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Male Health

# Analysis of the social and clinical factors affecting the age of children when receiving surgery for hypospadias: a retrospective study of 1611 cases in a single center

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We aimed to explore the associations between the age at which children undergo surgery for hypospadias and a range of social and clinical factors in a single center. Our aim was to promote the early surgical treatment of children with hypospadias. For a 6-year period, social and clinical data were collected from all children undergoing surgery to repair hypospadias in Children's Hospital of Chongqing Medical University (Chongqing, China), located in southwest of China. We analyzed the correlations between age at surgery and a range of social and clinical factors. A total of 1611 eligible cases were recruited, with a mean age of 54.3 months and a median age of 42 months: 234 cases (14.5%) were classified into a "timely operation" group, 419 (26.0%) cases into a "subtimely operation" group, and 958 (59.5%) cases into a "delayed operation" group. According to multivariate regression analyses, the higher the regional economic level, the closer the urethral opening to the perineum, and the higher the educational level of the guardians was, the younger the children were when they underwent the initial surgery for hypospadias; this was also the case for families without other children. Our subgroup analysis showed that the primary educational level of the guardians was a risk factor for subtimely surgery in their children (odds ratio [OR] = 1.52, 95% confidence interval [CI]: 1.08–2.15,  $P < 0.05$ ). A lower regional economic level (OR = 1.87, 95% CI: 1.26–2.78,  $P < 0.01$ ), a lower educational level of the guardians (OR = 3.84, 95% CI: 2.31–6.41,  $P < 0.01$ ), and an anterior-segment urethral opening (OR<sub>1</sub> [vs middle hypospadias] = 2.07, 95% CI: 1.42–3.03; OR<sub>2</sub> [vs posterior hypospadias] = 2.63, 95% CI: 1.75–3.95;  $P < 0.01$ ) were all risk factors for delayed surgery in children.

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**Keywords:** age; children; hypospadias; surgery

## INTRODUCTION

Hypospadias is a common congenital anomaly in males with a prevalence rate of approximately 0.2%–0.3%.<sup>1–3</sup> Previous research has shown that the incidence of hypospadias varies with race and region. Surgery is the only curative method and relies upon the technique of urethroplasty, one of the most common forms of pediatric urological surgery. International consensus advocates that surgery to correct hypospadias should be carried out at an appropriate age.<sup>4</sup> However, there are many factors that can exert influence over the time at which surgery for hypospadias can take place, including the surgical environment, the influence of anesthesia, the size of the penis, and the potential psychological impact on the children themselves. Children begin to develop gender consciousness from around the age of 18 months; this will inevitably lead to noncooperation postoperatively and thus increase the risk of postoperative recovery.<sup>5</sup> After 3 years of age, children become more adaptable and can cooperate better during surgical treatment and

postoperative recovery. However, after children have attained the age of 3 years, they will have to attend preschool in the vast majority of regions and therefore experience a variety of social roles. Hypospadias is associated with the need to squat. Furthermore, children often wet their pants due to the abnormalities in the urinary system. These factors will have a certain impact on social and psychological development. Age is not an absolute contraindication to anesthesia, although in recent years, some studies have demonstrated the negative impact of anesthetic drugs on the neurodevelopment of children; a correlation with the age of children when they receive anesthesia has not been proven, and the issue of anesthetic risk needs further investigation.<sup>6,7</sup> It is believed that the degree of penile development has little effect on surgery in young children. The penis only grows moderately during the preschool period; thus, the benefits of delaying surgery are not significant. In 2019, the European Association of Urology (EAU) Guidelines on Pediatric Urology recommended that children

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should be 6–18 months or 6–24 months of age at the time of surgery for hypospadias.<sup>4,8,9</sup> An American study further reported that genital surgery should be performed in children at the age of 6–12 months when feasible.<sup>10,11</sup> In Mainland China, the proportion of children with hypospadias who undergo surgery at an age that is above the upper threshold is relatively high.<sup>12,13</sup> Furthermore, the Chinese Urological Association states that all surgical procedures should be completed during the preschool period.<sup>14</sup> Chen *et al.*<sup>15</sup> investigated the factors associated with delayed surgery in Taiwan, China, and identified a number of factors, including the age and specialty of the physician at the first visit, the place of residence, and the presence of comorbidities in the children; however, the sample size analyzed in this study was very small (only 89 cases). Similar studies have yet to be carried out in Mainland China, where there are many children with hypospadias. Consequently, there is a clear need to investigate the factors that might influence the age at which children undergo surgery for hypospadias in China. By determining these factors, we may be able to guide local medical health-care plans and improve the physical and mental health of children with hypospadias.

## PATIENTS AND METHODS

We analyzed children undergoing initial surgery for hypospadias between January 2014 and October 2019 in the Urology Clinic of the Children's Hospital of Chongqing Medical University (Chongqing, China). Signed and informed consent from guardians was acquired, and the study was approved by the Ethics Committee of Children's Hospital of Chongqing Medical University (approval number: 2020195). Because of data duplication, we excluded patients who underwent surgery in two stages or underwent a second round of surgery. We also excluded referred children who received surgery at another hospital but came to our hospital due to complications. For each patient, we collected a range of key data, including the age at admission (months), the place of residence, whether there were extra children in the family, the type of hypospadias, comorbidities, surgical methods, surgical duration, hospitalization expenses, guardians' highest education level, and medical insurance status. According to the place of residence, and the year of admission, we downloaded data from the national and local bureaus of statistics. Regional economic data were determined using the per capita Gross Domestic Product (GDP). The guardians' highest educational level referred to primary education (primary school and junior high school), secondary education, and higher education (junior college and above). The regional economic level was classified into three levels based on the per capita GDP: (1) per capita GDP <5000 United States dollars (USD), (2) per capita GDP of 5000–10 000 USD, and (3) per capita GDP >10 000 USD. When retrospective data were collected, there was a deviation in whether the urethral opening was located within the posterior one-third of the penis.<sup>16</sup> Therefore, the urethral opening was classified into anterior hypospadias (glans and coronary sulcus), middle hypospadias (corpus penis), and posterior hypospadias (penile root, scrotum, and perineum), based on the coronary sulcus and the junction of the penis and scrotum. Based on age, the patients were divided into three subgroups: "timely operation" group (aged <24 months), "subtimely operation" group (aged 25–36 months), and "delayed operation" group (aged >36 months).

### Statistical analyses

Statistical analysis was performed using SPSS 22.0 software (SPSS Inc., Chicago, IL, USA). Normally distributed and nonnormally distributed continuous variables were compared using one-way analysis of variance (ANOVA) and the Kruskal–Wallis test, respectively.

Categorical variables were compared using the Chi-squared test. We also performed correlation analysis between age at surgery and the social and clinical data collected. This analysis involved Spearman's correlation method depending on the type of variable involved. Significant variables that were identified in the correlation analysis were then included in regression analysis. The associations between age and the statistical data described above were analyzed via multivariate linear regression analysis. The associations between the three groups and the statistical data described above were analyzed by multinomial logistic regression. "Complications and payment method" was not included in the multivariate analysis. We also excluded "comorbidities, payment method, and additional children" from the group analysis.  $P < 0.05$  was considered statistically significant.

## RESULTS

A total of 1611 children were enrolled in our study (**Table 1**). We found that the age of surgery for children with hypospadias in southwest China is much older than that in the guidelines and developed countries. Moreover, posterior hypospadias accounted for about 27% of cases, higher than other reports in the literature.<sup>17</sup> Both hydrocele testis and oblique inguinal hernia were evident as scrotal masses in children. Consequently, these conditions were merged into one common condition for the sake of this study.

The economic level of the children's place of residence, the position of the urethral opening, the highest educational level of the guardians, and whether there were extra children in the family, all had an impact on the age at surgery (**Table 2**). The higher the regional economic level was, the closer the urethral opening was to the perineum; the higher the guardians' educational level was, and without additional children in family, the younger the children tended to be at the time of surgery (all  $P < 0.05$ ).

According to the EAU Guidelines on Pediatric Urology (6–24 months),<sup>4</sup> only 14.4% of children underwent prompt surgery (**Figure 1**); this was far lower than the proportion of cases reported in other regions.<sup>12</sup> The proportion of children undergoing prompt surgery was the highest in 2014 (19.1%). Based on the expert consensus of the Chinese Urological Association,<sup>14</sup> children aged 25–36 months at surgery were enrolled into the subtimely operation group (26.0%).

We found that there were obvious differences in the economic development level, type of hypospadias, and educational level among the three groups. According to logistic regression analysis (**Table 3**), the guardians' highest educational level was different when compared between the subtimely operation group and the timely operation group, and the probability of subtimely surgery in the case of primary education was 1.52-fold higher than that for higher education (odds ratio [OR] = 1.52, 95% confidence interval [CI]: 1.08–2.15,  $P < 0.05$ ). When compared with those in the timely operation group, a lower regional economic level (OR = 1.87, 95% CI: 1.26–2.78,  $P < 0.01$ ), a lower educational level of the guardians (OR = 3.84, 95% CI: 2.31–6.41,  $P < 0.01$ ), and anterior-segment urethral opening (anterior hypospadias vs middle hypospadias: OR<sub>1</sub> = 2.07; anterior hypospadias vs posterior hypospadias: OR<sub>2</sub> = 2.63;  $P < 0.01$ ) were identified as risk factors for delayed surgery in children in the delayed operation group. In addition, we found that the length of the surgical procedure was shorter in older children; we therefore performed further analyses to investigate whether age affects surgical duration. Linear regression analysis confirmed that the surgical duration was significantly correlated with the position of the urethral opening ( $P < 0.01$ ) but not patient age ( $P > 0.05$ ), as shown in **Table 4**.

**Table 1: Characteristics of social and clinical data from 1611 cases**

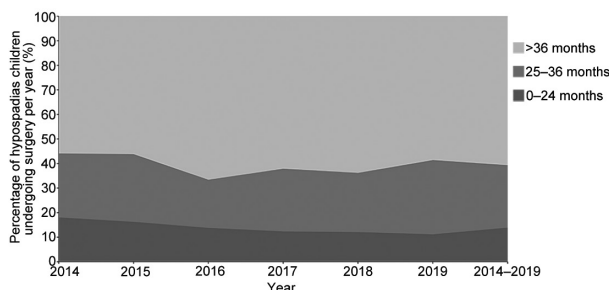
Characteristic	Total (n=1611)	TOG (n=234)	STOG (n=419)	DOG (n=958)	$F/\chi^2$	P
Age at surgery (month), mean±s.d.	54.3±36.1	19.5±3.8	30.5±3.5	73.2±35.8	NA	NA
Regional real GDP per capita (USD), mean±s.d.	7084.5±3513.4	7514.5±3672.7	7524.0±3775.8	6788.2±3322.8	14.32	0.001
Total cost in hospital (USD), mean±s.d.	2094.9±268.3	2096.3±235.8	2071.9±282.0	2104.6.0±269.2	3.19	0.203
Operation time (h), mean±s.d.	1.30±0.43	1.37±0.42	1.32±0.42	1.27±0.43	10.85	0.004
Main diagnosis, n (%)					31.46	0.000
Anterior hypospadias	485 (30.1)	46 (19.7)	106 (25.3)	333 (34.8)		
Middle hypospadias	687 (42.6)	109 (46.6)	179 (42.7)	399 (41.6)		
Posterior hypospadias	439 (27.3)	79 (33.8)	134 (32.0)	226 (23.6)		
Guardians' education level, n (%)					37.11	0.000
Primary education level	271 (16.8)	21 (9.0)	60 (14.3)	190 (19.8)		
Secondary education level	867 (53.8)	113 (48.3)	228 (54.4)	526 (54.9)		
Higher education level	473 (29.4)	100 (42.7)	131 (31.3)	242 (25.3)		
Payment method, n (%)					5.24	0.263
Self-supporting	666 (41.3)	94 (40.2)	160 (38.2)	412 (43.0)		
Rural medical insurance	40 (2.5)	3 (1.3)	10 (2.4)	27 (2.8)		
Urban medical insurance	905 (56.2)	137 (58.5)	249 (59.4)	519 (54.2)		
Comorbidity, n (%)					6.23	0.795
None	1380 (85.7)	202 (86.3)	356 (85.0)	822 (85.8)		
Inguinal hernia and hydrocele	76 (4.7)	9 (3.8)	21 (5.0)	46 (4.8)		
Cryptorchidism	23 (1.4)	5 (2.1)	8 (1.9)	10 (1.0)		
DSDs	20 (1.2)	3 (1.3)	6 (1.4)	11 (1.1)		
Genital-related diseases	112 (7.0)	15 (6.4)	28 (6.7)	69 (7.2)		
Additional children, n (%)					8.87	0.012
With additional children	597 (37.1)	93 (39.7)	130 (31.0)	374 (39.0)		
No additional children	1014 (62.9)	141 (60.3)	289 (69.0)	584 (61.0)		

s.d.: standard deviation; TOG: timely operation group; STOG: sub-TOG; DOG: delayed operation group; NA: not available; USD: United States dollar; DSDs: disorder of sex development; GDP: Gross Domestic Product

**Table 2: Multiple linear regression analysis of factors associated with the age at which hypospadias surgery was performed**

Factor	B	s.e.	t	P
Low economic level versus moderate economic level	4.50	1.95	2.31	0.021
Higher economic level versus moderate economic level	-4.73	2.21	-2.14	0.033
Anterior hypospadias versus middle hypospadias	10.09	2.03	4.96	0.000
Posterior hypospadias versus middle hypospadias	-4.46	2.09	-2.13	0.033
Primary education level versus secondary education level (guardians)	20.41	2.38	8.59	0.000
Higher education level versus secondary education level (guardians)	-8.51	1.95	-4.36	0.000
With additional children	-6.21	1.76	-3.53	0.000

s.e.: standard error; B: regression coefficient; t: t-test



**Figure 1:** The proportion of patients with hypospadias receiving surgery from 2014 to 2019 by age category.

## DISCUSSION

In addition to clinical complications and surgical success rates, it is also necessary to consider a child's psychological development, social adaptation, postoperative care, and penis development when considering surgery for hypospadias.<sup>11,18</sup> A previous study involving

children aged 2–12 years reported that younger children had a lower incidence of postoperative maladaptive behavior than older children, and this was mainly characterized by a higher frequency of anxiety and tantrums.<sup>5</sup> We believe that early surgery is also necessary for those children who missed the optimal age for surgery. In a previous study, Jones *et al.*<sup>19</sup> reported that when surgery was completed before the age of 5 years, boys will not have perioperative memory, and the lack of such surgical memory will improve their satisfaction as they grow up with regard to their body. Two other studies found that children with hypospadias are likely to suffer from adverse psychological behavior, such as depression, poor communication, and enhanced aggression,<sup>20,21</sup> these two studies considered children who were 6–14 years of age and 4–8 years of age, respectively, and therefore, most had already started school.<sup>20,21</sup> Early surgery can also reduce the psychological burden on parents.<sup>22,23</sup>

Previously, it was believed by surgeons that the success rate of surgery for hypospadias did not change with increased age at surgery.<sup>8,24,25</sup> In recent years, however, an increasing number of

**Table 3: Multinomial logistic regression analysis of factors associated with timely versus subtimely, timely versus delayed operation group**

Factors between groups	B	s.e.	Wald	OR (95% CI)	P
Subtimely operation group versus timely operation group					
Primary education level versus higher education level (guardians)	0.42	0.18	5.61	1.52 (1.08–2.15)	<0.05
Secondary education level versus higher education level (guardians)	0.79	0.29	7.65	2.21 (1.26–3.88)	<0.01
Delayed operation group versus timely operation group					
Low economic level versus higher economic level	0.63	0.20	9.63	1.87 (1.26–2.78)	<0.01
Moderate economic level versus higher economic level	0.39	0.19	4.35	1.48 (1.02–2.15)	<0.05
Primary education level versus secondary education level (guardians)	0.69	0.25	7.32	1.99 (1.21–3.27)	<0.01
Primary education level versus higher education level (guardians)	1.35	0.26	26.63	3.84 (2.31–6.41)	<0.01
Secondary education level versus higher education level (guardians)	0.66	0.16	17.01	1.93 (1.41–2.65)	<0.01
Anterior hypospadias versus middle hypospadias	0.73	0.19	14.16	2.07 (1.42–3.03)	<0.01
Anterior hypospadias versus posterior hypospadias	0.97	0.21	21.77	2.63 (1.75–3.95)	<0.01
Middle hypospadias versus posterior hypospadias	0.24	0.17	1.90	1.27 (0.90–1.78)	0.17

s.e.: standard error; B: regression coefficient; OR: odds ratio; CI: confidence interval

**Table 4: Multiple linear regression analysis of factors associated with surgical duration**

Factor	B	s.e.	t	P
Age at surgery	0.01	0	0.24	0.813
Urethral opening position	0.40	0.013	17.20	0

s.e.: standard error; B: regression coefficient; t: t-test

studies have shown that the incidence of complications is lower in younger patients undergoing surgery.<sup>9,26,27</sup> However, the occurrence of complications may also be affected by many other factors, such as the position of the urethral opening, the presence or absence of infections, penis development, and surgical duration.<sup>28</sup> If postoperative complications occur, multiple operations are needed, and early surgery can also reserve time for subsequent re-operation, thus reducing the impact of the second operation.

Socioeconomic factors, such as the economic level of the children's place of residence and the guardians' educational level, were related to the children's age at surgery and delayed surgery. This finding may indicate that there are more and better health-care institutions and specialized pediatricians in highly developed areas, and that the proportion of mothers who give birth in hospitals is also higher; thus, unhealthy infants are more likely to receive professional initial diagnosis. Owing to an absence of pediatric surgeons in the United States over the last century, the age of 3–4 years was considered more appropriate for surgery in this particular country.<sup>29</sup> Furthermore, the highest educational level of the guardians had the greatest impact on the age at surgery. We found that the proportion of guardians with higher education was 42.7% in the timely operation group, far higher than that (25.3%) in the delayed operation group, but secondary education of guardians had no obvious impact on the age at surgery across the three groups. The differences in the educational level of the guardians may cause differences in the recognition of the disease across the whole family. In the absence of guidance from professional physicians, guardians with a higher educational level may still gain a deeper understanding of hypospadias through the internet and books, thereby promoting surgical intervention.

The position of the urethral opening was related to the children's age at surgery. We speculated that children whose urethral opening is located at the posterior coronary sulcus can be diagnosed more easily because this is more likely to cause abnormal urination postures. Moreover, severe hypospadias often leads to confusion with regard to gender and genital dysplasia; consequently, the parents of such children

seek medical treatment earlier. In our study, we found that there was no relationship between children with cryptorchidism and their age at surgery. However, it was reported in Taiwan, China, that children who were complicated with cryptorchidism were older than those with hypospadias alone.<sup>15</sup> The incidence of cryptorchidism was 1.4% in our present cohort, lower than that reported in other literature (9%).<sup>14,30</sup> We believe that this was because the mean age at surgery was higher and because the data relating to cryptorchidism showed deviation. Unexpectedly, disorders of sex development (DSDs) had no impact on the age at surgery, probably because some children were diagnosed only with DSDs, rather than hypospadias, and because some children with DSD underwent gonadal biopsy but did not receive urethroplasty, thus resulting in biased results. In a previous study, Oswald<sup>31</sup> argued that severe hypospadias should be strictly distinguished from DSD, to ensure a normal gender identity and optimal surgical treatment. Initially, we found that in older children, the procedure was shorter. However, subsequent analysis showed no significant effect of surgical age on surgical procedure. We speculate that this may be because of the shorter operation time and simpler surgical procedure in older children with more anterior hypospadias.

The data used in this study were derived from a single medical center and most of the patients were from southwest China. Except for downtown Chongqing, the economic conditions and educational level of other regions were below the average of China, thus resulting in selection bias. Very few studies have been published relating to the factors affecting the age at which children undergo surgery for hypospadias. Over 1600 cases were enrolled in this study, and the data were complete and reliable. Some retrospective data could not be verified, such as family income, although this may have caused bias in our results. The local level of economic development is more representative and more relevant for health promotion and health guidance. With regard to waiting lists for surgery, the hospital waiting time for all of the children included in this cohort was about 1 month. Although the waiting time increased with the age at which surgery is performed, this interval is short and there was no significant difference in waiting time among children. Consequently, we do not consider that this has a significant impact on our findings.

## CONCLUSIONS

Our analysis revealed that the economy of the area in which the family resides, the location of the urethral opening, and the educational level of the guardians were all risk factors for delayed surgery in children with hypospadias. In less economically and educationally developed



areas, it is necessary to strengthen education and health promotion for children with hypospadias and pay more attention to children with mild hypospadias.

### AUTHOR CONTRIBUTIONS

ZCZ designed the study, collected, organized, and analyzed data, and drafted the manuscript. XL contributed to study design and helped to draft and revise the manuscript. HSC and YS helped collect data. TL, DWH, and YTL participated in statistical analyses. GHW helped revise the manuscript. All authors read and approved the final manuscript.

### COMPETING INTERESTS

All authors declared no competing interests.

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