Testing the undescended testis

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Conservative policy for acquired undescended testes is warranted

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Submitted
ABSTRACT

Purpose
There is no consensus on the management of acquired undescended testes (UDT). This study evaluates a conservative approach to acquired UDT. It assesses spontaneous descent and short-term and long-term testicular volumes.

Methods
Boys referred for acquired UDT were treated by awaiting spontaneous descent until puberty and, in case of non-descent, by performing a pubertal orchidopexy. Annual follow-up, both before and after reaching scrotal position, included physical examination and ultrasonographic measurement of testicular volume. Results were compared with normative values.

Results
A total of 410 boys were included with 487 acquired UDTs. Of these acquired UDTs, 347 testes had reached scrotal position by the end of the study period: 79.3% by spontaneous descent and 20.7% as a result of pubertal orchidopexy. An analysis was performed of 1,404 testicular volume measurements in 349 boys. At all ages, the volumes of the acquired UDTs were found to be smaller than the 50th percentile of normative values for testicular volume. From the age of 17, spontaneously descended UDTs were larger than pubertal orchidopexied UDTs.

Conclusion
Conservative approach of acquired UDTs results in volumes smaller than normal but comparable to acquired UDTs orchidopexied at diagnosis. If treated conservatively until puberty, acquired UDTs descend spontaneously in nearly 80% of the cases. Therefore, a conservative policy of acquired UDT is warranted.
INTRODUCTION

Undescended testis (UDT) is a common pediatric urological abnormality. It is a well-established risk factor for later subfertility and testicular cancer. For congenital UDT, orchidopexy is recommended at 6 to 12 months of age. However, for acquired UDT, there has been considerable controversy in terms of its management. It is often maintained that surgical correction after diagnosis is mandatory. Nevertheless, both the underlying aetiology and the timing of the treatment may differ considerably between these two conditions. In the Netherlands, a conservative policy towards acquired UDT is usually followed in accordance with the Dutch consensus on non-scrotal testes, and orchidopexy is only performed at puberty in case of non-descent. So far, insufficient information has been available on the results of this conservative policy. These results should be compared to the results of orchidopexy at diagnosis. Therefore, we studied the results of a conservative policy of acquired UDTs in terms of ultrasonographically measured testicular volumes.

PATIENTS AND METHODS

A testis was defined as undescended if a non-scrotal testis could not be brought into a stable scrotal position and traction on cord structures was painful. A non-scrotal testis was defined as retractile testis if it could be brought into the scrotum to a low stable position where it remained until the cremaster reflex was elicited and traction on cord structures was not painful.

The position of the UDT was further classified as high scrotal, inguinal and non-palpable. We defined a congenital UDT as a UDT which had not been descended from birth, whereas an acquired UDT had previously been situated in the scrotum. Data on the previous testicular positions were obtained from the Youth Health Care Institution “Hollands Noorden”.

Study design

From 1996 - 2012, we followed a cohort of boys who had been referred to our outpatient clinic for non-scrotal testis. If a diagnosis of acquired UDT was made, patients were treated conservatively and were invited for an annual follow-up visit. Surgery was
deferred and spontaneous descent was awaited until at least Tanner stage 3 was reached.9 If spontaneous descent still had not occurred at this stage, orchidopexy was performed. We continued the annual follow-up after spontaneous descent as well as after orchidopexy until the boys were 19 years old. None of the patients received any hormonal treatment.

**Inclusion and exclusion criteria**

Boys were included if acquired UDT had been diagnosed, either unilateral or bilateral, and if at least one ultrasound measurement of testicular volume had been performed. Boys were excluded if they had had previous inguinoscrotal surgery, chromosomal disorders, endocrine abnormalities such as growth hormone deficiency or if orchidopexy had been performed at diagnosis (request of the parents). Additionally, ultrasound measurements were excluded for testicular volume analyses if they had been performed at ages higher than 18 years or in boys with contralateral groin surgery and/or testicular abnormalities.

**General characteristics**

Ethnical background, gestational age, birth weight and medical history were analysed.

**Annual follow-up**

Annual follow-up included physical examination to assess puberty stage and testis position. Puberty stage was determined according to the Tanner stages.9 Testis position was assessed by a two-handed technique with the boy in a supine and crossed-legged position.

In 2006, ultrasonographical measurement of testicular volume was introduced. All ultrasound examinations were performed with the same equipment (Falco Auto Image, Tomsk, Russia), using a 12-MHz linear array transducer. To prevent shape distortion of the testis, only gentle pressure was applied. Each testis was measured in the transverse and longitudinal dimensions and the volume was calculated using the approximation for a prolate ellipsoid: volume = length x width x height x π/6 ml. Of each testis, three separate measurements were performed and the highest value was taken as volume measurement. The epididymis was not included in the images. Parenchymal disturbances and Doppler flow were not performed. All examinations were performed by the same physician (WH).
Subsequently, testicular volumes were compared with recently developed normative values,\textsuperscript{10} which had been determined with the same equipment and formula. Strong correlations were found between researchers WH and JG (\(R = 0.988\)).\textsuperscript{11}

**Orchidopexy**

Surgical repositioning of the testis within the scrotal sac was performed by the same surgeon (RM). After inguinal exploration, if present, the open processus vaginalis was separated from the cord structures and ligated. Separation of the cremaster muscle and retroperitoneal funiculolysis were performed to mobilize the cord. Finally, the testis was fixated in the scrotum in a created Dartos pouch.

**Statistical analysis**

All data were managed and analyzed with SPSS, version 20.0. Due to skewed distributions of ages and testicular volume, non-parametric statistical tests were used. The Mann-Whitney U test was used to calculate the differences in age and testicular volume for spontaneously descended testes versus testes orchidopexied during puberty. The Wilcoxon test was used to calculate the difference in testicular volume with the normative values, matched for age. The chi-squared test was used to test the relation between testis position at referral and outcome. We used multivariate regression techniques to analyze the effect on testicular volume of testis position at referral, age at referral, and duration of non-descent, corrected for age. A p-value of less than 0.05 was considered statistically significant.

**RESULTS**

**Study population**

During the period 1996 – 2012, 961 boys were referred to the outpatient clinic because of a non-scrotal testis. The testis was diagnosed as undescended in 733 boys. In 49 cases, the UDT could not be classified, as previous testicular position was not available. In 180 boys (mean age 2.4 ± 1.8 years; range 0.1 - 10.1 years), the UDT was classified as congenital. In the remaining 504 boys (mean age 9.1 ± 2.5 years; range 2.1 - 18.1), the UDT had previously been situated in the scrotum and was diagnosed as acquired. In 55 of these boys, no ultrasound had been obtained as they had been referred before 2006.
and 39 boys were excluded for other reasons (listed in Figure 1). Consequently, 410 boys were included (mean age 9.1 ± 2.4 years; range 2.1 - 18.0 years). Of these, 333 patients (2.1 - 18.0 years; median 9.1) had a unilateral acquired UDT (199 right-sided, 134 left-sided), whereas 77 patients (4.3 - 14.9 years; median 8.4) had bilateral acquired UDT (p = 0.146); this resulted in 487 included acquired UDTs (Figure 1).

Figure 1 Flowchart of acquired undescended testes (number and age of boys) enrolled in this study and the outcome of testicular descent at the end of the study.

General characteristics
In 369 of the 410 boys (90.0%), additional general characteristics were obtained. The majority of the boys were White (91.3%), 12 were Mediterranean (3.3%), 3 Asian (0.8%), and 17 were of mixed races (4.6%). Birth weight was more than 2500 grams in 307 (83.2%) boys. Duration of pregnancy was 37 weeks or more in 329 (89.4%) boys.

Follow-up data
At the end of the study period, 347 of the 487 (71.3%) acquired UDTs had reached a
Conservative policy for acquired undescended testes

Scrotal position. Spontaneous descent occurred in 275 of these 347 testes (79.3%), while in the remaining 72 testes (20.7%) pubertal orchidopexy was performed. The mean age at spontaneous descent was 12.7 ± 1.4 years (range 9.8 - 16.8) and at orchidopexy it was 14.3 ± 1.4 years (range 11.0 - 18.3; p < 0.001). One boy was referred at the age of 18 years with an acquired UDT and was treated with orchidopexy. In three patients (12.5, 14.4 and 16.1 years of age) orchidopexy was indicated, but they underwent orchiectomy due to an atrophic testis.

At referral, of the 487 acquired undescended testes, 357 testes (73.3%) were in high scrotal position and 130 (26.7%) in inguinal position. Spontaneous descent occurred significantly more often in high scrotal forms (83.3%) than in inguinal forms (69.6%; p = 0.004).

Ultrasonographical examinations

Inclusion and exclusion
Ultrasound measurement were excluded in 37 boys because of contralateral groin surgery (n=17), epididymis cyste (n=12), hydrocele (n=5) and varicocele (n=3). In addition, in 24 boys ultrasound measurements were only available over the age of 18; consequently, they were excluded. As a result, we included 1404 ultrasound examinations, in 349 boys, for testicular volume analysis.

The mean age at ultrasound was 12.2 ± 2.6 years (range, 4.1 - 18.5). Ultrasound measurement was performed once in 79 boys, twice in 80 boys, three times in 89 boys and four times or more in 162 boys.

Testicular volume
Figure 2 shows the ultrasound measurements of testicular volumes, performed prior to testicular descent, compared to normative values. Different lines indicate the final outcome, i.e. spontaneous descent, pubertal orchidopexy or still in follow-up. At the ages of 11, 12 and 13 years, the UDTs were significantly smaller for testes which finally descended spontaneously compared to those which needed pubertal orchidopexy (p < 0.05).

Figure 3 shows the mean testicular volume according to age, after reaching a scrotal position. Different lines indicate whether scrotal position had been reached by spontaneous descent or by orchidopexy. At the ages of 17 and 18 years, the mean
volume of the spontaneously descended testes was higher than the mean volume of the orchidopexied ones. At the age of 18, this was 10.7 ± 2.9 vs 7.6 ± 2.4 ml (p = 0.001). In both groups, the mean volume was significantly smaller than the 50th percentile of the normative values for the same age, at all ages above 13 years (p < 0.001).

There was no significant correlation between testis position or age at referral and final testicular volume corrected for age (p = 0.81). The mean duration of non-descent (measured from referral to the last visit in which the testis was undescended) was 3.5 ± 2.2 years (range, 0.1 - 13.0). No correlation was found between the duration of non-descent and final testicular volume corrected for age (p = 0.36).
Figure 2 Mean volume (ml) of acquired undescended testes as measured by ultrasound prior to testicular descent. Different lines indicate final outcome; spontaneous descent (-----), orchidopexy (- - -) and still in follow up (• • •). Reference lines are normative values for testicular volume (10th, 50th and 90th percentile).
Figure 3 Mean volume (ml) of acquired undescended testes as measured by ultrasound after reaching scrotal position by spontaneous descent (——) or pubertal orchidopexy (- - -). Reference lines are normative values for testicular volume (10th, 50th and 90th percentile).
DISCUSSION

This study shows that if a conservative policy until puberty is followed for acquired UDTs, testis volume is smaller than normative values, both before and after reaching scrotal position. From the age of 17 years, spontaneously descended acquired UDTs are significantly larger than those needing pubertal orchidopexy. Moreover, it becomes clear from this study that if a conservative policy is followed until puberty, nearly 80% of the acquired UDTs descend spontaneously.

In congenital UDTs, orchidopexy is recommended at the age of 6 - 9 months. These recommendations are based on studies that show that early surgery gives a better germ cell development and catch-up growth of the testis. Recent data shows that the longer the congenital UDTs reside supra-scrotally, the more they exhibit impaired growth. In addition to congenital UDT, the acquired form of UDT has been recognized. It affects 1.5% of prepubertal boys with a peak age between 6 and 12 years. However, there is no consensus on the best treatment for this form of UDT. In contrast to congenital UDT, an acquired UDT is located in the scrotum during the first years of life. This results in a normal postnatal germ cell development. Therefore, the extrapolated urge to bring the acquired UDT down as soon as possible after diagnosis is debatable.

Recently, we studied the long-term testicular volumes measured by ultrasound of acquired UDTs after orchidopexy at diagnosis; these were found to be smaller than normative values. The current study evaluates the volumes measured by ultrasound of the acquired UDTs treated conservatively, with pubertal orchidopexy in case of non-descent. We found smaller volumes at almost all ages, both before and after reaching scrotal position, for the spontaneously descended as well as for the pubertal orchidopexied acquired UDTs. Focusing on the age of 18 years, we found a mean testicular volume of 9.5 ± 3.1 ml in the current study. There was no significant difference between this volume and the mean testicular volume of 8.1 ± 3.7 ml after orchidopexy at diagnosis (n = 38, p = 0.06). In addition, no correlation could be established between the duration of non-descent and the final testicular volume (p = 0.36). These findings support that diminished testicular growth is the result of testicular intrinsic abnormalities rather than thermal effects.

In summary, it appears that the volume of the acquired UDT is smaller than normative values. Performing orchidopexy at diagnosis or following a conservative approach does not lead to any differences in long-term testicular volume.
However, there are other aspects of surgery at diagnosis versus a more conservative approach that should be considered. As shown in earlier reports\textsuperscript{11,23} and confirmed by the present study, in 3 out of 4 boys an orchidopexy appears to be redundant if a conservative approach is chosen. Besides economic benefits, there are individual advantages in forgoing these operations; for example, anaesthesia on children can be harmful\textsuperscript{24} and surgery has a considerable psychological impact on children and their parents.\textsuperscript{25}

The natural history and testicular growth of part of the current study population has been reported previously.\textsuperscript{11} In this study, testicular volume was nearly always within the normal range, both after spontaneous descent and after pubertal orchidopexy. The difference between these results and our findings may be explained by the method used. In the earlier study, testicular volumes were assessed by Prader orchidometry and compared to the normative values according to Mul.\textsuperscript{26} Although Prader orchidometry correlates closely with the measurements by ultrasound, it overestimates the testicular volume, especially in small testes. Ultrasound measurements, as used in the present study, are found to be more accurate.\textsuperscript{27,28}

The limitations of this study need to be addressed. Firstly, the diagnosis of acquired UDT is complicated. The physical examination and the distinction between retractile and UDT can be difficult. Furthermore, the distinction between congenital and acquired UDT was based on data on previous testis position, which were obtained from investigators of the Youth Health Care Institution. The accuracy of these data could not be tested. Secondly, as the number of volume measurements and the period of follow-up per boy differs, the influence per boy on the data varies. Finally, we used testicular volume as a parameter for long-term outcome. Although several studies show strong correlations between testicular volume and testis functioning,\textsuperscript{29,30} testicular volume remains an indirect measurement of testicular function.

Based on our results we state that a randomised controlled trial on the management of acquired UDT is indicated; it should compare the results of orchidopexy at diagnosis and a more expectative approach, in order to reach final conclusions on the best treatment of acquired UDT. The long-term outcome on both fertility and the potentially increased risk of testicular malignancies should both be taken into account. Until then, physicians should inform boys and their parents about the two different options to choose from in the management of acquired UDT: awaiting spontaneous descent until puberty or orchidopexy at diagnosis.
An expectative policy of acquired UDT results in nearly 80% of the UDTs reaching the scrotum by spontaneous descent. With regard to testicular volumes, all acquired UDTs are smaller than normative values, both before and after reaching the scrotum. However, these volumes are comparable to volumes after orchidopexy at diagnosis. Therefore, awaiting spontaneous descent does not seem to be detrimental, and a conservative policy of acquired UDT is warranted.
Chapter two

References

Conservative policy for acquired undescended testes