Timing of Orchiopexy for Undescended Testis in Israel: A Quality of Care Study

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ABSTRACT: Background: Strong evidence suggests that in order to prevent irreversible testicular damage surgical correction (orchiopexy) for undescended testis (UDT) should be performed before the age of 1 year.

Objectives: To evaluate whether orchiopexy is delayed in our medical system, and if so, to explore the pattern of referral for orchiopexy as a possible contributing factor in such delays.

Methods: We conducted a retrospective chart review of all children who underwent orchiopexy for UDT between 2003 and 2013 in our institution. We collected data on the age at surgery and the child's health insurance plan. We also surveyed pediatricians from around the country regarding their pattern of UDT patient referral to a pediatric urologist or surgeon for surgical correction.

Results: A total of 813 children underwent orchiopexy in our institute during the study period. The median age at surgery was 1.49 years (range 0.5–13). Only 11% of the children underwent surgery under the age of 1 year, and 53% between the ages of 1 and 2 years. These findings were consistent throughout the years, with no difference between the four health insurance plans. Sixty-three pediatricians who participated in the survey reported that they referred children to surgery at a median age of 1 year (range 0.5–3 years).

Conclusions: Our results demonstrate delayed orchiopexy in our medical system. There is a need to improve awareness for early specialist consultation in order to facilitate earlier surgery and better care.

KEY WORDS: orchiopexy, undescended testis (UDT), quality of care study, cryptorchidism, pediatrics

Undescended testes (UDT) are common, found in 3.4–5.8% of term boys and up to 30% of premature male infants. In most of these cases the testes descend spontaneously within the first few months of life and rarely after 6 months of age. By the age of 1 year 1% of male children have UDT [1]. UDT are associated with a higher risk of testicular malignancy [2] and torsion [3], reduced fertility and endocrine function [1]. In addition, in most cases there is a patent processus vaginalis, which if not treated may, albeit rarely, turn into a clinical indirect inguinal hernia [4]. Lastly, UDT is an esthetic problem with psychological consequences of an ipsilateral empty scrotum especially in puberty and adulthood [5].

Strong evidence [6–9] suggests that in order to prevent irreversible testicular damage surgical correction (orchiopexy) should be performed before the age of 1 year. Those studies showed that any delay in orchiopexy will increase the risk of testicular growth failure, histological changes such as fibrosis, as well as low sperm count. In 1996 the American Academy of Pediatrics (AAP) published clinical guidelines stating that orchiopexy for UDT should be performed before the age of 1 year. Recently, a large database study [10] using the PHIS (Pediatric Hospital Information System) database that included over 28,000 patients from 41 children's hospitals in the United States showed that despite the AAP guidelines, only 16% of children with UDT underwent orchiopexy before 1 year of age and 43% before the age of 2 years. In addition, a recent study from Germany [11] found that only 18.7% underwent orchiopexy before 1 year of age, 24.3% at 1–2 years, and 57% after age 2 years. In reality, some of the cases, even today, are operated at a later age.

Those results were the basis of this study which aimed to determine the age of patients with UDT at the time of the surgical correction (phase I); and if there was a delay, to explore the pattern of referral for orchiopexy as a possible contributing factor to such delays (phase II).

PATIENTS AND METHODS
This study received Institutional Review Board approval. Phase I was a chart review. Participation in phase II was voluntary and anonymous.

PHASE I: PATIENT POPULATION
We used our institutional electronic medical records to collect data on all patients who underwent orchiopexy between 2003 and 2013. Inclusion criteria included orchiopexy due to UDT between 0 and 18 years. We collected data on each child's
co-morbidity and health insurance plan (one of four in Israel). We excluded cases of orchiopexy due to testicular torsion and iatrogenic UDT post-inguinal surgery. To avoid dual counting of two-stage orchidopexies, bilateral orchiopexy or redo procedures, only the first surgical procedure for any individual patient was included in the final data set. In order to examine trends in practice during the study period, the year of procedure was also documented.

Our primary outcome of interest was patient age at the time of orchiopexy (1 year, 2 years, etc.)

**PHASE 2: PEDIATRICIANS SURVEY**

We conducted a short survey of active pediatricians in the community. The survey was distributed to community-based pediatricians during a continuous medical education lecture gathering. All were asked three questions:

- In your everyday practice, what is the age for referral of a patient with UDT to a specialist (pediatric urologist or surgeon)?
- What health insurance plan do you belong to?
- How many years have you been in practice?

**RESULTS**

**PHASE 1**

We identified 947 surgeries for orchiopexy in our institution between 2003 and 2013. After exclusion of 144 patients who had orchiopexy for a reason other than UDT, 803 children remained in the study group. The median age at surgery was 1.49 years. Eleven percent of the patients underwent surgery at age less than 1 year, 53% were operated on at age 1–2 years, and 36% underwent orchiopexy after age 2 years [Figure 1]. We found that these findings were stable throughout the years of the study period (range 1.17–1.67 years). We did not observe any difference in the timing of orchiopexy between the four health insurance plans. Seventy-nine patients (9.7%) had other major background diseases, mostly other congenital anomalies. In that group of patients the median age at surgery was 2 years.

**PHASE II**

Sixty-three general pediatricians who work both in the community and in academic hospitals claimed to refer their patients for surgery at a median age of 1 year (range 0.5–3 years). No difference was found between physicians affiliated to the four different health insurance plans. The number of years in practice and the age of referral were not significantly different between physicians [Table 1].

**DISCUSSION**

The primary aim of this study was to determine the age at which orchiopexy is performed in our institution and to examine factors associated with delay in surgery. Contrary to our expectations, many orchidopexies were performed after the age of 2 years. In addition, this figure remained constant during the study period, despite the presence of robust literature and guidelines recommending early surgery.

Given that the evidence for early repair of congenital cryptorchidism is extremely strong, delays in surgery are worrisome. Kollin et al. [6] showed in a randomized controlled study that catch-up growth of the cryptorchid testis occurred after orchiopexy at 9 months, but not when surgery was delayed until age 3 years. Biopsy at the time of orchiopexy has shown that testicular histology tends to worsen with age. Moreover, interstitial fibrosis and poor tubular characteristics are more common in UDT repaired after 2 years [7]. Hadziselimovic and co-authors [8] found that in the case of intraabdominal testes, germ-cell counts may be normal in the newborn period, but if left untreated beyond 2 years of age there is a 30–40% chance of complete spermatogenic failure. Similarly, Canavese et al. [9] noted that both sperm counts and motility are higher in young men who underwent orchiopexy before the age of 1 year.

These robust literature data of the past few decades reveal that the recommended age for orchiopexy has been consistently lowered. In 1975, the American Academy of Pediatrics (AAP) still recommended surgery at age 4–6 years for undescended testis [12]. Once it became clear that the histological changes in testicular tissue associated with this condition are not congenital but in fact develop from the age of 6 months onward, the AAP and other international pediatric associations [13-15] devised
guidelines recommending orchiopexy at age 1 year. The rare reported cases of spontaneous testicular descent after the age of 6 months should not be cited to support a general policy of watchful waiting. Such observations are likely due to a missed distinction between retracted and undescended testis [16].

In 2014 the American Urological Association (AUA) published its guidelines on cryptorchidism. Statement 11 clarifies: “In the absence of spontaneous testicular descent by six months (corrected for gestational age), specialists should perform surgery within the next year (Standard; Evidence Strength: Grade B)” [17]. The current European Urological Association (EAU) guidelines confirmed that orchiopexy should be performed by age 12 months, or 18 months at the latest [18]. In the present study we have shown that for 50% of our patients these new more flexible guidelines were followed.

Physicians should be aware that the potential rare complications of orchiopexy – such as anesthesia-related incidents, hemorrhage, wound infection, recurrent undescended testis, testicular atrophy and injury to the vas deferens – are not more common when the procedure is undertaken in the child's first year compared to later, as long as it is performed by an experienced and well-trained pediatric urologist or surgeon [19].

In this study we showed that despite the conclusive guidelines the surgery is still performed much later than the recommended time. We also showed that pediatricians tend to refer patients at a median age of 1 year. The fact that 50% of the pediatricians initiate the process after the recommended age of surgery may be one of the major causes of delay in surgery. Another possible cause of delay might be that surgeons do not operate at the recommended age.

Another potential delay in surgery may be that despite AAP well-child guidelines [20,21], which explicitly state that a physical exam should be performed at every child visit and includes examination for testicular descent, studies in the USA have shown that only a minority of practicing pediatricians regularly follow such guidelines [22]. So, delay in referral may well be due to delay in diagnosis.

The results of this study emphasize the importance of early diagnosis and referral of children with UDT by primary care physicians and pediatricians. We recommend referral at age 6 months since the chance of spontaneous descent is very low and anesthesia is safe at this age, and because in many public institutions in Israel the time from referral to surgery might take several months. We believe that educating pediatricians and parents about the importance of early surgery should be the next step in improving management of these patients.

Our findings should be interpreted in light of their limitations, mainly the retrospective nature of the study. Data are limited to tertiary care, and as such, the patient population may not be generalizable to other academic or community hospitals in Israel. In phase II of the study, when a questionnaire was distributed to pediatricians, a regional bias might have occurred as we sampled pediatricians from a specific region of the country.

Ascending testes (testicles that are in the scrotum at birth and ascend later in life) may have been a confounder in our results. Although delayed diagnosis or treatment of cryptorchidism beyond the neonatal period is well documented, the relative proportion of cases of true testicular asent vs. congenital cases that were not identified or referred early for care remains unclear. Given the potential for change in testicular position throughout childhood, careful evaluation of the scrotum should be performed at every scheduled well-child examination [17].

Other than ascending testes we are not aware of any specific important confounders not included in the model; however, given the observational nature of this investigation, there may be unmeasured confounding influences on our results.

In conclusion, in our institute, half of the children with UDT underwent orchiopexy before age 1.5 years and most of them before age 2. These results are better than those of the USA and Germany but are not optimal. A major factor contributing to the delay in surgery is that pediatricians tend to refer the patient to surgery too late. Improving awareness regarding the best orchiopexy timing among primary care pediatricians and surgeons is mandatory.

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References

**Capsule**

**Risk factors for Middle East Respiratory syndrome coronavirus infection among health care personnel**

Health care settings can amplify transmission of Middle East respiratory syndrome coronavirus (MERS-CoV), but knowledge gaps about the epidemiology of transmission remain. Alraddai et al. conducted a retrospective cohort study among health care personnel in hospital units that treated MERS-CoV patients. Participants were interviewed about exposures to MERS-CoV patients, use of personal protective equipment, and signs and symptoms of illness after exposure. Infection status was determined by the presence of antibodies against MERS-CoV. To assess risk factors, the authors compared infected and uninfected participants. Health care personnel caring for MERS-CoV patients were at high risk for infection, but infection most often resulted in a relatively mild illness that might be unrecognized. In the health care personnel cohort reported here, infections occurred exclusively among those who had close contact with MERS-CoV patients. *Emerg Infect Dis* 2016; 22: 1915

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**Capsule**

**Personalized medicine by another name**

A vision of the Human Genome Project was that molecular profiling would enable identification of the molecular underpinnings of disease on an individual basis; “personalized medicine” became a watchword. However, a rebranding has been occurring since roughly 2012 in which the concept has been transmogrified into “precision medicine.” Juengst and colleagues describe conclusions from interviews and case studies conducted since 2011 with 143 supporters of personalized genomic medicine. The terminology change may minimize unrealistic expectations. However, a shift from “personal” could mean a reversal of the trend toward patient autonomy in decision making. The need for population-level sequencing to identify groups with particular molecular profiles carries its own risks in terms of pressures to participate and the possibility of stigmatization. *Hastings Cent Rep* 2016; 46: 21

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**Capsule**

**Worms remodel immune responsiveness**

Rural populations in less developed countries commonly show poor immunogenicity in vaccination programs. Helminth infestations remain common in some rural areas, and cellular immune hyporesponsiveness is a hallmark of chronic helminth infections. Community deworming programs are in general believed to be a good thing to reverse the morbidity that a large worm burden can impose on children. Wammes et al. set up a 2 year clinical trial to systematically test the immunological consequences of deworming in > 1000 villagers in Indonesia. After treatment, subjects showed significant immune remodeling, with reduced expression of CTLA-4 (cytotoxic T lymphocyte-associated antigen 4) and elevated pro-inflammatory cytokine responses to malaria parasite antigens. The challenge in the longer term could be that restored immune responsiveness might increase the prevalence of inflammatory diseases. *Proc Natl Acad Sci* 2016; 10.1073/pnas.1604570113

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