Early Warning Model Construction and Validation for Urinary Tract Infection in Patients with Neurogenic Lower Urinary Tract Dysfunction (NLUTD): A Retrospective Study

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Background. This study was performed to construct and validate an early risk warning model of urinary tract infection in patients with neurogenic lower urinary tract dysfunction (NLUTD). **Methods.** Eligible patients with NLUTD admitted to Shenzhen Longcheng hospital from January 2017 to June 2021 were recruited for model construction, internal validation and external validation. The first time point of data collection was within half a month of patients first diagnosed with NLUTD. The second time point was at the 6-month follow-up. The early warning model was constructed by Logistic regression. The model prediction effects were validated using the area under the Receiver Operating Characteristic curve, the Boostrap experiment and the calibration plot of the combined data. The model was externally validated using sensitivity, specificity and accuracy. **Results.** Six predictors were identified in the model, namely patients≥65 years old (OR=2.478, 95%CI: 1.215 ～5.050), female (OR=2.552, 95%CI: 1.286 ～5.065), diabetes (OR=2.364, 95%CI) : 1.182 ~4.731), combined with urinary calculi (OR=2.948, 95%CI: 1.387 ～6.265), indwelling catheterization (OR=1.988, 95%CI: 1.003 ～3.940) and bladder behavior training intervention time ≥2 weeks (OR=2.489, 95%CI: 1.233 ～5.022); and the early warning model formula was Y = 0.907 × age+ 0.937 × sex + 0.860 × diabetes+ 1.081 × combined with urinary calculi+ 0.687 ×indwelling catheterization+ 0.912 ×bladder behavior training intervention time-2.570. The results show that the area under the ROC curve is 0.832, which is close to that of 1,000 Bootstrap internal validation (0.828). The calibration plot shows that the early warning model has good discrimination ability and consistency. The external validation shows the sensitivity is 62.5%, the specificity is 100%, and the accuracy is 90%. **Conclusion.** The early warning model for urinary tract infection in patients with NLUTD is suitable for clinical practice, which can provide targeted guidance for the evaluation of urinary tract infection in patients with

NLUTD.

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[Abstract]

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23 first diagnosed with NLUTD. The second time point was at the 6-month follow-up. The early

24 warning model was constructed by Logistic regression. The model prediction effects were

25 validated using the area under the Receiver Operating Characteristic curve, the Boostrap

26 experiment and the calibration plot of the combined data. The model was externally validated

27 using sensitivity, specificity and accuracy.

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30 95%CI) : 1.182 ~4.731), combined with urinary calculi (OR=2.948, 95%CI: 1.387 ～6.265),

31 indwelling catheterization (OR=1.988, 95%CI: 1.003 ～3.940) and bladder behavior training

32 intervention time ≥2 weeks (OR=2.489, 95%CI: 1.233 ～5.022); and the early warning model

33 formula was Y = 0.907 × age+ 0.937 × sex + 0.860 × diabetes+ 1.081 × combined with urinary

34 calculi+ 0.687 ×indwelling catheterization+ 0.912 ×bladder behavior training intervention time-

35 2.570. The results show that the area under the ROC curve is 0.832, which is close to that of

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38 sensitivity is 62.5%, the specificity is 100%, and the accuracy is 90%.

39 **Conclusion.** The early warning model for urinary tract infection in patients with NLUTD is

40 suitable for clinical practice, which can provide targeted guidance for the evaluation of urinary

41 tract infection in patients with NLUTD.

42 [Keywords] Neurogenic lower urinary tract dysfunction; Neurogenic bladder; Urinary tract

43 infection; Early waring model; Risk factors

44 **INTRODUCTION**

45 Neurogenic lower urinary tract dysfunction (NLUTD) refers to abnormal function of either the

46 bladder, bladder neck, and/or its sphincters caused by lesions to the central or peripheral nervous

47 system (Jahromi et al., 2014; Panicker et al., 2013) It is often clinically manifested as poor

48 urination, urinary retention, abnormal ejaculation and other symptoms such as lower urinary tract

49 and sexual dysfunction (Amarenco et al., 2017). NLUTD could cause a series of urinary

50 complications, such as hydronephrosis, pyelonephritis and urinary tract infection (UTI) (Lima et

51 al., 2015; Manack et al., 2011). Significantly, UTI is the most common complication. Unsal-

52 Delialioglu et al. reported that 70% of febrile spinal cord injury patients with NLUTD in

53 rehabilitation units developed urinary tract infections (Unsal-Delialioglu et al., 2010).

54 Meanwhile, another study also shows the prevalence of UTI is>50% among patients with

55 NLUTD (Nicolle et al., 2005). Once a patient develops UTI, it will seriously affect the

56 rehabilitation of the primary disease and may further cause secondary damage to the upper

57 urinary tract, leading to renal function damage and even death (Amarenco et al., 2017;

58 Wagenlehner & Pilatz, 2018). Furthermore, UTI is an independent risk factor leading to renal

59 damage, and UTI has serious adverse effects on the prognosis of patients with NLUTD (Chow et

60 al., 2018).

61 As for effective preventive measures, intermittent catheterization may be associated with fewer

62 urinary tract infections (Hooton et al., 2010; Siroky, 2002). The evidence showed that bladder

63 irrigations, the use of hydrophilic catheters and the frequency of intermittent self-catheterization

64 can reduce the risk of UTI (Cox et al., 2017; Lapides et al., 1972; Vo et al., 2013). However,

65 there is no consensus among current studies on the effects of prophylactic antibiotics for

66 preventing UTI. Catheters impregnated with antibiotics or silver-coated catheters have shown

67 short-term effects on bacteriuria and infection (Prieto et al., 2017; Salameh et al., 2015).

68 However, with prolonged use, antibiotic resistance may develop (Salameh et al., 2015). In

69 addition, aseptic bacteriuria should not be treated because treatment of asymptomatic bacteriuria

70 does not prevent febrile urinary tract infection or infection recurrence and increases bacterial

71 resistance and virulence due to antibiotics (D'Hondt & Everaert, 2011; Vasudeva &

72 Madersbacher, 2014). Bacterial interference may promise to prevent UTI, but more evidence is

73 currently needed (Dinh et al., 2019).

74 Given the high incidence and severe impacts of UTI among NLUTD patients, early identification

75 of risk factors for UTI in patients with NLUTD is essential. Common risk factors of UTI in

76 patients with NLUTD include diabetes mellitus, hypoalbuminemia, long-term indwelling

77 catheter, multiple intermittent catheterization, frequent bladder irrigation and intervention time

78 for bladder function retraining (Fang et al., 2018; Kinnear et al., 2020; Pang & Li, 2013; Zhang

79 et al., 2021). However, identifying clinical risk factors for UTI is based on experts' opinions,

80 without using contemporary modelling techniques, which is not helpful in accurately classifying

81 patients. Furthermore, some researchers have shown that independent risk factors for UTI in

82 patients with NLUTD include indwelling catheter, bladder capacity <200ml, increased bladder

83 pressure and bladder emptying method (Anderson et al., 2019; Zhang et al., 2021). However, no

84 study has investigated whether bladder treatment-related parameters are predictors for urinary

85 tract infection in patients with NLUTD. Therefore, this study collected general information,

86 disease characteristics and bladder treatment-related parameters of patients with NLUTD to

87 construct the early warning UTI model among NLUTD patients. This study could provide novel

88 insights for clinical early screening of such patients, which could strengthen the prediction of

89 UTI in patients with NLUTD during rehabilitation and adopt active individuals for patients with

90 different risk levels.

91 **MATERIALS AND METHODS**

92 **Participants**

93 Eligible patients with NLUTD admitted to Shenzhen Longcheng Hospital from December 2017

94 to December 2020 were retrospectively selected as construction and internal validation research

95 subjects, and patients from January 2021 to June 2021 were selected as external validation

96 research objects. The inclusion criterion was patients first diagnosed with NLUTD (ICD-10 code

97 N31.901), while the exclusion criteria were ① UTI co-existing with pulmonary infection, wound

98 infection, etc., namely secondary UTI; ② cannot obtain the required medical records, such as

99   lack of blood routine, renal function, urological imaging data or urodynamic; ③ patients did not

100   complete the 6-month follow-up.

Data collection

102   We collected the following predictors half-month after patients diagnosed with NLUTD: (1)

103   General clinical data: including gender, age, body mass index (BMI), diabetes, hypertension,

104   urinary calculi, etc.; (2) Disease characteristics and bladder treatment-related data: including

105   NLUTD type based on clinical manifestation (detrusor overactivity type, detrusor inactivity type

106   and mixed type), catheterization method (voiding/intermittent catheterization and indwelling

107   catheterization), preventive use of antibacterial drugs, time to start the bladder behavior training,

108   serum albumin, serum creatinine, total serum bilirubin and blood urea nitrogen. Time to start the

109   bladder behavior training <2 weeks means that the training started within two weeks of the first

110   diagnosis of NLUTD. The bladder behaviour training included scheduled urination, delayed

111   urination, reflex urination, anal stretch techniques, and pelvic floor muscle training. Patients with

112   indwelling catheterization only performed anal stretch techniques and pelvic floor muscle

113   training.

114   The end point outcome observation time is at six-month follow-up. All patients underwent

115   routine urinalysis and urine culture tests. The clinical diagnosis of UTI met the relevant

116   standards in the "Guidelines on urological infections" formulated by the European Association of

117   Urology (European Association, 2021). Clinical symptoms of UTI include urgent urinary,

118   frequent urination, urinary retention, dysuria, lumbago, and urination pain. Physical signs

119   included fever, costovertebral angle tenderness/pain and suprapubic tenderness. Patients with an

120   axillary temperature of > 37.5 were considered febrile. According to the above clinical

121   manifestations, this study assesses UTI with "yes" if one of the following conditions is met and

122   with one of above clinical manifestations: (1) Diagnosis of UTI in medical records; (2) Positive

123   urine culture; (3) Fresh urine specimens were centrifuged and examined by phase contrast

124   microscopy (400x). Bacteria were observed in half of every 30 visual fields.

125 **Ethical approval**

126 This study was approved by the Medical Ethics Committee of Shenzhen Longcheng Hospital

127 (LCLL(3)--2021). Since this study is a retrospective study and there is no medical risk to the

128 patients, the patient's informed consent was exempted with the approval of the Medical Ethics

129 Committee.

130 **Statistical analysis**

131 The data was analyzed by SPSS 22.0 software and R statistics version 3.6.3, utilizing the ROCR

132 package for all analyses. The count data of patients' age, BMI and diabetes were described by

133 frequency and percentage. The comparison between UTI and non-UTI groups was performed by

134 univariate regression analysis. P < 0.05 indicated that the difference was statistically significant.

135 The logistic regression model was used to construct the risk prediction model. The prediction

136 ability of the model was evaluated by the AUROC (Are Under Receiver Operating Characteristic)

137 curve, C-index and the calibration curve. Bootstrapping with 1,000 resamples was done to

138 calculate a relatively accurate C-index for internal cross-validation (Steyerberg, 2019; Van

139 Calster et al., 2016; Van Calster & Vickers, 2015). The external validation was conducted by

140 using sensitivity, specificity and accuracy (Steyerberg, 2019).

141 **RESULTS**

142 There were 206 patients for the model construction and internal validation (See Figure 1). The

143 age ranged from 35 to 88, and their mean age was 62.79 ± 18.95. Among them, 60 (29.1%) had

144 UTI, while 146 patients did not develop UTI. There were 30 patients for the external validation,

145 19 males and 11 females. The age ranged from 20 to 86 (51.72 ± 13.51).

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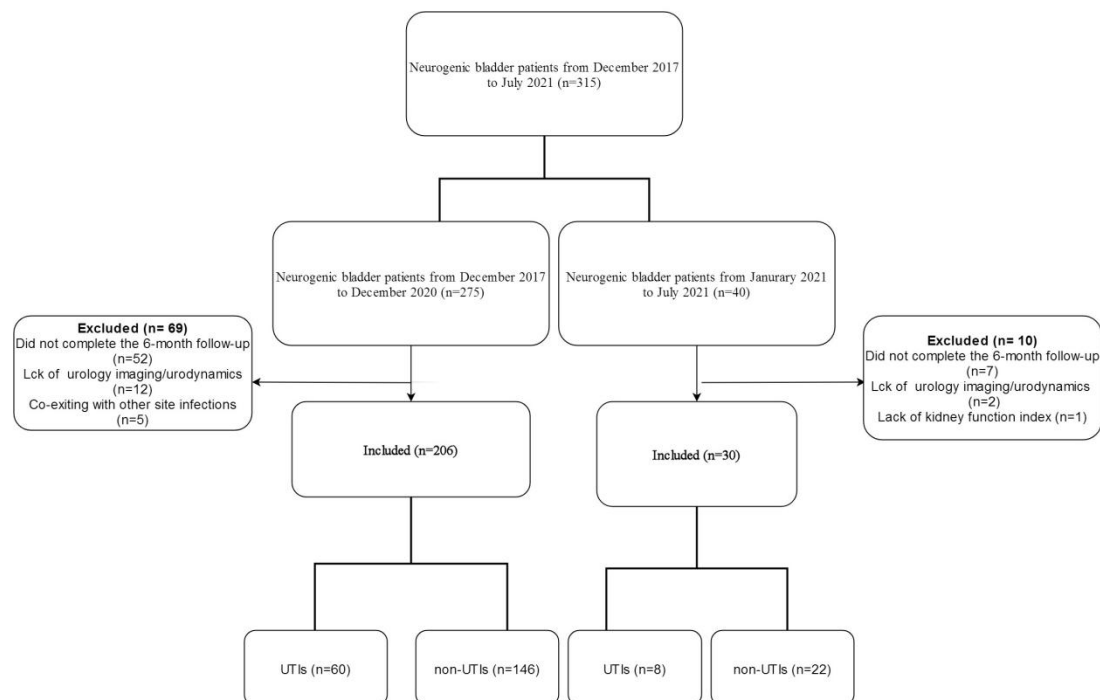


Figure 1 Flowchart of inclusion

Univariate regression analysis of NLUTD patients between groups

The clinical data of patients with UTI and those without UTI was analyzed by univariate analysis. The results showed that the proportion of ≥65 years old, complicated with diabetes, urinary calculi, hypoproteinemia and female patients in the UTI group was significantly higher than that of the non-UTI group. The proportion of patients with intermittent catheterization and time to start bladder training <2 weeks was significantly lower in the UTI group than in the non-UTI group (P <0.05). See Table 1.

Table 1 Univariate analysis among NLUTD patients with or without UTI (n=206)

Factor	UTI Group (N=60)	Non-UTI group (n=146) (N=146)	x 2	P

Age			6.898	0.009
≥65	42 (70.0)	73 (50.0)		
<65	18 (30.0)	73 (50.0)		
Gender			6.967	0.008
Male	28 (46.7)	97 (66.4)		
Female	32 (53.3)	49 (33.6)		
BMI (kg/m 2)			0.833	0.361
≥24	22 (36.7)	44 (30.1)		
<24	38 (63.3)	102 (69.9)		
Hypertension			2.513	0.113
Yes	26 (43.3)	81 (55.5)		
No	34 (56.7)	65 (44.5)		
Diabetes			6.668	0.010
Yes	29 (48.3)	43 (29.5)		
No	31 (51.7)	103 (70.5)		
Urinary calculi			7.688	0.006
Yes	23 (38.3)	29 (19.9)		
No	37 (61.7)	117 (80.1)		
NLUTD type			1.142	0.565
Detrusor overactivity	5 (8.3)	18 (12.3)		

type

Detrusor inactivity type	40 (66.7)	99 (67.8)		
Mixed type	15 (25.0)	29 (19.9)		
Catheterization method			6.154	0.013
Intermittent catheterization	31 (51.7)	102 (69.9)		
Indwelling catheterization	29 (48.3)	44 (30.1)		
Preventive use of antibacterial drugs			2.598	0.107
Yes	39 (65.0)	77 (52.7)		
No	21 (35.0)	69 (47.3)		
Time to start the bladder behavior training (weeks)			6.467	0.011
<2 weeks	22 (36.7)	82 (56.2)		
≥2 weeks	38 (63.3)	64 (43.8)		
Hypoproteinemia			4.875	0.027
Yes	17 (28.3)	22 (15.1)		
No	43 (71.7)	124 (84.9)		
Serum creatinine			2.184	0.139
Normal	45 (75.0)	94 (64.4)		

Abnormal	15 (25.0)	52 (35.6)		
Serum total bilirubin			1.303	0.254
Normal	53 (88.3)	136 (93.2)		
Abnormal	7 (11.7)	10 (6.8)		
Diagnosis			1.099	0.577
Spinal cord injury	42 (71.3)	107 (73.5)		
Cerebrovascular accident/ brain tumor/ stroke	12 (19.6)	21 (14.4)		
Peripheral neuropathy (such as diabetes)	6(10.1%)	18 (12.1)		

157 Notes: NLUTD, neurogenic lower urinary tract dysfunction, UTI, urinary tract infection

158 **Multivariate regression analysis among NLUTD patients with UTI**

159 The statistically significant factors in the univariate analysis were used as independent

160 variables, and whether the patient had a UTI during the follow-up period was used as the

161 dependent variable, and binary logistic regression analysis was performed (see Table 2). The

162 results showed that under the premise of controlling for other confounding factors, patients

163 age ≥65(OR=2.478 , 95%CI : 1.215 ～5.050), female patients (OR=2.552 , 95%CI : 1.286 ～

164 5.065), diabetes (OR= 2.364 , 95% CI : 1.182 ~ 4.731), combined urinary calculi (OR =

165 2.948 , 95% CI : 1.387 ~ 6.265), indwelling catheterization embodiment (OR = 1.988 , 95%

166 CI : 1.003 ~ 3.940) and bladder behavior training intervention time ≥ 2 weeks

167 (OR=2.489 , 95%CI : 1.233 ~ 5.022) were independent risk factors for UTI in patients with

168 NLUTD (P <0.05). The final formula was Y = 0.907 × age + 0.937 × female gender + 0.860

169 × diabetic + 1.081 × urinary calculi + 0.687 × indwelling catheterization + 0.912 ×Time to start

170 bladder behavior training ≥ 2 weeks + 0.547 × hypoproteinemia -2.570 . See Table 2 for details.

171 Y means the calculated UTI risk prediction score.

172 Table 2 Multivariate regression analysis among NLUTD patients (n=206)

factor	Assignment method	Regression coefficients	Standard error	Wald value	P	OR	95% confidence interval Upper limit	Lower limit
Age	≥65 years old = 1 , <65 years old = 0	0.907	0.363	6.235	0.013	2.478	1.215	5.050
Gender	Female =1 , Male =0	0.937	0.350	7.173	0.007	2.552	1.286	5.065
With diabetes	Yes =1 , No =0	0.860	0.354	5.912	0.015	2.364	1.182	4.731
Combined with urinary calculi	Yes =1 , No =0	1.081	0.385	7.898	0.005	2.948	1.387	6.265
Catheterization method	Indwelling catheterization =1 , Intermittent catheterization =0	0.687	0.349	3.870	0.049	1.988	1.003	3.940
Time to start bladder behavior	≥2 weeks =1 , <2 weeks =0	0.912	0.358	6.476	0.011	2.489	1.233	5.022

training								
Hypoproteine mia	Yes =1 , No =0	0.547	0.422	1.674	0.196	1.727	0.755	3.952
constant		-2.570	0.638	16.223	0.000	0.077		

173 Notes: NLUTD, neurogenic lower urinary tract dysfunction

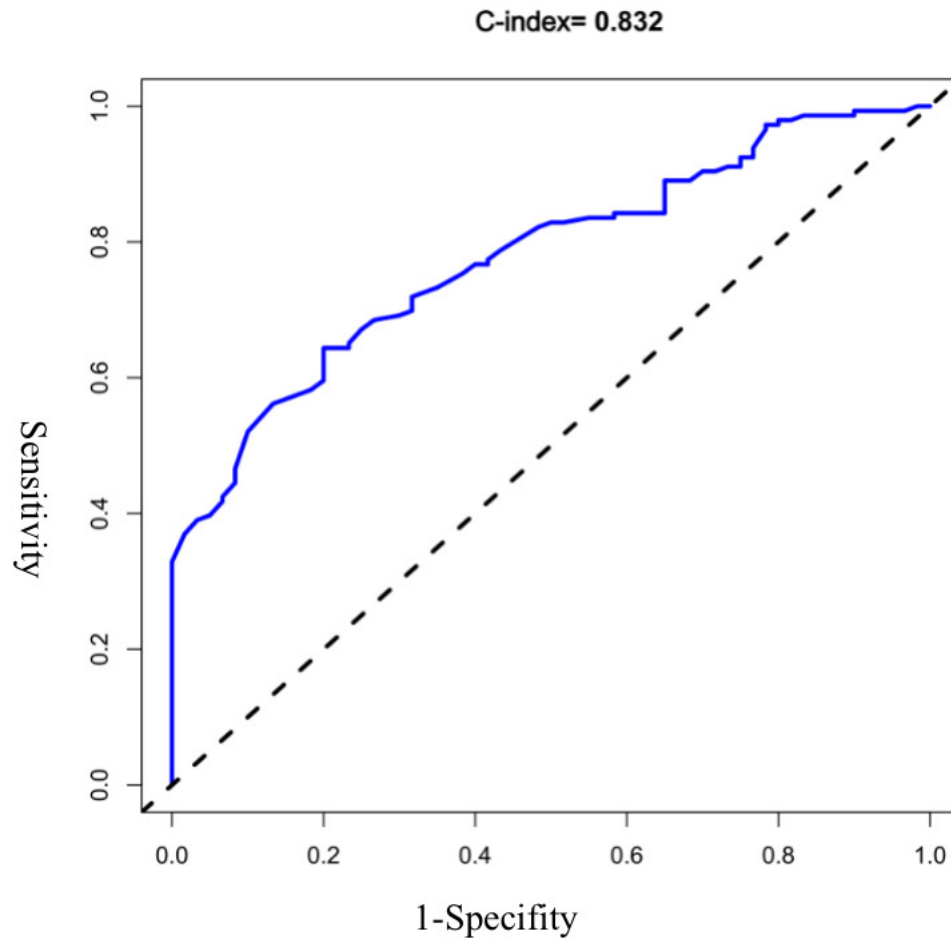
174 **Internal evaluation of the early warning model**

175 The AUROC of the model was evaluated, and the initial C-index was 0.832 (see Fig 2). The

176 Youden index was 0.82+0.59-1= 0.41. The C-index of 1,000 Bootstrap internal validations was

177 0.828 (see Fig 3). The calibration curve showed that the predicted value of the model and the

178 observed value had a certain correlation (see Fig 4), indicating that the model had a higher

179 probability of predicting the occurrence of UTI and the actual probability of occurrence.

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181   Fig 2. ROC curve of the initial early warning model

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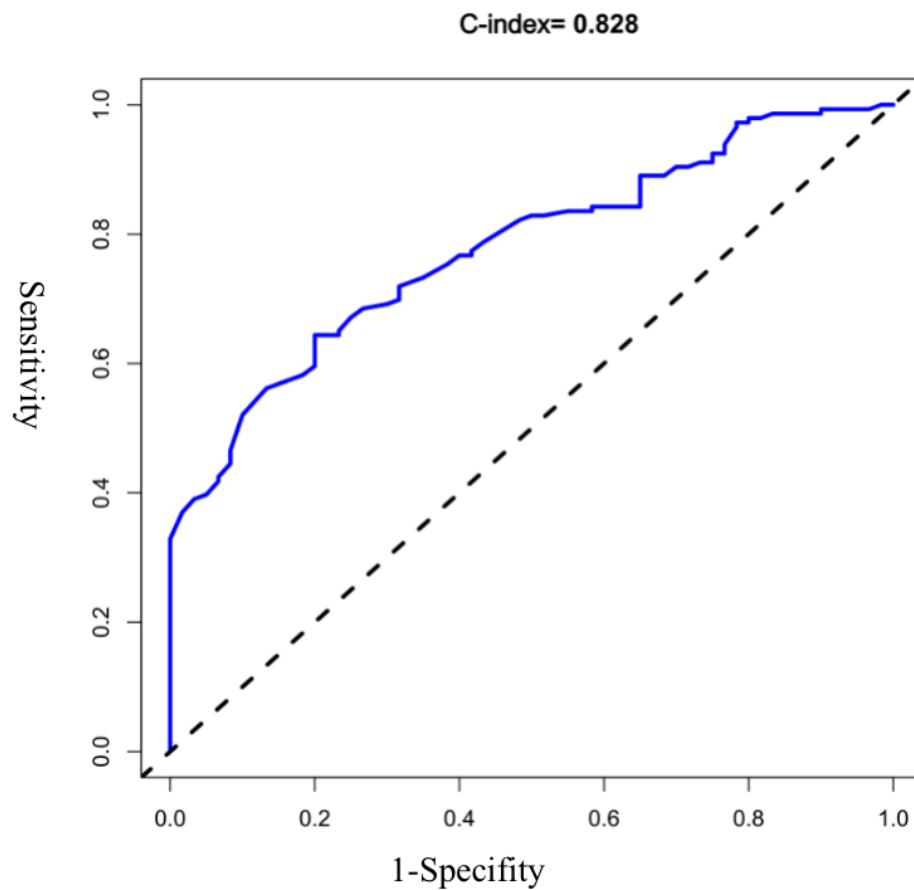
Fig 3. ROC curve of 1,000 Bootstrap internal validations

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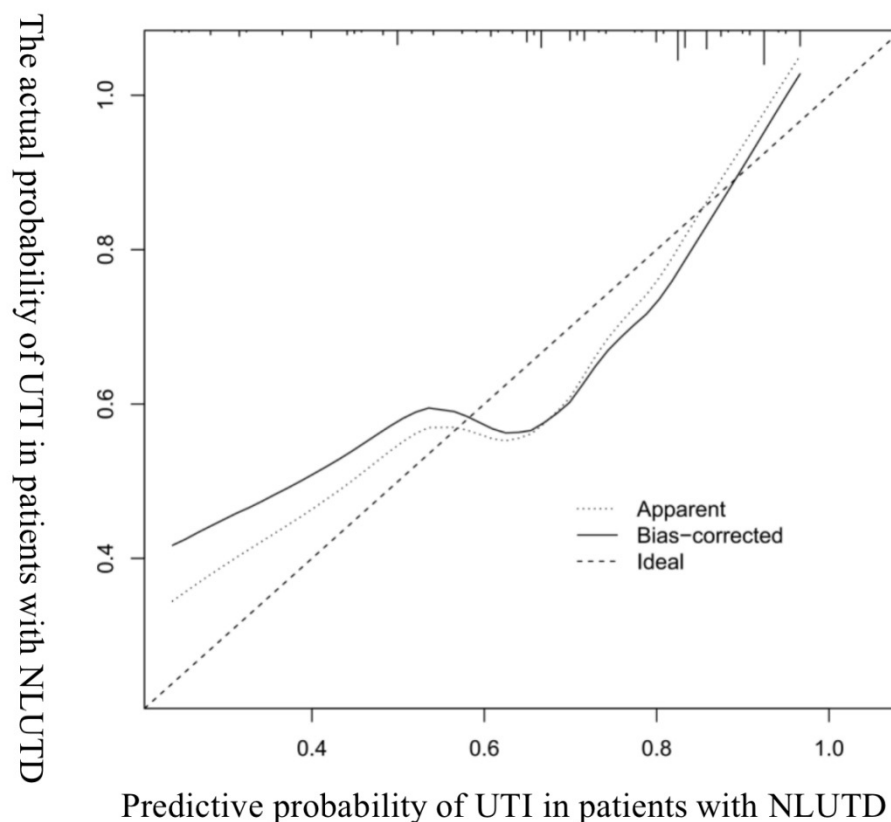
186   Fig 4. Calibration curve diagram of UTI in patients with NLUTD

187   **External validation of the early warning model**

188   Thirty eligible patients with NLUTD treated in Shenzhen Longcheng hospital from January to

189   June 2021 were included for external validation. There were 19 males and 11 females. The age

190   ranged from 20 to 86 (51.72 ± 13.51). According to the formula of this prediction model, when

191   calculated UTI prediction score $\geqslant 0.41$, it is considered that the patient will occur UTI. This

192   model predicts that 5 patients will occur UTI and 25 patients will not occur UTI within 6-month

193   follow-up. The results were that UTI occurred in 8 patients and non-UTI occurred in 22 patients.

194   Compared with the actual results, the sensitivity of the prediction model is 62.5%, the specificity

195   is 100%, and the accuracy is 90%.

196   **DISCUSSION**

197   The risk factors of UTI in patients with NLUTD are complex, which is the result of the multiple

198   influencing factors. The occurrence is related to the localized bacterial colonization,due to

199   patient's decreased ability to urinate autonomously and the loss of urine flushing in the urethra,

200   and also associated with the patients' own physiological and pathological factors,as welas

201   treatment methods. In this study, we found that age ≥65 years old, female patients, combined

202   with diabetes, urinary calculi, indwelling catheterization and bladder behavior training

203   intervention time ≥ 2 weeks could be used to identify the high risk of UTI in patients with

204   NLUTD. Sixty patients occurred UTI in 206 patients with NLUTD; the incidence rate was

205   29.1%, significantly lower than the 45.37% (Shi et al., 2020) and 45.59% (Pang & Li, 2013)

206   reported by the other domestic researchers. The main reason may be the difference of the

207   NLUTD pathogenic factors between this study and other studies. In Shi and Ling's analysis,

208   most reported research objects are mainly NLUTD patients caused by elderly cerebrovascular

209   accidents. Such patients often have a poor prognosis, and their bedtime is significantly longer,

210   which leads to a substantially higher risk of UTI. In the study, 70% of patients had NLUTD

211   caused by spinal cord injury, while about 20% patients had cerebrovascular accidents, stroke, or

212   brain tumor. Therefore, the incidence of UTI in this study was significantly lower than in other

213   reports.

214   **The research significance of the early warning model**

215   UTI is one of the common complications of NLUTD. Because of a variety of complex

216   factors, it can often manifest as recurrent episodes, which not only aggravates the clinical

217   symptoms of NLUTD, but also affects the renal parenchyma damage, and ultimately lead to a

218   decline in the quality of life of patients and shortened life expectancy (Van Calster & Vickers,

219   2015). Therefore, it must be actively prevented and controlled.

220   Identification of clinical risk factors for UTI is previously based on experts' opinions

221   without using contemporary modelling techniques, which is not helpful to accurately classify

222   patients, leading to insufficient prevention and treatment of UTI (Chow et al., 2018). The

223   establishment of the predictive model shifts the focus from interventions when UTI occurs to the

224   purposeful and focused prevention of UTI in people with high-risk NLUTD. This early warning

225   model intuitively displays the relevant risk factors and their correlation with the occurrence of

226   UTI, which could arouse the attention of medical staff, improve prevention, and finally reduce

227   the workload of medical staff.

228   **The prediction effect of the early warning model**

229   In this study, the ROC curve was used to test the model's fit, with specificity as the abscissa and

230   sensitivity as the ordinate. The area under the ROC curve obtained in this study is 0.832, and the

231   area under the ROC curve verified internally is 0.828. The optimal value of the area under the

232   ROC curve is 1. Moreover, the results of the calibration chart in this study are better, and its

233   slope is basically the same as the standard curve. The external validation results also showed a

234   specificity of 100% and an accuracy of 90%.

235   **Elderly female patients are prone to UTI**

236   Elderly patients are prone to infections due to decreased estrogen levels, broad and short urinary

237   tract, poor nutritional status, and reduced immunity. Studies have shown that with age, the

238   probability of occurrence of UTI increases significantly because female patients have a broad

239   and short urinary tract,which is close to the anus, leading to bacterial colonization and

240   retrograde infection (Kakde et al., 2018). Especially in elderly menopausal female patients, due

241   to the decline of ovarian function, the level of estrogen decreases significantly, which eventually

242   leads to the degeneration of the reproductive system, a decrease in blood supply to the urinary

243   tract, and a reduction in muscle tone that maintains the bladder and urethra (Jung & Brubaker,

244   2019).

245   **Patients with diabetes and urinary calculi are prone to UTI**

246   Many studies have confirmed that diabetes is closely related to UTI, and the incidence of UTI

247   has positively correlated with the course of diabetes, blood sugar levels and glycosylated

248 haemoglobin (He et al., 2018; Zubair et al., 2019). The reduction of substance metabolism in
249 diabetic patients reduces the body's synthesis of immunoglobulins, antibodies and complement,
250 thus minimizing the chemotaxis, phagocytosis and sterilization of inflammatory cytokines.
251 Therefore, the body's cellular immune barrier is destroyed, causing the drop of the immunity
252 system. In addition, patients with a long course of diabetes may be accompanied by peripheral
253 nerve and vascular disease, which may cause urinary tract blood supply disorders and lead to
254 local neurological abnormalities, degrading the genitourinary system and causing infection (Hine
255 et al., 2017). Studies have shown that urinary calculi are closely related to the occurrence of UTI,
256 and patients with urinary calculi (diameter of 2 cm or more) are at higher risk of recurrent UTI
257 (Wang & Li, 2020). The main reason is that bacteria tend to colonize on the irregular surface of
258 urinary calculi, which prevents the antibacterial drugs from reaching the site of action, resulting
259 in poor effects of antibacterial treatment.

260 **Patients who use indwelling catheterization are prone to UTI**

261 Intermittent urinary catheterization is strongly recommended for patients with NLUTD, which is
262 suitable for reducing the incidence of UTI. Still, the indwelling catheterization method had to be
263 used for some severely ill patients (extreme weakness or ureteral reflux patients) (Han et al.,
264 2017). However, as a foreign body, the urinary catheter can cause reactive inflammation when it
265 comes in contact with the urethral mucosa and bladder mucosa. The urethral mucosa is damaged
266 during the catheter operation, which further reduces the urethra physical barrier function and
267 may cause infection after bacteria enter the urethra retrogradely from the urethral orifice to
268 outside the official cavity (Menegueti et al., 2019). For patients with indwelling catheterization,
269 patients should use the closed drainage catheter system (Nicolle et al., 2005), and indwelling
270 catheters should not be replaced systematically but in the event of an obstruction, hematuria, or
271 UTI (Hooton et al., 2010). UTI may be reduced by early anal stretch techniques and pelvic floor
272 muscle training,which could help patientsimprove bladder function recovery, and reduce
273 bladder residual urine output (Ginsberg, 2013).

The correlation between hypoproteinemia and UTI remains to be verified

The study showed that the decrease of serum albumin levels in patients with NLUTD is related to UTI. The reason may be the decreased immunity of patients with hypoalbuminemia (Jiao, 2020). In this study, univariate analysis showed statistical significance between groups (P <0.05). However, regression analysis showed no statistical difference between hypoproteinemia and UTI. The main reason for this difference may be that hypoalbuminemia in this study mainly occurred in elderly patients. And the hypoalbuminemia may be excluded as a confounding factor of this model. In addition, It may also be due to the small sample size of patients with hypoproteinemia (n=39). Future studies are needed to explore whether hypoproteinemia could be used to predict UTI among patients with NLUTD.

Strengths and limitations of this research

 This study attempts to develop and validate an early warning model of UTI among patients with NLUTD compared with previous studies. This model has the characteristics of simple data acquisition and quick evaluation, which can provide purposeful and focused prevention of UTI in people with NLUTD (Autumn et al., 2018). The limitation of this study lies in that it was only verified in one hospital. This study suggests that it still needs to be verified by a large sample, multi-centre, and prospective study before the model is routinely applied to pre-clinical applications. To develop a model that was easy to use in clinical settings, we dichotomized the continuous age variable into a binary variable. This may lose more information on the variable itself.

CONCLUSION

The predictive effect of this early warning model for UTI in patients with NLUTD is suitable for clinical practice, which can provide targeted guidance for the early prediction of UTI in patients with NLUTD.

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Univariate analysis among NLUTD patients with or without UTI (n=206)

1 Table 1 Univariate analysis among NLUTD patients with or without UTI (n=206)

Factor	UTI Group (N=60)	Non-UTI group (n=146) (N=146)	x 2	P
Age			6.898	0.01
≥65	42 (70.0)	73 (50.0)		
<65	18 (30.0)	73 (50.0)		
Gender			6.967	0.01
Male	28 (46.7)	97 (66.4)		
Female	32 (53.3)	49 (33.6)		
BMI (kg/m 2)			0.833	0.36
≥24	22 (36.7)	44 (30.1)		
<24	38 (63.3)	102 (69.9)		
Hypertension			2.513	0.11
Yes	26 (43.3)	81 (55.5)		
No	34 (56.7)	65 (44.5)		
Diabetes			6.668	0.01
Yes	29 (48.3)	43 (29.5)		
No	31 (51.7)	103 (70.5)		
Urinary calculi			7.688	0.01
Yes	23 (38.3)	29 (19.9)		
No	37 (61.7)	117 (80.1)		
NLUTD type			1.142	0.57
Detrusor overactivity type	5 (8.3)	18 (12.3)		
Detrusor inactivity type	40 (66.7)	99 (67.8)		
Mixed type	15 (25.0)	29 (19.9)		
Catheterization method			6.154	0.01

Intermittent catheterization	31 (51.7)	102 (69.9)		
Indwelling catheterization	29 (48.3)	44 (30.1)		
Preventive use of antibacterial drugs			2.598	0.11
Yes	39 (65.0)	77 (52.7)		
No	21 (35.0)	69 (47.3)		
Time to start bladder behavior training (weeks)			6.467	0.01
<2 weeks	22 (36.7)	82 (56.2)		
≥2 weeks	38 (63.3)	64 (43.8)		
Hypoproteinemia			4.875	0.03
Yes	17 (28.3)	22 (15.1)		
No	43 (71.7)	124 (84.9)		
Serum creatinine			2.184	0.14
Normal	45 (75.0)	94 (64.4)		
Abnormal	15 (25.0)	52 (35.6)		
Serum total bilirubin			1.303	0.25
Normal	53 (88.3)	136 (93.2)		
Abnormal	7 (11.7)	10 (6.8)		
Diagnosis			1.099	0.577
Spinal cord injury	42 (71.3)	107 (73.5)		
Cerebrovascular accident/ brain tumor/ stroke	12 (19.6)	21 (14.4)		
Peripheral neuropathy (such as diabetes)	6 (10.1)	18 (12.1)		

2   Notes: BMI, body mass index, NLUTD, neurogenic lower urinary tract dysfunction, UTI,
3   urinary tract infection

Multivariable regression analysis

1   Table 2 Multivariate regression analysis among NLUTD patients (n=206)

factor	Assignment methods	Regression coefficients	Standard error	Wald value	P	OR	95% confidence interval Upper limit	Lower limit
Age	≥65 years old = 1 , <65 years old = 0	0.907	0.363	6.235	0.01	2.478	1.215	5.050
Gender	Female =1 , Male =0	0.937	0.350	7.173	0.01	2.552	1.286	5.065
Combined with diabetes	Yes =1 , No =0	0.860	0.354	5.912	0.02	2.364	1.182	4.731
Combined with urinary calculi	Yes =1 , No =0	1.081	0.385	7.898	0.01	2.948	1.387	6.265
Catheterization method	Indwelling catheterization =1 , Intermittent catheterization =0	0.687	0.349	3.870	0.04	1.988	1.003	3.940
Time to start bladder behavior training (week)	≥2 weeks =1 , <2 weeks =0	0.912	0.358	6.476	0.01	2.489	1.233	5.022

Hypoproteinemia	Yes =1 , No =0	0.547	0.422	1.674	0.19	1.727	0.755	3.952
constant		-2.570	0.638	16.223	0.001	0.077		

2 Notes: NLUTD, neurogenic lower urinary tract dysfunction

Figure 1

Flowchart of inclusion
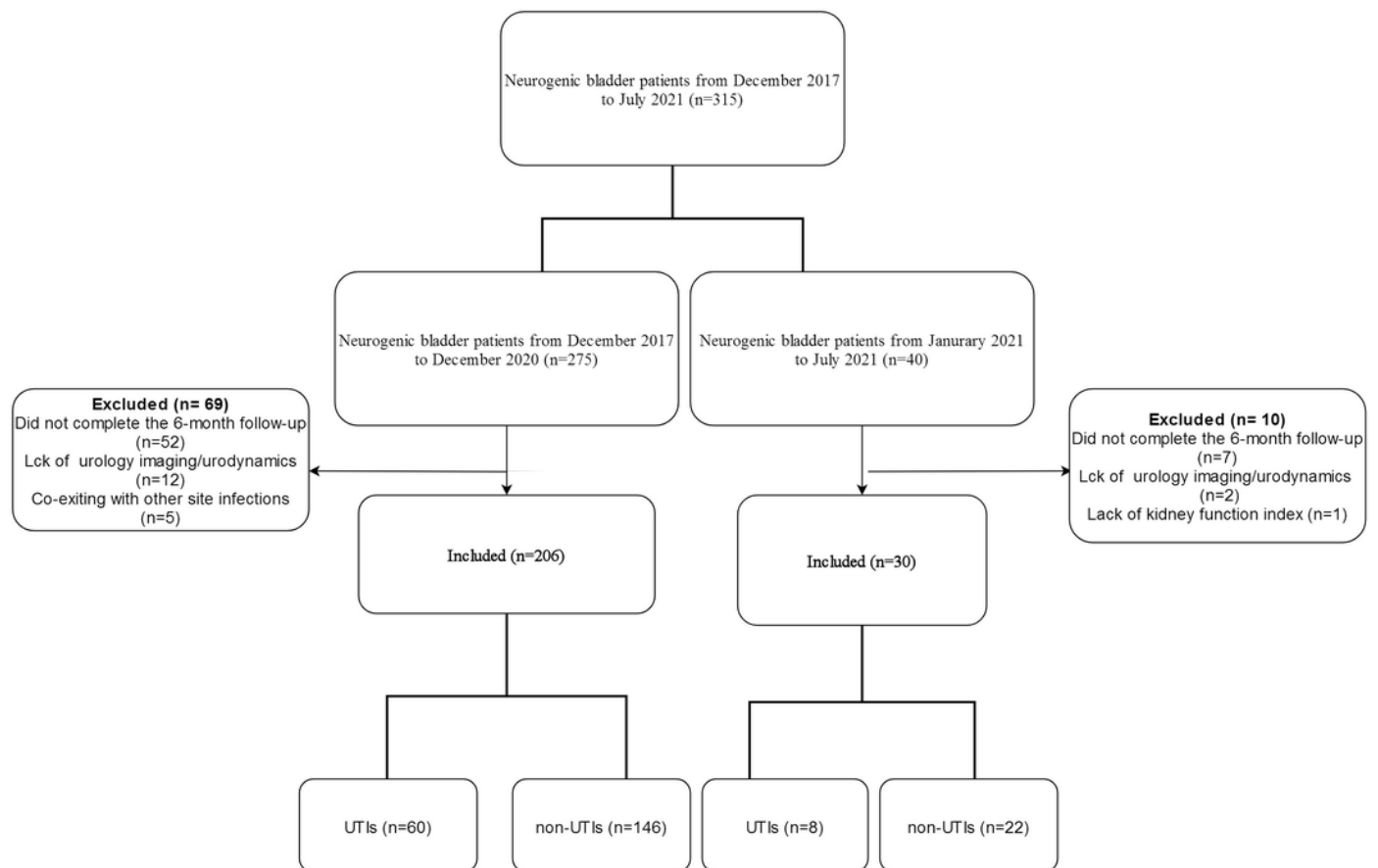
Figure 2

ROC curve of the initial early warning model
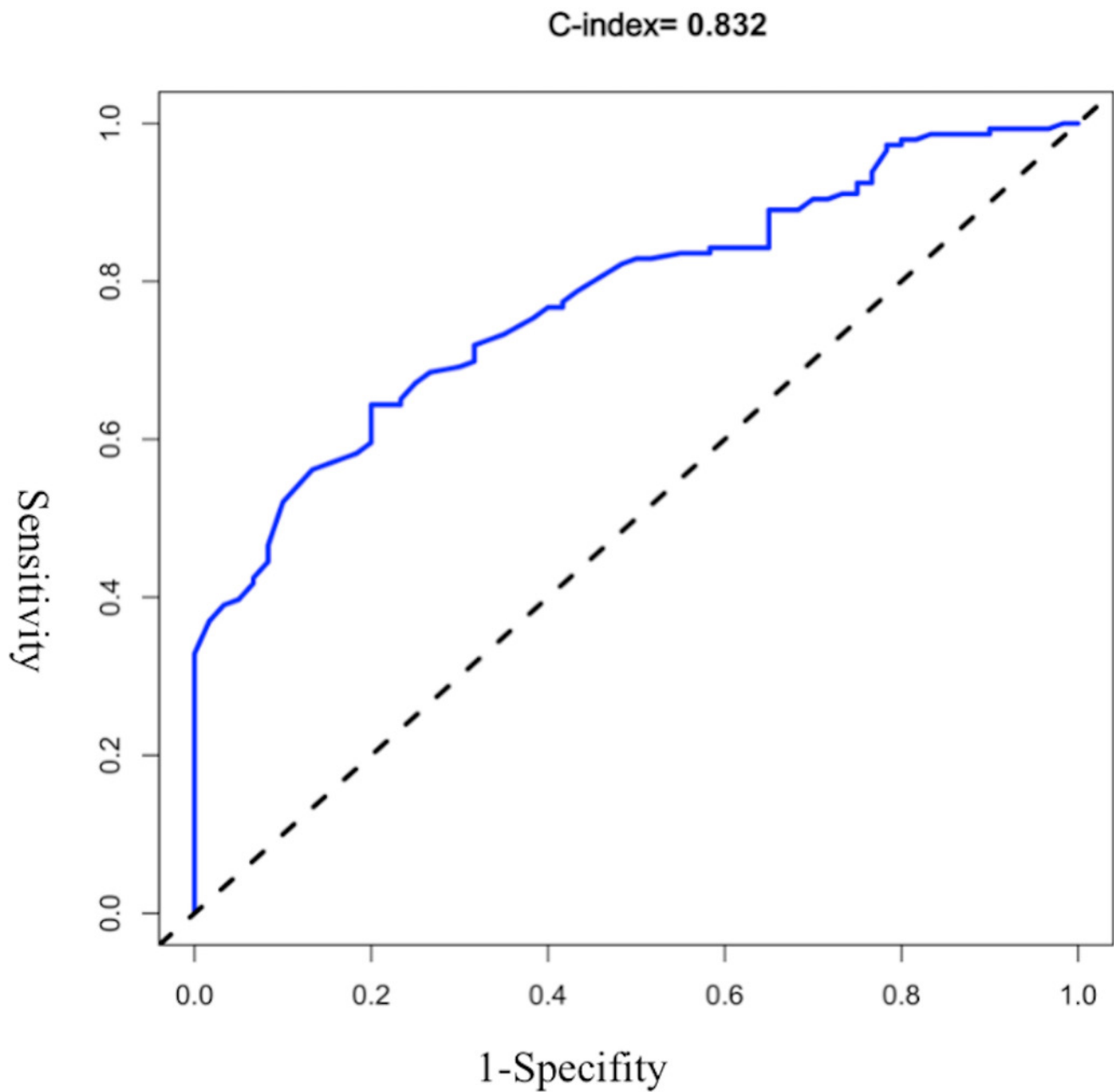
Figure 3

ROC curve of 1,000 Bootstrap internal validations

C-index= 0.828
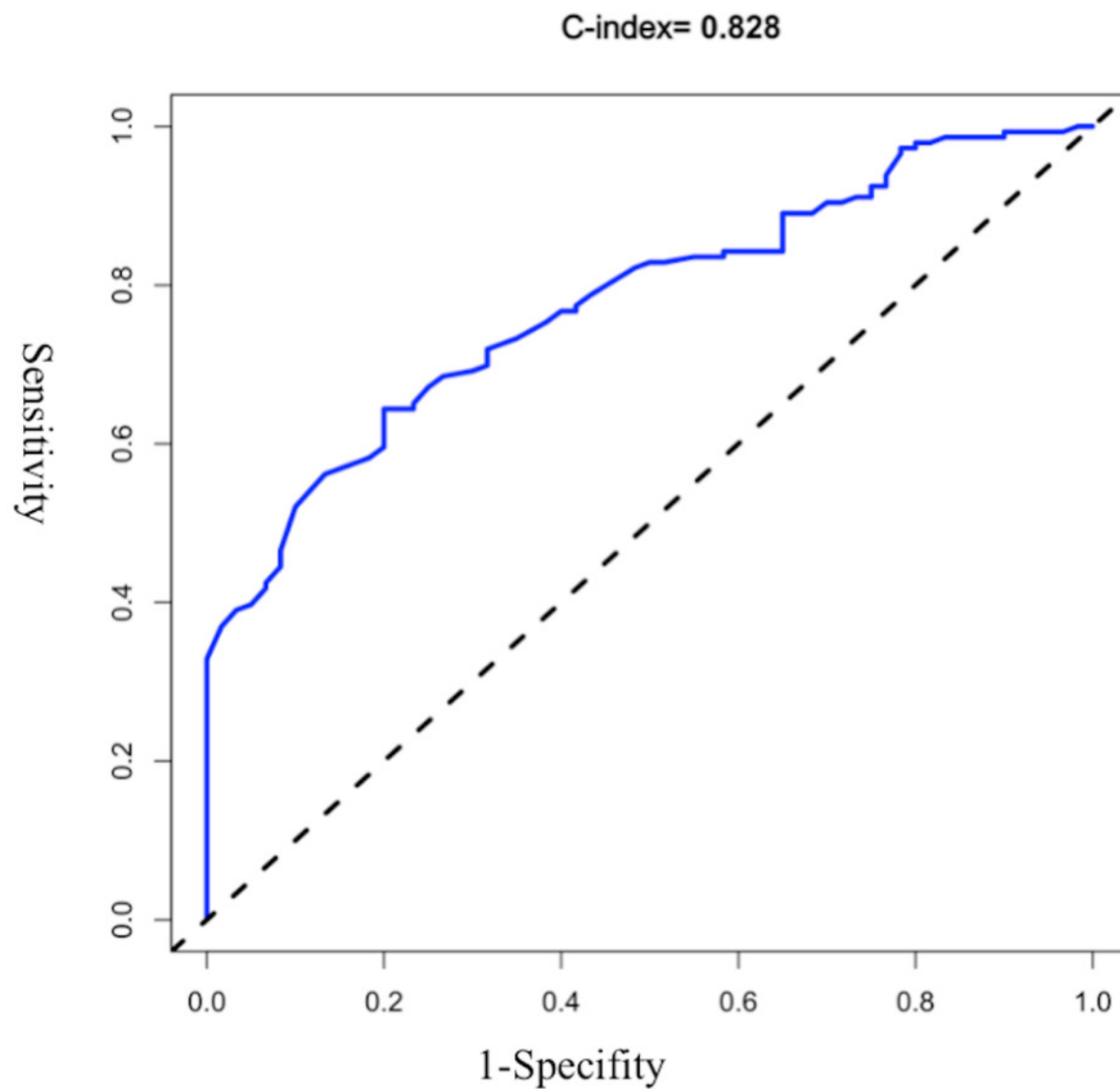
Figure 4

Figure 4 Calibration curve diagram of UTI in patients with NLUTD