INTRODUCTION
Cryptorchidism is a common condition in children; it refers to a testis that does not descend into the scrotum. These undescended testes are low in volume, which is associated with decreased reproductive function. In cases of unilateral cryptorchidism, normal testes opposite the cryptorchid testes can be used as a control reference to evaluate their growth. The testicular atrophy index (TAI) and its usefulness were first described by Niedzielski et al. in 2003. TAI or the testicular volume ratio between operated and control testes was used to evaluate the degree of damage to the cryptorchid testis and the effects of human chorionic gonadotropin (hCG) therapy and orchidopexy. The relationship between TAI and age may be used to evaluate the timing of treatment for cryptorchidism; however, this relationship remains unclear. In the present study, the TAI values of undescended palpable testes were reviewed, and their correlation with age was analyzed.

PATIENTS AND METHODS
The present study was conducted in The Third Affiliated Hospital of Zhengzhou University (Zhengzhou, China). Clinical data of cryptorchidism obtained between October 2013 and June 2021 were selected for retrospective analysis. Ethical approval was obtained by the Ethics Committee of The Third Affiliated Hospital of Zhengzhou University (Medical Ethics Review No. 2022-086-01). All experimental protocols involving human data were in accordance with the principles of the Declaration of Helsinki. The requirement for informed consent was also waived due to the retrospective nature of this study.

We selected patients who underwent surgery for unilateral palpable cryptorchidism. We studied 228 cases (age range: 6–53 months). Scatter plots were constructed, and Loess curves were fitted, revealing a turning point at 24 months of age. The patients were divided into age groups of 6–24 months and 25–53 months. Testicular volume of the cryptorchid side was smaller than that of the normal side in both groups (both P < 0.001). In the 6–24-month group, the testicular atrophy index was positively correlated with age, testicular volume on the cryptorchid side was not correlated with age, and testicular volume was positively correlated with age on the normal side. In the 25–53-month group, testicular atrophy index and testicular volumes on either side were not correlated with age. A palpable unilateral cryptorchid testis is smaller than the contralateral testis. The testicular atrophy index increases with age between 6 months and 24 months, but not between 25 months and 53 months. Testicular volume increased with age on the normal side between 6 months and 24 months, but not on the cryptorchid side. Trends in testicular atrophy index with age contribute to the decision of operation time.

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Keywords: cryptorchidism; testicular atrophy index; testicular volume
volume on both sides. Spearman’s rank correlation analysis was used to determine the relationship between the data, and the Loess method was used to draft the fitting curve. Statistical analyses were performed using SPSS version 26 software (IBM Corp., Armonk, NY, USA). Statistical significance was set at $P < 0.05$.

**RESULTS**

In total, we analyzed 228 cases of unilateral palpable cryptorchidism, with ages ranging from 6 months to 53 months.

Spearman’s rank correlation analysis revealed no relationship between TAI and age in all cases ($r = 0.082; P = 0.215$). Scatter plots were constructed, and Loess curves were fitted, showing that there was a turning point at 24 months of age. The patients were then divided into two age groups of 6–24 months and 25–53 months (Figure 1). The testicular volume of the cryptorchid side was lower than that of the normal side in both groups (both $P < 0.001$). There was no difference in testes volume between both age groups on the cryptorchid side ($P = 0.064$); however, the volume on the normal side increased in the 25–53-month group ($P = 0.020$), as shown in Table 1.

In the 6–24-month group, TAI ($P = 0.015$) and testicular volume on the normal side ($P = 0.047$) were positively correlated with age, whereas testicular volume on the cryptorchid side ($P = 0.422$) was not correlated with age (Table 2). In the 25–53-month group, TAI ($P = 0.325$), testicular volume on the cryptorchid side ($P = 0.103$), and testicular volume on the normal side ($P = 0.121$) were all not correlated with age (Table 2).

**DISCUSSION**

Normally, in noncryptorchid individuals, testicular size does not differ considerably between sides. We observed lower testicular volume on the cryptorchid side than that of the contralateral normal testis. Thus, cryptorchidism affects testicular volume growth.

A previously published article reported that mean testicular volume increased markedly during the first 5 months, decreased at 9 months, and remained stable during the following years. We found that testicular volume on the normal side was positively correlated with age between 6 months and 24 months, but there was no longer an association with age between 25 months and 53 months.

The average cryptorchid testicle volume decreased after the sixth month, and the reduction in testicular size correlated with the increasing distance between the cryptorchid tests and the scrotum. In this study, we focused on palpable undescended testes in the inguinal canal and found that the volume of cryptorchid testes between the ages of 6 months and 53 months was not significantly correlated with age.

However, TAI has been reported to differ in unilateral cryptorchid boys younger than 1 year of age compared to those older than 1 year of age. The difference in the present study lies in the analysis of the correlation between TAI and age in boys with a unilateral cryptorchid testis, and then the difference of the above correlation is found between 6–24 months and 25–53 months.

Müller and Skakkebaek found that the volume of testes differed between those younger than 1 year of age and those aged 1–4 years old, and we obtained a similar result. Compared with the 6–24-month group, there was no difference in the volume of testes on the cryptorchid side, but the volume on the normal side was higher in the 25–53-month group. This result is due to delayed growth on the cryptorchid side between 6 months and 24 months and the accumulation of growth on the normal side over time.

**Table 1: Testicular volume and testicular atrophy index**

| Factor                          | 6–24-month group | 25–53-month group | $P$  |
|---------------------------------|------------------|-------------------|------|
| Patients ($n$)                  | 167              | 61                |      |
| Age (month), median (IQR)       | 16 (12–19)       | 32 (27–43)        |      |
| Volume of the cryptorchid testis (ml), median (IQR) | 0.19 (0.13–0.24) | 0.19 (0.14–0.31) | 0.064 |
| Volume of the normal testis (ml), median (IQR) | 0.38 (0.30–0.47)$^a$ | 0.47 (0.31–0.59)$^a$ | 0.020 |
| TAI, median (IQR)               | 0.49 (0.34–0.61) | 0.50 (0.26–0.63) | 0.818 |

$^aP < 0.001$, volume of normal compared to that of undescended testis. TAI: testicular atrophy index; IQR: interquartile range.


Trend of TAI with age in cryptorchidism

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Table 2: Spearman’s rank correlation analysis results with age

| Factor                                  | 6–24-month group (n=167) | 25–53-month group (n=61) |
|-----------------------------------------|--------------------------|--------------------------|
|                                         | r           | P         | r           | P         |
| Volume of the cryptorchid tests         | -0.063      | 0.422     | 0.211       | 0.103     |
| Volume of the normal tests              | 0.154       | 0.047     | 0.200       | 0.121     |
| TAI                                     | 0.187       | 0.015     | -0.128      | 0.325     |

n: Spearman’s rank correlation coefficient; TAI: testicular atrophy index

Testicular volume reflects the number of germ cells. The testicular volume in individuals with cryptorchidism is positively correlated with their germ cell index. Testicular volume is also correlated with sperm density. Therefore, changes in the testicular volume of cryptorchidism can reflect impaired fertility potential to some extent.

Substantial qualitative and quantitative changes in the Sertoli cell population occur after birth. The postnatal proliferation of primarily Sertoli cells and germ cells results in testicular growth. A peak in the total number of germ cells per boy between 50 days and 150 days after birth was observed. The present study found that the size of the testes in the normal position increased with age between 6 months and 24 months. One downside of the current study was the lack of data before six months. The testicles may not grow as much as those on days 50 and 150, but they still grow.

Undescended testes can be treated surgically, and a primary goal of surgery is to preserve reproductive function. Undescended testes have a monthly rate of increased damage to the supporting and germ cells, thus surgical timing is important. Currently, several pieces of evidence suggest that early treatment of cryptorchidism can achieve better results. Surgery appears to be required before the age of 1 year; however, more evidence is needed to confirm this. In the present study, the correlation between the TAI of cryptorchid testes and age was investigated further. The TAI worsened with age between 6 months and 24 months. Theoretically, performing surgery before testicular atrophy increases with age will yield better results.

A limitation of this study is that it was a single-center retrospective study. The patients ranged from 6 months to 53 months in age; however, further studies on the effect of age on TAI in a larger age range would be beneficial. In addition, studies to determine the relationship between TAI and the age of surgery in long-term follow-up will allow the exact age of surgery that yields the greatest benefits to be elucidated. This may provide scope for future research.

Unilateral palpable cryptorchid testes are smaller than their contralateral testes, as shown by an increase in testicular volume on the normal side with age between 6 months and 24 months, but not on the cryptorchid side. TAI also increases with age between 6 months and 24 months, but does not change with age from 25 months to 53 months. Trends in testicular atrophy index with age contribute to the decision of operation time.

AUTHOR CONTRIBUTIONS

PQL conceived the study, participated in its design and data collection, performed the statistical analysis, and drafted the manuscript. FYL conceived the study, participated in its design, performed the statistical analysis, and helped draft the manuscript. YH participated in study design and data collection, and helped in statistical analysis. All authors read and approved the final manuscript.

COMPETING INTERESTS

All authors declare no competing interests.

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