

# Undescended testis: 513 patients' characteristics, age at orchidopexy and patterns of referral

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## **Abstract**

### **Objective**

Undescended testis (UDT) affects 1-6% of males. Current recommendations are to correct maldescent by 1 year of age. We identify the population characteristics of children referred and managed for UDT, age at referral and orchidopexy, and patterns of referral.

### **Design, Setting and Patients**

Retrospective 5 year review of all patients operated for UDT from 2007-2011 in our institution. Patient demographics, neonatal diagnosis of UDT, age at referral, referral source and age at first orchidopexy were recorded. Data are reported as median(range).

### **Results**

There were 513 boys with 576 undescended gonads; 450(88%) had unilateral UDT. Congenital (present at birth) UDT was diagnosed in 287(56%) children. Seventy-nine(15%) were premature births, 41(8%) had associated major genitourinary abnormalities. Median age at referral was 1.1(0-16.2) years; median age at first orchidopexy was 1.6(0-17.2) years. When corrected for age, those with a history of prematurity and associated major genitourinary malformations were referred and operated on earlier. There was no difference in age at referral and orchidopexy when comparing unilateral versus bilateral maldescent, and palpability of UDT. Of those with congenital UDT, 70% were operated at beyond 1 year of age. Those referred from public tertiary hospitals were younger than those referred from community clinics( $p<0.0001$ ) and private healthcare institutions( $p=0.003$ ).

### **Conclusions**

Despite early diagnosis in many patients with UDT, most are referred and operated after 1 year of age, even in congenital UDT. Premature babies, those with major genitourinary anomalies, and those seen in public tertiary hospitals are referred earlier. Community health initiatives must emphasise prompt referral to allay the impact of delayed surgery.

### **Keywords**

Cryptorchidism, testicular maldescent, children, age at referral, age at orchidopexy

### **Introduction**

Testicular maldescent or undescended testis (UDT) is found in up to 6% of full term male births. Early postnatal descent of the testis may occur, resulting in an incidence of approximately 1-2% in males more than 6 months of age (1).

The association of UDT with subfertility and testicular malignancy is well described in the literature. Some reports have elegantly demonstrated that older age at orchidopexy adversely affects spermatogonic potential of the testis (2). This effect is worsened in bilateral disease where fertility rates are significantly lower than that seen in unilateral UDT (3). Thus, many groups have suggested that correction of the UDT should be carried out between 6 – 12 months of age (4,5,6). This is a reduction from the previously recommended age of 18 months - 2 years. In our institution, we started to recommend early orchidopexy before 1 year old in 2004.

The risk of malignancy, although low, is also increased in the presence of UDT, with increasing risk associated with older age at orchidopexy (7,8,9,10).

As the age when surgical correction is carried out appears to play a central role in prevention of these two problems of infertility and malignancy, it becomes imperative that an early diagnosis is achieved in order to set the patient on an appropriate referral pathway in a timely manner.

The aim of our study is to identify the population characteristics of children referred and managed for UDT in our institution, age at referral and orchidopexy, and patterns of referral. Our institution is a publicly funded tertiary hospital with the largest paediatric surgical unit in the country, receiving the bulk of referrals from a stable population with easy access to good primary care.

## **Methods**

This was a retrospective review of all patients operated for UDT in our institution between 2007 and 2011. Ethical approval for the study was obtained from the institutional review board (No 2012/534D).

A list of patients was obtained from operative log books and relevant case notes were retrieved. Information from physical case records were supplemented by electronic medical records where available. We excluded those who had their first surgery elsewhere and those who had their first surgery prior to 2007.

Data collected included patients' demographics and clinical characteristics, neonatal diagnosis of UDT, sources of referrals, time first seen by a paediatric surgeon, wait time for surgery, age at orchidopexy and operative details. Where prior

documentation of scrotal position of the testis was available, this was noted. The UDT was considered ‘congenital’ when the testis was undescended at birth, and ‘acquired’ when previously recorded to be scrotal in position.

#### *Associated genitourinary malformations*

We defined ‘minor’ anomalies as those that did not require surgical intervention. These included mild renal pelviectasis, hydrocoele, and mild phimosis. ‘Major’ anomalies were those that required surgical correction, e.g. ureterocoele, hypospadias.

#### *Sources of referral*

These were classified into the following categories: (a) internal referrals, where referrals were made from doctors within our institution, (b) other publicly funded hospitals (c) publicly funded community clinics, (d) private healthcare clinics and institutions, (e) school health service, which is a public health screening service that carries out well child examinations in schoolchildren, and (f) self-referrals, where patients were brought by caregivers without a medical referral. When comparing sources of referral, we excluded those from the school health service to remove selection bias, as these patients would only be diagnosed upon entering primary school at 6 years of age. However, these children were included in the analysis of all other covariates.

#### *Age at referral, wait time for operation, age at orchidopexy*

Age at referral was calculated using the actual date the patient was referred. When this was not available, the date first seen by a paediatric surgeon was used as a surrogate.

Wait time for operation was the time lapsed between the age at referral and age at orchidopexy.

Age at orchidopexy was calculated from the date of first procedure. For example, where the procedure was staged, such as a Fowler-Stephens procedure, the age at orchidopexy was calculated using the date of the first stage of the procedure.

When there was a history of prematurity, we corrected for age, taking birth at 37 completed weeks of gestation and beyond as term.

### *Operative details*

Intraoperative site of the cryptorchid testis was categorized as follows: (a)impalpable (b)palpable (c)retractile (d)absent/atrophic (e)ectopic. Intra-abdominal testes were categorized as impalpable. All UDT distal to the deep inguinal ring were considered palpable, except for retractile, atrophic and ectopic testes which were considered separately. Retractable testes were those found to remain comfortably in the scrotum without requiring traction during physical examination. Absent (or atrophic) testes were diagnosed in patients who had blind-ending testicular vessels without visible testicular tissue. Ectopic testes were those sited away from the embryological line of descent of the testis.

### *Statistical analysis*

Covariates analysed were unilaterality/bilaterality of disease, history of prematurity, presence/absence of associated genitourinary abnormalities, and intraoperative site of the cryptorchid testis. We used chi-squared tests for categorical data, and Wilcoxon rank sum tests for continuous non-parametric data.

When comparing median age among sources of referral and intraoperative site of the UDT, we used a Kruskal-Wallis test. Pair-wise comparisons were carried out using the Wilcoxon rank sum test.

Data are reported as median and range. A P-value of 0.05 was considered significant.

## **Results**

A total of 534 boys were operated for UDT between 2007 and 2011. Twenty-one boys were not analysed due to our exclusion criteria, leaving 513 boys in our study with 576 undescended gonads (Table 1).

There were 287(56%) children who had the diagnosis made as neonates. Of the 221 boys born in our institution, 165(75%) were diagnosed at birth. Seventy-nine (15%) were premature, born at 35(25-37) weeks of gestation. In 91(18%) boys, the cryptorchid testis was noted to be scrotal in position on previous physical examination. Details of scrotal examination in the neonatal period were not available in 135(26%) boys.

A total of 642 procedures were performed, including 520 orchidopexies, 23 Fowler-Stephens, 15 staged orchidopexies, 42 orchidectomies and 2 redo orchidopexies. The majority of the 'orchidectomies' consisted of removal of testicular remnant tissue in cases of atrophic testis.

### *Associated malformations*

Associated congenital anomalies were seen in 115(22%) boys and occurred most frequently in the genitourinary tract. Major genitourinary malformations involved 41(8%) children; the most common was hypospadias, which was seen in 15 boys.

#### *Sources of referral (Table 2)*

Internal referrals from within our own institution formed the largest proportion of children operated for UDT (219, 43%).

#### *Age at referral, wait time for operation, age at orchidopexy (Figure 1)*

Median age at referral was 1.1(0-16.2) years and median age at first orchidopexy was 1.6(0-17.2) years. Wait time for operation was 3.9(0-96) months. There were 393(77%) patients above 1 year old, and 216(42%) above 2 years old at first surgery. A bimodal distribution was seen with peaks at 1 and 7 years.

#### *Factors influencing age at referral and age at orchidopexy (Table 3)*

When corrected for age, we found that those with history of prematurity were referred ( $p<0.0001$ ) and operated earlier ( $p=0.0001$ ).

When we looked at all associated genitourinary malformations, there was no difference in age at referral and age at orchidopexy. However, when we eliminated 'minor' malformations, we found that those with major genitourinary malformations were diagnosed ( $p<0.001$ ) and operated earlier ( $p=0.01$ ).

When we compared sources of referral, those referred from all public tertiary hospitals, including our institution, were younger than those referred from community clinics ( $p<0.0001$ ) and private healthcare institutions ( $p=0.003$ ).



We also assessed the impact of scrotal examination in the neonatal period, information on which was available in 378 patients (Figure 2). Those with congenital UDT were referred and operated earlier than those with acquired UDT. However, even in the presence of a congenital UDT, only 30% were operated before 1 year of age, rising to 68% by 2 years of age.

There was no difference in age at referral and orchidopexy when comparing unilateral versus bilateral maldescent, and palpability of the cryptorchid testis.

## **Discussion**

We demonstrate that a large number of boys with undescended testes are referred and surgically corrected beyond the recommended age of 1 year, even in the presence of congenital UDT.

The recommended age at orchidopexy has steadily decreased in recent decades, due to awareness of the associated risks of testicular malignancy and infertility, which may be attenuated by early surgery (8). In 1996, the Section of Urology of the American Academy of Pediatrics first recommended surgical correction by one year of age (4). However, it is only in the past 5 years or so that the global paediatric surgical community has followed suit, releasing a number of consensus statements (5,6).

Wood et al reviewed existing data on the risk of testicular tumour with cryptorchidism, and noted an overall relative risk of 2.75 to 8(7). Similar to Pettersson et al post-pubertal orchidopexy was associated with approximately double the risk of

testicular malignancy compared to pre-pubertal orchidopexy (8). As the majority of our patients are operated pre-pubertally, the incidence of UDT-associated testicular malignancy is unlikely to be high. Nevertheless, concerns about malignant potential mean that all our patients are followed up into adolescence.

The effect of age at orchidopexy appears even more pronounced when considering the issue of fertility. In a study by Tasian et al, age at orchidopexy was associated with germ and Leydig cell depletion where each month of undescend corresponded to 2% severe germ cell loss and 1% Leydig cell depletion (2). In our population with a low fertility rate of 1.2 per female, this has far-reaching implications(11). However, despite these dramatic results, many would agree that the true test of fertility is paternity. Miller et al showed that unilateral cryptorchidism did not correlate with reduced fertility, nor did age at orchidopexy, preoperative testicular location or preoperative testicular size(12).

In our study, factors that contributed to earlier referrals were history of prematurity and source of referral(13). This is unsurprising as prematurity is a risk factor for UDT, affecting up to 30% of premature males. As public tertiary hospitals see a high volume of premature neonates, neonatologists frequently encounter the pathology and make prompt referrals. Even so, nearly 40% of patients with a neonatal diagnosis of UDT were referred beyond the age of 1 year, revealing a critical gaps either in the referral pathway or in complete and proper physical examination.

Another factor that contributed to earlier diagnosis was the presence of associated major genitourinary malformations. It may be that the presence of these anomalies

triggered more detailed physical examinations leading to earlier referral or resulted in earlier paediatric surgical consultations during which the testes were examined. Our findings are somewhat similar to the report by Bayne et al where the presence of concomitant penile anomalies resulted in earlier referral(14).

Unexpectedly, having bilateral UDT did not affect age at referral. This may have been due to the interplay of factors that negated each other. The absence of scrotal asymmetry could potentially delay diagnosis leading to later referral(13). Conversely, the abnormally 'flat' hypoplastic appearance of the scrotum in bilateral UDT should lead to earlier diagnosis, as evaluation for disorders of sexual development should be performed. Both these scenarios may have played out leading to no effect overall. Palpability of the testis also made no difference, unlike other reports(14).

The entity of the 'ascending testis' or the 'acquired' UDT appears to have contributed to the high number of delayed orchidopexies as nearly one fifth of our patients were previously recorded to have a scrotally positioned testis(15,16). Little is known about the implications on fertility in the context of a previously descended testis – current evidence is difficult to interpret as it is largely retrospective and definitions are heterogenous (17,18). There have been case reports of testicular tumours in ascending testes, but no clear evidence to support an increased risk of malignancy (19,20). Similar to Hack et al, we saw a bimodal distribution in age at referral and age at orchidopexy, with peaks seen at 1 year and 7 years, which they attributed to acquired UDT(16). In our case, we believe the rise in incidence at age 7 was due to new cases picked up by the school health service which is a national health screening programme carried out in all primary schoolchildren. Regardless, this fails to explain

the majority of boys with congenital UDT who experienced delayed referral and surgery, other than the lack of a good physical examination.

Age at orchidopexy may be useful in itself as a proxy marker to assess the effectiveness of a regional public health service(21,22,23). Singapore is a small city state with healthcare facilities located in close proximity to its urban resident population. Local health indices such as the low infant mortality and high vaccination rates, are reflective of first world standard of care. Assuming that healthcare is thus easily accessible and of excellent quality, it was regrettable to find the large number of boys with delayed referrals, especially when referred from providers outside our institution. We postulate that this may be due a lack of awareness of the condition and its appropriate management among general practitioners and community paediatricians, as well as the general public. Certainly, as reported by Yiee et al and Springer et al, the type of referring provider plays a central role, where family practitioners and community paediatricians tend to refer later, even when possessing appropriate levels of knowledge of the condition(22,24).

One particular problem with UDT is the multiple changes in guidelines that have transpired in a fairly short period of time, thus placing a burden on community paediatricians and general practitioners to maintain up-to-date practices. Hack et al have demonstrated that it is possible to have effective screening for the detection of acquired UDT (25). However, it may require more intensive and coordinated outreach efforts from paediatric surgeons to disseminate knowledge and achieve early diagnosis with improved referral patterns.

This is one of the largest studies of its kind in the literature – many other reports utilize computerized population registration systems which allow mining of data for patients numbering thousands, but cannot provide more patient-specific information such as history of prematurity, associated malformations, and source of referral(8,26). The overwhelming majority of previous studies originate from mainly Caucasian populations, whilst ours provides insight into the populous yet largely unknown Asian demographic.

However, we acknowledge that the retrospective nature of our study did not provide the necessary data for certain analyses. For example, it would be interesting to evaluate the post-pubertal boys as a subgroup to identify factors that contributed to the delay in referral. There was also a lack of information from the neonatal period in many of our patients, which did not allow us to assess the true incidences of congenital and acquired UDT. We also could not ascertain the specific reasons for delayed referral in many of those with congenital UDT – where information was available, among the reasons given for delay were parental concerns regarding costs of treatment, inaccurate information provided to caregivers regarding recommended timing of surgery, and the misguided hope that the UDT ‘might come down’ despite medical advice to the contrary. Certainly, a prospective database would be ideal in allowing us to assess these patterns of referral in further detail. Following on from this study, we intend to evaluate knowledge levels of UDT amongst healthcare providers to allow targeted community outreach initiatives.

In conclusion, despite early diagnosis in many patients with UDT, most are referred and operated after 1 year of age, including those with congenital UDT. Premature

babies, those with major genitourinary anomalies and those seen in public tertiary hospitals are referred earlier. The entity of the 'ascending testis' may contribute in part to older age at diagnosis. Community health initiatives must emphasise prompt referral to allay the impact of delayed surgery

What is already known about this topic

- Previous recommendation for undescended testis was for orchidopexy by 2 years of age. Several new guidelines have lowered the recommended age to 1 year old.
- ‘Acquired’ undescended testis (ascending testis) accounts for some of the delay in age at orchidopexy
- Most previous studies describe a mainly Caucasian population

What this study adds

- This is the largest study on UDT in Asians with relevant clinical information
- Delays in referral and surgery continue to occur in those diagnosed with congenital undescended testis and despite easy access to excellent primary care services
- UDT management by the present routine of diagnosis and referral by primary providers is suboptimal. Dedicated outreach or screening programmes may be required

### **Footnotes**

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were involved in critical revision and final approval of the paper. CCPO was involved in writing and final approval of the paper.

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### **Legend**

Figure 1: (a) Overall age at referral and (b) overall age at orchidopexy. A bimodal distribution was seen with peaks at approximately 1 year and 7 years.

Figure 2: (a) Age at referral and (b) age at orchidopexy in patients with previously documented position of testis.

Table 1: Characteristics of 513 patients operated for undescended testis

Characteristic	No (%) or median (range)
Total patients	513
Total gonads	576
Unilateral : bilateral disease	450 (88) : 63 (12)
Right UDT : Left UDT	277 (48) : 299 (52)
Congenital UDT : Acquired UDT*	287 (56) : 91 (18)
History of prematurity Yes : No	79 (15) : 434 (85)
Associated major genitourinary malformations Yes : No	41 (8) : 472 (92)
Intraoperative site of cryptorchid testis	
Impalpable	394 (68)
Palpable	77 (13)
Retractile	27 (5)
Absent/atrophic	39 (7)
Ectopic	14 (2)
NA	25 (4)
Overall age at referral (years)	1.1 (0-16.2)
Overall age at orchidopexy (years)	1.6 (0-17.2)
Overall wait time for operation (months)	3.9 (0-96)

NA = Information not available

\* Only those with prior documentation of testicular position were included in this analysis

Table 2: Sources of referral

	No (%)	Age at referral <sup>#</sup> (years)	Age at orchidopexy <sup>#</sup> (years)
Internal	219 (43)	0.8 (-0.1, 16.2)	1.3 (-0.1, 17.2)
Public community health clinics	150 (29)	1.3 (0, 15.7)	1.7 (0.6, 16.0)
School health service	68 (13)	7.1 (5.3, 12.7)	7.5 (5.7, 12.8)
Self-referrals	40 (8)	1.8 (0.3, 12.2)	2.2 (0.8, 12.4)
Private healthcare practitioners / institutions	23 (5)	1.1 (0.1, 10.4)	1.6 (0.8, 12.4)
Other public hospitals	11 (2)	0.9 (0, 1.3)	1.0 (0.8, 2.5)
Not available	2 (<1)	-	-

<sup>#</sup> age corrected for prematurity where appropriate

Data = median (range)

Table 3: Age at referral and age at orchidopexy comparing history of prematurity vs term delivery, presence vs absence of major genitourinary anomalies, congenital vs acquired UDT, unilateral vs bilateral disease and palpable vs impalpable UDT

	Age at referral (years) <sup>#</sup>	p-value	Age at first orchidopexy (years) <sup>#</sup>	p-value
Premature (n=79) vs Term (n=434)	0.2 (-0.1, 9.2) 1.1 (0, 16.2)	<0.0001*	0.7 (-0.1, 9.4) 1.6 (0, 17.2)	0.0001*
Associated major genitourinary malformations (n=41) vs No major genitourinary malformations (n=472)	0.2 (-0.1, 12.3) 1.1 (0, 16.2)	<0.001*	1.3 (0, 12.8) 1.7 (0.1, 17.2)	0.01*
Congenital UDT <sup>§</sup> (n=287) vs Acquired UDT (n=91)	0.8 (-0.1, 16.2) 1.3 (-0.1, 15.7)	0.03*	1.3 (0, 16.3) 1.9 (0, 15.8)	0.006*
Unilateral UDT (n=450) vs Bilateral UDT (n=63)	1.0 (-0.1, 16.2) 0.9 (-0.1, 14.4)	0.8	1.5 (-0.1, 16.3) 1.5 (0, 17.2)	0.4
Palpable UDT (n=394) vs Impalpable UDT (n=77)	1.1 (-0.1, 16.2) 1.0 (0, 14.4)	0.1	1.7 (0, 16.3) 1.5 (0-17.2)	0.2

\*statistically significant

<sup>#</sup> age corrected for prematurity where appropriate

<sup>§</sup>only those with prior documentation of testicular position were included in this analysis

Data = median (range)