석사 학위논문

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## - Reasons and effects of delayed orchiopexy -

2014년 2월

서울대학교 대학원

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by

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A thesis submitted to the Department of Urology in partial fulfillment of the requirements for the Degree of Master of Science in Clinical Medical Science at Seoul National University College of Medicine

Feb 2014

Approved by Thesis Committee:

Professor 정성진 Chairman

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# Abstract

# Reasons for delayed orchiopexies in a Korean tertiary care hospital

**서울대학교 대학원**

**임상의과학과**

**안현수**

**Introduction:** Since the 1990s, it has been well known orchiopexies should be performed no later than 2 years of age. Nevertheless, studies from other countries report a substantial number of delayed orchiopexies. Based on the analysis of a tertiary care hospital database, we aimed to investigate the incidence of delayed orchiopexies performed in patients after 5 years of age, and to understand the causes of such delays and the possible consequences.

**Methods:** We retrospectively analyzed the surgical database of our institution between 2004 and 2012, and detected patients who underwent orchiopexy later than 5 years of age. Reasons for delayed orchiopexies were studied and the possible consequences of delayed orchiopexies were assessed with respect to surgical difficulty and testicular volume.

**Results:** We found 160 cases of delayed orchiopexies, which accounted for about 15% of all orchiopexies performed. Two major reasons for delay were related to the parents of the child; i.e. parental delay and parental request for

the treatment of persistent retractile testis. Acquired cryptorchidism was found in 21 (13.1%) cases, mainly associated with hypospadias. Surgical difficulty, especially due to short testicular cord, was encountered in 48 cases (30.2%), and a comparison with age matched normative values showed substantially smaller testicular volume.

**Conclusions:** Despite well established guidelines for optimal age of surgery, 15% of orchiopexies were not performed at a proper time. Improved propagation of an optimal age limit is necessary for reducing the rate of delayed orchiopexies considering increases in surgical difficulty and potential testicular growth retardation.

**Keywords:** Cryptorchidism, Orchiopexy, Tertiary Care Centers
**Student Number: 2012-22705**

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# INTRODUCTION

Cryptorchidism is the most common genital anomaly identified in males at birth with a prevalence of about 1% at 1 year of age. (1,2) After the first year of life spontaneous testicular descent is unlikely to occur and it has been postulated that testicular position at that time might be final, or that in some cases, testicular ascent may occur. (3) Since cryptorchidism is associated with infertility, malignancy and cosmetic concerns, orchiopexy has been proven necessary for prevention of such conditions.

Although various guidelines (4-6) may differ regarding the age at which an orchiopexy should be performed, it is agreed that it should be performed at least before 18 months of life. These recommendations are based on medical and psychological postulations such as a higher risk of malignancy and infertility in the undescended testes (UDT). (4) The Nordic consensus on treatment of UDT (5) advocates treatment at 6-12 months of age. However, reports from several countries (7-10) have indicated that these theoretical advantages or guidelines for early orchiopexy have not been applied in clinical practice. Data from many surgical divisions in different countries show that orchiopexies are still being performed late in childhood despite several national and international recommendations. Iatrogenic trapping by previous surgery, parental delay and delay in referral have been speculated, but the data is sparse and researchers could not elucidate possible causes.

Another interesting explanation for delayed orchiopexy is the

presence of acquired cryptorchidism (AC). Although a testis can be found in the scrotum during a previous examination, it can ascend as the child grows older. According to Hack and associates (11) the prevalence of AC can reach 73.4% and the median age of orchiopexy can be postponed until 8.4 years of age. Thus, this could be another explanation of late orchiopexy, though its presence has not been verified in Korean published data.

Retractile testis (RT) is regarded as a normal variant of UDT and does not require orchiopexy, since the testis will descend spontaneously. However, the distinction between RT and AC is not clear, which may explain the wide range of prevalence of testicular ascent among patients who were followed up for RT. (12-14) Furthermore, the usefulness and feasibility of annual follow-up until puberty, when both AC and RT are likely to spontaneously descend, has not been established.

In tertiary care hospitals, children with serious medical conditions often miss the optimal surgical timing for orchiopexy. Due to the more urgent need for treatment of coexisting medical conditions, which affect more vital organs, the presence of UDT is often forgotten. Only after the more serious illnesses have been treated, underoging delayed orchiopexies finally become the main focus. This may be a plausible scenario, but relevant statistics supporting such a hypothesis have not been reported so far.

To provide additional information to our current database, we analyzed the data of delayed orchiopexies performed at our institution. Since there has been only one report in the setting of a tertiary referral hospital, our data may be valuable to classify and understand the possible reasons of delayed orchiopexies. Another objective of our study was to evaluate the effects of delayed orchiopexies. Based on our surgical data, we tried to study

the potential effects of delayed orchiopexies on surgical difficulty and testicular volume. We assumed that a delay in surgery might be associated with shortness of cord length, leading to difficulty in surgery. Moreover, it could result in retarded testicular growth compared to the mean normative value of age matched Korean boys. (15)

# MATERIALS AND METHODS

We retrospectively analyzed the records of all orchiopexies for UDT performed in patients older than 5 years of age from January 2004 through June 2012. We reviewed medical records and analyzed data concerning the age at operation, reasons of delayed surgery, laterality, testis size measured during operation and difficulty in cord lengthening.

The reasons of delayed surgery were categorized as follows: [1] AC, [2] parental request for the treatment of persistent RT, [3] delay due to coexisting medical conditions (missed the surgical timing due to treating other medical conditions), [4] re-operative orchiopexy (iatrogenic trapping following previous orchiopexies or herniorrhaphies), [5] parental delay (parents did not do nothing despite the presence of overt cryptorchidism), and [6] delayed referral by the primary physician.

We defined AC when there had been a previous medical record confirming scrotal location of testis. Parental delay included unintentional late detection (recent parental recognition of an empty scrotum without prior knowledge of the testicular position) and intentional negligence (parents knew that their son's testis was elevated, but did not seek medical consultation).

Orchiopexy was performed using the conventional technique of placing the testis in the subdartos space. Difficulty in lengthening was defined when the testis did not reach the mid-scrotum following the release of the processus vaginalis and cremasteric muscle during orchiopexy.

The effect of delayed orchiopexies was assessed by comparing the size of operated testes with those of age-matched Korean boys.[15] Data were

entered and expressed using SPSS 18 for Windows (SPSS Inc, Chicago, IL, USA). Chi square was used to examine the difference of proportion. p value lower than 0.05 was considered significant.

# RESULTS

We analyzed 963 patients from our database, who underwent 1084 orchiopexies during the period of this study. A total of 125 (12.9%) patients underwent 160 (14.6%) delayed orchiopexies (81 right, 79 left-sided). Their median age at operation was 8.0 (5-15) years. The incidence of orchiopexies increased from the age of 5 and peaked between 8-9 years of age, then abruptly decreased after 10 years of age (Figure 1).

The reasons of delayed orchiopexies in this population are described in Table 1. Parental delay and parental request for the treatment of persistent RT accounted for more than half of cases. Of the 54 cases of parental delay,

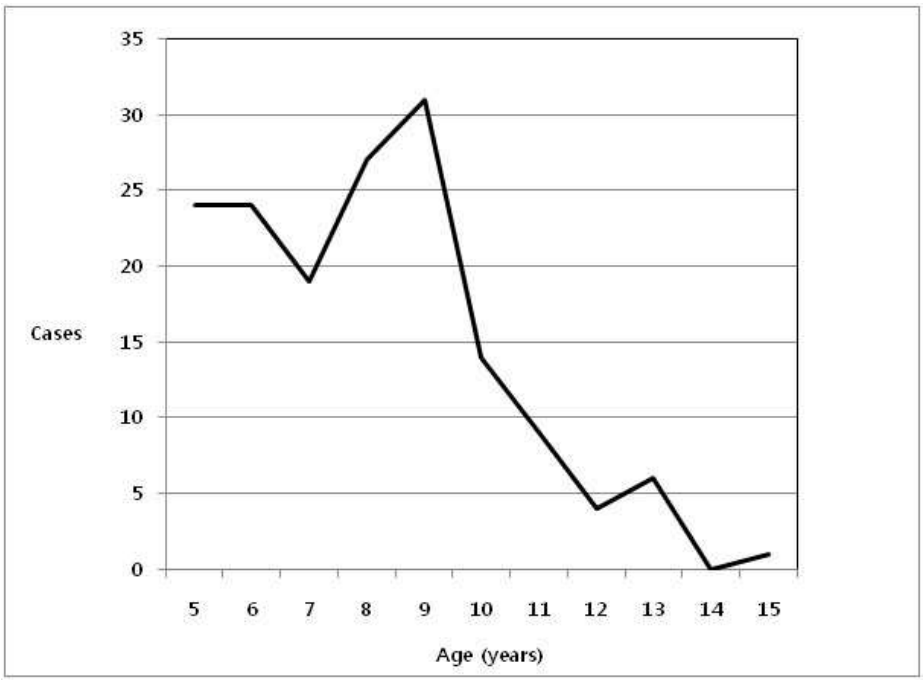


**Figure 1.** Age distribution of all patients who underwent delayed orchiopexy regardless of age

**Table 1.** Reasons of delayed orchiopexy

| Reasons | N = 160 | % |
|---|---|---|
| Acquired cryptorchidism | 21 | 13 |
| Parental request for persistent retractile testis | 33 | 21 |
| Iatrogenic after previous orchiopexy or inguinal surgery | 24 | 15 |
| Delay due to other medical conditions | 14 | 9 |
| Parental delay | 54 | 34 |
| Delayed referral | 13 | 8. |
| Unknown | 1 | 1 |

**Table 2.** Association of various reasons of delayed orchiopexy with the difficulty in cord lengthening (N=159, except 1 case of unknown reason)

| Reasons (N) | Difficult cord lengthening (N/%) | |
|---|---|---|
| | Yes | No |
| Acquired cryptorchidism (21) | 5 (24) | 16 (76) |
| Persistent retractile testis (33) | 1(3) | 32 (97) |
| Iatrogenic (24) | 10 (42) | 14 (58) |
| Delay due to other medical conditions (14) | 6 (43) | 8 (57) |
| Parental delay (54) | 22 (41) | 32 (59) |
| Delayed referral (13) | 4 (31) | 9 (69) |

28 and 26 cases were attributed to unintentional late detection and intentional negligence despite prior recommendation by primary physician, respectively. AC was found in 21 (13.1%) of cases. Of these cases, 16 (76%) had comorbidities including hypospadias (11 patients), Prader-Willy syndrome (2 patients) and cerebral palsy (2 patients).

During operation, difficulty in cord lengthening was noted in 48 (30.2%) cases (Table 2). Except for the case of the RT, which showed

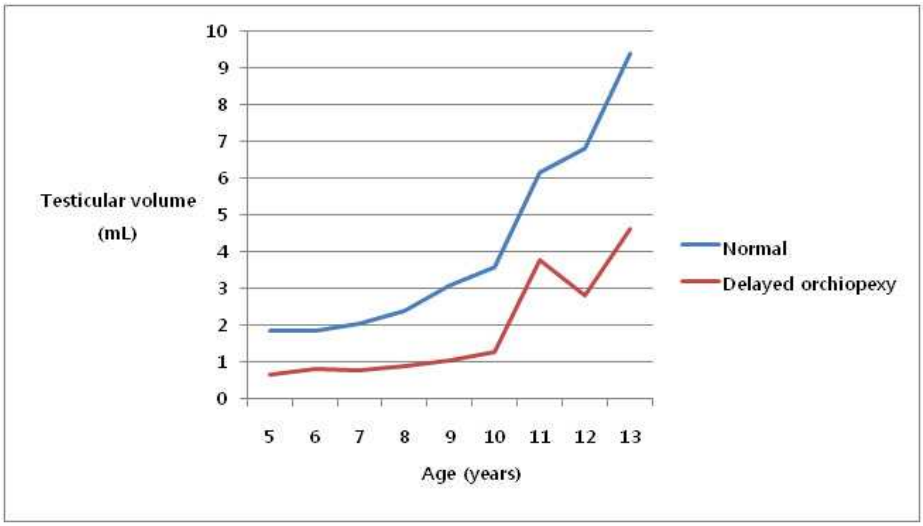


**Figure 2.** Mean age matched testicular volume of those who underwent delayed orchiopexy. For comparison, age matched values of Korean boy are depicted

**Table 3.** Age-matched comparison of measured testicular volume of those who underwent delayed orchiopexy and Korean normative value.

| Age (yr) | Measured testicular volume (mL)* | Korean normative value (mL) | P value† |
|---|---|---|---|
| 5 | 0.675 | 1.855 | <0.001 |
| 6 | 0.824 | 1.860 | <0.001 |
| 7 | 0.776 | 2.075 | <0.001 |
| 8 | 0.876 | 2.410 | <0.001 |
| 9 | 1.039 | 3.070 | <0.001 |
| 10 | 1.261 | 3.600 | <0.001 |
| 11 | 3.759 | 6.150 | 0.050 |
| 12 | 2.812 | 6.795 | N/A |
| 13 | 4.594 | 9.375 | N/A |

N/A: not assessed due to nonnormal distribution

*calculated using modification of the Lambert formula: 0.71 x (length) x (width) x (depth)

†using one-way t-test

difficulty in only 1 case, the difficulty was nonspecifically distributed to each reason ($p>0.05$).

Data for testicular volume measurement was available in 116 cases. Figure 2 showed the mean testicular volume in accordance with age. Compared to the mean Korean normative data which was depicted for reference, significantly lower mean testicular volume was observed in the present study (Table 3).

# DISCUSSION

In this study, we reviewed the database of our hospital in order to detect factors that can contribute to delayed orchiopexies. Such delays have been reported elsewhere, but the causes have not been well clarified, especially in a tertiary care setting. Since delays in orchiopexies can lead to testicular growth retardation, can be detrimental to future fertility, and may increase risk of testicular cancer development, it is necessary to know why orchiopexies were not performed at a proper time. Understanding such causes could be helpful when implementing proper strategies to solve this problem.

During the 8.5-year study period, we discovered that 160 orchiopexies were performed in a delayed fashion. This is not a small number, considering that orchiopexies account for about 15% of the surgeries performed in our hospital. An even larger number of delayed orchiopexies was reported in other studies. McCabe and Kenny evaluated hospital statistics of all orchiopexies performed in England over a 9-year period, and reported that only 20% of boys are operated on within the age of 24 months. (8) Guven and Kogan (16) conducted a similar study to ours in a tertiary care center setting and reported 33% were delayed surgeries between 1997 and 2006, though their age limit was lowered to 4 years. The above-mentioned studies indicate that regarding the age limit of surgery, current guidelines of orchiopexy have not been well observed even in the tertiary care center.

Considering that most textbooks or guidelines published after the 1980s recommend orchiopexy to be performed no later than 2 years old, it is

surprising that so many orchiopexies were conducted after 5 years. Reports from other countries speculated that the possible reason may be delayed referral from primary physicians, differences of referral habit between pediatricians and primary physicians, cultural differences, parental delay, re-operative orchiopexy due to iatrogenic trapping of testis, and the presence of AC. (7-14) Our data adds new reasons to the current database, such as delay due to other medical conditions and parental request for persistent RT. These new reasons may be due to the difference in the study setting or may reflect cultural differences, i.e. a study in tertiary care hospital setting in Korea. These additional reasons could broaden our knowledge and aid us to understand and solve the problem of delayed orchiopexy.

Considering the preventable nature of complications related to cryptorchidism, it is frustrating that parental delay and delayed referral (by primary physician) contributes to more than 40% of delayed orchiopexies. Regarding parental delay, a similar proportion of unintentional or intentional delay was identified. Due to the retrospective nature of study, we could not identify the exact cause of these delays. However, we expect that improved education or propagation concerning the consequences of untreated cryptorchidism to parents will reduce the incidence of delayed surgery. Despite the fact that more than 20 years have passed since the controversy concerning optimal age for orchiopexy has been settled, our data still showed that unexplained delayed referral by a physician was responsible for delayed orchiopexies in about 8% of patients. This may be related to failure to determine the correct testicular position or misunderstanding of the optimal age for orchiopexy or the occurrence of AC. This portrays the clear necessity for primary physicians to be familiar with testicular palpation, and to know the

optimal age for orchiopexy. Putting on advertisement on medical newspaper may be an effective way to lower the proportion of delayed orchiopexy.

Intriguingly, parental request to correct RT accounted for more than 20% of cases. Despite the fact that all RT spontaneously descend, the distinction between RT and AC remains unclear. This explains the wide ranges of testicular ascent reported in those who were presumed to have RT. (13,17) In addition, the need to follow-up until puberty may instigate an impatient parent to consent to have an orchiopexy performed, since the long duration of surveillance into puberty may seem too long for the parent to regularly evaluate the normal testicular position of their son.

AC also referred to as ascending testis, is also a significant reason for delayed orchiopexy. This ascent was first noted in 1966 and data regarding similar cases was accumulated in subsequent studies. The risk of ascent was reported to increase in the presence of RT, cerebral palsy and proximal hypospadias. (18,19) As far as we know, our data of AC is the first report in Korea. Our data shows that AC significantly contributes to delayed orchiopexy, although the proportion was not as large as that reported in an American tertiary care center study. (16) Moreover, as previous reports have indicated, about half of AC patients in our study had a history of hypospadias, supporting the results of previous studies.

Considering the fact that hypospadias is the result of low androgenic action and that androgen plays a critical role for proper signaling of the genitofemoral nerve via Calcitonin Gene Related Peptide (CGRP) and subsequent testicular ascent in animal study, (20,21) it may be assumed that a low androgenic milieu could lead to disruption of innervations of CGRP positive nerves and possibly testicular ascent afterwards. In Prader-Willy

syndrome, a similarly low androgenic milieu may play a role. In case of cerebral palsy, the cremasteric muscle spasticity may be implicated. Based on these results, careful testicular palpation should be included in follow-up tests for patients who have a history of operation for proximal hypospadias, Prader-Willy syndrome, and cerebral palsy.

The most critical point of orchiopexy is cord lengthening by division of the processus vaginalis and dissection of cremasteric muscle and fascia. We observed a rate of difficulty which was approximately 30% in cord lengthening in delayed cases of orchiopexy. This is unusually high compared to the 3%-5% range of incidence of difficulty in lengthening in younger children. (22,23) Although difficult cord lengthening could be expected in iatrogenic cases, it is interesting that a similarly high rate of difficulty was noted in all other causes of delay but the cases for RT. As Hack et al (24) assumed, failure of the spermatic cord to elongate in proportion to increasing body length may play a role in the case of delayed orchiopexy and this may be responsible for the difficulty in cord lengthening in some patients regardless of reasons.

The deleterious effect of delayed orchiopexy may be reflected in comparison of testicular size. The mean testicular size of patients who underwent delayed orchiopexy was substantially lower than the age matched normative one. Moreover, the fact that such discrepancy was found in all age ranges supports the harmful effect of delayed orchiopexy. These findings underscore the proper timing of orchiopexy. Whether this effect can be applied to all causes could not be evaluated due to the small number of cases in each reason.

This study has some limitations. Since it was performed in a

retrospective nature, the determination of causes may not be discriminative and is liable to response bias. For example, what we described to be a case of delayed referral may actually be a case of a parent trying to hide his or her mistake of postponement of surgery, despite appropriate referral. Additionally, the low incidence of AC may result from the fact that some cases might have been spuriously categorized as parental delay or delayed referral. The physical examination performed by parents and primary physicians was not as accurate as pediatric urologist, thus resulting in incorrect assessment for testicular positions. Furthermore, an age-matched normative volume of testis was measured by Prader orchidometery, while testicular volume in our study was measured directly by ruler during operation. This difference in measuring testicular volume may have affected the difference of the testicular size. Lastly, surgical difficulty in cord lengthening was determined by surgical records written by numerous urologic residents. The relationship between surgical difficulty and delayed orchiopexy needs to be further clarified.

# CONCLUSIONS

Substantial number of patients with cryptorchidism missed the proper timing for orchiopexy and underwent delayed surgery. Several reasons were attributable for this delay, and underscored the necessity of improved propagation of the optimal age for orchiopexy. Similar to previous reports in other countries, AC plays a significant role in the Korean cohort. The increased number of AC in cases of hypospadias suggests the need for vigilant follow-up, even after the completion of urethroplasty. The harmful effects of delayed orchiopexy were reflected in difficult cord lengthening and retarded testicular growth.

# REFERENCES

1. Berkowitz GS, Lapinski RH, Dolgin SE, Gazella JG, Bodian CA, Holzman IR. Prevalence and natural history of cryptorchidism. Pediatrics 1993;92:44-9.

2. Thong M, Lim C, Fatimah H. Undescended testes: incidence in 1,002 consecutive male infants and outcome at 1 year of age. Pediatr Surg Int 1998;13:37-41.

3. Barthold JS, González R. The epidemiology of congenital cryptorchidism, testicular ascent and orchiopexy. J Urol 2003;170:2396-401.

4. Timing of elective surgery on the genitalia of male children with particular reference to the risks, benefits, and psychological effects of surgery and anesthesia. American Academy of Pediatrics. Pediatrics 1996;97:590-4.

5. Ritzén EM, Bergh A, Bjerknes R, Christiansen P, Cortes D, Haugen SE, et al. Nordic consensus on treatment of undescended testes. Acta Paediatr 2007;96:638-43.

6. Tekgul S, Riedmiller H, Gerharz E, Hoebeke P, Kocvara R, Nijman R, et al. Guidelines on pediatric urology. Arnhem: European Society for Pediatric Urology; 2009;8-11.

7. Springer A, Huber C, Reck CA, Fengler D, Horcher E. Delayed referral despite appropriate knowledge in cryptorchidism as a cause of delayed orchidopexies in Austria. Klin Padiatr 2010;222:248-51.

8. McCabe JE, Kenny SE. Orchidopexy for undescended testis in England: is it evidence based? J Pediatr Surg 2008;43:353-7.

9. Golabek T, Kiely E. Patterns of referral and treatment of undescended testis: a 12-year experience in a single centre. Ir J Med Sci 2010;179:511-4.

10. Kokorowski PJ, Routh JC, Graham DA, Nelson CP. Variations in timing of

surgery among boys who underwent orchidopexy for cryptorchidism. Pediatrics 2010;126:576-82.

11. Hack WW, Meijer RW, van der Voort-Doedens LM, Bos SD, Haasnoot K. Natural course of acquired undescended testis in boys. Br J Surg 2003;90:728-31.

12. Atwell JD. Ascent of the testis: fact or fiction. Br J Urol 1985;57:474-7.

13. Stec AA, Thomas JC, DeMarco RT, Pope JC 4th, Brock JW 3rd, Adams MC. Incidence of testicular ascent in boys with retractile testes. J Urol. 2007;178:1722-4.

14. Hack WW, Meijer RW, van der Voort-Doedens LM, Bos SD, De Kok ME. Previous testicular position in boys referred for an undescended testis: further explanation of the late orchidopexy enigma? BJU Int 2003;92:293-6.

15. Song JE, Yi YY, Hwang IT, Lee HR, Lim JS, Yang S. Testicular Volume in Korean Boys. J Korean Soc Pediatr Endocrinol 2010;15:14-18.

16. Guven A, Kogan BA. Undescended testis in older boys: further evidence that ascending testes are common. J Pediatr Surg 2008;43:1700-4.

17. Agarwal PK, Diaz M, Elder JS. Retractile testis--is it really a normal variant? J Urol 2006;175:1496-9.

18. Tasian GE, Zaid H, Cabana MD, Baskin LS. Proximal hypospadias and risk of acquired cryptorchidism. J Urol. 2010;184:715-20.

19. Itesako T, Nara K, Matsui F, Matsumoto F, Shimada K. Acquired undescended testes in boys with hypospadias. J Urol 2011;185:2440-3.

20. Shono T, Zakaria O, Imajima T, Suita S. Does proximal genitofemoral nerve division induce testicular maldescent or ascent in the rat? BJU Int 1999;83:323-6.

21. Nazir Z, Masood R, Rehman R. Sensory innervation of normal and

hypospadiac prepuce: possible implications in hypospadiology. Pediatr Surg Int 2004;20:623-7.

22. Kirsch AJ, Escala J, Duckett JW, Smith GH, Zderic SA, Canning DA, et al. Surgical management of the nonpalpable testis: the Children's Hospital of Philadelphia experience. J Urol 1998;159:1340-3.

23. Banieghbal B, Davies M. Laparoscopic evaluation of testicular mobility as a guide to management of intra-abdominal testes. World J Urol 2003;20:343-5.

24. Hack WW, Goede J, van der Voort-Doedens LM, Meijer RW. Acquired undescended testis: putting the pieces together. Int J Androl 2012;35:41-5.

# 초 록

# Reasons for delayed orchiopexies in a Korean tertiary care hospital

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**서론:** 잠복고환 환아에서 고환 고정술은 2세 이전에 시행되는 것이 추천되나 현재 많은 고환고정술이 지연된 형태로 시행되고 있다. 이 연구에서는 3차 병원의 자료를 분석하여, 5세 이후 지연된 고환 고정술이 시행되는 비율을 파악하고, 수술이 지연된 원인과 이에 따르는 영향을 분석해보고자 하였다.

**방법:** 2004년부터 2012년까지 본 병원에서 5세 이후에 시행된 고환 고정술에 대한 자료를 후향적으로 분석하였다. 수술이 지연된 원인을 파악하였고, 이에 대한 영향은 짧은 정삭으로 인한 수술의 어려움과 수술 당시 측정한 고환의 크기를 통해 평가하였다.

**결과:** 총 160건의 고환고정술이 5세 이후에 시행되었고, 이는 전체 고환고정술의 15%에 해당하였다. 수술 지연의 주요한 원인 중 2가지가 환아의 부모와 직접적으로 관련이 있었다: 병원에 환아를 늦게 데리고 온 것, 그리고 지속되는 퇴축고환에 대해 수술을 원하는 것. 후천성 잠복고환은 21건(13%)에 해당하였고, 이 중 절반 이상이 요도하열을 가지고 있었다. 48건

(30%)에서 짧은 정삭으로 인한 수술의 어려움이 있었다. 각 연령대에서 평균 고환 크기는 정상 참조치와 비교하여 현저하게 작았다.

**결론:** 적정한 수술 시기에 대한 확립이 이루어져 있음에도 불구하고, 잠복고환에서 고환고정술은 15%에서 지연된 형태로 시행되었다. 수술의 어려움과 작은 고환크기를 고려할 때, 지연된 고환고정술을 줄이기 위한 노력이 필요할 것으로 생각된다.

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**주요어:** Cryptorchidism, Orchiopexy, Tertiary Care Centers

**학번: 2012-22705**