Early outcome of orchiopexy - a retrospective review of patients treated for cryptorchidism at Örebro University Hospital

Version 2

Author: Fanny Bergman
Supervisor: Beata Persson, MD
Department of Urology
Örebro University Hospital
ABSTRACT

Introduction: Cryptorchidism, clinically known as undescended testes, is the most common genital anomaly in boys, in which one or both of the testes are not found at their normal position in the scrotum. Cryptorchidism is a strong risk factor for both infertility and the development of testicular cancer later in life. The treatment is surgical with orchiopexy, where the testis is brought down and placed in the scrotum. The Nordic guidelines states that surgery should be performed between the ages of six to 12 months, to prevent the development of cancer and generate the best possible conditions for normal testicular growth and spermatogenesis.

Objective: The objective of this retrospective study is to analyze the quality of the surgical treatment for cryptorchidism at the Urology Department of Örebro University Hospital, in terms of age at orchiopexy and anatomical outcome.

Material and methods: The study is a retrospective descriptive study. The medical records at the Department of Urology were searched to identify patients who underwent orchiopexy for cryptorchidism during the time period 2010-11-19 – 2013-11-28. A total of 86 patients with 106 undescended testes were included. The patients’ medical records were viewed and selected variables were registered and analyzed.

Results: Out of the 104 primary orchiopexies performed, 83% had an anatomically successful outcome after one orchiopexy, and 91% had a successful outcome after reoperation. The median age at first surgery was 2.6 years (range 0.9-12.7 years) and the mean age was 4.25 years. The highest number of orchiopexies was performed on patients at the age of 1-2 years.

Conclusion: This review shows that the anatomical outcome after surgery is similar to the results reported in published studies. However, the recommendations that boys with cryptorchidism should be operated between the ages of six to 12 months are not followed.
CONTENTS

ABSTRACT .......................................................................................................................... 2

INTRODUCTION .................................................................................................................. 4

MATERIAL AND METHODS .............................................................................................. 6

RESULTS ............................................................................................................................ 8

DISCUSSION ...................................................................................................................... 11

CONCLUSION .................................................................................................................... 14

REFERENCES .................................................................................................................... 15
INTRODUCTION

Background
Cryptorchidism, clinically known as undescended testes, is the most common genital anomaly in boys, in which one or both of the testes is not found at their normal position in the scrotum. This condition affects up to 6% of newborns, and the prevalence is even higher, 17% in preterm newborns. Approximately 70% of these testes descend spontaneously during the first year of life, especially during the first three months, and the overall prevalence among one-year-old boys is 1-2%. Bilateral cryptorchidism is seen in 10-12% of cases. [1,2]

Cryptorchidism is either congenital or acquired (ascending testes). Congenital cryptorchidism is associated with low birth weight and length, early gestational age and short penile length at birth. Boys with ascending testes have the same weight and length as non-cryptorchid boys, but with a shorter penile length. [2] Even though the majority of boys born with undescended testes experience spontaneous postnatal descent, up to 22% of these so called “late descenders” are later found with a retained testis. [3] Wohlfahrt-Veje et al distinguishes this condition from acquired cryptorchidism where the testes have a normal scrotal position at birth, and defines it as recurrent cryptorchidism. [4] The causes for undescended testes are still unknown. Since the descent of the testes depends on both anatomical, endocrine, mechanical and paracrine factors, it is believed that disturbances in any of these factors can contribute to the genesis of the condition. [5] At 12 weeks of gestation the testes are located in the inguinal region, the migration through the inguinal canal takes place at around week 28 and the testes reach the scrotum at approximately week 33. [6] The location of the undescended testis can be abdominal, inguinal or upper scrotal depending on where the descending of the testis was arrested. [7]

A strong risk factor for congenital cryptorchidism is prematurity. Associated risk factors are low birth weight, with a gradient of increasing risk with decreasing birth weight, and being small for gestational age. [8,9] An increased risk is also seen in firstborn boys. [9,10] Other well-known risk factors are breech presentation and substantial vaginal bleeding. A Swedish study published in 2008 showed an increased risk for cryptorchidism with maternal use of nicotine substitutes, but not with
maternal smoking, during pregnancy. The study also showed an increased risk with infertility treatment by intrauterine insemination. [9]

It is well described in the literature that cryptorchidism is a strong risk factor for infertility as well as testicular cancer. [11,12] Untreated bilateral cryptorchidism results in infertility due to severely impaired spermatogenesis. [12] The impaired spermatogenesis is at least partly due to a relative hyperthermia in the suprascrotal position, which causes germ cell depletion. [13] It is also shown that men with former bilateral cryptorchidism who underwent surgery in childhood have a significantly lower sperm count and paternity rate compared to control groups. Men with former unilateral cryptorchidism have a small decrease in sperm count but the paternity rate approaches that of the control group. [12] The lifetime relative risk of developing testicular neoplasia (carcinoma in situ and invasive tumors) among men treated for cryptorchidism before the age of 13 is 2.2 compared to the general population. Among men treated after the age of 13, the relative risk increases to 5.4 compared to the general population. This shows that early treatment is important to prevent the development of cancer later in life. [14]

Historically, cryptorchidism has been treated with two principally different methods, hormonal therapy with human chorionic gonadotropin (hCG) or gonadotropin releasing hormone (GnRH), or primary surgery. The hormonal therapy is no longer recommended due to poor efficacy, and has gradually been replaced with surgery. In the Nordic countries, consensus has been reached and the recommended treatment is surgical with orchiopexy, in which the testicle is brought down to its normal position in the scrotum. [15] Orchiopexy can be performed with several different techniques, and the main goal is to establish the testicle in the scrotum without iatrogenic atrophy and without it ascending again. There are two different surgical techniques for fixation of the testicle in the scrotum. The classical way is to put a suture through tunica albuginea of the testis and the scrotal wall and thereby prevent the testicle from moving upwards. This method is associated with a risk of damaging the testicle, leading to atrophy and infertility. A newer method consists of creating a pouch in the dartos fascia in the scrotum, into which the testicle is put, and the window closed. This method has been seen to have a smaller risk of atrophy and infertility and is thereby preferred, even though there is a risk of the testicle ascending again. [16]
It has long been debated at which age surgery should be performed to optimize testicular growth and spermatogenesis. [15,17] It is shown that the greatest results in testicular catch-up growth occur when surgery is performed before the patient is two years old. [17] Testicular volume reflects the number of germ cells very well in early childhood. Furthermore, the number of germ cells shows great depletion if surgery is carried out at the age of 36 months compared to nine months. [18] It has also been debated whether surgery at an early age is more difficult and has a higher risk for complications and non-satisfactory anatomical position that demand reoperation. Studies have reported inferior results in patients operated at an early age, and it has been discussed whether the benefits from early surgery outweigh the increased risk. [19,20] Nevertheless, the Nordic recommendations now state that surgery should be performed after the age of six months, because of the high number of late descending testicles during the first months of life, and before the age of 12 months, to generate the best possible conditions for normal testicular growth and spermatogenesis. If the undescended testis is diagnosed after the age of 12 months, surgery should be performed as soon as possible. [15] Studies have shown anatomical success rates of orchiopexies to be 85-95%. [16]

**Objective**
The objective of this retrospective study is to analyze the quality of the surgical treatment for cryptorchidism at the Urology Department of Örebro University Hospital, in terms of age at orchiopexy and anatomical outcome.

**MATERIAL AND METHODS**

*Design*
The study is a retrospective descriptive study where the patients’ medical records were viewed.

*Patient population and selection*
All patients with cryptorchidism who underwent their first orchiopexy at Örebro University Hospital (USÖ) during the time period 2010-11-19 – 2013-11-28 were included in the study. These patients were found by searching the hospital’s medical
records in the database “Kliniska Portalen” for the procedure code KFH00 (surgery code for orchiopexy). A total of 118 patients were identified. Out of these, 32 patients were excluded due to following reasons: 14 patients had at least one orchiopexy prior to 2010-11-19; seven patients underwent orchiopexy because of other reasons than cryptorchidism (for example testis torsion or hydrocele); two patients had moved and follow-ups could not be found; one patient had died prior to the follow-up and eight patients were found in the register twice because of reoperations. Ultimately, 86 patients, with a total of 106 undescended testes, were included in the study. Reviews of the patients’ medical records were made in November 2014.

Study variables
All the information in the patients’ medical journals from the Urology Department was viewed. The variables registered were: age at first surgery; if the cryptorchidism was unilateral or bilateral; whether the testis could be palpated prior to surgery; any other medical condition; whether the testis could be brought into the scrotum at surgery; whether the testis were removed; clinical position of the testis at follow-up; need for a reoperation; and if any operative or postoperative complications occurred.

Definitions
The surgery was considered anatomically successful if the testis were palpable in the scrotal area at the postoperative control that was carried out about six months after surgery. If successful, the patient did not need further follow-up. If unsuccessful, the patient was re-operated and had another postoperative control after six months. Postoperative complications were defined as having sought medical treatment for complications that occurred after and were related to the surgery.

Ethics consideration
The head of the department of Urology at USÖ have approved analysis of the medical records. Since this study is a quality audit with the aim to improve medical quality, and is not to be published, no consent has been collected from the patients. Nonetheless, the patients have been de-identified and given a patient number.
RESULTS

Surgical outcome

A total of 86 patients with 106 undescended testes were reviewed. Out of these, 61 testes (58%) were palpable before surgery. The cryptorchidism was bilateral in 20 patients (23%). Out of the 106 undescended testes, 99 (93%) testes were successfully brought down into the scrotum at first surgery. In two cases (1.9%), the testicle was found to be missing at the operation. By the time for postoperative follow-up, 86 out of the 104 (83%) orchiopexies performed were considered anatomically successful (Figure 1).

Figure 1. Flowchart of the 106 undescended testes.
Follow-ups had not yet been carried out by the time of data collection in two patients and their results are therefore unknown. In one of the non-successfully operated patients it was decided that orchiectomy should be carried out once the patient has gone through puberty. Due to unacceptable testicular position, fifteen patients had a reoperation. Out of these, nine were considered anatomically successful by the time of follow up. Orchiectomy was performed on two patients due to atrophied testicular tissue. Follow-ups had not yet been carried out in three patients and the results on them are therefore unknown. One patient has undergone two reoperations with still no acceptable result by the time of this review.

Out of the 104 operated undescended testes, 95 (91%) had an anatomically successful final result. A total of five patients had not been followed up by the time of data collection and the results of their surgery remain unknown.

Complications
One perioperative complication occurred, where the vas deferens was accidentally cut during the procedure. Postoperative complications occurred in two patients. One of them searched medical treatment four days after the surgery due to a wound infection. The infection was successfully treated and no further complications followed. Another patient experienced severe pain in his right groin six weeks after surgery and had to be reoperated acutely. The reoperation was successful and the patient did not have any further complications.

Age at surgery
The median age at first surgery was 2.6 years (range 0.9-12.7 years) and the mean age was 4.25 years. The highest number of orchiopexies was performed on patients at the age of 1-2 years (Figure 2).
Figure 2. Age distribution at the time for first surgery (n=106).

The best results were seen in patient groups “0-1 years” and “10-12 years” where the surgery was successful in 89% of the cases (Table 1). The poorest results were seen when the first operation was performed at the age of three years, where the surgery was successful in 57% of the cases. The three patients who experienced surgery-related complications were seen in different age groups, with the ages of 2.7, 3.0 and 4.4 years, respectively.

Table 1. Outcome of first surgery related to age.

<table>
<thead>
<tr>
<th>Age at first orchiopexy</th>
<th>Total n</th>
<th>Unacceptable position n</th>
<th>Follow-up missing n</th>
<th>Successful n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0-1</td>
<td>35</td>
<td>4</td>
<td></td>
<td>31 (89)</td>
</tr>
<tr>
<td>2</td>
<td>23</td>
<td>3</td>
<td>2</td>
<td>18 (78)</td>
</tr>
<tr>
<td>3</td>
<td>7</td>
<td>3</td>
<td></td>
<td>4 (57)</td>
</tr>
<tr>
<td>4-6</td>
<td>7</td>
<td>1</td>
<td></td>
<td>6 (86)</td>
</tr>
<tr>
<td>7-9</td>
<td>23</td>
<td>4</td>
<td></td>
<td>19 (83)</td>
</tr>
<tr>
<td>10-12</td>
<td>9</td>
<td>1</td>
<td></td>
<td>8 (89)</td>
</tr>
</tbody>
</table>

Other medical conditions or anomalies
A total of 11 patients (10%) had other medical conditions or anomalies in addition to their cryptorchidism, where the most common was phimosis followed by hypospadias (Table 2). The first surgery was anatomically successful in nine (82%) of these patients and two patients had a successful result after one reoperation.
Table 2. Other medical conditions and anomalies in the 86 patients treated for cryptorchidism.

<table>
<thead>
<tr>
<th>Medical condition or anomaly</th>
<th>No. of patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>Phimosis</td>
<td>3</td>
</tr>
<tr>
<td>Hypospadias</td>
<td>2</td>
</tr>
<tr>
<td>Downs syndrome</td>
<td>1</td>
</tr>
<tr>
<td>Ehler-Danlos syndrome</td>
<td>1</td>
</tr>
<tr>
<td>Fetal alcohol spectrum disorder</td>
<td>1</td>
</tr>
<tr>
<td>Pericentric inversion of chromosome 2</td>
<td>1</td>
</tr>
<tr>
<td>Cleft lip and palate + pulmonary valve stenosis</td>
<td>1</td>
</tr>
<tr>
<td>Sacral agenesis, esophageal atresia and imperforate anus</td>
<td>1</td>
</tr>
</tbody>
</table>

**DISCUSSION**

*Surgical outcome*

The review of the results of surgical treatment for undescended testes showed that 83% had an anatomically successful outcome after one orchiopexy, and 91% had a successful outcome after reoperation.

A large review made 2006 by Taran et al reports orchiopexy success rates for inguinal testes to be over 95% and between 85-90% for abdominal testes. [16] The outcome after first orchiopexy in Örebro did not meet these high rates. The reasons for that might be that many of the studies included in their review had different inclusion criteria, for example that the testis had to be palpable before surgery, and thus had a more selected patient population. The present study included everyone who went through orchiopexy for undescended testes at USÖ during the time period, and were not specifically selected, and this might contribute to the results. If patients in this study with no follow-up were excluded, a total of 96% (95 out of 99) would have had a successful final result, and the result would have approached the international standard. Another factor to consider is that many of the published studies in this field are made at large specialized hospitals with large patient populations where orchiopexies are frequently performed. Smaller hospitals with inferior results, where orchiopexies are not performed as often, are probably less likely to publish their results, which could lead to publication bias.
A recent retrospective study from a regional hospital in Norway reports that orchiopexies were immediately anatomically successful in 81% of the cases, and 94% were successful after reoperation. [20] This is similar to the results in this study, and a relevant comparison since it is made in a Nordic country where the surgery guidelines are the same and where it is likely that the study population is very similar. Also, they had very similar inclusion criteria, including all patients that underwent orchiopexy during the years 2001 to 2010 at Telemark Regional Hospital.

Age at orchiopexy

The Nordic guidelines [15] as well as the American guidelines [21] now recommend that orchiopexy should be performed between the ages of six to 12 months. The present study shows that this is not achieved in our hospital. Only one patient was operated before the age of 12 months. The mean age at first surgery was 4.25 years and 35% were operated before the age of two years. Other authors have presented similar findings. The Norwegian study reports a mean age of 5.1 years and median age 3.7 years by the time for first orchiopexy. [20] In a Danish study from 2011 the mean age at first surgery was 3.3-3.8 years. [22] A large American study, with over 28,000 boys who underwent orchiopexy, showed that mean age for first surgery was 4.4 years. Of these patients, 18% underwent orchiopexy before the age of one year and 43% did so before the age of two years. [23] The mean age is similar to our findings, but the amount of patients operated during the first year of life is significantly higher in the American study. The finding that so many of the patients with undescended testes are operated outside the recommended time frame is thus not unique for our institution, but rather a common concern among hospitals in many countries.

There may be several explanations as to why so many patients are operated at an older age than 12 months. Before coming to the Urology Department the boys have to be referred from their district health care centre where they first get examined. It is possible that this process is delayed, due to late recognition of the condition or due to the waiting period before the patient gets to see a urologist at the hospital. When a urologist has confirmed the cryptorchidism the patient will be placed on the waiting list for surgery. There may be a waiting period of several months before the patient finally gets operated. This is a factor of potential improvement. Another reason why
surgery is performed at an older age may be that many of the patients undergoing orchiopexy have acquired cryptorchidism. This is a reasonable explanation as to why the number of orchiopexies performed reaches a new peak at the ages of seven to eight years in this review. In a Dutch study from 2003 the mean age at referral for acquired cryptorchidism was 8.4 years [24], which corresponds very well to the findings in the present study.

This review showed that the best results were seen in patients operated at one year of age, and 10 to 12 years of age, respectively. These results differ from published studies that have reported inferior results in the youngest patients and a higher success rate with higher age. [19,20] However, it is not possible to make any conclusions out of the present review since the number of patients varied a lot in the different age groups. The age group with the poorest results had only seven patients. Although, the success rate of 89% in the 35 patients operated before two years of age should be considered a satisfactory result. Only three cases of surgery related complications were seen, and they were found in different age groups. This suggests that complications occur randomly and is not increased in a specific age group. Although, it is not possible to draw any general conclusions regarding complication rates due to the small study population.

Method
There are some weaknesses in this retrospective review. The medical notes were very differently written and sometimes very short, depending on which doctor the patient has had. Only the procedure code KFH00 were reviewed and it is possible that some surgeons have used a different code and that not all orchiopexies were included. A total of five patients included in the study had not yet been followed up and the results on them could potentially alter the final results, although not significantly. Another weakness is the lack of blindness in the follow up examinations, where many of the boys were examined by the same doctor that performed the surgery, which could potentially lead to false-positive results. This is probably not a real issue since the boys are followed by their district health care centre or school and would have been referred to the Department of Urology and reoperated if the testes were not found in the scrotum at the regular examinations. Another limitation is the number of patients
reviewed. Conclusions regarding age at orchiopexy could not be made because some age groups were too small.

CONCLUSION
The purpose of the current study was to investigate the quality of the surgical treatment for cryptorchidism at Örebro University Hospital. This review shows that the anatomical outcome after surgery is similar to the results reported in published studies. However, the recommendations that boys with cryptorchidism should be operated between the ages of six to 12 months are not followed. These findings suggest that this is a factor of potential improvement and it is desirable that action is taken to improve adherence to current guidelines.

This study only reviews early anatomical outcome after orchiopexy and does not say anything about the function of the operated testis. It would be interesting to investigate the testicular function in adult patients who underwent orchiopexy for cryptorchidism in childhood, in terms of sperm count and paternity rate. This could be an object for a later study.
REFERENCES


