The following full text is a publisher's version.

For additional information about this publication click this link.
https://hdl.handle.net/2066/226763

Please be advised that this information was generated on 2021-07-01 and may be subject to change.
Development of a prediction model for postoperative complications after primary hypospadias correction

Elisabeth MJ Dokter a,⁎, Loes FM van der Zanden a, Susanne JM Laumer a, Priya Vart a, Barbara BM Kortmann b, Robert PE de Gier b, Wout FJ Feitz b, Nel Roeleveld a, Iris ALM van Rooij a

a Radboud Institute for Health Sciences, Department for Health Evidence, Radboud University Medical Center, P.O. Box 9101, 6500, HB, Nijmegen, The Netherlands
b Department of Urology, Paediatric Urology, Radboudumc Amalia Children's Hospital, P.O. Box 9101, 6500, HB, Nijmegen, The Netherlands

ARTICLE INFO

Article history:
Received 6 September 2019
Received in revised form 20 March 2020
Accepted 28 March 2020

Key words: Hypospadias
Postoperative complications
Prognosis
Model development
Prediction model

ABSTRACT

Purpose: To develop a prediction model for postoperative complications after primary one-stage hypospadias correction to improve preoperative parental counseling.

Materials and methods: In this retrospective cohort study, data were collected from 356 patients with anterior or middle hypospadias who had a one-stage hypospadias correction from 2003 onwards. Potential treatment- and patient-related factors were selected and used to develop a prediction model for postoperative complications within one year (wound-related complications, urinary tract infections, fistulas, stenosis, and prepuce-related complications). Multivariable logistic regression analysis with stepwise backward selection and a p-value of 0.20 was used to select the final model, which was internally validated using the bootstrap procedure.

Results: Complications within one year postoperatively occurred in 66 patients (19%), of which 13% and 37% were seen in anterior and middle type of hypospadias, respectively. Hypospadias phenotype, surgical technique, chordeectomy, and surgeon's experience were included in the final prediction model, whereas none of the patient-related factors were. The final model had a good discriminative ability (bias corrected C statistic 0.70) and calibration.

Conclusion: Using easily obtainable information, this model showed good accuracy in predicting complications within one year after hypospadias surgery. It is a first step towards individualized risk prediction of postoperative complications for anterior and middle hypospadias and can assist in preoperative parental counseling.

Type of study: Prognostic study.
Level of evidence: Level II.

© 2020 The Authors. Published by Elsevier Inc. This is an open access article under the CC BY license (http://creativecommons.org/licenses/by/4.0/).

Hypospadias is a congenital malformation in boys with estimated prevalence in Europe ranging between 1.7 and 3.8 per 1000 live births [1,2]. Surgical treatment of hypospadias is usually performed within the first or second year of life [3]. Although surgical correction is indicated in most patients [1], this is usually an elective procedure with long-term complication rates as high as 50% [4]. After hypospadias surgery, approximately half of the parents experience decisional regret, with postoperative complications as risk factor for regret according to Lorenzo et al., but not according to Ghidini et al. [5,6]. An objective perspective of the complication risk may improve preoperative parental counseling and help parents make better informed decisions on whether or not they will have their son operated upon.

Several studies tried to identify risk factors for the development of complications and most agree that hypospadias phenotype (e.g. anterior, middle, or posterior), preoperative existence of chordee (for which surgery is indicated), surgeon’s experience, and surgical technique influence number complications [7–11]. However, the risk factors identified have never before been combined in a prediction model.

Although treatment-related factors were investigated most frequently, factors concerning the neonatal period, such as mode of delivery and breast feeding, and other patient-related factors, such as exposure to smoking in the first years of the child’s life, may also play an important role. The effects of these factors on the child’s general health or immune status [12–14] may influence the risk of postoperative complications. Some factors were studied in association with surgical complications before [12,14], but never for patients with hypospadias. The aim of this study was to develop and internally validate a prediction model using treatment- and patient-related factors to predict the risk of postoperative complications within one year after primary hypospadias correction. This prediction model may help physicians with preoperative parental counseling.

https://doi.org/10.1016/j.jpedsurg.2020.03.030
0022-3468/© 2020 The Authors. Published by Elsevier Inc. This is an open access article under the CC BY license (http://creativecommons.org/licenses/by/4.0/).
1. Materials and methods

1.1. Study population

In this retrospective cohort study, patients were derived from AGORA (Aetiologic research into Genetic and Occupational/environmental Risk factors for Anomalies in children), a large ongoing data and biobank coordinated by the Radboud university medical center (Radboudumc), the Netherlands, including diagnostic and questionnaire data and DNA samples from children with congenital malformations and their parents. Routine patient recruitment for AGORA started in 2004, and details about this are described elsewhere [15]. Patients who had primary hypospadias correction in the Radboudumc were selected for this study. Patients were excluded when medical records contained insufficient information, preoperative meatal location was posterior or unknown, or surgery was performed as multistage correction or before 2003. Follow-up of less than one year after initial hypospadias correction was also reason for exclusion unless a complication occurred within the first year.

1.2. Data collection

At inclusion in the AGORA data- and biobank, the patients’ parents were asked to complete the AGORA questionnaire concerning demographics, lifestyle before, during, and after pregnancy, and pregnancy outcome. Relevant clinical information, treatment characteristics, and postoperative outcome were obtained from medical records by a medical doctor (ED) supported by medically trained research assistants using structured data forms, which was carried out in 2015. Between April and August 2015, parents were invited to complete an online questionnaire concerning the neonatal period and the patient’s health and exposures in the first two years of life.

Ethical approval was granted by the Regional Committee on Research involving Human Subjects. All parents gave written informed consent for the study.

1.3. Definitions of outcome and prognostic variables

We used the occurrence of postoperative complications within one year after initial hypospadias surgery as described in the medical records as outcome variable. There is a follow-up at the outpatient clinic after one week, six weeks, and six and twelve months. Hypospadias-related complications were described as wound-related complications (wound dehiscence, wound infection, or mental retraction), urinary tract infections (UTIs), urethrocutaneous fistulas, meatal or urethral stenosis, and prepucce-related complications (prepucce fistulas, prepucce dehiscence, or phimosis). For patients who needed reintervention within one year after initial surgery (n = 29, 8%), only complications after the initial repair were analyzed.

We selected potential prognostic variables based on importance according to the literature. Because we aimed to develop a model that could be used for preoperative risk prediction, only variables available during preoperative parental consultation were selected. The definition and categories of all variables taken into consideration for the prognostic model can be found in Table 1.

1.4. Statistical analysis

Descriptive statistics were used to provide an overview of all relevant variables and to perform a nonresponse analysis for the online parental questionnaire. Method of anesthesia, perioperative use of antibiotics, and type of postoperative bandage were excluded as prognostic variables because of little variation among current patients owing to the present-day standard of care. Eleven candidate prognostic factors remained for modeling of which five were treatment-related (hypospadias phenotype, type of surgery, surgeon’s experience, chordectomy, and type of prepucce reconstruction) and six patient-related (birth weight, mode of delivery, breast feeding, child age and weight-for-age at time of surgery, and exposure to smoking in the first two years of life).

Missing values were imputed with 50 data replicates using multiple imputation by the chained equations (MICE) method [16], in which all prognostic variables were considered and the outcome variable (postoperative complications) were taken into account. Using multivariable logistic regression and stepwise backward selection (with individual variable p-values of 0.20), variables were selected for the final model. The p-values were derived from the significance of the pooled estimate for that variable obtained from the imputed datasets. Estimates were pooled using Rubin’s rule [17].

1.5. Model performance and validation

The model’s performance was examined with discrimination and calibration statistics [18]. Discrimination was assessed by the C statistic, also known as the area under the receiver operating characteristic (ROC) curve (AUC) and calibration by the Hosmer–Lemeshow test. To provide a more accurate estimate of model performance, 1000 random bootstrap samples were drawn from each imputed data set to obtain a corrected C statistic for each set [19]. The mean of these corrected C statistics was used to indicate model discrimination. Compared to other methods of internal validation, such as split-sample and cross-validation modeling, bootstrap resampling techniques produce stable and nearly unbiased estimates of predictive accuracy with better efficiency [19].

All statistical analyses were performed using SPSS Statistics, Version 22.0 for Windows (IBM SPSS Inc., Chicago, IL, USA) and RStudio version 1.0.143 (RStudio: Integrated Development for R. RStudio, Boston, MA, USA http://www.rstudio.com/).

2. Results

2.1. Study population

Of the 945 hypospadias patients available in the AGORA data- and biobank (Fig. 1), 589 patients were excluded, mostly because of surgery before 2003 (n = 308), insufficient medical information (n = 86), proximal hypospadias (n = 54), or multistage correction (n = 43), leaving 356 patients for analysis. The online parental questionnaire was completed for 235 patients (66%). Nonresponse analysis showed that sons of responders more often had prepucce reconstruction and a higher birth weight than those of nonresponders (65% vs 52%, and 3400 g vs 3135 g, respectively).

The majority of patients were of Caucasian origin and the median follow-up after hypospadias correction was 3.2 years (5–95% range: 1.2–8.9 years). The preoperative meatal location was anterior in 77% and middle in 23% of patients (Table 2). Anterior hypospadias was most frequently corrected using MAGPI/meatoplasty/meatal or urethral advancement (57%), whereas TIP/tubularization was most common for middle hypospadias (63%). A chordectomy was performed in 66% of patients, prepucce reconstruction in 61%, and circumcision in 34%. The prepucce was left untouched in 5% of patients on specific request of the parents. Ninety percent of corrections were performed by one of the three current pediatric urologists. The median surgeons’ experience was 9.9 (0.9–17.7) years.

Median birth weight was 3330 (1978–4262) g and 22% of the children were born by caesarean section. Seventy-seven percent of children were breast fed, with a median duration of 4.0 (0.2–11.2) months. Median age at time of surgery was 13.5 months (9.8 months–5.0 years). Approximately 27% of patients were exposed to smoking in the first two years of life.
2.2. Prediction model

One or more hypospadias-related complications within one year after initial one-stage hypospadias repair were found in 66 patients (19%), of which 45 patients had a reintervention. Wound-related complications were the most frequent (n = 40). Fistulas (n = 11), UTIs (n = 8), stenosis (n = 4), and prepuce-related complications (n = 14) occurred in 1%-4% of patients.

A number of patients had missing information on prognostic variables mostly owing to incomplete online questionnaires: chordectomy (n = 2, <1%), prepuce surgery (n = 4; 1%), surgeon's experience (n = 3; <1%), birth weight (n = 23; 6%), mode of delivery (n = 182; 51%), breast feeding (n = 125; 35%), weight-for-age at time of surgery (n = 19; 5%), and exposure to smoking (n = 130; 37%). By multiple imputation of these missing values, however, the total study population could be used in development of the prediction model.

In the final model, no patient-related variables remained, but the treatment-related variables hypospadias phenotype, surgical technique (no urethroplasty vs. others and MAGPI/meatusplasty and meatal or urethral advancement vs. others), chordectomy, and surgeon's experience were included. These variables are presented in Table 3, with their coefficient estimates and standard errors and the corresponding odds ratios (ORs) with 95% confidence intervals (CIs). Performing no urethroplasty or performing a MAGPI/meatusplasty and meatal or urethral advancement instead of another surgical technique seemed to decrease the risk of postoperative complications, whereas having a middle hypospadias, chordectomy, and more years of surgical experience was associated with increased complication risks.
By inserting the type of hypospadias and the relevant treatment information for a patient in the logistic regression model with the coefficients from Table 3, probability estimates can be calculated for the individual patient’s postoperative complication risk. The model demonstrated good discrimination (C statistic = 0.76; bias-corrected C statistic = 0.70) and calibration, as no substantial deviation from the 45° line of perfect fit was observed (Hosmer–Lemeshow test $\chi^2 = 5.9; p = 0.66$) (Fig. 2).

3. Discussion

This is the first study to develop and internally validate a prediction model for the risk of postoperative complications after hypospadias surgery. Hypospadias phenotype, surgical technique, chordectomy, and surgeon’s experience were found to be prognostic factors and the model had a good discriminative ability and calibration. The model may improve preoperative counseling by giving parents an estimate of the postoperative complication risk.

3.1. Strengths and limitations

The strengths of this study are the extensive (partially routine) data collection and the availability of a relatively large number of patients who had hypospadias surgery in one clinic. Therefore, many variables could be included in the initial prediction model, including various patient-related factors, and be assessed for their effects on postoperative complications. A limitation of the study is the retrospective nature of the data. Although medical records were reviewed to gather information on treatment-related factors and complications, these were not always reported in a standardized manner and were based on the clinical opinion of the evaluating physician or nurse practitioner. As observed in previous studies, complication registration in medical records may be incomplete [20,21], which could have reduced the accuracy of the model.

Most patient-related factors were collected using self-reported questionnaires, sometimes completed a long time after the time period of interest. This may have introduced some misclassification, but except
for smoking, these variables (i.e. birth weight, mode of delivery, and breast feeding) were clearly defined and easy to recall, especially since birth of a child is a major life event. Owing to nonresponse and incomplete parental questionnaires, however, some patient-related variables contained a large number of missing values. This was remedied by multiple imputation, assuming that missingness was completely at random, although nonresponse analysis showed some differences between the responders (66%) and nonresponders (34%) in birth weight and prepuce surgery. As these factors were not included in the final prediction model, we expect these differences not to have had large consequences. To have a suitable number of events per variable for the development of the multivariable prediction model, the number of potential prognostic factors was reduced by excluding factors that have little variation in present-day standard of care [22].

Table 2
Characteristics of the total study population and divided by the occurrence of main complications within 1 year after hypospadias repair.

| Totala | No complications | Complications within 1 yearb |
|--------|------------------|-------------------------------|
| n = 356| n = 290          | n = 66                       |

| Treatment-related factors |          |          |          |
|---------------------------|----------|----------|----------|
| Hypospadias phenotype     |          |          |          |
| Anterior                  | 274 (77.0) | 238 (82.1) | 36 (54.5) |
| Middle                    | 82 (23.0)  | 52 (17.9)  | 30 (45.5) |
| Surgical technique        |          |          |          |
| No urethroplastyd         | 53 (14.9)  | 45 (15.5)  | 8 (12.1)  |
| TIP / Tubularizationd     | 99 (27.8)  | 68 (23.4)  | 31 (47.0) |
| MAGPI / meatusplasty and meatal advancementd | 172 (48.3) | 157 (54.1) | 15 (22.7) |
| Prepuce flapsf            | 20 (5.6)   | 11 (3.8)   | 9 (13.6)  |
| Mathieu and other techniques | 12 (3.4)  | 9 (3.1)    | 3 (4.5)   |
| Chordectomy               |          |          |          |
| Yes                       | 233 (65.8) | 178 (61.8) | 55 (83.3) |
| No                        | 121 (34.2) | 110 (38.2) | 11 (16.7) |
| Prepuce surgery           |          |          |          |
| Prepuce reconstruction    | 213 (60.5) | 181 (63.3) | 32 (48.5) |
| Circumcision              | 120 (34.1) | 89 (31.1)  | 31 (47.0) |
| No reconstruction performed | 19 (5.4)  | 16 (5.6)   | 3 (4.5)   |
| Surgeon's experience in years, median (90% range) | 9.9 (0.9–17.7) | 9.6 (0.8–17.4) | 11.4 (1.0–19.3) |
| Patient-related factors   |          |          |          |
| Birth weight in grams, median (90% range) | 3330 (1978–4262) | 3340 (1997–4285) | 3280 (1515–4280) |
| Mode of delivery          |          |          |          |
| Natural birth             | 136 (78.2) | 112 (77.8) | 24 (80.0) |
| Caesarean section         | 38 (21.8)  | 32 (22.2)  | 6 (20.0)  |
| Breastfeeding             |          |          |          |
| Yes                       | 178 (77.1) | 146 (77.7) | 32 (74.4) |
| No                        | 53 (22.9)  | 42 (22.3)  | 11 (25.6) |
| Child age at time of surgery |          |          |          |
| < 18 months               | 273 (76.7) | 221 (76.2) | 52 (78.8) |
| ≥ 18 months               | 83 (23.3)  | 69 (23.8)  | 14 (21.2) |
| Weight-for-age at time of surgery as z-score, mean (SD) | −0.18 (1.19) | −0.16 (1.2) | −0.29 (1.15) |
| Exposure to smoking in the first two years of lifeg |          |          |          |
| Yes                       | 61 (27.0)  | 49 (26.3)  | 12 (30.0) |
| No                        | 165 (73.0) | 137 (73.7) | 28 (70.0) |

a Numbers do not add up to total owing to missing values.
b Main complications are wound problems, urinary tract infections, fistulas, stenosis, and prepuce-related complications. The total number of these complications exceeds the number of main complications since patients can have multiple complications.
c The group 'No urethroplasty' entailed patients in which preputial reconstruction or circumcision and/or correction of the penile curvature were performed, but no urethral reconstruction.
d Tubularization using the tubularized incised plate urethroplasty (TIP) or another type of tubularization plasty.
e Meatal advancement with glansplasty incorporated (MAGPI).
f The group 'Preputial flaps' contained patients in which corrections, such as onlay flap, Duckett, or double faced onlay flap were performed.
g Exposure to smoking in the household or vicinity of the child.

Table 3
Variables included in the final prediction model with regression coefficient, standard error, adjusted odds ratio and 95% confidence interval.

| Variables                  | β coefficient | Standard error | Adjusted odds ratio | 95% Confidence interval |
|---------------------------|---------------|----------------|---------------------|-------------------------|
| Intercept                 | −1.65         | 0.41           |                     |                         |
| Middle hypospadias        | 0.56          | 0.35           | 1.75                | 0.88–3.49               |
| Surgical technique        |               |                |                     |                         |
| No urethroplastyd         | −0.78         | 0.48           | 0.46                | 0.18–1.18               |
| MAGPI / meatusplasty and meatal advancementd | −1.38 | 0.38 | 0.25 | 0.12–0.53 |
| Chordectomy performed     | 0.80          | 0.37           | 2.23                | 1.07–4.62               |
| Surgeon's experiencec     | 0.39          | 0.16           | 1.48                | 1.08–2.01               |

a The patients in this group had prepuce reconstruction or circumcision and/or correction of the penile curvature without urethral reconstruction.
b Meatal advancement with glansplasty incorporated (MAGPI).
c Additional risk for every additional year of experience.
3.2. Our findings in light of existing literature

Many studies have tried to identify factors influencing complication risk after hypospadias surgery, mostly focusing on treatment-related factors [7–11,23,24]. Although we expected patient-related factors to contribute to this risk as well, these factors were dropped from the prediction model in our analyses. The study showed that treatment-related factors (hypospadias phenotype, surgical technique, chordectomy, and surgeon’s experience) indeed play an important role in the risk of complications. The model presented is the first to combine these treatment-related factors to predict the individual risk. Middle hypospadias phenotype and the need for a chordectomy resulted in higher complication risks which correspond with findings in previous studies, as are the results that certain surgical techniques have a lower risk than others [7,8,10,24]. However, whereas other studies showed improved results with more years of surgical experience [7,9], more experience seemed to have the opposite effect in our model. This is most likely because of the more experienced surgeons performing surgery on the more complicated cases in our hospital. Therefore, years of surgical experience should be considered as a proxy variable for one or more underlying treatment-related factors. Moreover, the results of the separate variables in the model are not strictly to be seen individually, but only in the view of the entire model. Although we took many variables into account in development of the model, several other variables may play a role in decision making around hypospadias surgery, which leave room for improvement of our model.

3.3. Clinical implications

Ideally, we would have developed a prediction model to optimize surgical circumstances, for example determining the type or timing of surgery with the lowest risk of complications. However, this was not possible with the observational data available for model development [25]. Our model was based on primary one-stage corrections for anterior or middle hypospadias performed in a university hospital. For posterior hypospadias, multistage corrections are mostly used, which have a higher complication rate [26]. Since reoperations have different
complication rates as well [27,28], this prediction model should not be used to predict complications after multistage corrections or repeat surgery.

Patients in our hospital are usually discharged after one overnight stay with a urethral dripping catheter in place. A nurse practitioner contacts the parents a few days later to ask for complications, and the patient visits the outpatient clinic one week after surgery to remove the postoperative dressing and urethral catheter. Medical care applied and postoperative follow-up may vary between medical institutions, potentially resulting in different reported complications rates. Therefore, external validation is advised before introducing this model in another hospital setting.

Because hypospadias correction is not required in all patients, it is important to provide parents with an objective perspective of the expected postoperative outcome and the complication risk during preoperative consultation, to help them make a well-informed decision. Our prediction model can inform and prepare parents regarding the development of complications, which will hopefully reduce decisional regrets afterwards.

4. Conclusion

To our knowledge, this study is the first to develop and internally validate a prediction model for complication risk after one-stage surgery for anterior and middle hypospadias. The final model included the factors hypospadias phenotype, surgical technique, chordectomy, and surgeon’s experience and showed a good discriminative ability and calibration. We found patient-related factors not to predict postoperative complication risk. Although external validation is still needed, this model is a first step towards an effective individualized risk prediction of complications after hypospadias surgery and may improve preoperative parental counseling.

References

[1] Pierik FH, Burdorf A, Nijman JR, et al. A high hypospadias rate in the Netherlands. Hum Reprod. 2002;17:1112–5.
[2] Nissen KI, Udesen A, Garne E. Hypospadias: prevalence, birthweight and associated major congenital anomalies. Congenit Anom (Kyoto). 2015;55:37–41.
[3] Kass E, Kogan S, Manley C, et al. Timing of elective surgery on the genitalia of male children with particular reference to the risks, benefits, and psychological effects of surgery and anesthesia. Pediatrics. 1996;97:590–4.
[4] Nuijinaa JE, De Gier RP, Verschuren R, et al. Long-term outcome of different types of 1-stage hypospadias repair. J Urol. 2005;174:1544–8.
[5] Ghidini F, Sekuловić S, Castagnetti M. Parental decisional regret after primary distal hypospadias repair: family and surgery variables, and repair outcomes. J Urol. 2016;195:720–4.
[6] Lorenzo AJ, Salle JLP, Zlateska B, et al. Decisional regret after distal hypospadias repair: single institution prospective analysis of factors associated with subsequent parental remorse or distress. J Urol. 2014;191:1558–63.
[7] Cimador M, Vallasciana S, Manzioni G, et al. Failed hypospadias in paediatric patients. Nat Rev Urol. 2013;10:657–66.
[8] Eassa W, Jednak R, Capolicchio JP, et al. Risk factors for re-operation following tubularized incised plate urethroplasty: a comprehensive analysis. Urology. 2011;77:716–20.
[9] Lee OT, Durbin-Johnson B, Kurzrock EA. Predictors of secondary surgery after hypospadias repair: a population based analysis of 5,000 patients. J Urol. 2013;190:251–6.
[10] Prat D, Nataša A, Polak A, et al. Surgical outcome of different types of primary hypospadias repair during three decades in a single center. Urology. 2012;79:1350–3.
[11] Sarhan OM, El-Hefawy AS, Hafez AT, et al. Factors affecting outcome of tubularized incised plate (TIP) urethroplasty: single-center experience with 500 cases. J Pediatr Urol. 2009;5:378–82.
[12] Chiswell C, Akram Y. Impact of environmental tobacco smoke exposure on anaesthetic and surgical outcomes in children: a systematic review and meta-analysis. Arch Dis Child. 2017;102:123–30.
[13] Salminen S, Gibson C, McCartney A, et al. Influence of mode of delivery on gut microbiota composition in seven year old children. Gut. 2004;53:1388–9.
[14] Talbot LJ, Sinyard RD, Riaison KL, et al. Influence of weight at enterostomy reversal on surgical outcomes in infants after emergent neonatal stoma creation. J Pediatr Surg. 2017;52:35–40.
[15] van Rooij IA, van der Zanden LF, Borgers EM, et al. AGORA, a data-and biobank for birth defects and childhood cancer. Birth Defects Res A Clin Mol Teratol. 2016;106:675–84.
[16] Van Buuren S, Groothuis-Oudshoorn K. mice: Multivariate imputation by chained equations in. R J Stat Softw. 2011;45.
[17] Rubin DB. Multiple imputation for nonresponse in surveys. New York: John Wiley & Sons; 2004.
[18] Steyerberg EW, Vickers AJ, Cook NR, et al. Assessing the performance of prediction models: a framework for some traditional and novel measures. Epidemiology. 2010;21:128.
[19] Steyerberg EW, Harrell FE, Borsboom GJ, et al. Internal validation of predictive models: efficiency of some procedures for logistic regression analysis. J Clin Epidemiol. 2001;54:774–81.
[20] Sethi MVA, Zimmer J, Ure B, et al. Prospective assessment of complications on a daily basis is essential to determine morbidity and mortality in routine pediatric surgery. J Pediatr Surg. 2016;51:630–3.
[21] Dokter EM, Goosen EE, van der Zanden LF, et al. Level of agreement on postoperative complications after one-stage hypospadias correction comparing medical records and parent reports. J Pediatr Surg. 2019;54:1825–31.
[22] Moons KG, Royston P, Vergouwe Y, et al. Prognosis and prognostic research: what, why, and how? BMJ. 2009;338:b3375.
[23] Bush NC, Holzer M, Zhang S, et al. Age does not impact risk for urethroplasty complications after tubularized plate repair by hypospadias in prepubertal boys. J Pediatr Urol. 2013;9:252–8.
[24] Spinoti A-F, Poeault F, Van Praet C, et al. Grade of hypospadias is the only factor predicting for re-intervention after primary hypospadias repair: a multivariate analysis from a cohort of 474 patients. J Pediatr Urol. 2013;11:70.e1–6.
[25] Harrell FL, Laura. outcome prediction vs. optimal treatment selection: EHRs and RCTs; 2017 [1-8-2017]. Available from: http://www.fharrell.com/post/ehrs-rcts/.
[26] Aigner Y, Cheikhellah A, Lottmann H, et al. Hypospadias: surgery and complications. Horm Res Paediatr. 2010;74:218–22.
[27] Manzioni G, Marroco G. Reoperative hypospadias. Curr Opin Urol. 2007;17:268–71.
[28] Mousavi SA, Aarabi M. Tubularized incised plate urethroplasty for hypospadias reoperation: a review and meta-analysis. Int Braz J Urol. 2014;40:588–95.