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Trends in the treatment of undescended testes: a pediatric tertiary care center experience from Croatia

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ABSTRACT

Objective Undescended testes (UDT) is the most common anomaly of the male genitourinary tract. The guidelines suggest that orchidopexy in congenitally UDT should be performed between 6 months and 18 months of age, while in acquired UDT, orchidopexy should be performed before puberty. Delay in treatment increases the risk of cancer and infertility. The main aim of this study was to determine whether we meet international standards in the treatment of UDT.

Methods The present study included all boys who underwent orchidopexy either due to congenital or acquired UDT in 2019 (from January 1 to December 31). For each group, laterality, location, associated anomalies, premature birth and in how many cases ultrasound was applied were determined. Additionally, for each group, the types of surgery, the number of necessary reoperations, and in how many cases atrophy occurred were determined. Finally, ages of referral, of clinical examination, and of orchidopexy were determined.

Results During this period, 198 patients with 263 UDT underwent orchidopexy. The median time of orchidopexy for the congenital group was 30 months, while that for the acquired group was 99 months. In the congenital group up to 18 months of age, orchidopexy was performed in 16 (16%) boys, while in the acquired group up to 13 years of age, orchidopexy was performed in 95 (96.94%) boys.

Conclusion Given the well-known risks of late treatment of UDT, orchidopexy needs to be performed much earlier, especially in the congenital group.

INTRODUCTION

Undescended testes (UDT) is the most common congenital anomaly of the male genitourinary tract. In patients with UDT, testes can most often stop in the abdominal cavity or in the inguinal canal on their way.¹ Congenital UDT occurs predominantly unilaterally in preterm infants. Most testes that do not descend at birth will complete the descent within the first 3 months of life, while spontaneous descent after the sixth month is extremely rare.²⁻³ After a series of studies reporting the negative effects of such laid testes, the recommendation from some associations is that treatment should begin

WHAT IS ALREADY KNOWN ON THIS TOPIC

- ⇒ The guidelines suggest that orchidopexy in congenitally undescended testes (UDTs) should be performed between 6 months and 18 months of age, while in acquired UDTs, orchidopexy should be performed before puberty.
- ⇒ Delay in treatment increases the risk of cancer and infertility.

WHAT THIS STUDY ADDS

- ⇒ In the largest Croatian tertiary pediatric center for the treatment of UDTs, orchidopexy, in the congenital group, is not performed on time.

HOW THIS STUDY MIGHT AFFECT RESEARCH, PRACTICE OR POLICY

- ⇒ In the largest Croatian tertiary pediatric center for the treatment of UDTs, orchidopexy should be performed much earlier, especially in the congenital group.

as early as 6 months and end no later than 18 months.⁴⁻⁶ Acquired UDT occurred in a group of boys whose testes are palpable in the scrotum and can be observed during neonatal and infant life, but will ascend over time.⁷⁻⁸ In this group of boys, it is important to note that orchidopexy before puberty can significantly reduce the risk of testicular cancer.⁹ Due to low success rates, there are fewer and fewer proponents of hormone therapy. Since hormonal treatment can improve fertility indices, it is recommended as an additional tool in addition to orchidopexy, especially in boys who have UDT on both sides.¹⁰⁻¹¹ The most common technique with a high success rate is Dartos pouch technique. For non-palpable intra-abdominal testes, the simplest and most accurate way of locating is diagnostic laparoscopy, after which Fowler-Stephens orchidopexy is most often used for testicular locating,¹²⁻¹³ but there are other techniques currently available that have not been used in our hospital.¹⁴⁻¹⁵ The severity of the outcome of untreated UDT, especially infertility and

cancer, requires early referral of such boys for definitive treatment.

METHODS

Study population and selection

The present research was conducted at the Children's Hospital Zagreb, the largest pediatric tertiary center for the treatment of children in Croatia. The total number of children aged 0–18 living in the area under the jurisdiction of our hospital is 300 000. We retrospectively analyzed the data of patients undergoing orchidopexy in 2019 (from January 1 to December 31, prepandemic year) by searching the hospital information system (IN2 BIS) of our institution. The information system was searched according to the following International Classification of Diseases, 10th Revision, codes: Q53.1 (undescended testicle, unilateral), Q53.2 (undescended testicle, bilateral), and Q53.9 (undescended testicle, unspecified). This study included all patients who underwent orchidopexy due to congenital or acquired, unilateral or bilateral UDT. Patients who underwent orchidopexy due to ectopic testis or had testicular agenesis were excluded from the study.

Study variables and outcomes

The primary outcome of this research was to determine the cumulative number of orchidopexy in 2019 and the distribution of orchidopexy performed on congenital and acquired UDT. For each group, the number of right-sided, left-sided and bilateral UDT, and in how many cases ultrasound was initiated preoperatively was determined separately. Depending on the position of the testes, the number of abdominal and inguinal testes was determined. In addition, we analyzed how many patients had inguinal hernia or hydrocele and how many children were born at term or prematurely. Finally, we determined from whom the patients were referred to the pediatric surgeon and the relevant associated anomalies.

The secondary outcome was to determine the method of surgical treatment (Dartos pouch technique or laparoscopic Stephen-Fowler procedure) and the number of necessary reoperations in relation to the initial position and side of the UDT.

The third and main outcome was to determine the age of the boys' referral at our institution, the age at which the boys were examined, and the age of the operative treatment, as well as the time between referral, clinical examination, and the orchidopexy. Regarding the valid consensus,⁶ we determined how many patients in the congenital UDT group were operated on before 18 months and how many patients in the acquired UDT group were operated on before 13 years of age, so until puberty.

Statistical analysis

Descriptive statistics were used to characterize the patient cohort. Categorical variables within and between the

observed groups were expressed as frequency and were analyzed using χ^2 test. Collected measurements were analyzed for normal distribution using the Shapiro-Wilk test. Continuous variables were expressed as mean with standard deviation (SD) and median (Mdn) with interquartile range (IQR) and were analyzed using the Student t-test or the Mann-Whitney U test as appropriate. The obtained data were analyzed using the Microsoft Excel software program (XLSTAT) for Windows V.2020.5.1 (Microsoft Corporation, Redmond, Washington, USA). The significance level of 0.05 was used.

RESULTS

During the 1-year period of 2019, a total of 204 children under the diagnosis of Q53 (undescended and ectopic testicle) were surgically treated at our institution. Six children were excluded because they had testicular agenesis or ectopy. A total of 198 children were included in the study. A total of 12 pediatric surgeons participated in the treatment of children with UDT.

Out of 198 children, 100 (50.51%) had congenital UDT, while 98 (49.49%) had acquired UDT (table 1). There were 31 (31%) bilateral cases in boys with congenital UDT, while in boys with acquired UDT, there were 34 (34.69%). As a result, a total of 263 orchidopexies were performed. In both congenital (62.32%) and acquired (67.19%) cases, the right side was predominantly affected. In the inguinal canal, there were 123 (93.89%) congenital and 126 (95.45%) acquired UDTs. Of the eight abdominal testes in the congenital group, four were within one side (two right and two left) of bilateral UDT, while of the six abdominal testes in the acquired group, two were within one side (one right and one left) of bilateral UDT. In the congenital group, 35.88% of patients with UDT had associated inguinal hernia or hydrocele, while in the acquired group, the prevalence was 21.21% ($p=0.0084$). In the congenital group, inguinal hernia or hydrocele was present bilaterally in seven boys (7%), while in the acquired group, it was present in only one boy (1.02%) ($p=0.0326$). Before the surgery, ultrasound was done in 67% of boys in the group of congenital UDT, while in the group of acquired UDT, 60.2% of cases underwent ultrasound. In the group of congenital UDT, 16% of boys were born before 37 weeks, while in the group of acquired UDT, 4.08% were born before term ($p=0.0054$). In both groups, patients were most often referred to pediatric surgeons by primary pediatricians (83% vs 40.82%), but parents themselves (23.47%) and school physicians (29.59%) played a significant role in the acquired group. In the congenital group, 19% of patients had associated anomalies, while in the acquired group, 11.22% had associated anomalies ($p=0.1271$) (table 2).

Out of a total of 263 orchidopexies performed, 249 (94.68%) were performed using the Dartos pouch technique (123 in congenital group and 126 in acquired group), while 14 (5.32%) were performed using the single-stage Fowler-Stephens procedure (eight in

Table 1 Characteristic indicators in patients undergoing orchidopexy

Variables	Congenital UDTs (100 patients, 131 orchidopexies)	Acquired UDTs (98 patients, 132 orchidopexies)	P value
Side, n (%)			
Right	43 (43)	43 (43.88)	0.5573
Left	26 (26)	21 (21.43)	
Position, n (%)			
Inguinal	123 (93.89)	126 (95.45)	0.5728
Abdominal	8 (6.11)	6 (4.55)	
Inguinal hernia/hydrocele, n (%)			
Yes	47 (35.88)	28 (21.21)	0.0084
No	84 (64.12)	104 (78.79)	
Ultrasound performed, n (%)			
Yes	67 (67)	59 (60.2)	0.3203
No	33 (33)	39 (39.8)	
Birth, n (%)			
Preterm/early term	16 (16)	4 (4.08)	0.0054
Full/late term	84 (84)	94 (95.92)	
Referred by, n (%)			
Primary pediatrics	83 (83)	40 (40.82)	<0.0001
School age medicine	2 (2)	29 (29.59)	
The parents themselves	9 (9)	23 (23.47)	
By surgeon (incidental finding)	6 (6)	6 (6.12)	
Referral time* (month)	14.00 (23.25)	74.50 (61.75)	<0.0001
Age of clinical examination* (month)	17.50 (26.25)	80.50 (54.50)	<0.0001
Age of surgery* (month)	30.00 (37.50)	99.00 (51.75)	<0.0001

*Data are presented with median (IQR).
IQR, interquartile range; UDT, undescended testis.

Table 2 Associated anomalies in children with congenital and acquired undescended testes

Congenital group (n=19)	Acquired group (n=11)
Dysmorphia (n=4)	Autism (n=2)
Prenatal hydronephrosis (n=2)	Trigonocephalus
Down syndrome (n=2)	Schizencephaly
Hip dysplasia	Atrial septal defect
Morbus Hirschsprung	Microcephaly
Microcephaly	Urinary tract malformation
Hypertrophic pyloric stenosis	Focal cortical dysplasia
Macrocrania	Congenital anemia
Arthrogryposis	Dandy-Walker syndrome
18q deletion syndrome	Multiple cardiac anomalies
Focal cortical dysplasia	
Ventricular septal defect	
Greig cephalopolysyndactyly syndrome	
Congenital hypogammaglobulinemia	

congenital group and six in acquired group). Within the congenital group, seven reoperations were performed due to inadequate position of the testis within the scrotum (six inguinal testis with four of the left side and two of the right side) and one abdominal left testis, while in the acquired group, three reoperations were performed (one inguinal right testis and two abdominal right testis). In total, 10 patients were reoperated and followed up for 2 years. During follow-up, all testes undergoing orchidopexy were palpated in the scrotum, but atrophy (>50% loss of volume after orchidopexy) was verified by ultrasound in nine (3.42%) testes (five in the congenital group and four in the acquired group).

The referral time to our institution, age at which the patient underwent clinical examination, and age at which the patient received surgery are summarized in [table 1](#). The Mdn time from referral to clinical examination was 3.5 months in the congenital group and 6 months in acquired group ($p=0.007$). The Mdn time from clinical examination to orchidopexy was 12.5 months in

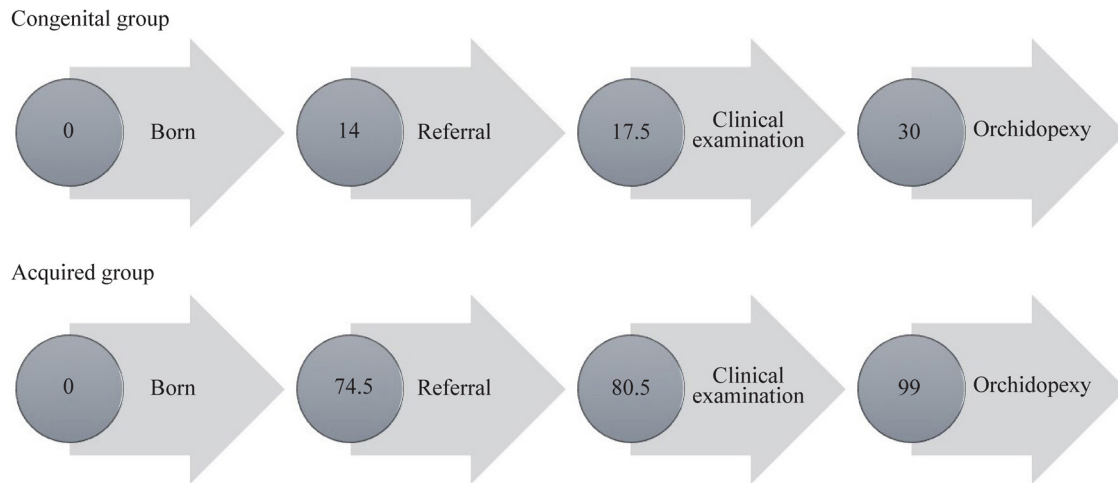


Figure 1 Median times (months) from birth to orchidopexy (born→referral→clinical examination→orchidopexy).

the congenital group and 18.5 months in the acquired group ($p=0.003$) (figure 1). In the congenital group up to 18 months of age, orchidopexy was performed in 16 (16%) boys, while in the acquired group up to 13 years of age, orchidopexy was performed in 95 (96.94%) boys (figure 2).

DISCUSSION

Our single-center retrospective study aimed, in addition to general characteristics, to determine whether children with congenital and acquired UDT were surgically treated on time, as negative repercussions of untimely treatment were clearly identified.¹⁶ At the end of the 20th century, scientists made it clear that the optimal time for treatment of congenital UDT is within the first year of life and that there are no harmful effects or risks to the child.¹⁷ Although the first comprehensive research on this topic did not clearly distinguish the group of congenital from acquired testes, the researchers expressed concern, since in less than 50% of boys orchidopexy was performed by the age of 2 years.¹⁸ Already in the same

year, it was considered necessary to determine whether there was a tendency to reduce the age at which orchidopexy was performed. For the Irish child population, the mean time of orchidopexy in one decade has been reduced by 3 years, while in the Danish population, for 6 years, the reduction was half a year, which instilled optimism.^{19 20} In two decades, the Mdn of orchidopexy performed in the Chinese population was reduced by 7 years, although only 2% of healthcare practitioners knew the recommended age for orchidopexy.²¹ Researchers in Germany have recognized that the theoretical knowledge of primary pediatricians and early referral is extremely important.²² Steckler *et al* reported in their study that only 30% of pediatricians and 14% of family physicians recommended orchidopexy between 6 months and 12 months of age.²³ Gerber *et al* pointed out the suspicion that poor quality clinical examination by pediatricians may also be a factor that may influence the untimely diagnosis of this condition.²⁴ The study by Cho *et al* showed that the intervention by an interactive survey aimed at general practitioners had positive effects on reducing referral time.²⁵

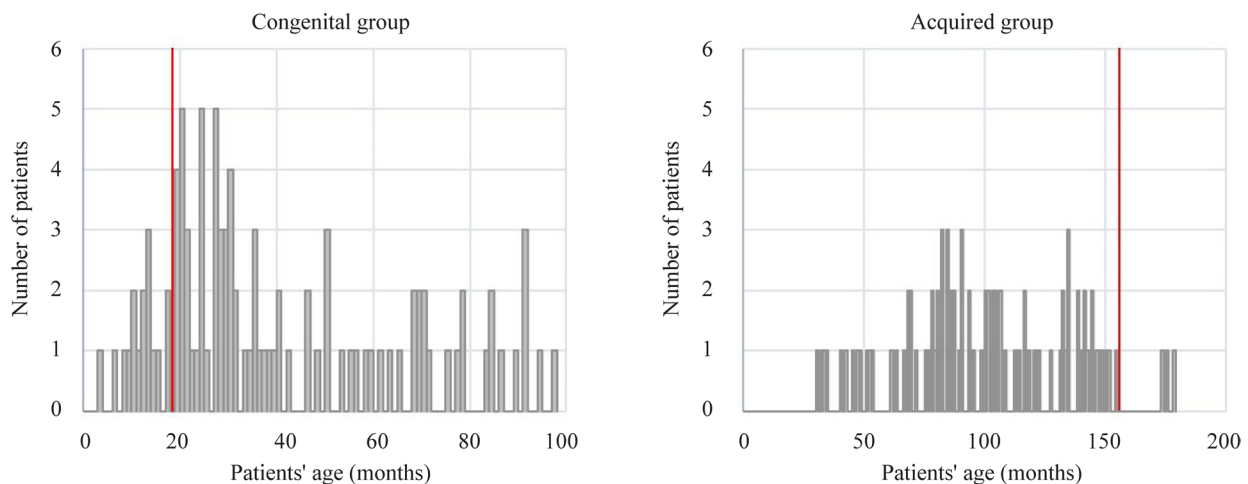


Figure 2 Number of patients by age (months) when orchidopexy was performed. The red line indicates the recommended age by which orchidopexy should be performed.

We also believe that the time of referral to our institution must be significantly reduced, especially for the congenital group. In addition to the pediatrician's and general practitioner's theoretical knowledge, several other factors have been identified that are significantly related to the time to surgery, such as the age of the diagnosing physician, the age of the surgeon performing the surgery, and the urbanization of the patient's residence.^{26–28} The study from the neighboring country also states that the residence of patients is extremely important, given that 28.13% of boys from urban areas underwent surgery by 18 months of age, while from rural areas, this percentage was only 15.46. A total of 22.6% of boys compared with our 16% underwent surgery before 18 months of age.²⁹ Compared with our study, a New Zealand study showed that the Mdn waiting time from referral to clinical examination was only 1.84 months (vs 3.5 months), while the Mdn from clinical examination to orchidopexy was only 2.95 months (vs 12.5 months).³⁰ At a single-center in Saudi Arabia, the Mdn waiting time for elective orchidopexy was 4.8 months, while in another center, the time was 8.1 months, but they had a slightly higher Mdn from referral to clinical examination (4.1 months).^{31,32} There is no doubt that we need to do orchidopexy for our patients faster than the day when the clinical examination was performed. It is interesting to note that even countries with a Mdn age for surgery of 1.05 and 1.49 years show a tendency towards a lower Mdn in the future.^{30,33} In a study by Chen *et al*, similar to our results, 32% of boys had an associated inguinal hernia, but in our study, we had more boys with bilaterally UDT (32.82% vs 11.3%).²⁶ On the other hand, according to a study by Zhao *et al*, only 14% of boys had an inguinal hernia or hydrocele, while 15.2% had bilaterally UDT. Analogous to our results, only 16.9% of boys underwent surgery by 18 months of age.²⁸ According to Marret *et al*, during the Mdn follow-up of 5.5 years, ultrasound verified atrophy in 11% of cases, while during our 2-year follow-up, atrophy was recorded in 3.42% of cases.³⁴ Although in our study the rate is not high, according to Elzeneini *et al*, the rate of testicular atrophy is much lower in two-stage Fowler-Stephens orchidopexy, which should guide us in the future.³⁵ Although meta-analysis concluded that ultrasound cannot reliably locate non-palpable testes and that ultrasound is unnecessary in preoperative evaluation of boys with UDT because it does not affect final surgical management, according to a study by Soto-Palou *et al*, 46.4% of boys underwent ultrasound preoperatively.^{36,37} In our study, as many as 63.6% of patients underwent ultrasound, which certainly extended the time to orchidopexy. Ultrasound was mostly requested by pediatric surgeons. This habit will certainly need to be reduced by adequate education of all stakeholders involved in treatment. Comprehensive studies that clearly distinguish congenital from acquired UDT began to appear only a few years ago. In the study of Boehme *et al*, almost identical results were observed in the proportion of congenital and acquired UDT, which is confirmed by our study. The study also

found that there were more children born prematurely in the congenital group than in the acquired group (51% vs 34%), which was confirmed by our results (16% vs 4%). Regarding patients who had an associated inguinal hernia, a significantly higher number was recorded in the congenital group (50% vs 18%), which was confirmed by our study (36% vs 21%).³⁸ It should be emphasized that the time interval, from diagnosis to orchidopexy, was only 3 months. Regarding the congenital UDT, a study by Zvizdic *et al*, analogous to our results, found that the right side is more often affected. An almost identical percentage of boys had an associated congenital inguinal hernia. Although we had a better Mdn referral time (14 months vs 23 months), the Mdn time of orchidopexy was far worse (30 months vs 24 months).³⁹

In the future, we must strive to surgically treat children with congenital UDT much earlier, up to 18 months of age, in order to prevent long-term consequences of untimely treatment. Children with undescended testicles will have to get more priority appointments for surgery. Also, unnecessary referrals to ultrasound should be reduced, except in specific indications that require it. It will certainly be necessary to conduct extensive education and public health intervention for pediatricians and family physicians in order to move the time of referral to an earlier age. We will examine the real reasons for the delay in referral with a questionnaire that we plan to conduct and analyze soon.

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