Normative Values for Testicular Volume Measured by Ultrasonography in a Normal Population from Infancy to Adolescence

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Key Words
Testicular volume \(
\text{Prader orchidometer} \) \text{Ultrasound}

Abstract
Background/Aims: We obtained reference data for testicular volume measured by ultrasound in asymptomatic boys aged 0.5–18 years. In addition, we assessed the validity of the Prader orchidometer per age group by correlating it with the volume measurement by ultrasound. Methods: The study only included healthy boys with two scrotal testes at birth and at the time of the examination. For each boy the testicular volume of both testes was measured by ultrasound and the Prader orchidometer. Testicular volumes were measured for boys aged from 1 to 18 years. The boys’ ages were rounded down to the last birthday if it had occurred less than 6 months previously or rounded up to the next birthday if it was going to be within 6 months. Results: The volume measurement by the Prader orchidometer according to reference curves showed a statistically significant correlation. Moreover, the testicular volumes measured by the Prader orchidometer showed an accurate goodness of fit with US measurements (\(R^2 = 0.956\)). Conclusion: Normative values are provided for testicular volume measured by ultrasound in boys aged 0.5–18 years. An accurate correlation was found between volume measurements by ultrasound and by the Prader orchidometer (\(R^2 = 0.956\)). Therefore, volume measurement by the Prader orchidometer, as generally used in the practice by doctors, can be used as a valid parameter for monitoring testicular growth.

Introduction
Testicular function has a direct correlation with testicular volume, since seminiferous tubules and germinal elements comprise approximately 98% of testicular mass [1, 2]. Reduction in testicular size is mainly caused by reduction of these histological elements due to primary dysplasia or secondary damage and can therefore result in disturbed spermatogenesis [3]. Therefore, accurate measurement of testicular volume is important to define the onset of puberty and in the evaluation of boys with a variety of disorders affecting testicular growth and development, such as varicocele and undescended testis (UDT), and after testicular torsion.
Currently, a number of methods for testicular volume measurement are being used, including Prader orchidometry and ultrasonography (US). The Prader orchidometer is widely used in clinical settings. However, scrotal ultrasound offers the potential for greater accuracy in testicular measurement compared to the Prader orchidometer [4–7]. The true volume is only slightly overestimated by ultrasound, whereas the orchidometer overestimates the true volume more significantly [8]. It is unknown whether the reliability of the Prader orchidometer is age dependent.

Testicular volume assessment in individual boys measured by US is only useful if reference data from a healthy population are available for comparison. Recently, normative values have been published for testicular volume measured ultrasonographically in boys aged 0–6 years [9]. However, no reference values were available for ultrasonographically measured testicular volume in boys from infancy to adolescence.

The primary aim of this study was to obtain reference data for testicular volume measured by US in boys from the age of 6 months to 18 years. In addition, we investigated the validity of the Prader orchidometer per age group by relating it to the testicular volume measurement by US.

Methods

Study Design

From October 2007 until August 2009, data were collected from 932 boys aged 6 months to 19 years who lived in the vicinity of the Medical Centre Alkmaar. The boys’ ages were rounded down to the last birthday if it had occurred less than 6 months previously, or rounded up to the next birthday if it was going to be within 6 months. As a result, seven 18-year-old boys over 18.5 years were classified as 19 years old. However, the testicular volumes of these boys were comparable to the boys in the age group of 18 years (independent t test, p = 0.192) and were therefore added to the group of 18-year-old boys.

Recruitment and Enrolment

To ensure that there were enough boys to participate in our study, an invitation letter was sent to 2,600 boys and/or their parents (100–200 letters per age group). These boys were randomly selected from the records of the Youth Health Care Institutions of the Gemeenschappelijke Gezondheidsdienst Hollands-Noord and Eeven-Gezondheidszorg. Moreover, all boys from a local secondary school received an invitation. However, prior to sending these invitation letters, we initiated a publicity campaign. Several media, such as newspapers, the hospital website and a local radio and TV station, were employed to persuade boys to participate in the study. Brothers of boys who had been treated for UDT in our clinic were also contacted and invited to take part.

Inclusion Criteria

Healthy boys with two descended testes at birth and at the time of the examination were included in the study.

Exclusion Criteria

Boys with UDT at the time of the physical examination or at birth were excluded from the study, as well as boys who suffered from syndromes, growth disorders or other conditions that could influence testis growth or who had undergone surgery in the urogenital region. UDT, hydrocele and varicocele were also criteria for exclusion, and boys with a history of scrotal pathologies such as epididymitis, trauma or testicular torsion were excluded as well. It is debatable whether retractile testes are a variant of normal. However, since there is still no consensus about the real entity of the retractile testis, we also excluded boys with retractile testes.

Definitions

Testis Position

‘Descent’ is defined as a spontaneously stable position of the testis at the bottom of the scrotum. A ‘retractile testis’ is defined as a testis which can be brought into a low scrotal position and which remains there until the cremasteric reflex is elicited, while traction on cord structures is not painful. An ‘undescended testis’ is defined as a testis which cannot be manipulated into a stable scrotal position, while further tension on cord structures is painful. A ‘high scrotal testis’ is defined as a UDT which can be brought into a high scrotal position by manipulation through the scrotal entrance, while further traction on cord structures is painful.

Study Protocol

Questionnaire

At the outpatient paediatric clinic, a questionnaire was filled out by the investigator screening patient and parents on the following items: medical problems, medication, major surgery, prior groin surgery, gestational age and ethnicity. Adenotonsillectomy and/or middle ear drainage were not taken into account, nor were the various reasons or motivations for participating in the study.

Physical Examination

A full physical examination was not routinely performed. The height and weight of all the boys was measured while they were wearing only underwear. The height was measured with a ruler which was routinely used at the outpatient clinic and the weight was determined with calibrated balance scales. All the physical examinations and height and weight measurements were performed by the same physician (J.G.). Testicular examination of the left testis was carried out first, followed by examination of the right testis, with the boy in supine and crossed-legged position. The testis position was classified as low scrotal, high scrotal, inguinal or absent; testes were classified as descended, retractile, undescended or absent. To assess retractile testes, the cremasteric reflex was elicited by lightly stroking the superior and medial part of the thigh. This reflex draws the testis back into the groin region. The presence of varicocele was determined in the standing position, by observation of each spermatic cord before and during a Valsalva manoeuvre.

Testicular Volume

After the physical examination, the volume of the left testis was measured first, followed by the right testis, using US and the
Prader orchidometer. We performed US measurements first, so we were blinded to the orchidometer examinations.

All 932 US were performed by the same physician (J.G.) with the same equipment (Falco Auto Image, Falco Software, Tomsk, Russia), using a 12-MHz linear array transducer. To measure the testicular volume, the scanner was placed on the scrotum while exerting light pressure to avoid distorting the testicular shape. Grey-scale images of the testes were obtained in the transverse and longitudinal planes. Three separate transverse and longitudinal images were recorded for each testis. Figure 1 shows an example of a longitudinal and transverse plane. The epididymis was not included in the images. After maximum length, width and height were obtained in the ultrasonogram, these were measured and the volume was calculated with the formula for an ellipsoid:

\[
\text{Volume} = \frac{4}{3} \pi \times \text{length} \times \text{width} \times \text{height}.
\]

All values were collected in a database. For each testis, the highest value of the three testicular volumes was taken as volume measurement. Lastly, additional findings, such as hydrocele and testicular microlithiasis, were assessed. Parenchymal disturbances were not studied and Doppler flow studies to assess testicular blood flow were not performed.

After assessing testis volume by US, testicular size was determined with the testis models of a Prader orchidometer, after the scrotal skin had been stretched over the testis in a warm room. The orchidometer consists of 12 ellipsoid models ranging in volume from 1 to 25 cm³ (1 to 6, 8, 10, 12, 15, 20 and 25 cm³). Estimated in-between values were recorded as well.

Validity of Measurements

To validate the precision of the measurement of testicular volume, three observers, blinded to each other, measured the testicular volumes of 128 boys on the same day at the same sitting. In 84 boys, another investigator (W.H.) measured testicular volume by US and by the orchidometer. A different investigator (K.S.) performed the same measurements on an additional 44 boys. We compared the measurement of testis volume for three age groups (<7 years, between 7 and 12 years and ≥12 years) between the investigators.

Data Recording and Statistical Methods

The statistical package SPSS for Windows, version 14.0, was used for all calculations and statistical analyses. The measured data were listed in special forms and were not added to the boys’ medical files.

The independent t test was used to investigate differences in testicular volume between boys who had been born prematurely or who had an ethnic background other than Caucasian. Correlations between the volume measurements by US and orchidometer were calculated with the Pearson correlation coefficient.

To obtain reference curves for testicular volume in relation to age, percentiles were used. It was not possible to determine 95% confidence intervals because this led to trend-line breaks in 12-year-old boys. Furthermore, the 95% confidence intervals could not be obtained due to the difference in the gradient of the first and the second part of the curve (cut-off 12 years) due to the difference in the number of participants in the different age groups and due to the small number of boys in the higher age categories. Finally, we smoothed the data to have a practical use of the reference curves.

To quantify the goodness of fit between testicular volume measurements by the Prader orchidometer and US, we measured the R². We also measured the goodness of fit in three different age groups (<7 years, between 7 and 12 years and ≥12 years) to investigate whether the R² varies between the age groups.

Ethical Approval

The study was approved by the Ethical Committee of the hospital (reference No. M06-056).

Results

Between October 2007 and August 2009, 936 patients were enrolled in this study (see fig. 2). Testicular volume of both testes could be measured in 932 of the cases (99.6%), whereas 4 boys (0.4%) refused measurement by
US due to embarrassment or fear. The ages of the 932 participating boys ranged from 0.6 to 19.0 years (mean 8.7 years, median 8.4 years).

**Included and Excluded Boys**

Excluded from the study were 163 boys (17.5%; mean 7.3 years, median 7.0 years). In 108 cases (66.2%; ages 0.8–13.0 years, mean 6.0 years, median 6.3 years), this was due to retractile testis: 70 bilateral and 38 unilateral. In 20 cases (12.3%; aged 4.2–12.6 years, mean 9.1 years, median 9.7 years), this was due to UDT. Eighteen boys (11.0%; aged 3.4–17.9 years, mean 10.3 years, median 10.8 years) were excluded due to a history of groin surgery/scrotal pathologies, whereas 7 boys (4.3%; aged 4.1–14.4 years, mean 8.7 years, median 7.2 years) were reported to suffer from syndromes or growth disorders which could influence testicular growth. Varicocele was found in 5 cases (3.0%; aged 11.1–18.4 years, mean 14.3 years, median 13.9 years) and hydrocele in 3 cases (1.8%; aged 4.9, 8.7 and 15.6 years). Two boys (1.2%; aged 5.5 and 8.4 years) were excluded as a result of hernia inguinalis (fig. 2).

Eventually, a total of 769 boys (aged 0.6–19.0 years, median 9.0 years, mean 9.0 years) were included in the study.

**General Characteristics**

Of the 769 boys who were included, 647 (84.1%) had no significant pathology by history, 64 (8.3%) suffered from asthma, and 24 boys (4.4%) had other medical problems. Twenty-four boys (3.2%) suffered from a psychiatric disorder. Ninety boys (11.7%) took some kind of medication.

Sixty boys (7.8%) had been born prematurely. The ethnic background was Caucasian for 716 of the boys (93.1%), African-American for 16 boys (2.1%), Asian for 18 boys (2.3%), Turkish for 12 boys (1.6%), North-African for 4 boys (0.5%) and Hispanic for 3 boys (0.4%).

Boys who had been born prematurely (independent t test, \( p = 0.57 \)) or who had an ethnic background other than Caucasian (independent t test, \( p = 0.21 \)) showed testicular volumes comparable to boys who had been born at term or who had Caucasian ethnicity.

Height and weight for each age group were compared with reference data for Dutch boys [10]. No significant difference was found. Boys who had an ethnic background other than Caucasian showed comparable height and weight to boys who had Caucasian ethnicity (independent t test, respectively \( p = 0.96 \) and \( p = 0.81 \)).
The mean testicular volumes measured by US ranged from 0.23 to 20.23 ml (mean 2.85 ml, median 0.76 ml). The testicular volume of the left testis ranged from 0.20 to 20.13 ml (mean 2.80 ml, median 0.74 ml) and the volume of the right testis ranged from 0.24 to 20.91 ml (mean 2.85 ml, median 0.77 ml). The mean testicular volume at 1 year of age was 0.48 ml. At 10 years of age it was 0.97 ml. The largest difference between the testicular volumes in one age group was found in the 14-year-old boys (range 1.69–19.98 ml) and the smallest difference was found in the 2-year-old boys (range 0.32–0.78 ml). Figure 3 shows the reference curve for testicular volumes measured by US (fig. 3a) and an enlargement of the first part of the curve (fig. 3b).

**Testicular Volume Measured by Prader Orchidometer**

The 769 mean testicular volumes measured by Prader orchidometer ranged from 1 to 30 ml (mean 6.4 ml, median 2.0 ml). The volume of the left testis ranged from 1 to 30 ml (mean 6.3 ml, median 2.0 ml) and the volume of the right testis ranged from 1 to 30 ml (mean 6.4 ml, median 2.0 ml). Comparable to the measurements by US, the largest difference between the mean testicular volumes was found in the 14-year-old boys (range 4.0–30.0 ml). The smallest difference was found in the 5-year-old boys (range 1.0–3.0 ml).

Table 1 shows the testicular volumes measured by US and the Prader orchidometer. Figure 4 shows the reference curve for the Prader orchidometer.

**Measurement of Testicular Volume by US versus Prader Orchidometer**

There was a statistically significant correlation between measured volume by the Prader orchidometer and reference curves [11] (Spearman’s correlation coefficient; all correlations significant at p < 0.01). Furthermore, the testicular volumes measured by the Prader orchidometer showed an accurate goodness of fit with US measurements ($R^2 = 0.956$; see fig. 5a). Figure 5b shows the tes-
Table 1. Volume of the right and left testis of the boys included in this study measured by ultrasound and Prader orchidometer (n = 769)

<table>
<thead>
<tr>
<th>Age years</th>
<th>Boys</th>
<th>Ultrasound, ml</th>
<th>Prader orchidometer, ml</th>
</tr>
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<tr>
<td></td>
<td>n</td>
<td>left volume</td>
<td>SD</td>
</tr>
<tr>
<td>1</td>
<td>40</td>
<td>0.48</td>
<td>0.14</td>
</tr>
<tr>
<td>2</td>
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<td>0.18</td>
</tr>
<tr>
<td>4</td>
<td>38</td>
<td>0.52</td>
<td>0.18</td>
</tr>
<tr>
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<td>0.15</td>
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<td>7</td>
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<td>0.18</td>
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<td>8</td>
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<td>9</td>
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</tr>
<tr>
<td>18</td>
<td>23</td>
<td>13.67</td>
<td>3.49</td>
</tr>
<tr>
<td>Total</td>
<td>769</td>
<td>2.8</td>
<td>4.16</td>
</tr>
</tbody>
</table>

Fig. 5. a Correlation between volume measurement by the Prader orchidometer and ultrasound. b Correlation between volume measurement by the Prader orchidometer and ultrasound in three different age groups.
ticular volumes measured by US and the Prader orchidometer in three different age groups (R² in 1- to 6-year-old boys: 0.429, in 7- to 12-year-old boys: 0.827 and in 13- to 18-year-old boys: 0.908).

Interobserver Variation
In 84 boys (10.6%), testicular volume was measured ultrasonographically and by the orchidometer additionally to the first investigator (J.G.) by a second investigator (W.H.) and in 44 boys (5.7%) additionally to the first investigator (J.G.) by a third investigator (K.S.). Both were blinded to the first investigator (J.G.). Table 2 represents the number of boys, the groups into which they were divided and the correlation coefficients between the measurements of J.G. and W.H. and between the measurements of J.G. and K.S.

Discussion
This study provides normative values of the ultrasonographically measured testicular volume for boys from the age of 6 months to 18 years. In addition, we found a strong correlation between US and orchidometer measurements for all ages.

Estimation of testicular volume in boys is important in several clinical conditions. For example, in patients with varicocele or UDT, impaired testicular growth may result in an earlier indication for operative correction. There are different means for measuring testicular volume, such as calipers, rulers, orchidometers, water displacement and US. The Prader orchidometer is widely used for the clinical assessment of testicular volume in the doctor’s office because it is practical and less time-consuming than US. However, US is more precise for humans as well and has been used in several studies [5, 7, 12, 14]. The orchidometer measures the epididymis as well as the scrotal skin, and, as a result, it tends to overestimate testicular volume, especially in small testes, in which the epididymis is large in comparison to the total testicular volume. Because of its practical use, the Prader orchidometer is one of the main instruments in the analysis of puberty. However, because of its accuracy in the follow-up of testicular growth, US has an additional role in the development of puberty.

A few studies comparing the orchidometer and US found that both methods correlated well [4, 8, 13, 14]. In our study, the comparison between the orchidometer and ultrasound demonstrated a strong linear relationship (R² = 0.96). Divided into three age groups, we found the weakest correlation in the youngest group (age 1–6 years; R² = 0.43). This may be due to the overestimation of the testicular volume in young boys and to the relatively large differences in the size of the orchidometer beads. The strongest correlation was found in the oldest age group (age 13–18 years; R² = 0.91) unless the spread in the US measurements related to the Prader orchidometer seems to increase with age.

Various formulas have been used to calculate the testicular volume measured by US. One recent study found 0.71 × length × width × height to be an accurate formula to estimate the volume of canine testes [5]. This formula, introduced by Lambert [15] in 1951, seems to be accurate for humans as well and has been used in several studies [16]. Other studies have used the formula π/6 × length × width² [2, 6, 17]. This formula would be correct if testicular width equals height, but this is not always the case. To measure testicular volume, we used in this study the formula for a prolate ellipsoid: π/6 × length × width × height, which was also used in several other studies [18, 19]. Furthermore, the highest value of three testicular volumes was taken as the true volume. Earlier studies chose to calculate testicular volume by recording the largest of three measurements for each of the three testicular dimensions [5, 7, 12, 14, 20]. Since the testis is an elastic organ, during measurement it might easily become compressed resulting in distorting the shape and dimensions. Compression of the testis would result in a larger length and smaller width in the trans-

<table>
<thead>
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<th>Correlation</th>
<th>Testes</th>
<th>Correlation</th>
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<tbody>
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<td>J.G.-W.H.</td>
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<td>J.G.-W.H.</td>
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<td>0.513</td>
<td>J.G.-K.S.</td>
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<tr>
<td>J.G.-W.H.</td>
<td>0.964</td>
<td>J.G.-K.S.</td>
<td>0.999</td>
</tr>
</tbody>
</table>

Table 2. Comparison of measurement of testis volume for three age groups (<7 years, between 7 and 12 years and ≥12 years) by Prader orchidometer and US between two investigators (J.G., W.H.) and between two other investigators (J.G., K.S.)

a Pearson’s r.
b All correlations were significant at p < 0.01.
verse plane. Without compression the length would be smaller and the width would be larger. Therefore, in our opinion, it is more accurate to use only the largest of the three volume measurements.

If the largest of the three measurements for each of the three testicular dimensions had been used in this study, the average testicular volume would have been 6% higher. Furthermore, in this study the largest instead of the mean measured volumes was taken as true volume as some of the individual measurements might not have included the full dimension of the testis. If the mean of the three measurements had been taken, the real testicular volume would be 4.8% higher.

We compared height and weight in our study group with normative values of the Dutch growth study and indicated that height and weight in our study group were comparable to the Dutch reference [10]. The Dutch growth study studied pubertal development in boys aged 9 years and older and determined testicular volume only by the orchidometer [11].

In this study, measured by US, the testicular volume of 9-year-old boys was significantly higher than in 1-year-old boys (mean volumes were 0.48 and 0.79 ml, respectively; independent t test p < 0.001). Testicular growth before puberty was previously documented by Rey [21] and is essentially the result of Sertoli cell proliferation. Earlier studies may not have detected prepubertal testicular growth due to a lack of accuracy of the orchidometer [11]. However, we also found a significant difference in the testicular volumes measured using the orchidometer between 9- and 1-year-old boys (mean volumes 2.32 and 1.64 ml, respectively; independent t test p < 0.001).

The limitations of this study need to be addressed. To promote participation in our study, we sent an invitation letter to more than 2,500 boys. Only some of these boys decided to participate. It is unclear why a great number declined to participate, which makes this a possible selection bias. Furthermore, brothers of boys who were treated for UDT were invited to take part in the study. This might have led to a selection bias, although UDT is generally not hereditary.

In each boy, a testicular examination was performed and the testis position was classified. The location of the retractile testis is variable, so the testis position in boys with retractile testis might be interpreted as scrotal at the time of the testicular examination. As testicular volume in retractile testis may be lower, this may have influenced the values of the normal population of boys. Although we asked parents whether their sons suffered from syndromes, growth disorders or other conditions that could influence testis growth, we cannot fully exclude any of these conditions since no full physical examination was performed.

In the general population, the prevalence of boys with acquired UDT varies between 1.2 and 2.2% [22]. It is possible that pubertal boys enrolled in this study may unknowingly have suffered from acquired UDT which descended spontaneously at puberty. These boys might have a smaller testicular volume as a result of the formerly acquired UDT.

We found a strong correlation between volume measurement by the orchidometer and US. The examiner performed both US and Prader orchidometer measurements at the same sitting, thus potentially biasing the results of the study. However, measurement by the orchidometer was performed following US during the same session, and as a result the examiner was not blinded to the findings of the orchidometer examination. This may have contributed to the strong correlation between both measurements. Furthermore, because the examiner was not blinded to the findings of the orchidometer examination, the volume measurement by the orchidometer could be influenced.

This study included 53 non-Caucasian boys. It is known that ethnic background can influence testicular volume in adult men [23]. In children, no studies have been published on the comparison of testicular volume between various ethnic groups. We found no differences in testicular volume between boys from various ethnic backgrounds. However, we could not assess the influence of testicular volume in different ethnic groups because only a small number of non-Caucasian boys were included in this study. Therefore, further research is necessary to assess the testicular volume in boys of non-Caucasian origin.

**Conclusion**

This study provides normative values for testicular volume measured by US in boys aged 0.5–18 years, and these values can be used as a reference for different testicular abnormalities. Furthermore, we found an accurate correlation between the volumes measured by the Prader orchidometer and by US (R² = 0.956). Therefore, volume measurement by the Prader orchidometer, as generally used in practice by doctors, can be used as a valid parameter for monitoring testicular growth.
Acknowledgements

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