Journal of the Formosan Medical Association (2014) **113**, 915–920

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ORIGINAL ARTICLE

Factors related to the time to cryptorchidism surgery—A nationwide, population-based study in Taiwan

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Received 3 October 2012; received in revised form 28 May 2013; accepted 4 June 2013

KEYWORDS
cryptorchidism;
infertility;
orchiopexy;
surgery;
testicular cancer;
undescended testis

Background/Purpose: Current guidelines recommend that the optimal timing for cryptorchidism surgery is by the age of 12 months. This study investigated the trend of surgical timing and examined the factors associated with time to surgery for cryptorchidism in Taiwan by using a nationwide, population-based database.
Methods: The present study utilized the Longitudinal Health Insurance Database 2005, a subset of the National Health Insurance Research Database, which contains data on all paid medical benefit claims over the period 1997–2007 for a subset of 1 million beneficiaries randomly drawn from 22.72 million individuals enrolled in the National Health Insurance program in 2005. We analyzed the timing of surgery in boys younger than 18 years with diagnosis of cryptorchidism.
Results: We identified 547 boys who underwent surgery under 18 years of age. Approximately 79.2% of study participants received surgery after the age of 12 months. A multivariate analysis showed that several factors were significantly associated with time to surgery: age of the physician making the diagnosis, age of the surgeon performing the surgery, age of the patient

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http://dx.doi.org/10.1016/j.jfma.2013.06.001

at the first diagnosis of cryptorchidism, and number of previous clinic visits with the diagnosis of cryptorchidism and urbanization level of the patient's residence.
Conclusion: A surprisingly high rate (79.2%) of all study participants underwent surgery beyond the optimal timing. Certain doctor and patient factors were associated with time to cryptorchidism surgery. Improving the alertness and education of parents and specialists may lead to earlier surgeries.

Introduction

Cryptorchidism is one of the most common congenital anomalies in newborns.[1,2] Previous studies showed that the prevalence rate of cryptorchidism at birth varies from 1% to 9%.[3–6] Histologic deterioration was observed in cryptorchidism by the age of 12 months.[7,8] In addition, cryptorchidism has been reported to increase the risk of testicular cancer by 3- to 8-fold.[9] The risks of infertility and malignancy after cryptorchidism may be lowered by earlier orchiopexies.[10–12] Additional considerations related to the timing of surgery for cryptorchidism include age-related anesthetic risks and psychological effects of genital surgery.[13,14] Therefore, the current recommendation for the optimal timing of cryptorchidism treatment suggests that orchiopexy should be performed before 6—12 months of age.[14–17] Several hospital-based studies have indicated that a considerable number of orchiopexies were performed beyond 1 year of age.[17–20] However, the reasons for the delays have not been well studied.[20] By looking beyond hospital-based research, we investigated the age of cryptorchidism surgery by analyzing the data from the National Health Insurance Research Database (NHIRD). Furthermore, we aimed to elucidate the factors associated with delayed surgery for cryptorchidism.

Materials and methods

Data source

National Health Insurance Research Database

The NHI Bureau of Taiwan has collected claims records covering all inpatient and outpatient medical benefit claims for nearly the entire population of Taiwan from the inception of its single-payer NHI program in 1995. By 2005, the NHI covered nearly 99% of the population in Taiwan, and the NHI registry of beneficiaries numbered 22.72 million. The entire data collection is known as the NHIRD.[21]

Longitudinal Health Insurance Database 2005

The present study utilized a subset of the NHIRD known as the Longitudinal Health Insurance Database 2005 (LHID2005), which contains all inpatient and outpatient medical benefit claims from 1997 to 2007 for a sample of 1 million beneficiaries randomly drawn from the 22.72 million individuals in the NIH Registry for Beneficiaries at any part of the calendar year 2005. The 1 million deidentified individuals included in the LHID2005 provide a good statistical representation of the entire population of Taiwan.

Study sample

From the LHID2005, we first selected all boys younger than 18 years of age whose claims records included the specific diagnosis of undescended testis as defined by the *International Classification of Diseases, Ninth Revision, Clinical Modification* (ICD-9-CM) codes 752.51 and primary surgical treatment for cryptorchidism (an orchiectomy or orchiopexy). Age-at-treatment was based on the surgical date. Concomitant birth defects identified by ICD-9-CM codes 740—759 of all patients were also considered in the analysis.

Key variables of interest

The following variables were included in the analyses. (1) Patient characteristics included the calendar year of birth, Charlson Comorbidity Index (CCI), insurance fee, type of surgical procedure (orchiopexy vs. orchiectomy), number of associated congenital anomalies, number of outpatient clinic visits with the diagnosis of cryptorchidism prior to surgery, number of well-baby clinic visits prior to surgery, geographic location of the residence, and urbanization level of the residence locality. (2) Doctor characteristics included the specialty of the physician making the initial diagnosis, specialty of the surgeon performing the surgery, sex, number of board certifications, years since board certification(s), and age (the last 2 characteristics being surrogates for practical experience). (3) Hospital characteristics included the hospital level, ownership, and urbanization level of the hospital locality, and geographic area of hospital locality. The hospital level indicates whether the hospital was a medical center, a regional hospital, a district hospital, or a private clinic. Hospital ownership was recorded as one of three types: public, private not-for-profit, or private for-profit. The hospital level served as a proxy for clinical service capabilities. The hospital teaching status was not included in the analyses, because all medical centers and regional hospitals in Taiwan are teaching hospitals.

Urbanization level

The 359 municipalities in Taiwan were stratified into eight groups according to standards published by the National Health Research Institutes, Taiwan, with 1 indicating "most urbanized" and 8 indicating "least urbanized". These standards include the population density, proportion of the population with a college education or above, proportion of the population older than 65 years, proportion of agricultural workers in the population, and number of physicians per 100,000 population.[21,22]

Charlson Comorbidity Index

The CCI predicts mortality for a patient who may have a range of 17 comorbid conditions. Each condition is assigned with a score of 1. Then the scores are summed up and given a total score that predicts mortality.[23]

Statistical analyses

Statistical analyses were performed using the SAS version = 9.1 (SAS Institute, Cary, NC, USA). Continuous data were expressed as the mean (standard deviation [SD]). Percentages were calculated for categorical variables. Chi-square test or Fisher's exact test was used to analyze the categorical data. Multivariate analyses were conducted by fitting a multiple Cox's proportional hazards model to the data to predict the factors associated with the time from birth to cryptorchidism surgery. Basic model-fitting techniques for: (1) variable selection, (2) goodness-of-fit assessment, and (3) regression diagnostics were used in our regression analyses to ensure the accuracy of the results. A two-tailed $p < 0.05$ was considered statistically significant.

Results

The study sample comprised 547 patients who underwent surgery for cryptorchidism before the age of 18 years, including unilateral orchiopexies in 474 patients (86.7%), bilateral orchiopexies in 62 patients (11.3%), and orchiectomies in 11 patients (2.0%). The mean time to cryptorchidism surgery in all individuals was 44.7 months. The estimated probability of nonoperation versus patient age, calculated by Kaplan—Meier analysis, is shown in Fig. 1. A surprisingly high rate (79.2%) of all study participants underwent surgery beyond the optimal age of 12 months. Approximately 30.3% of study participants received surgery after the age of 60 months. In terms of the time to cryptorchidism diagnosis, approximately 56.7% of patients with cryptorchidism were diagnosed after the age of 12 months. Fig. 2 shows the mean age of surgery for cryptorchidism by year. The issue of delayed surgery for cryptorchidism has existed during the study period, 1997—2006.

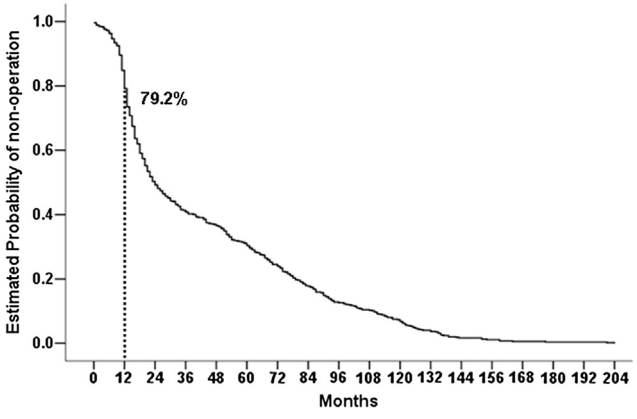

Figure 1 Kaplan—Meier estimate showing the estimated probability nonoperation versus patient age.

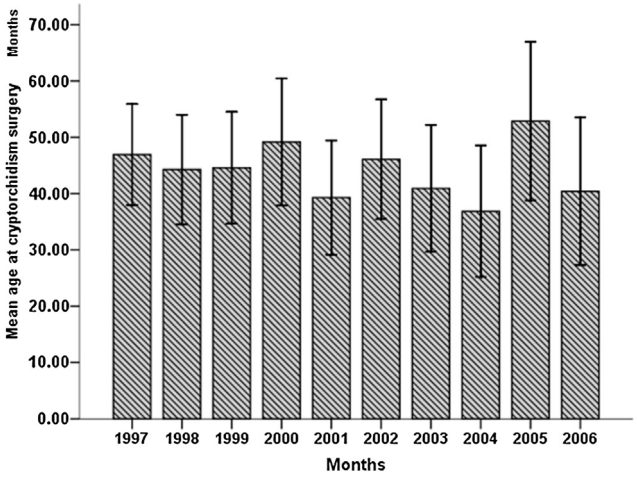

Figure 2 Mean time to cryptorchidism surgery by year during the period 1997—2006.

The characteristics of patients, doctors, and hospitals as associated risk factors with delayed surgery for cryptorchidism are shown in Table 1. The three most common associated anomalies were an inguinal hernia in 175 patients (32%), cardiovascular diseases in 50 patients (9.1%), and prematurity with low body weight in 38 patients (6.9%). Approximately 258 (47.2%) individuals lived in the northern area, and 156 individuals lived in the southern area. A total of 343 patients lived in urban areas and 204 patients lived in rural area. In terms of hospital characteristics, 330 patients (60.3%) received surgery in hospitals at the medical center level, and 474 patients (86.7%) underwent surgery in hospitals located in urban areas. Most of the procedures were performed by male surgeons older than 40 years.

Table 2 shows the results of the multivariate analyses of associated factors with the age of surgery for cryptorchidism, computed by means of Cox's proportional hazards model. The significant associated factors with time to cryptorchidism surgery are as follows: age of the patient at the first diagnosis of cryptorchidism, number of clinic visits with the diagnosis of cryptorchidism prior to surgery, urbanization level of the patient's residence, age of the physician making the initial diagnosis, and age of the surgeon performing the surgery.

Some patient characteristics were significantly associated with time to cryptorchidism surgery. The age of patient at the first diagnosis of cryptorchidism was significantly associated with time to surgery. The earlier the initial diagnosis is made, the earlier the surgery is performed [hazard ratio (HR) = 0.998; 95% confidence interval (CI), 0.998—0.998; $p < 0.0001$]. Moreover, patients who lived in areas of higher urbanization level (level: 1—4) underwent surgery earlier compared with those who lived in areas of lower urbanization level (level: 5—8; HR = 1.518; 95% CI, 1.234—1.868; $p < 0.0001$). The number of clinic visits with the diagnosis of cryptorchidism prior to surgery was also significantly associated with time to surgery. The number of clinic visits increased, the later the patient received surgery (HR = 0.868; 95% CI, 0.832—0.906; $p < 0.0001$). Certain physician characteristics were also significantly related to time to cryptorchidism surgery.

Table 1 Clinical and demographic characteristics of all study participants, hospitals, and doctors ($n = 547$).

Variables	Patient no.	%
Patient characteristics	547	100
Geographic area of residence		
Northern	258	47.2
Central	126	23.0
Southern	156	28.5
Eastern	7	1.3
Urbanization level of residence		
Urban area (level 1—4)	343	62.7
Rural area (level 5—8)	204	37.3
Associated anomalies		
Inguinal hernia	175	32.0
Cardio	50	9.1
Premature and low body weight	38	6.9
Others	61	11.2
Surgical modality		
Unilateral orchidopexies	474	86.7
Bilateral orchidopexies	62	11.3
Orchiectomy	11	2.0
Hospital characteristics		
Geographic location		
Northern	268	49.0
Central	109	19.9
Southern	165	30.2
Eastern	5	0.9
Level of hospital		
Medical center	330	60.3
Regional hospital	156	28.5
District hospital	55	10.1
Private clinic	6	1.1
Urbanization level of hospital location		
Urban area (level 1—4)	474	86.7
Rural area (level 5—8)	73	13.4
Doctor characteristics		
Physicians making the diagnoses		
Age (y)		
≤ 40	206	46.9
41—50	256	37.7
>50	85	15.5
Sex		
Male	535	97.8
Female	12	2.2
Physician's specialty		
Urology	205	37.5
Pediatrics	476	87.0
Surgery	40	7.3
Other specialties	38	7.0
Surgeons performing the surgery		
Age (y)		
≤ 40	214	39.1
41—50	249	45.5
> 50	84	15.4
Sex		
Male	538	98.4
Female	9	1.6
Surgeon's specialty		
Urology	221	40.4
Pediatric surgery	301	55.0
Other specialties	25	4.6

Surgery for cryptorchidism was performed later if the initial diagnosis was made by a younger physician (HR = 1.039; 95% CI, 1.024—1.054; $p < 0.0001$). In addition, surgery for cryptorchidism was performed later if the surgeon was older (HR = 0.954; 95% CI, 0. 0.942—0.967; $p < 0.0001$).

Discussion

The mainstay of therapy for cryptorchidism is surgery. Earlier surgery can minimize histopathological changes and prevent infertility.[17,24] Late orchiopexy appeared to have an adverse effect on future fertility.[25,26] Moreover, the subsequent development of testicular cancer may be lowered by early surgical treatment.[10,12] The prevailing view is that for a healthy child, the optimal time for cryptorchidism surgery is 6—12 months of age.[14—17]

The only previous study using a nationwide database—the Pediatric Health Information System in the United States—to determine the factors associated with the timing of surgery also showed that only 43% of patients had surgery by 2 years of age, and the associated factors with the timing of orchiopexy included patient race, insurance status, and the hospital in which surgery was performed.[20]

This study was based on the database from a nationwide, population-based cohort covered by a single payer insurance (NHI program), which also minimizes the bias from differences in medical access. We showed that some factors were significantly associated with time to surgery: age of patients at the first diagnosis of cryptorchidism, number of clinic visits with the diagnosis of cryptorchidism prior to surgery, urbanization level of the patient's residence, age of the physician making the initial diagnosis, and age of the surgeon performing the surgery.

In most cases, cryptorchidism can be diagnosed at birth. However, the diagnosis of cryptorchidism depends to a large extent on the experience of the investigator and the examination setup.[1] Actually, delayed diagnoses and delayed referral of cryptorchidism have been reported to be major problems.[27] Sinha et al[27] conducted a retrospective review of 298 testes, and the time to referral, time to surgery, complications, and final outcomes were assessed. The mean age at referral was 57 months. Only 24% of cases were operated on before the age of 2 years.[27] Similar patterns of delayed diagnoses and surgery, and referral by pediatricians were also observed in our study. In our study sample, there is also a high percentage of patients with cryptorchidism (56.7%) who were diagnosed after the age of 12 months. We likewise found that certain doctor factors such as age of the physician making the initial diagnosis and age of the surgeon performing the surgery were both associated with time to surgery. Special training to improve professionalism enables physicians and care providers to achieve early diagnosis and timely referral.

The present study is based on records generated by Taiwan's highly accessible and well-used NHI system.[21] The NHIRD offers several advantages when analyzing factors associated with the time interval from birth to a diagnosis of cryptorchidism. First, the NHIRD is a nationwide population-based database, which includes all medical claims for more than 22 million Taiwanese enrollees, representing more than 99% of the island's population. The results represent the general population as a whole. Second, the database

Table 2 Multivariate analyses of the risk factors associated with time to surgery (months) for cryptorchidism by using Cox's proportional hazards model (n = 547).

Variable	Parameter estimate	SE	Chi-square test	HR	95% CI	p
Age of patient at the first diagnosis of cryptorchidism (d)	−0.002	0.0001	713.553	0.998	0.998−0.998	<0.0001
Urbanization level of patient's residence (high vs. low)[a]	0.417	0.106	15.538	1.518	1.234−1.868	<0.0001
Number of clinic visits with the diagnosis of cryptorchidism prior to surgery	−0.141	0.022	42.024	0.868	0.832−0.906	<0.0001
Age of physician making the initial diagnosis (y)	0.038	0.007	27.025	1.039	1.024−1.054	<0.0001
Age of surgeon performing the surgery (y)	−0.047	0.007	45.786	0.954	0.942−0.967	<0.0001

CI = confidence interval; HR = hazard ratio; SE = standard error.
[a] High urbanization level: 1−4; low urbanization level: 5−8 .

contains original claim records that are not designed for academic study, thereby attenuating bias in patient selection. Third, the NHIRD included all inpatient and outpatient data. It should be noted that cryptorchidism treatment is sometimes performed on an outpatient basis; thus, we removed the bias underestimating the quantity in previous studies that includes only inpatient data. Above all, boys with retractile testis were excluded in this study, thereby minimizing the confounding effects from different indications for retractile testis treatment.

The study also had several limitations. First, it is a retrospective study. Second, the NHIRD lacks some clinical and demographic data such as the position of the testes, family history, and socioeconomic data. Third, the insurance claims data inevitably include some diagnostic errors. However, all claims records of the NHI system are subject to a quality control process in which the actual medical charts are spot-checked by qualified record review teams. Finally, despite the fact that NHIRD includes all medical claims from more than 99% of Taiwan's entire population, the study may have missed those individuals whose medical services were not covered by the NHI.

In conclusion, this nationwide study addresses an important clinical issue. Approximately 79.2% patients with cryptorchidism received surgical correction beyond the optimal age of 12 months. To minimize the possibility of delayed surgery for cryptorchidism, it is important to increase the alertness and education of parents and specialists who make the diagnosis or perform the surgery.

Acknowledgments

This study was based in part on data from the NHIRD provided by the Bureau of National Health Insurance, Department of Health, Taiwan, and managed by the National Health Research Institutes, Taiwan.

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