartile range (IQR) 25-75]; P-values for comparing testicular volume between the 'mild TM' and TM and 'severe TM'; P^a-values for comparing the right testicular volume; p^b-values for comparing the left testicular volume; p-values for comparing the average testicular volume; P-values were obtained using the Mann-Whitney U test; p-value <0.05 was considered significant

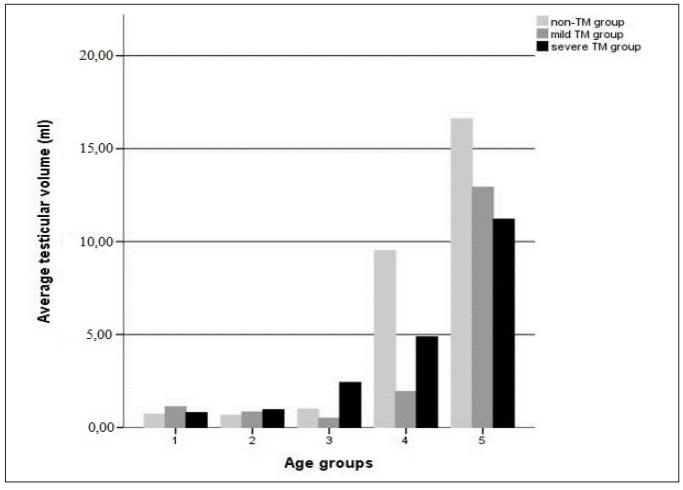

Figure 4. Testicular volume (mL) distribution in children without testicular microlithiasis (non-TM group), 'mild TM', and 'severe TM' among different age groups [Group 1 (0-2 years), Group 2 (3-6 years), Group 3 (7-10 years), Group 4 (11-14 years), Group 5 (15-18 years)]

TM: Testicular microlithiasis

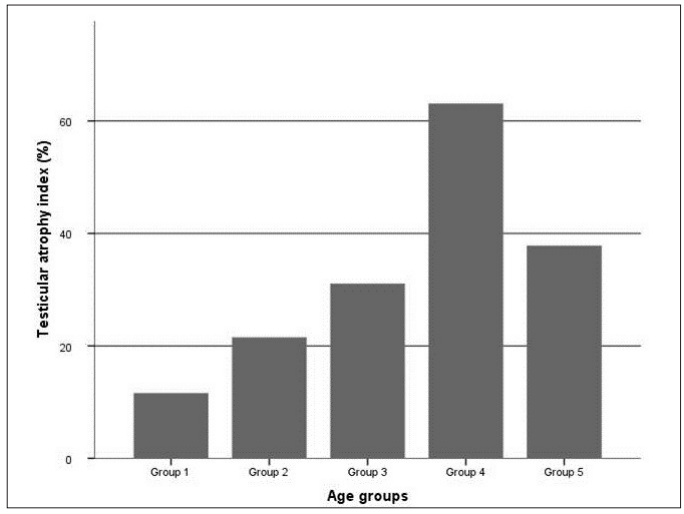

Figure 5. The distribution of the mean testicular atrophy index according to age groups [Group 1 (0-2 years), Group 2 (3-6 years), Group 3 (7-10 years), Group 4 (11-14 years), Group 5 (15-18 years)]

The mean TAI was 36% and ranged from 0% to 93%. Twenty-six patients (37%) had a mean TAI of more than 50%. The significantly higher TAI values were found in the older age groups (>11 years) (p=0.037) (Figure 5). TAI was not significantly different between the mild and severe TM subgroups (p=0.747).

DISCUSSUON

The present study reported no significant association in the overall testicular volume between boys with TM and controls, however, in the age-specific comparisons, significantly lower testicular volumes were found in boys above 11 years with TM compared to those without TM. Moreover, significantly lower testicular volumes were found in 11-14-y-old boys with 'mild TM' than in those with 'severe TM'. The testicular volumes were lower in older boys (≥15 years) with 'severe TM' compared to those with 'mild TM', however, these changes were not significant.

TM is the deposition of microcalcifications in the seminiferous tubules which are visualized as small, non-shadowing, and hyperechogenic foci on testicular ultrasound [1,2]. The first case of TM was reported in a 4-year-old boy by Priebe and Garret in 1970 [17]. The ultrasonographic appearance of TM was first noted by Doherty et al. [18] in 1987. TM is usually bilateral, asymptomatic, and found incidentally on ultrasonographic imaging [1,2]. TM does not seem to be related to testicular malignancy during childhood, however, in the presence of risk factors, an association between TM and testicular malignancy has been confirmed in adults. A potential relationship between testicular atrophy and TM in childhood might increase the risk of testicular malignancy and infertility in adulthood [1,19,20]. Therefore, we aimed to determine the effect of the presence of TM on testicle volume by comparing the testicular volumes between boys with TM and controls.

In our study, the average testicular volumes were 1.44 mL in boys with TM and 3.09 mL in the age-matched subjects without TM. Although there was no statistically significant association between the testicular volume in boys with TM compared with those without TM, there was a tendency for a lower testicular volume in patients with TM. Bayramoglu et al. [13] measured the testicular volume in 23 pediatric patients with bilateral TM (median age 12 years, age range, 5-14 years) using ultrasound and reported no significant difference in the testicular volume between the control and study groups (2.3 mL vs. 3.0 mL, p=0.320, respectively). Cebeci et al. [11] found TM in 9 (36%) patients with Down syndrome and showed that their testicular volumes did not change significantly compared to the control group. Goede et al. [9] investigated the TM in 79 subjects (mean age 8.44 years, age range, 2.0-19.3 years) with Down syndrome and demonstrated smaller testicular volumes in boys with TM than in those without TM.

In the study by Pedersen et al. [4], the testicular volume measurements of 91 patients with TM (median age 48 years, age range, 19-94 years) were compared with those of age-matched control subjects. The testicular volume in patients with TM tended to be lower compared to those without TM, however, this difference did not reach statistical significance (14.3 mL vs. 14.5 mL, p=0.370, respectively) [4]. The median testicular volumes in adult patients with 'limited' TM (<5 microliths) and 'classic' TM (≥5 microliths) were reported as 20.5 mL and 15.5 mL, respectively, by Von Eckardstein et al. [21].

We also found no significant differences in the testicular volume between subjects with 'mild TM' (5-20 microliths) and 'severe TM' (>20 microliths). This result agreed with a previous study by Bayramoglu et al. [13], who described no significant difference in the testicle volume between boys with ≤15 microliths and those with >15 microliths (p=0.210). According to Pedersen et al. [4], severe testicular atrophy (≤8 mL) was more often seen in adult patients with TM compared to controls (p=0.02). In our study, significantly higher TAI values were found in boys above 11 years of age (p=0.037).

Serum levels of follicle-stimulating hormone (FSH), luteinizing hormone (LH), testosterone, and testicular volume are good indicators of the hormonal and spermatogenic function of the testicles [22-25]. Ruiz-Olvera et al. [22] reported significant differences in the testicular volume between controls and patients with primary or secondary hypogonadism. Several studies suggested that the FSH, LH, and testosterone levels were significantly lower in major thalassemia patients with secondary hypogonadism [23-25]. In the study by Fariborzi et al. [23], 3.2% of 62 beta-thalassemia adult patients had testicular volume under 4 mL. Hypogonadism and TM were seen in 22.6% and 4.8% of the patients, respectively [23]. Ohana Marques Coelho de Carvalho et al. [26] found testicular adrenal rest tumors in six and TM in two out of 12 patients with a history of congenital adrenal hyperplasia by ultrasound, suggesting a possible link between congenital adrenal hyperplasia and TM.

Study Limitations

Several limitations deserve comments. The present study was a single-institution retrospective study. The exclusion criteria for controls were the same as for the study group, however, some subjects in the control group were admitted to the hospital because of scrotal or groin pain. Further comparison and discussion of our results were limited since most studies in the literature were conducted on adults, subjects with Down syndrome, and only one, so far, was conducted on a small sample of children. Our study was not designed to evaluate the association between the testicular volume and hormonal status or hypogonadism, thus, further studies including more participants are needed to assess this topic. Furthermore, we did not consider the pubertal status of the boys in the analysis which could be addressed in future studies.

Conclusion

In conclusion, we found no significant association in the testicular volume between boys with TM and age-matched controls, however, a trend towards lower testicular volume was observed in boys with TM. Although insignificant, a lower testicular volume was detected in children above 15 years of age with 'severe TM' compared to those with 'mild TM'. These findings might suggest that clinical follow-up could be considered in patients over 15 years of age with "severe TM >20 microliths".

Ethics

Ethics Committee Approval: This comparative and cross-sectional study conformed to the Declaration of Helsinki and was approved by the University of Health Sciences Turkey, İzmir Dr Behçet Uz Pediatric Diseases and Surgery Training and Research Hospital Clinical Research Ethics Committee (approval number: 2021/16-06, date: 21.10.2021).

Informed Consent: Since our study had a retrospective design, informed consent was not obtained from the patients.

Peer-review: Externally peer-reviewed.

Author Contributions

Surgical and Medical Practices: E.Ç., B.Ö., Concept: E.Ç., B.Ö., Design: E.Ç., B.Ö., Data Collection and/or Processing: E.Ç., Analysis and/or Interpretation: E.Ç., B.Ö., Literature Search: E.Ç., Writing: E.Ç.

Conflict of Interest: The authors have no conflict of interest to declare.

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REFERENCES

1. t Hoen LA, Bhatt NR, Radmayr C, Dogan HS, Nijman RJM, Quaedackers J, et al. The prognostic value of testicular microlithiasis as an incidental finding for the risk of testicular malignancy in children and the adult population: A systematic review. On behalf of the EAU pediatric urology guidelines panel. J Pediatr Urol. 2021;17(6):815-31. doi: 10.1016/j.jpurol.2021.06.013.
2. Kim B, Winter TC 3rd, Ryu JA. Testicular microlithiasis: clinical significance and review of the literature. Eur Radiol. 2003;13(12):2567-76. doi: 10.1007/s00330-003-2014-5.
3. Trout AT, Chow J, McNamara ER, Darge K, Ramirez Grueso R, Munden M, et al. Association between Testicular Microlithiasis and Testicular Neoplasia: Large Multicenter Study in a Pediatric Population. Radiology. 2017;285(2):576-83. doi: 10.1148/radiol.2017162625.
4. Pedersen MR, Osther PJS, Rafaelsen SR. Ultrasound Evaluation of Testicular Volume in Patients with Testicular Microlithiasis. Ultrasound Int Open. 2018;4(3):E99-E103. doi: 10.1055/a-0643-4524.
5. Aizenstein RI, Hibbeln JF, Sagireddy B, Wilbur AC, O'Neil HK. Klinefelter's syndrome associated with testicular microlithiasis and mediastinal germ-cell neoplasm. J Clin Ultrasound. 1997;25(9):508-10. doi: 10.1002/(sici)1097-0096(199711/12)25:9<508::aid-jcu9>3.0.co;2-r.
6. DeCastro BJ, Peterson AC, Costabile RA. A 5-year followup study of asymptomatic men with testicular microlithiasis. J Urol. 2008;179(4):1420-3. doi: 10.1016/j.juro.2007.11.080.
7. Varela-Cives R, Mendez-Gallart R, Estevez-Martinez E, Rodriguez-Barca P, Bautista-Casasnovas A, Pombo-Arias M, et al. A cross-sectional study of cryptorchidism in children: Testicular volume and hormonal function at 18 years of age. Int Braz J Urol. 2015;41(1):57-66. doi: 10.1590/S1677-5538.IBJU.2015.01.09.
8. Christman MS, Zderic SA, Kolon TF. Comparison of testicular volume differential calculations in adolescents with varicoceles. J Pediatr Urol. 2014;10(2):396-8. doi: 10.1016/j.jpurol.2013.12.007.
9. Goede J, Weijerman ME, Broers CJ, de Winter JP, van der Voort-Doedens LM, Hack WWM. Testicular volume and testicular microlithiasis in boys with Down syndrome. J Urol. 2012;187(3):1012-7. doi: 10.1016/j.juro.2011.10.167.
10. Vachon L, Fareau GE, Wilson MG, Chan LS. Testicular microlithiasis in patients with Down syndrome. J Pediatr. 2006;149(2):233-6. doi: 10.1016/j.jpeds.2006.03.051.
11. Cebeci AN, Aslanger A, Ozdemir M. Should patients with Down syndrome be screened for testicular microlithiasis? Eur J Pediatr Surg. 2015;25(2):177-80. doi: 10.1055/s-0034-1370779.
12. Nakamura M, Moriya K, Nishimura Y, Nishida M, Kudo Y, Kanno Y, et al. Prevalence and risk factors of testicular microlithiasis in patients with hypospadias: a retrospective study. BMC Pediatr. 2018;18(1):179. doi: 10.1186/s12887-018-1151-6.
13. Bayramoglu Z, Kandemirli SG, Comert RG, Akpinar YE, Caliskan E, Yilmaz R, et al. Shear wave elastography evaluation in pediatric testicular microlithiasis: A comparative study. J Med Ultrason (2001). 2018;45(2):281-6. doi: 10.1007/s10396-017-0837-y.
14. Richenberg J, Belfield J, Ramchandani P, Rocher L, Freeman S, Tsili AC, et al. Testicular microlithiasis imaging and follow-

up: guidelines of the ESUR scrotal imaging subcommittee. Eur Radiol. 2015;25(2):323-30. doi: 10.1007/s00330-014-3437-x.

15. Mbaeri TU, Orakwe JC, Nwofor AME, Oranusi CK, Mbonu OO. Ultrasound measurements of testicular volume: Comparing the three common formulas with the true testicular volume determined by water displacement. African Journal of Urology. 2013;19:69-73. doi: 10.1016/j.afju.2012.11.004.
16. Zvizdic Z, Milisic E, Halimic A, Zvizdic D, Zubovic SV. Testicular volume and testicular atrophy index as predictors of functionality of unilaterally cryptorchid testis. Med Arch. 2014;68(2):79-82. doi: 10.5455/medarh.2014.68.79-82.
17. Priebe CJ Jr, Garret R. Testicular calcifications in a 4-year-old boy. Pediatrics. 1970;46(5):785-8.
18. Doherty FJ, Mullins TL, Sant GR, Drinkwater MA, Ucci AA Jr. Testicular microlithiasis. A unique sonographic appearance. J Ultrasound Med. 1987;6(7):389-92. doi: 10.7863/jum.1987.6.7.389.
19. Silveri M, Bassani F, Colajacomo M, Orazi C, Adorisio O. Management and follow-up of pediatric asymptomatic testicular microlithiasis: are we doing it well? Urol J. 2011;8(4):287-90.
20. Kocaoğlu M, Bozlar U, Bulakbaşi N, Sağlam M, Uçöz T, Somuncu I. Testicular microlithiasis in pediatric age group: ultrasonography findings and literature review. Diagn Interv Radiol. 2005;11(1):60-65.
21. von Eckardstein S, Tsakmakidis G, Kamischke A, Rolf C, Nieschlag E. Sonographic testicular microlithiasis as an Indicator of premalignant conditions in normal and infertile men. J Androl. 2001;22(5):818-24.
22. Ruiz-Olvera SF, Rajmil O, SanchezCurbelo J-R, Vinay J, Rodriguez-Espinosa J, Ruiz-Castañé E. Association of serum testosterone levels and testicular volume in adult patients. Andrologia. 2018;50(3). doi: 10.1111/and.12933.
23. Fariborzi MR, Hashemi SM, Aflatoonian M, Abeshoori EJ, Mohammadi S, Mohammadnia A, et al. Testicular Ultrasound Assessment in Thalassemic Men. Imaging J Clin Medical Sci. 2016;3(1):020-023. Doi: 10.17352/2455-8702.000031.
24. Wasniewska M, Raiola G, Teresa A, Galati MC, Zirilli G, Catena MA, et al. Gynecomastia disclosing diagnosis of Leydig cell tumour in a man with thalassemia, secondary hypogonadism and testis microlithiasis. Acta Biomed. 2009;80(3):286-8.
25. De Sanctis V, Elawwa A, Angastiniotis M, Eleftheriou A, Kattamis C, Karimi M,et al. Highlights from the First Thalassaemia Forum on Growth and Endocrine Complications in Thalassemia Doha, (October 2-3, 2011). Pediatr Endocrinol Rev. 2012;9(3):672-9.
26. Ohana Marques Coelho de Carvalho L, Miguel Garcia Lora R, Renata Rezende Penna C, Calland Ricarte Beserra I. Testicular Adrenal Rests Tumors and Testicular Microlithiasis in a Brazilian Case Series with Classic Congenital Adrenal Hyperplasia. Int J Endocrinol Metab. 2016;15(1):e40611. doi: 10.5812/ijem.40611.