ORIGINAL RESEARCH

Analysis of Risk Factors of Pelvic Organ Prolapse in Postmenopausal Women and Construction of Prediction Model

Xiaohong Xie, MS; Jiejie Shen, MS

ABSTRACT

Background • The incidence of Pelvic organ prolapse (POP) was as high as 50% in women, with the main symptoms of vaginal tissue prolapse, accompanied by urination, defecation, and sexual dysfunction, which affected patients' quality of life. POP is more prominent in postmenopausal women due to various factors. By constructing a model, we predict POP and expect to reduce the incidence of POP.

Objective • To explore the risk factors for POP in postmenopausal women and develop a predictive model that can identify high-risk individuals early so that targeted preventive measures can be taken to reduce the burden of POP.

Methods • Using retrospective studies, 290 menopausal women treated in the Department of Gynecology of the Ninth People's Hospital of Suzhou from January 2019 to December 2022 were selected as the study subjects. Women with menopause were divided into the POP group (62 cases) and a non-POP group (228 cases) according to whether or not POP occurred. Single factor analysis was performed on the two data groups. The risk factors of POP in menopausal women were screened by multivariate logistic regression analysis. Based on the screening results, a graph prediction model expressed as a nomogram is constructed. The model's effectiveness was analyzed by the goodness of fit test and receiver operating characteristic curve (ROC) curve. The decision curve was used to analyze the clinical effectiveness of the model.

Results • Multifactor logistic regression analysis showed that Older age (OR = 2.309, P = .007), more childbirth frequency (OR = 3.121, P = .002), low expression of estradiol (E_2) (OR = 1.499, P = .023), low expression of serum 25-hydroxyvitamin D3[25-(OH)D_3] (OR = 2.073, P = .011), and lower blood calcium (OR = 21.677, P = .014) were all risk factors for POP in menopausal women. Based on the above indicators, a risk prediction model is constructed. The model has been proved to have good recognition ability, areas under curve (AUC) = 0.887 (95%CI: 0.845-0.926), The best cutoff value is 0.37, The sensitivity and specificity were 0.885 and 0.840, respectively; The goodness of fit test showed that the predicted value of the model had no statistical significance with the actual value. The threshold probability is in the range of 1%~99%. The net benefit of menopausal women is higher than the other two extreme curves. It shows that the model is clinically effective.

Conclusion • Age, times of delivery, E_2, 25-(OH)D_3, and blood calcium are related to POP in menopausal women. A nomogram model based on these 5 indicators can effectively assess the risk of POP in postmenopausal women. The clinician can use this column chart to calculate the risk of POP occurrence for each patient and make clinical recommendations accordingly. (*Altern Ther Health Med.* 2024;30(1):265-269).

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INTRODUCTION

Pelvic organ prolapse (POP) is a kind of pelvic floor supporting tissue weakness caused by various reasons (pelvic floor fascia, ligament, muscle, soft tissue attachment and other supporting structures weakness or damage), resulting in pelvic organ descending and displacement leading to organ position and function abnormalities.[1] The main symptom of POP is vaginal tissue prolapse, and It may be accompanied by urination, defecation, and sexual dysfunction; it affects the quality of life of patients to varying degrees.[2,3] A series of endocrine disorders caused by decreased sex hormone levels caused by decreased ovarian function in women during menopause will mediate related molecular biological changes, such as collagen degradation, cellular oxidative damage, signaling pathway disorders, etc., making menopausal women prone to POP.[4-7] The incidence of POP in

women is as high as 50%,[8] and the incidence of POP will gradually increase with the increase of women 's age, especially women after menopause who are more likely to have POP.[9] Surgery is recommended for the treatment of patients with severe POP. However, for the elderly with mild or older age, drugs, pessary, pelvic floor electromagnetic stimulation, and other treatment methods are often adopted.[10] Although the symptoms of POP can be alleviated after treatment, they cannot be cured.[11] Can we identify the possible risk of POP in menopausal women, To take early preventive measures to reduce the incidence of POP in menopausal women? At present, there is no intuitive and reliable tool to evaluate and identify the high-risk population of a POP in postmenopausal women. The construction of a POP prediction model for menopausal women has a certain value in reducing the occurrence of POP. Therefore, this study analyzes the data of menopausal women, and it aims to find out the risk factors of a POP in menopausal women and build a reliable risk prediction model. This model is represented by a nomogram to objectively present the variables of the prediction model, the corresponding scores of each variable, and the predicted incidence of events, so as to provide a reference for clinical evaluation of the risk of POP in menopausal women and formulation of preventive measures, thereby reducing the incidence of POP and improving the quality of life of the patients.

MATERIALS AND METHODS

Study population

Using a retrospective study, 290 menopausal female patients treated in the Department of Gynecology of the Ninth People's Hospital of Suzhou from January 2019 to December 2022 were selected as the study subjects. Inclusion criteria: (1) 50~70 years old; (2) In menopause, estradiol (E_2) < 40 nmol/L; (3) No intellectual defect or consciousness obstacle; (4) The first diagnosis was POP; (5) The patient suffered from irregular menstruation and was accompanied by symptoms such as anorectal distension or pain in the perineal region, and casual vaginal spasm during sexual life, It is required to evaluate the status of pelvic organs by using the quantitative POP staging (POP-Q). Exclusion criteria: (1) Patients with acute abdomen; (2) Patients with huge pelvic space-occupying disease; (3) Patients with malignant tumor; (4) Previous history of pelvic surgery or lumbosacral and spinal trauma; (5) The clinical data required for the study were incomplete. According to the diagnosis results of POP-Q, they were divided into the POP group (62 cases) and the non-pOP group (228 cases). This study was conducted in accordance with ethical guidelines and has been approved by the Medical Ethics Committee of Suzhou Ninth People's Hospital.

Methods

Material gathering. Log in to the information system of Suzhou Jiu People's Hospital,Refer to patient electronic records, blood test results during medical treatment, and other data, Collect the patient's age, number of deliveries, body mass index (BMI), nature of work, underlying disease, and history of hysterectomy from the patient's electronic case record;Collect the patient's sex hormones [Luteinizing Hormone (LH), Follicle Stimulating Hormone (FSH), testosterone, progesterone, prolactin, E_2], white blood cell count, platelet count, serum 25-hydroxyvitamin D_3 [25-(OH) D_3], blood calcium, and other indicators from the patient's blood test sheet at the time of treatment.

POP Diagnostics

POP-Q method was used to assess whether menopausal women had POP.[12] After the subject urinates, Take bladder lithotomy position, Do Valsalva action, A senior basin bottom expert measures each point. Take the hymen as a reference (point 0), and Point C refers to the farthest end of the cervical or vaginal stump after hysterectomy; the range is -TVL~+TVL (total vacuum length, TVL: normal range is about 10cm), Measure and record the measured values of Ba, C and Bp respectively, Each point represents the position of anterior pelvic cavity, middle pelvic cavity and posterior pelvic cavity in turn, (Fig.1). The pelvic prolapse was graded according to the distance from the farthest point of the maximum prolapse to the edge of the hymen; that is, 0 degree means no sag; Degree I indicates that the lowest point of the cervix is below the level of the ischial spine, But it did not reach the hymen margin; Grade II indicates that the cervix protrudes out of the vagina, But the uterus is still in the vagina; The third degree indicates that the cervix and body of the uterus are completely out of the vagina; Grade IV indicates that the lower genital tract is completely or almost completely dislocated. See Table 1.

Statistical analysis

Using SPSS19.0 software for data analysis, Enumeration data were expressed as %, and the χ^2 test was used to compare the findings between the two groups. Measurement data with a normal distribution were expressed as ($\bar{x} \pm s$), and an independent t test was used to compare groups. $P < .05$ indicates that the difference wasstatistically significant. The statistically significant variables were included in the multivariate logistic regression analysis to screen out the risk factors of POP in menopausal women, Then R language (R3.4.3) software to visualize the results of the multifactor analysis to obtain the POP risk prediction model of menopausal women expressed in Nomogram. The discriminability of the model was evaluated using the area under the receiver operating characteristic (ROC)

Table 1. The quantification of POP-Q

POP-Q/ Degree	Classification/Anatomy description	Standard/Position description
0	No prolapse	Point Aa,Ap,Ba and Bp are all at -3cm point,point C, D are high at least as high as the vaginal length -tvl~-(tvl-2)cm
I	Minimal prolapse	The prensenting part is >1cm above the hymen
II	1cm above or below hymenal ring	The leading edge is ≤1 cm above or below the hymen
III	More than 1cm below but not complete	The leading edge is >1 cm beyond the hymen but≤1cm less than tvl
IV	Basically total eversion of the vagina	Complete eversion

Abbreviations: POP-Q, Pelvic Organ Prolapse Quantification; tvl, total vacuum length.

Table 2. Single factor analysis of POP in menopausal women

Factors	POP group (n = 62)	Non-POP group (n = 228)	t/χ^2	*P* value
Age(years)	61.98±2.56	58.17±2.09	12.101	<0.001
BMI(kg/m²)	24.29±1.73	23.96±1.54	1.456	.146
Childbirth frequency (times)	1.95±0.36	1.45±0.19	14.760	<.001
Nature of work			1.221	.269
Stand	34(54.84)	107(46.93)		
Sitting	28(45.16)	121(53.07)		
Hypertension			0.467	.494
Yes	5(8.06)	13(5.70)		
No	57(91.94)	215(94.30)		
Combined diabetes			1.206	.272
Yes	8(12.90)	19(8.33)		
No	54(87.10)	209(91.67)		
Hyperlipidemia			1.219	.270
Yes	7(11.29)	16(7.02)		
No	55(88.71)	212(92.98)		
History of hysterectomy			2.223	.136
Yes	18(29.03)	46(20.18)		
No	44(70.97)	182(79.82)		
LH(U/L)	50.12±10.54	51.27±10.95	0.739	.460
FSH(U/L)	29.57±4.76	28.48±4.41	1.696	.091
Prolactin (ng/mK)	20.65±4.78	20.18±4.53	0.716	.475
Testosterone (ng/dL)	2.35±0.54	2.46±0.59	1.325	.186
Progesterone (ng/mL)	1.09±0.16	1.14±0.23	1.608	.109
E_2(pg/L)	25.87±5.12	27.92±4.86	2.911	.004
Platelet count(×10⁹/L)	248.54±42.78	252.49±46.91	0.599	.549
WBC count (×10⁹/L)	4.16±1.19	3.97±1.12	1.169	.244
25-(OH)D3(ng/mL)	23.95±5.28	28.82±5.83	5.834	<.001
Blood calcium (mmol/L)	2.16±0.47	2.59±0.64	4.938	<.001

Abbreviations POP, Pelvic Organ Prolapse; BMI, Body mass index; LH, luteinizing hormone; FSH, follicle stimulating hormone; E2, estradiol; WBC, White blood cell, 25-(OH)D3, 25-hydroxyvitamin D3.

curve (AUC), sensitivity, and specificity. The calibration of the model is tested using goodness of fit (referring to the degree to which the regression line fits the observed values). The clinical benefit rate of the model was evaluated using a decision curve.

RESULTS

Single factor analysis of POP in menopausal women

The age of the POP group (61.98 ± 2.56) was significantly higher than that of the non POP group (58.17 ± 2.09); The number of deliveries in the POP group (1.95 ± 0.36) was significantly higher than that in the non POP group (1.45 ± 0.19);The E_2 (25.87 ± 5.12), 25-(OH)D_3 (23.95 ± 5.28), and blood calcium (2.16 ± 0.47) in the POP group were lower than those in the non POP group E_2 (27.92 ± 4.86), 25-(OH)D_3 (28.82 ± 5.83), and blood calcium (2.59 ± 0.64),The difference was statistically significant ($P < .05$), See Table 2.

Multivariate logistic regression analysis of POP in postmenopausal women

Determined through multivariate logistic regression analysis,Older age, more times of delivery, low expression of E_2, low expression of 25-(OH)D_3, and low serum calcium were all risk factors for POP in menopausal women ($P < .05$), See Table 3.

Construction of a prediction model for the occurrence of POP in postmenopausal women

The five variables selected from the multifactor logistic analysis are used as the prediction indicators, Visualize it using the ggplot() function in R language to obtain a graphical representation of Nomogram, Present the results of multi factor analysis in a more intuitive graphical manner. The total score is obtained by adding the corresponding scores of each indicator value expressed in the graph,Translate the total score into the predicted probability of POP risk in postmenopausal women. Specific interpretation is as follows: The age of a menopausal woman=56 years old, the number of deliveries=2, E_2=24 pg/L, 25-(OH)D_3=24 ng/mL, and blood calcium=1.4 mmol/L, The total score is: 30+34+45+40.5+54=203.5, The corresponding POP risk is 38%, See Figure 2.

Table 3. Multi factor Logistic Regression Analysis of POP in Menopausal Women

Variable	*β*	*SE*	Wald χ^2	*P* value	OR(95%CI)
Age	0.837	0.310	7.290	.007	2.309(1.257~4.263)
Childbirth frequency	1.138	0.368	9.563	.002	3.121(1.517 ~ 6.417)
E_2	0.405	0.178	5.177	.023	1.499(1.058 ~ 2.125)
25-(OH)D3	0.729	0.287	6.452	.011	2.073(1.181 ~ 3.640)
Blood calcium	0.517	0.210	6.061	.014	1.677(1.110 ~ 2.532)

Figure 1. Schematic Diagram of Measuring Points and Diameters of POP-Q Indexing Method for Pelvic Organ Position

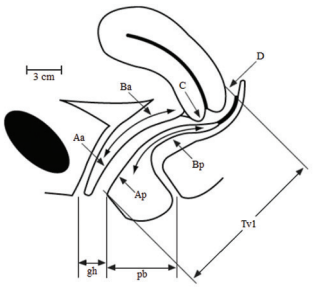


Figure 2. Nomogram expression of POP risk prediction model for menopausal women

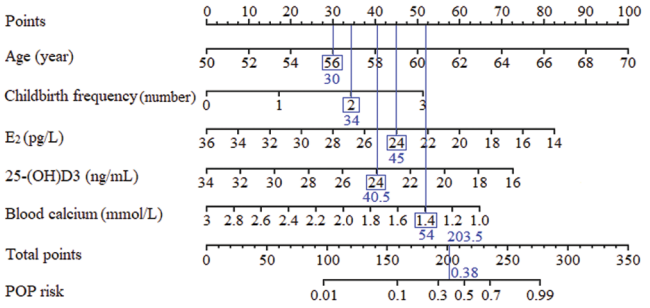
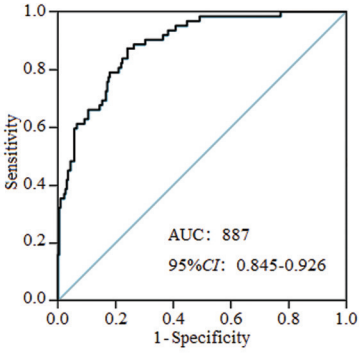
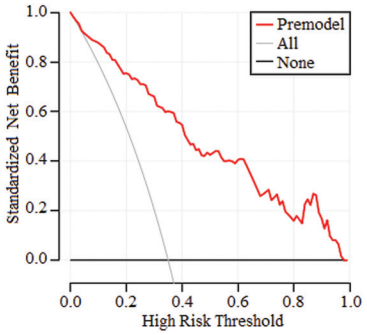


Figure 3. Evaluation of ROC curve of Nomogram model for predicting POP in menopausal women



Abbreviations: ROC, receiver operating characteristic curve; AUC, areas under curve.

Figure 4. Decision Curve Analysis of Nomogram Model



Validation of POP risk prediction model for menopausal women

According to the ROC curve analysis, the curve area of the model expressed by Nomogram to predict the POP risk of menopausal women is 0.887 (95% CI: 0.845-0.926), The best cutoff value is 0.37, and The sensitivity and specificity are 0.885 and 0.840 respectively, This indicates that the model has good discrimination, see Figure 3. The deviation between the predicted value and the actual value of the model is not statistically significant ($\chi^2 = 5.321$, $P = .723$) after the goodness of fit test, It shows that the model has no over-fitting phenomenon, The model has high consistency in predicting the POP risk of menopausal women with actual values. Decision curve analysis shows that The threshold probability is in the range of 1%~99%; the net benefit of menopausal women is higher than the other two extreme curves; it shows that the model is clinically effective. If the cutoff value of 0.37 for constructing the model is used as the threshold probability (37%) to determine whether intervention measures need to be taken,This predictive model can provide additional clinical net benefits, see Figure 4.

DISCUSSION

With the improvement of people's living standards, The average life is extended; women spend about 1/3 of their lives after menopause.[13] During the menopausal transition period, the pelvic floor muscles will become loose, the ligament elasticity will decrease, and the collagen will be lost due to the ovarian function decline and the hormone level change. It makes menopausal women prone to pelvic floor dysfunction,[14] and then induces POP. It affects the quality of life after menopause.[15] Therefore, it is necessary to strengthen the prediction of POP risk in menopausal women and research relevant mechanisms.

This study found that older age is a risk factor for POP in postmenopausal women. As age increases, the pelvic floor muscles and fascia begin to show a degenerative decline. A cross-sectional study of 21,449 women before and after menopause was conducted between 1997 and 1999. They found that the frequency of POP increased with age. Compared with women aged ≤ 51, the OR values of POP in women aged 52-55 and > 65 years old were 1.3 and 1.7.[16] In addition, many other studies have also shown the correlation between age and POP.[17,18] Possible aging, pelvic floor muscle and fascia decline.[19] This results in a lack of collagen in pelvic floor tissue, Making pelvic floor ligaments loose and pelvic floor muscle fibers have insufficient elasticity; the support structure system at the bottom of the basin is weak, Increasing the risk of POP.

This study found that frequent childbirth is a risk factor for the occurrence of POP in postmenopausal women. A meta-analysis of 14 studies also clearly pointed out that vaginal delivery is a risk factor for POP.[20] Consistent with the results of this study. The traction and expansion of the pelvic floor by women during childbirth are very likely to cause mechanical deformation or destruction of the supporting tissue of the pelvic floor, Such as excessive stretching or tearing of pelvic floor fascia and muscles. The repeated expansion and traction of pelvic floor muscles and fascia, caused by multiple deliveries, is very likely to cause nerve fiber breakage and connective tissue damage in the pelvic floor,[21] Increasing POP risk in the later stage.

This study found that low expression of E_2 is a risk factor for POP in postmenopausal women. E_2 is secreted by the ovary, follicle, and corpus luteum, It belongs to the most biologically active hormone, estrogen. Estrogen receptors are widely distributed in female pelvic floor tissue. The common E_2 target organs include the levator ani muscle's stroma, the uterus's main ligament, vaginal wall tissue, and fascia.[22] When E_2 binds to estrogen receptors, It can also regulate the electrolyte balance in the body, the homeostasis of the internal environment, bone metabolism, immunity, and other aspects. However, due to the factors of ovarian function degradation in menopausal women, Hormone secretion is seriously reduced.[23] It directly leads to decreased hormone secretion and synthesis, resulting in the lack of E_2; Lack of estrogen can lead to atrophy and decreased elasticity of female pelvic floor tissue, which can easily trigger POP.[24] This causes the contraction and closure of some blood vessels in the pelvic floor tissue, Causing the pelvic floor muscles to atrophy due to the insufficient blood supply; as a result, the basin bottom support system is weak, Raises POP. Lang et al.[25] The estrogen receptor was expressed in both pelvic ligament and muscle tissue, indicating that the pelvic floor site is one of the targets of estrogen action.

This study found that low expression of 25-(OH)D_3 and low blood calcium are both risk factors for the occurrence of POP in postmenopausal women.Vitamin D has been proven to regulate the physiological functions of muscles and bones.[26-29] 25-(OH)D_3 is the most stable and biologically active representative of vitamin D. After binding with receptors on muscle cells, It can promote the proliferation of muscle fiber cells and the synthesis of related proteins; however, the lack or insufficiency of 25-(OH)D_3 will lead to the decline of the body's antioxidant capacity, It causes nerve dysfunction and muscle strength reduction of muscles (including pelvic floor muscles), Then increase the risk of POP. Relevant research shows that 25-(OH)D_3 can activate calcium endoplasmic reticulum transport and increase calcium storage, Promoting muscle contraction.[30,31] This

suggests that 25-(OH)D_3 can directly regulate blood calcium. When menopausal women lack 25-(OH)D_3, It may lead to their inability to properly adjust the calcium and phosphorus balance system. Resulting in a disorder of calcium and phosphorus metabolism and Forming a negative calcium balance. A slight decrease in blood calcium can increase osteoclast activity, Limit osteoblasts' function, affects the strength of pelvic floor skeletal muscle, Make muscles contract and become loose, The posture stability of the pelvic floor support is reduced,[32] increase POP risk.

The incidence of POP in menopausal women is high; More reasons are that diagnosis and treatment are based on the occurrence of POP. There is no objective POP risk assessment for menopausal women before the disease occurs, It leads to insufficient early prevention. According to the risk factors of POP in postmenopausal women, this study constructs a prediction model expressed by nomogram, After verification, the area under the ROC curve of the model is greater than 0.85, And the deviation between the predicted POP value of menopausal women and the actual value of the model is not statistically significant after the analysis of goodness of fit test, It shows that this model has a good consistency in predicting the risk of POP in postmenopausal women and the actual occurrence. It may be that this study fully considers the interaction between factors, Multi-indicator joint prediction, Avoiding the shortage of single indicator forecast, and Effectively improving the prediction efficiency. In this study, the cutoff value of the ROC curve analysis of the model is 0.37 as the clinical net benefit threshold of the risk of POP in menopausal women; It can be seen that the clinical net benefit rate is higher than that of all the extreme methods with or without intervention, It shows that the model is clinically effective. The nomogram can clearly reflect the contribution rate of various factors, Then carry out risk quantification; it is suitable for individualized risk assessment of POP risk in menopausal women.In use, the score of each factor is determined by the corresponding point on the axis of the column chart corresponding to the different groups of each factor,The total score is obtained by adding up the scores of each factor,The point vertically downwards corresponding to the total score on the POP risk axis is the probability of POP risk for menopausal women.

In summary, This study found that the risk of POP in postmenopausal women is related to older age, more frequent deliveries, low E_2 expression, low 25-(OH)D_3, and low blood calcium indicators, based on this, the prediction model of POP risk in menopausal women is constructed, It can effectively assess the POP risk of menopausal women. In clinical work, doctors can predict the risk of POP in patients through model calculation and take further treatment measures by collecting basic information on these factors in patients, which is greatly beneficial to reducing the occurrence of POP.

DATA AVAILABILITY STATEMENT

The labeled dataset used to support the findings of this study are available from the corresponding author upon request.

CONFLICT OF INTEREST

The author declare no competing interests.

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This study did not receive any funding in any form.

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