

Diagnostic Effectiveness of Contralateral Testicular Hypertrophy in Children with Non-Palpable Testicles

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Purpose: To evaluate the effectiveness of contralateral testicular volume measurements in differentiating monorchidism from intra-abdominal viable testes in children with non-palpable testes (NPT).

Materials and Methods: The data of 179 patients who underwent surgery for undescended testes between January 2017 and January 2024 were retrospectively reviewed. The study included 33 patients with unilateral non-palpable testes. Testicular volumes were measured by ultrasonography 6-12 months prior to diagnostic laparoscopy, and the surgical findings were recorded.

Results: Diagnostic laparoscopy was performed on 33 children with non-palpable testes. For five patients, staged orchiopexy was planned due to the testes being 2 cm or more away from the internal inguinal ring. In 22 patients, inguinal orchiopexy was performed as the testes were around the internal inguinal ring (AIR). In the remaining six patients, no testes were found; the spermatic cord and vessels terminated at the internal inguinal ring (vanishing) or were atrophic (nubbin). There was a significant difference in the contralateral testicular volumes between patients with vanishing testes and those with intra-abdominal viable testes ($p < 0.001$). Additionally, there was a statistically significant difference in the contralateral testicular volumes between the AIR group and those with testes remote from the internal inguinal ring (RIR) ($p = 0.03$).

Conclusion: The preoperative ultrasonographic measurement of the contralateral testicular volume in children with a unilateral non-palpable testis can provide valuable information about the nature of the intra-abdominal testis. The presence of a hypertrophic contralateral testis can guide surgeons prior to laparoscopy and is valuable for counseling parents about potential diagnoses.

Keywords: contralateral testicular hypertrophy; non-palpable testis; monorchidism; ultrasonography; laparoscopy

INTRODUCTION

The undescended testicle (UDt) is the most common congenital anomaly in males, affecting around 2-4% of full-term newborns and 1% of one-year-olds. Since the descent of the testicle is an embryological process, this rate can reach up to 30% in premature newborns⁽¹⁾. Approximately 20% of these undescended testicles cannot be palpated during examination (non-palpable testicle, NPT)⁽²⁾. An NPT may be located in the abdomen (intra-abdominal testicle, IAt), may descend partially (peeping), or may even be absent (vanishing). Other less common causes include being in an ectopic position outside the abdomen or having a testicle size that is too small for a fatty body structure (10-30%)⁽³⁾. Unfortunately, neither magnetic resonance imaging (MRI) nor ultrasound (US) scans consistently identify nonpalpable testicles⁽⁴⁾. Laparoscopy is the gold standard for confirming or excluding the presence of a viable testicle (VT)⁽⁵⁾. Testicular hypertrophy is a natural response of the remaining testicle to compensate for what is missing, enabling physical maturation and sexual development. Laron and Zilka were pioneers in using contralateral testicular enlargement to predict missing or underdeveloped testicles, known as "nubbin testis"⁽⁶⁾. Further studies show that contralateral testicular hypertrophy (CTH) can predict monorchidism⁽⁷⁻¹⁰⁾.

Koff investigated this concept further and found that contralateral testicular hypertrophy typically occurs between 8 months and 3 years of age, suggesting that a contralateral testicular volume exceeding 2 ml has significant predictive value for monorchidism⁽¹¹⁾. While monorchidism can be explained by unilateral testicular hypertrophy, laparoscopic exploration is currently the gold standard for all patients with unilateral undescended testes due to its low clinical reliability. The hypothesis of this study is that if there is hypertrophy in the contralateral testis of children with an undescended testis compared to the control group of infants of the same age, then the probability of the undescended testis being intra-abdominal, vanishing, or a nubbin is very high. This is important to confirm the preoperative expectations of the surgeon. Therefore, this study aimed to investigate the relationship between the volume of the contralateral testis measured by ultrasound and the status of the undescended testis through retrospective evaluation of patient data.

MATERIALS AND METHODS

Study population

We analyzed the records of 179 children who had surgery for undescended testes at the Private Gebze Yüzyıl Hospital between January 2017 and January 2024.

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Table 1. Descriptive Statistics of Testicular Volumes by Group

Group	N	Age (Months, Mean)	Contralateral Testis Volume (cc, Mean ± SD)
Group 1: Control	30	7.5	0.61 ± 0.12
Group 2: V/N	6	8.4	0.85 ± 0.14
Group 3: AIR	22	9.2	0.51 ± 0.15
Group 4: RIR	5	7.6	0.70 ± 0.24

Notes: SD: Standard deviation. V/N: Vanishing/Nubbin Testis. AIR: Around the internal inguinal ring. RIR: Remote from internal inguinal ring.

Among them, 33 patients had non-palpable testes, meaning their testes could not be felt during the preoperative examination.

Children with bilateral non-palpable testes or a unilateral non-palpable testis that became palpable in the inguinal canal under anesthesia were excluded from the study.

We examined the volumes of the contralateral testes, measured by testicular ultrasonography, which is routinely done between six and twelve months before surgery for non-palpable testes. Additionally, we included a control group of 30 healthy male infants who were at the hospital for regular check-ups and showed no concerns beyond growth and development. We performed testicular ultrasonography on these infants to measure the sizes of their testes. Our study was structured as follows: Group 1 was designed as the control group,

consisting of healthy male infants where both right and left testicular volumes were measured, and average testicular volumes were calculated. The study group comprised 33 patients who underwent diagnostic laparoscopy due to non-palpable testes (**Figure 1**). Within this cohort, additional subgroups were delineated: Group 2 included patients with vanishing/nubbin testes (V/N) where no viable testis was found in the abdomen; Group 3 consisted of patients with testes around the internal inguinal ring (AIR); Group 4 included patients with testes remote from the internal inguinal ring within the abdomen (RIR), who underwent staged orchiopexy. Additionally, due to the presence of intra-abdominal viable testes in Groups 3 and 4, a separate Group 5 was formed specifically for intra-abdominal viable testes (VT). Our research aims to elucidate the relationship between contralateral testicular growth and the pres-

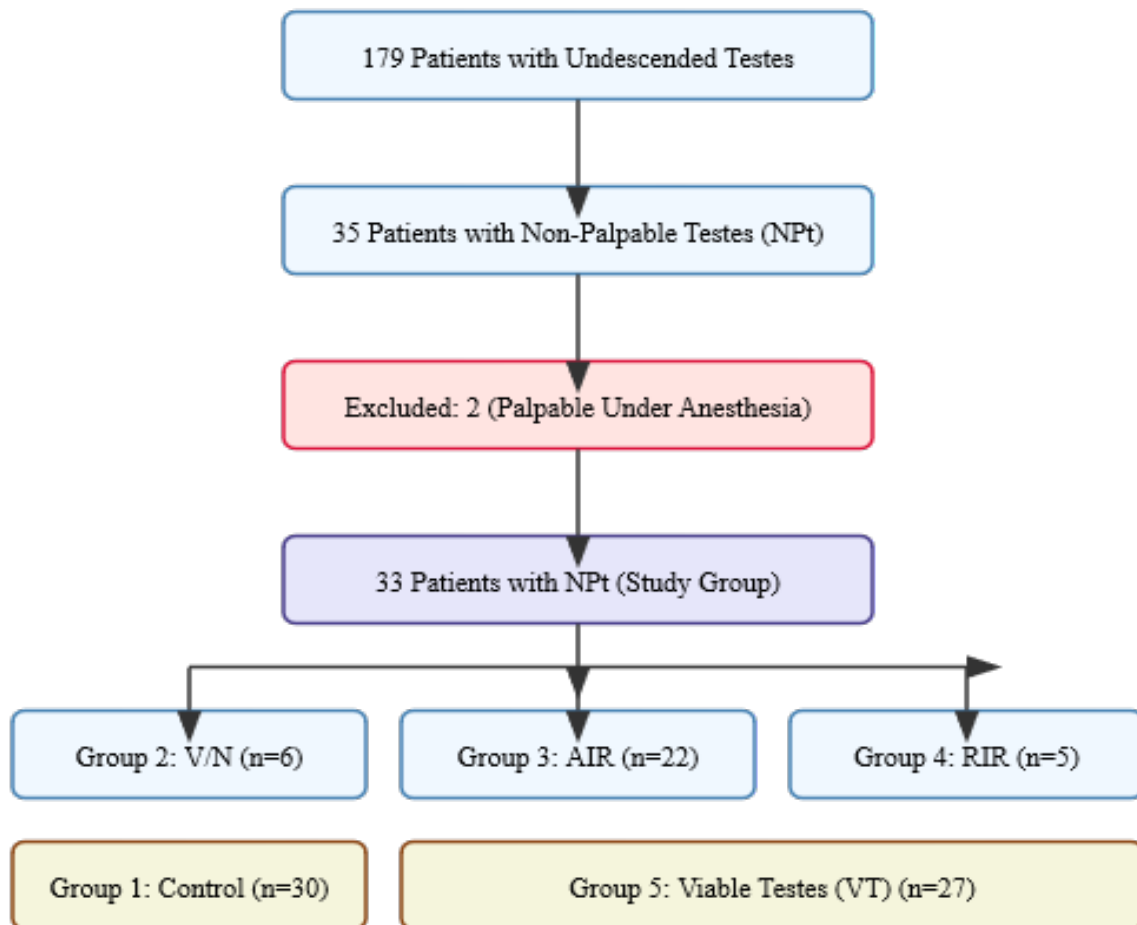


Figure 1. Algorithm showing the design of the study.

Table 2. Contralateral Testis Volume by Side of Non-palpable Testis

Side of Non-palpable Testis	N	Contralateral Testis Volume (Mean ± SD)	P-value
Right	10	0.56 ± 0.25	0.340(*)
Left	23	0.62 ± 0.24	

Notes: (*)Independent Samples Test. Statistically significant at $p \leq 0.05$. SD: Standard deviation.

ence of testes located intra-abdominally or in the inguinal region, as well as to understand the presence of V/N testes.

Study design

Our study commenced after receiving approval from the University Ethics Committee and Institutional Review Board on June 2, 2024 (Approval No: E-10840098-202.3.02-1453). The study was retrospective, examining the surgical records of patients who were referred due to non-palpable testes, with the cases reviewed retrospectively.

Measurement of Testicular Volume by Ultrasonography

Various clinical methods have been described to measure testicular volumes. While simple rulers or precise calipers can be used, testicular volume is most commonly measured using the Prader orchidometer in clinical settings today. These clinical methods calculate volumes using the ellipsoid equation ($Width^2 \times Length \times \pi \div 6$, $W^2 \times L \times 0.52$). However, these measurements tend to overestimate volumes compared to ultrasound measurements due to appendages such as scrotal skin and epididymal volume. It should be noted that the epididymal volume should not be included in the measurement⁽¹²⁾. Testicular volume is calculated using three common formulas: The ellipsoid formula (formula 1): $L \times W \times H \times 0.52$, Lambert’s empirical formula (formula 2): $L \times W \times H \times 0.71$, and the prolate spheroid formula (formula 3): $L \times W^2 \times 0.52$.

Recently, to bring ultrasound volumes closer to actual testicular volumes, studies have shown that the constant factor of 0.71 described by Lambert is the most reliable^(13,14). Therefore, in our study, to ensure standard measurements, we used the Lambert formula for both the control group patients and the children with only one palpable testis. All testicular volume measurements were performed by the same radiologist using ultrasonography.

Surgical Procedures

In this study, all patients with non-palpable testes were included in diagnostic laparoscopy and surgical planning after reaching six months of age. The age at surgery varied between 6 and 12 months, depending on the family's decision. All patients underwent surgery under general anesthesia with endotracheal intubation. Based on the findings of the laparoscopy, the patients were divided into three groups:

- Group 2 (V/N): The testis was a nubbin or vanishing (the testicular artery and cord ended blindly in the internal inguinal canal).

- Group 3 (AIR): The testis was viable and located very close to the internal ring of the inguinal canal (the distance from the testicular pedicle to the internal ring was less than 2 cm).

- Group 4 (RIR): The testis was viable, located within the abdomen, and more than 2 cm remote from the internal inguinal ring.

Patients in Group 3 underwent inguinal orchiopexy. For patients in Group 4, a two-stage laparoscopic-assisted orchiopexy was planned. In Group 2, no intervention was performed for those with blind-ending structures, while orchiectomy was conducted for those with atrophic or nubbin testes (Figure 2).

Outcome assessment

The statistical analysis was conducted using the IBM SPSS 22.0 statistical software package (IBM Corporation, Chicago, IL, USA). Initial descriptive analyses were performed to summarize the data. The normality of the variable distributions was assessed using the Shapiro-Wilk test, which indicated that testicular volumes followed a normal distribution. Accordingly, group comparisons were conducted using the parametric ANOVA test and the independent samples t-test, both suitable for this type of data. Post-hoc comparisons between groups were performed using the Tukey test. Results were reported as mean ± SD. Statistical significance was defined at a p-value of less than 0.05.

RESULTS

Our study included 33 male patients diagnosed with unilateral non-palpable undescended testis through clinical and sonographic examination, who subsequently underwent diagnostic laparoscopy. Two patients who had their testes palpable in the groin after general anesthesia and those with bilateral non-palpable testes were excluded. The ages of the patients ranged from 6 to 12 months, with a mean age of 7.5 ± 2.04 months. All patients were recommended laparoscopic evaluation and surgical planning after 6 months.

In Group 1 (Control), consisting of healthy male infants with an average age of 7.5 months, the mean contralateral testicular volume was 0.61 ± 0.12 cubic centimeters (mL). Group 2 (V/N), comprising infants with vanishing/nubbin testes and an average age of 8.4 months, exhibited a mean volume of 0.85 ± 0.14 mL. Group 3 (AIR), where testes were positioned around the internal inguinal ring and with an average age of 9.2 months, showed a mean volume of 0.51 ± 0.15 mL, while Group 4 (RIR), with testes remote to the internal inguinal ring and an average age of 7.6 months, had a mean volume of 0.70 ± 0.24 mL (Table 1).

Intra-abdominal Viable Testis Group	N	Contralateral Testis Volume (Mean ± SD)	P-value
Group 3 (AIR)	22	0.51 ± 0.15	0.031(*)
Group 4 (RIR)	5	0.70 ± 0.24	

Notes: (*)Independent Samples Test. Statistically significant at $p \leq 0.05$. SD: Standard deviation. AIR: Around the internal inguinal ring. RIR: Remote from internal inguinal ring.

Table 4. Post Hoc Multiple Comparisons (Tukey HSD)

Group Comparison	P-value
V/N vs. Control	0.002(*)
V/N vs. AIR	0.001(*)
AIR vs. Control	0.300

Notes: (*)Statistically significant at $p \leq 0.05$. V/N: Vanishing/Nubbin Testis. AIR: Around the internal inguinal ring. Control: Control Group.

The distribution of non-palpable testes was found to be 23 (69.7%) on the left side and 10 (30.3%) on the right side. Further analysis of contralateral testicular volumes among patients with non-palpable testes revealed no significant difference between the right (0.56 ± 0.25 mL) and left (0.62 ± 0.24 mL) sides (Table 2).

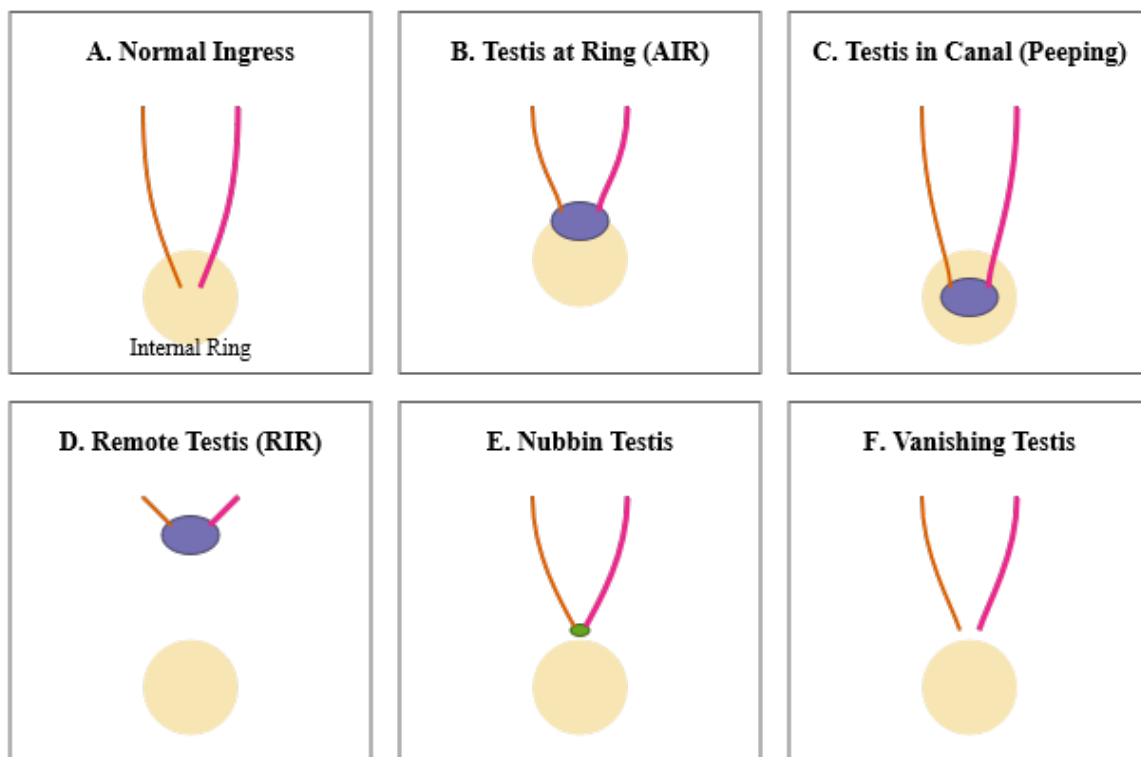
However, a comparison between Group 3 (AIR) and Group 4 (RIR) demonstrated a significant difference in contralateral testicular volume ($p = 0.031$), highlighting distinct growth patterns based on testis location within the abdomen (Table 3).

Post hoc analysis using Tukey's Honestly Significant Difference (HSD) test provided additional insights. Significant differences in testicular volumes were observed between Group 1 (Control) and Group 2 (V/N) ($p = 0.002$). Moreover, significant differences were noted between Group 2 (V/N) and Group 3 (AIR) ($p = 0.001$), underscoring the variability in contralateral testicular growth among different clinical presentations (Table 4) (Figure 3).

DISCUSSION

The non-palpable testis (NPt) comprises intra-abdominal viable testes, non-viable "nubbin" testes, agenetic "vanishing" testes, and inguinal viable or atrophic testes(2). While physical examination is the most critical step in distinguishing between palpable and non-palpable testes, additional methods are required to determine the exact localization of the testes. Ultrasound (US) is the most commonly used imaging modality for NPt diagnosis, with a specificity of 78% and sensitivity of 45%(15). Although MRI and computed tomography (CT) scans offer higher specificity and sensitivity, their use is limited by the need for sedation and the risks associated with radiation exposure(16,17). Consequently, laparoscopy, which also provides therapeutic options, has been advocated as the first-line approach without prior imaging(18).

However, some authors suggest scrotal and inguinal exploration before resorting to laparoscopy. They argue that the majority of cases involve inguinal or scrotal vanishing testes. In a study by Bae et al., intra-abdominal peeping testes were accessed via an inguinal incision, with laparoscopy needed in only three patients(19). Similarly, Snodgrass et al. reported that laparoscopy was required in only 23% of their patients(20). Given the low specificity and sensitivity of imaging modalities, the need for sedation, and the potential for radiation exposure, combined with the possibility of polyorchidism in these patients, we believe diagnostic laparoscopy should be the initial step.



A. Normal inguinal canal. B. Testis very close to the internal inguinal ring. C. Testis located within the canal. D. Testis distant from the internal inguinal ring. E. Nubbin testis. F. Vanishing testis.

Figure 2. Scenarios observed during diagnostic laparoscopy.

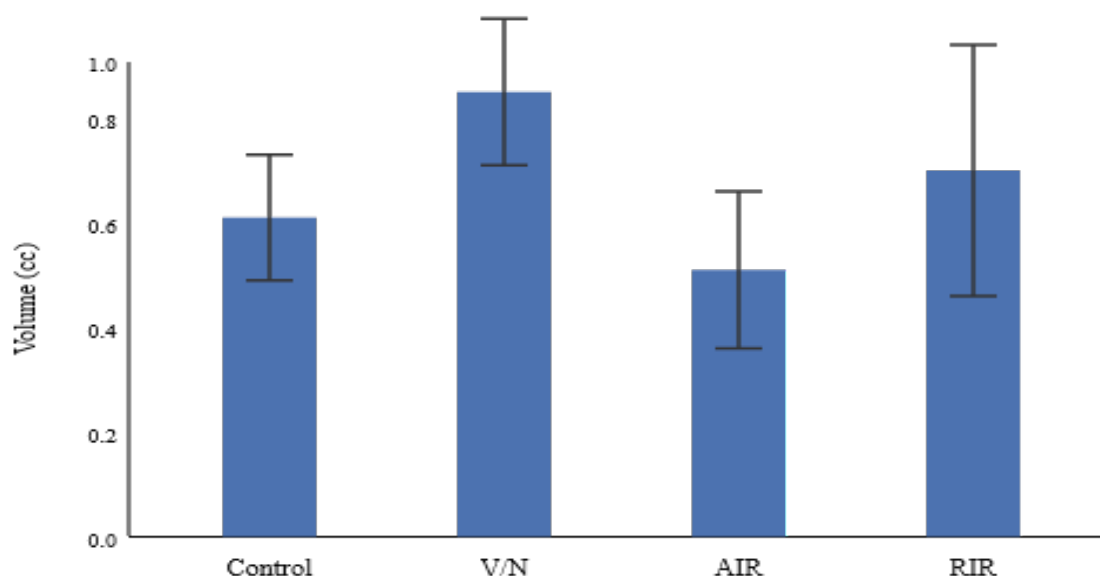


Figure 3. Graph showing the distribution of testicular volume among the groups.

Current literature recommends re-examination under general anesthesia for patients with NPt. Studies have shown that 18-34% of testes not palpable in outpatient settings can be palpated under general anesthesia⁽²¹⁾. In our study, 5.71% (2 out of 35) of patients diagnosed with NPt had their testes palpated under anesthesia, allowing for orchiopexy without the need for laparoscopy. This approach helps prevent unnecessary surgical interventions for patients. Contralateral testicular hypertrophy (CTH) is a well-known phenomenon in monorchidism and has been described by various authors as a highly reliable predictor of a vanishing testicle or testicular nubbin. The concept of CTH was first introduced by Laron and Zilka in 1969, by recording the size of hypertrophic testicles in prepubertal, pubertal, and postpubertal children using an orchidometer and caliper^(6,8-11,14). Testicular volumes can be measured using various types of orchidometers or calipers. The Prader orchidometer is the most commonly used; however, ultrasound (US) measurements of testicular volume are highly accurate, reproducible, and are considered by many experts to be the best method for assessing testicular volume⁽¹²⁻¹⁴⁾. Although there are publications reporting that the accuracy of Prader orchidometry for testicular measurements is similar to that of ultrasound⁽¹²⁾, there are also publications indicating the opposite⁽²²⁾. In our study, we decided to use ultrasound for testicular volume measurements. Since the reliability of ultrasound can be influenced by the operator's experience, all ultrasounds were performed by the same radiologist. In similar studies, cut-off values have been provided to measure testis size^(12,24,29). In this study, we also included a control group to evaluate the average testicular size in six-month-old children using the same radiologist and the same measurement method (Lambert)⁽¹³⁾.

CTH is a common finding in boys with a nonpalpable testis. This study demonstrated the value of CTH as a

predictor of monorchidism in patients with unilateral NPt. In our study, the mean contralateral testicular volume in boys with NPt was found to be 0.69 mL, compared to 0.61 mL in the control group ($p < 0.05$). When subdividing based on laparoscopy findings and considering vanishing or nubbin testes together, the mean volume was found to be 0.85 mL ($p = 0.002$).

Joustra et al. developed an age-based table for German children, providing a table depicting the average testicular volume from newborns to 18-year-olds^(22,23). Shirakawa et al. found the average volume to be 0.18 mL in Japanese newborns⁽²⁵⁾. In our study on healthy infants, we determined the average volume for both testes to be 0.61 mL. This value is higher compared to both studies. Contralateral testicular hypertrophy (CTH) is a well-known phenomenon. Despite numerous studies on this topic, researchers continue to show interest. Recent studies have measured testicular size using Prader orchidometry, calipers or rulers, and ultrasound. These studies have established cut-off values for testicular size in cases of intra-abdominal testis and monorchidism (caused by nubbin or vanishing testis syndrome). In the study conducted by Braga et al., which included 85 patients, calipers were used for measurements, and cut-off values of 18 ml, 19 ml, and 20 ml were identified. The ROC analysis yielded a 95% accuracy rate. However, we believe that the effectiveness of caliper measurements is limited in young children⁽²⁶⁾. In a study by Y. Wei et al., it was highlighted that contralateral testicular hypertrophy is a significant indicator for predicting monorchidism, with a cut-off value of ≥ 0.674 cm⁽²⁷⁾. Hurwitz et al. reported a 90% accuracy with a cut-off value of > 1.8 cm⁽²⁸⁾. Hodhod et al. found a sensitivity of 71.7% with a cut-off value of > 2 ml⁽⁸⁾. Elrouby et al. reported a sensitivity of 75% in their study with a cut-off value of ≥ 0.674 cm⁽²⁹⁾.

This study also showed that the volume of the contralateral testis varies with the position of intra-abdominal

testes. Testes in Group 4 (RIR) had a larger volume compared to those in Group 3 (AIR) (0.7 ± 0.24 vs. 0.51 ± 0.15 , $p = 0.031$). As the distance from the internal inguinal ring increases, the testis volume decreases while the contralateral testis volume increases. Elrouby et al. found that the contralateral testicular volume was significantly larger in cases where the intra-abdominal testis was absent or non-palpable. This supports the concept of compensatory hypertrophy, showing a direct relationship between the position of the intra-abdominal testis and the increased volume of the contralateral testis. Their findings reinforce the idea that testicular volume is affected by the intra-abdominal testis' proximity to the internal inguinal ring⁽²⁹⁾.

In a study by P. Shadpour et al.⁽³⁰⁾, the accuracy of contralateral testis volume in predicting the absence of a unilateral non-palpable testis was evaluated. In this group, which included both adult and pediatric patients, the results showed that in adults, scrotal testis volume moderately predicted monorchism with 64.3% sensitivity and 92.9% specificity. However, in patients under 18 years old, the accuracy was low (below 60%). This study evaluated the differences between adult and pediatric patients. Our study, which consisted solely of pediatric patients, showed that contralateral testis size was significantly compatible with surgical findings.

In the study conducted by J.S. Elder et al.⁽¹⁰⁾, in 111 boys with 124 impalpable testes, 45 testes (36%) were viable and suitable for orchiopexy, including 7 that were in the inguinal canal and 38 intra-abdominal testes. Another 79 testes (64%) were absent or vanishing. In our study, the occurrence of "vanishing" and "nubbin" testes is significantly lower compared to this study. This may be related to the fact that, according to current literature, a higher number of vanishing testes in the past could be attributed to later diagnosis and intervention for undescended testes.

There are studies in the literature indicating that the size of one testis may provide misleading information about the other testis. In the study conducted by D.S. Huff et al.⁽²⁴⁾, a biopsy was taken from the other testis, and the volumes of the contralateral testis were measured. Based on these findings, it was concluded that no conclusions could be made regarding the impalpable testis based on its volume.

Our study is consistent with the 2024 guidelines published by the European Association of Urology (EAU). According to these guidelines, it is recommended that patients with a non-palpable testis should first undergo examination under anesthesia, followed by diagnostic procedures with laparoscopy.

The major limitation of our study is the small sample size. While it is sufficient for statistical analysis, a larger cohort would greatly enhance the study's validity. Unfortunately, true non-palpable testes are rarer than expected; careful examination often reveals them in the inguinal canal or at the internal ring. We believe that the low number of patients with non-palpable testes in our study may be due to this factor.

CONCLUSIONS

The undescended testis is the most common congenital disorder of the male genital system. In this study, we evaluated the relationship between the volume of the contralateral testis and the presence or absence of intra-abdominal testicular remnants in children with

non-palpable testicles. Our findings indicate that the size of the contralateral testis is significantly larger when testicular remnants are absent. Conversely, when a viable testis is located within the abdominal cavity, the contralateral testis tends to be smaller. We propose that the measurement of the volume of the contralateral testis via ultrasound can serve as a predictor of monorchism and is a valuable tool for parental counseling.

SUMMARY

In boys with a non-palpable testis, ultrasound measurement of the descended testis helps predict if the missing one is absent. A larger testis often indicates the other is missing, providing vital information for surgeons and parents before surgery.

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