Infection and Drug Resistance

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ORIGINAL RESEARCH

Construction of a Risk Factor Model for Wound Infection After Ileostomy for Rectal Cancer and Its Relationship with Nucleotide-Binding Oligomerization Domain-Like Receptor Protein 3 (NLRP3) Gene Polymorphism

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Objective: To establish a predictive model for wound infection after ileostomy for rectal cancer and its relationship with nucleotide-binding oligomerisation domain-like receptor thermal protein domain-associated protein 3 *(NLRP3)* gene polymorphism.

Methods: A total of 347 samples were randomly divided into two groups: the model group (n = 260) and the verification group (n = 87). The patients in the model group were further divided into the infection group (n = 96) and the non-infection group (n = 164). Multivariate logistic regression was used to analyse the influencing factors of postoperative infection. The TaqMan probe method was used for genotyping.

Results: The results of multivariate logistic regression analysis showed that age >65 years, diabetes, operation time >105 minutes, loop colostomy and abnormal transepidermal water loss (TEWL) were independent risk factors. The risk value of postoperative wound infection predicted by the nomogram model reached 0.93, corresponding to a maximum predicted infection probability of 92.68%. The area under the receiver operating characteristic curve for the nomogram model was 0.869 ($P < 0.001$) and 0.861 ($P < 0.001$). The comparison of *NLRP3* genotypes between the two groups showed that the proportion of the GG genotype was significantly higher in the infection group than the CC and CG genotypes (51.43% vs 29.90% and 38.98%, respectively). In patients with the GG genotype, the associations between age >65 years, diabetes and abnormal TEWL with wound infection remained significant (all $P < 0.05$), indicating that these clinical risk factors are particularly prevalent among GG carriers.

Conclusion: This study identified the independent risk factors for postoperative wound infection. Patients with the G allele have a higher risk of postoperative infection, and *NLRP3* gene polymorphism is closely associated with the risk factors included in the model. The association between *NLRP3* gene polymorphisms and the risk of postoperative infection provides a new molecular biological indicator for prognostic evaluation.

Keywords: nucleotide, binding oligomerisation domain, like receptor thermal protein domain, associated protein 3, single, nucleotide polymorphism, ileostomy, wound infection

Received: 21 April 2025
Accepted: 3 September 2025
Published: 11 December 2025

Introduction

Rectal cancer is a malignant tumour of the digestive system that develops between the junction of the anal canal skin and rectal mucosa and the junction of the rectum and sigmoid colon. Its incidence is rising annually by 1.0%–2.4%. Surgical intervention is the primary clinical treatment for rectal cancer, often in combination with radiotherapy and chemotherapy.[1] In cases of mid to lower rectal cancer, the tumour's proximity to the anal sphincter complicates surgical resection. If the anus cannot be preserved, a permanent ileostomy is created by bringing the descending or sigmoid colon through the lower abdominal wall. In contrast, a preventive ileostomy is performed in patients undergoing anus-preserving surgery. This procedure is followed by a secondary closure 3–6 months later, during which the stoma is reversed and the resected rectal end is re-anastomosed within the abdominal cavity.[2] Studies indicate[3] that complications following ileostomy remain common, with postoperative wound infection being the most frequent, affecting over 35% of patients. If oedema or infection occurs around the anastomotic site, the stoma reversal procedure may be delayed. Postoperative infection not only compromises surgical outcomes but may also lead to systemic complications such as life-threatening sepsis.[4]

Genetic polymorphism, also known as gene polymorphism, describes the presence of two or more alleles with similar fitness at a specific gene locus within the same population, with allele frequencies exceeding 0.01. This phenomenon arises primarily from genetic mutations, including variations in DNA loci and fragment lengths.[5] Among DNA locus polymorphisms, single-nucleotide polymorphism (SNP) is a prominent type, defined as a mutation at a single nucleotide position in the genome, leading to genetic variation between populations or individuals.[6] In recent years, the nucleotide-binding oligomerisation domain-like receptor thermal protein domain-associated protein 3 *(NLRP3)* gene has attracted considerable attention in inflammation-related research. The *NLRP3* gene encodes a PYRIN domain protein that forms part of an inflammasome complex. As an upstream activator of the nuclear factor kappa-light-chain-enhancer of activated B cells signalling pathway, the *NLRP3* complex modulates proteins involved in apoptosis, immune responses and inflammatory signalling pathways, which potentially lead to wound infections.[7] Studies have shown that *NLRP3* gene polymorphism may influence the onset and progression of postoperative infection via inflammatory responses and immune regulation. Furthermore, alterations in *NLRP3* gene expression stability and messenger RNA translation efficiency have been linked to an increased risk of postoperative infection. Therefore, *NLRP3* gene polymorphism plays a pivotal role not only in the pathophysiology of rectal cancer but also in the prediction and prevention of ileostomy-related complications, particularly wound infections.[7] This study retrospectively analyses risk factors for postoperative wound infection in patients with rectal cancer who underwent ileostomy at our hospital. The objective is to develop a predictive model for wound infection risk factors following ileostomy in patients with rectal cancer and to investigate the relationship between *NLRP3* gene polymorphism and these risk factors.

Materials and Methods

General Data

A retrospective analysis was conducted on 347 patients with rectal cancer who underwent ileostomy at our hospital between June 2018 and June 2022. Among them, 213 were men and 134 were women, aged 28–79 years. The study population was randomly divided into a modelling group (n = 260) and a validation group (n = 87) using a random number table at a ratio of 3:1. The 260 patients in the modelling group were further categorised into an infection group (n = 96) and a non-infection group (n = 164) based on whether they experienced postoperative wound infection. The study details were thoroughly explained to the patients and their families, and all enrolled participants provided written informed consent. This study was conducted after obtaining approval from the hospital's ethics review committee (2024-S00510).

Inclusion and Exclusion Criteria

The inclusion criteria were as follows: (1) meeting the diagnostic criteria outlined in the Chinese Protocol of Diagnosis and Treatment of Colorectal Cancer (2023 edition);[8] (2) meeting the wound infection criteria confirmed by pathological histological examination;[9] (3) aged ≥18 years; 4) having received permanent or temporary ileostomy at our hospital with no surgical contraindications; (5) having stable postoperative vital signs; and (6) possessing complete clinical data, good

compliance and willingness to participate in the study and follow-ups. The exclusion criteria were as follows: (1) patients with metastatic or recurrent rectal cancer; (2) patients with mental or cognitive disorders; (3) patients with coexisting malignancies in other areas, infectious diseases or immune system disorders; (4) patients with coagulation disorders or impaired liver or kidney function; (5) patients with allergic constitutions; (6) patients undergoing emergency ileostomy due to trauma; and (7) patients with incomplete case data or who could not be contacted.

General Data Collection

The clinical data and information of the included patients were collected from electronic medical records. The collected data included sex, age, body mass index (BMI), underlying diseases (diabetes, cardiovascular diseases and respiratory diseases), medical history (postoperative complications and irritant dermatitis), rectal cancer staging, adjuvant radiochemotherapy (RCTx), duration of operation (DoO), ostomy type, postoperative length of hospital stay (LoHS), number of dressing changes during hospitalisation, postoperative stoma care guidance, postoperative adhesive bowel obstruction (ABO), prophylactic use of burn ointment and transepidermal water loss (TEWL).

Genotyping Method

All study participants underwent SNP genotyping before ileostomy following hospital admission. After an overnight fast of 8–12 hours, 2 mL of venous blood was collected the next morning at 8:00 a.m. under fasting conditions. Blood collection was performed with the patient in a supine or seated position for one minute to stabilise posture. The blood was placed in an anticoagulant collection tube and sent to the hospital laboratory. The sample was inverted several times to ensure thorough mixing and then left to stand for 30 minutes. It was centrifuged at a high speed of 3,500 rpm for 15 minutes, after which the plasma was stored at −80°C, and the blood cells were processed for DNA extraction within 24 hours. Genomic DNA was extracted from blood cells using a blood genomic DNA extraction kit (Axygen, CA, USA) following the manufacturer's instructions. Amplification of DNA was performed using TaqMan fluorescent probes (Thermo Fisher Scientific, MA, USA) on an ABI Prism 7500 fluorescence quantitative PCR system (ABI, MA, USA). The primer sequences for *NLRP3* (rs10754558) were as follows: 5′-GACAATGACAGCATCGGGTGTTGT-3′ (upstream primer), 5′-TCATCACAGCGCCTCAGTTAGAGGA-3′ (downstream primer). After amplification, fluorescence signals for *NLRP3* (rs10754558) SNP genotyping were interpreted using CFX Manager software. Fluorescence signals were categorised as follows: (1) CC genotype: FAM; (2) GG genotype: VIC; and (3) CG genotype: FAM + VIC. All procedures were conducted strictly according to the manufacturer's instructions. The remaining blood cells and DNA samples were stored at −20°C.

Development and Evaluation of the Predictive Model

The patients were randomly divided into a modelling group (n = 260) and a validation group (n = 87). In the modelling group, patients were further categorised into an infection group (n = 96) and a non-infection group (n = 164) based on whether they developed wound infections within 90 days postoperatively. Multivariate logistic regression analysis was conducted to identify factors influencing postoperative wound infection. Based on the identified independent risk factors, a nomogram predictive model was developed using R software. Each independent risk factor was assigned a corresponding score, and the total score was calculated to predict the risk of postoperative wound infection. The discriminative ability of the model was evaluated using the receiver operating characteristic (ROC) curve, and the area under the curve (AUC) was calculated. The model's calibration was assessed using a calibration curve, and the Hosmer–Lemeshow goodness-of-fit test was performed. External validation of the model was conducted using data from the validation group, with ROC and calibration curves applied again to evaluate the model's performance.

Postoperative Follow-up

Postoperative follow-up was conducted by two attending physicians and on-duty nurses. During hospitalisation, professional hospital staff managed dressing changes and monitored wound healing. After discharge, patients were required to return for regular outpatient visits, during which stoma conditions were verified through medical record reviews. The follow-up period lasted 90 days postoperatively, ending in September 2022. The primary follow-up outcomes were wound

healing status and the presence or absence of infection, recorded as 'infection", "no infection" or "lost to follow-up". No patients were lost to follow-up during the period, resulting in a follow-up rate of 100%.

Statistical Processing

Statistical analysis was performed using SPSS (IBM, Armonk, NY, USA) version 23.0. Continuous variables with a normal distribution were expressed as mean ± SD, and comparisons between groups were conducted using independent-sample t-tests. Non-normally distributed continuous variables were expressed as median (interquartile range, P25–P75), and comparisons between groups were performed using the Mann–Whitney *U*-test. Categorical variables were presented as frequencies (percentages) (n [%]), and between-group comparisons were conducted using the chi-square (χ^2) test. Univariate results were further analysed using multivariate logistic regression in GraphPad Prism 8.0 to identify risk factors for postoperative wound infection, with results expressed as odds ratios with 95% confidence intervals (CIs). Independent influencing factors identified through multivariate analysis were included in R software for model fitting, and a nomogram risk prediction model was developed. The predictive performance of the model was evaluated using the ROC curve, with the AUC used to assess its discriminative ability. Model calibration was evaluated using a calibration curve, and the Hosmer–Lemeshow goodness-of-fit test was conducted to assess model fit. Logistic regression analysis was also used to evaluate whether the prevalence of risk factors included in the nomogram (eg age, diabetes, TEWL) differed significantly across NLRP3 (rs10754558) genotypes. A significance level alpha (α) = 0.05 was used for all tests.

Results

General Data of the Modelling and Validation Groups

A total of 347 patients with rectal cancer were randomly divided into a modelling group (n = 260) and a validation group (n = 87) in a 3:1 ratio using a random number table The modelling group included 161 men and 99 women aged 28–79 years and was used to construct the risk prediction model for postoperative wound infection. The validation group comprised 53 men and 34 women aged 30–78 years and was used for external validation of the model's performance. There were no statistically significant differences between the two groups in terms of sex, age, BMI or postoperative wound infection (all P > 0.05) (see Table 1).

Clinical Data Analysis of Patients in the Modelling Group

Among 260 patients with rectal cancer who underwent ileostomy, 96 developed postoperative wound infection. Symptoms of wound infection included pain in 36 cases (37.50%), redness and swelling in 47 cases (48.96%) and purulent exudate in 30 cases (31.25%), resulting in a postoperative infection rate of 36.92%. Comparison of general data between the infection group and the non-infection group revealed no statistically significant differences in sex, history of postoperative complications, cardiovascular disease, respiratory disease, history of irritant dermatitis, rectal cancer staging, adjuvant RCTx or postoperative ABO (all P > 0.05). However, significant differences were observed between the two groups in age, BMI, diabetes, DoO, number of dressing changes, postoperative LoHS, stoma care guidance, ostomy type, prophylactic use of burn ointment and TEWL (P < 0.05) (see Table 2).

Table 1 Comparison of General Data Between the Modeling and Validation Groups

Group	Case (*n*)	Male, *n*(%)	Age (years)	BMI (kg/m²)	Postoperative wound infection, *n*(%)
Modeling	260	161 (61.92)	56.38±8.72	23.15±3.07	96 (36.92)
Validation	87	53 (60.92)	57.20±9.18	22.88±3.26	27 (31.03)
χ^2/*t*-value	—	0.041	0.352	0.901	0.602
p-value	—	0.852	0.719	0.375	0.428

Abbreviations: n, number of patients; BMI, body mass index; LoHS, length of hospital stay; χ^2, chi-square test; t-value, independent-sample t-test.

Table 2 Comparison of Clinical Data Between Infection and Non-infection Groups

Item	Infection Group (*n* = 96)	Non-infection Group (*n* = 164)	χ^2/t-value	*p*-value
Sex, *n*(%)	—	—	1.362	0.281
Male	54 (56.25)	107 (65.24)	—	—
Female	42 (43.75)	57 (34.76)	—	—
Age, *n*(%)	—	—	4.758	0.027
≤65 years	39 (40.63)	95 (57.93)	—	—
>65 years	57 (59.38)	69 (42.07)	—	—
BMI, *n*(%)	—	—	9.015	0.003
≤ 25 kg/m²	29 (30.21)	87 (53.21)	—	—
> 25 kg/m²	67 (69.79)	77 (46.79)	—	—
History of postoperative complications, *n*(%)	—	—	1.235	0.275
Yes	26 (27.08)	32 (19.51)	—	—
No	70 (72.92)	132 (80.49)	—	—
Diabetes, *n*(%)	—	—	5.215	0.022
Yes	34 (35.46)	33 (20.12)	—	—
No	62 (64.54)	131 (79.88)	—	—
Cardio-cerebrovascular disease, *n*(%)	—	—	0.014	0.915
Yes	17 (17.71)	27 (16.46)	—	—
No	79 (82.29)	137 (83.54)	—	—
Respiratory disease, *n*(%)	—	—	1.417	0.229
Yes	24 (25.00)	29 (17.68)	—	—
No	72 (75.00)	135 (82.32)	—	—
Irritant dermatitis, *n*(%)	—	—	0.455	0.487
Yes	26 (27.08)	36 (21.95)	—	—
No	70 (72.92)	128 (78.05)	—	—
Rectal cancer staging, *n*(%)	—	—	0.188	0.659
Stage 0–I	57 (59.38)	92 (56.10)	—	—
Stage II–III	39 (40.63)	72 (43.90)	—	—
Adjuvant RCTx, *n*(%)	—	—	0.148	0.686
Yes	30 (31.25)	47 (28.66)	—	—
No	66 (68.75)	117 (71.34)	—	—
DoO (min)	106.981±11.09	90.38±9.07	9.018	0.000
Number of dressing changes (n)	5.93±1.28	7.21±2.09	6.731	0.000
Postoperative LoHS (d)	14.21±3.11	12.03±3.01	4.212	0.000
Stoma care guidance, *n*(%)	—	—	8.518	0.003
Yes	18 (18.75)	66 (40.24)	—	—
No	78 (81.25)	98 (59.76)	—	—
Ostomy type, *n*(%)	—	—	5.120	0.021
End stoma	38 (39.58)	93 (56.71)	—	—
Loop stoma	58 (60.42)	71 (43.29)	—	—
Postoperative ABO, *n*(%)	—	—	0.317	0.509
Yes	14 (14.58)	18 (10.98)	—	—
No	82 (85.42)	146 (89.02)	—	—
Prophylactic use of burn ointment, *n*(%)	—	—	10.612	0.001
Yes	20 (20.83)	74 (45.12)	—	—
No	76 (79.17)	90 (54.88)	—	—
TEWL, *n*(%)	—	—	11.919	0.001
Normal	11 (11.46)	57 (34.76)	—	—
Abnormal	85 (88.54)	107 (65.24)	—	—

Abbreviations: n, number of patients; RCTx, adjuvant radiochemotherapy; DoO, duration of operation (minutes); LoHS, length of hospital stay (days); TEWL, transepidermal water loss; χ^2, chi-square test; t-value, independent-sample t-test.

https://doi.org/10.2147/IDR.S535810

Multivariate Logistic Regression Analysis of Risk Factors for Postoperative Wound Infection in Patients with Rectal Cancer Undergoing Ileostomy

Factors with statistically significant differences identified in the univariate analysis were included as independent variables in a multivariate logistic regression analysis, with postoperative wound infection as the dependent variable. As shown in Figure 1, age >65 years, diabetes, DoO >105 minutes, loop ileostomy and abnormal TEWL are independent risk factors for postoperative wound infection (all $P < 0.05$).

Development of a Nomogram Predictive Model

Based on the independent risk factors for postoperative wound infection in patients with rectal cancer undergoing ileostomy, a nomogram predictive model was constructed using R software. The nomogram scoring system demonstrated that the risk of postoperative wound infection increased with advancing age, the presence of diabetes, prolonged DoO, loop ileostomy and abnormal TEWL. The contribution of each factor to the model

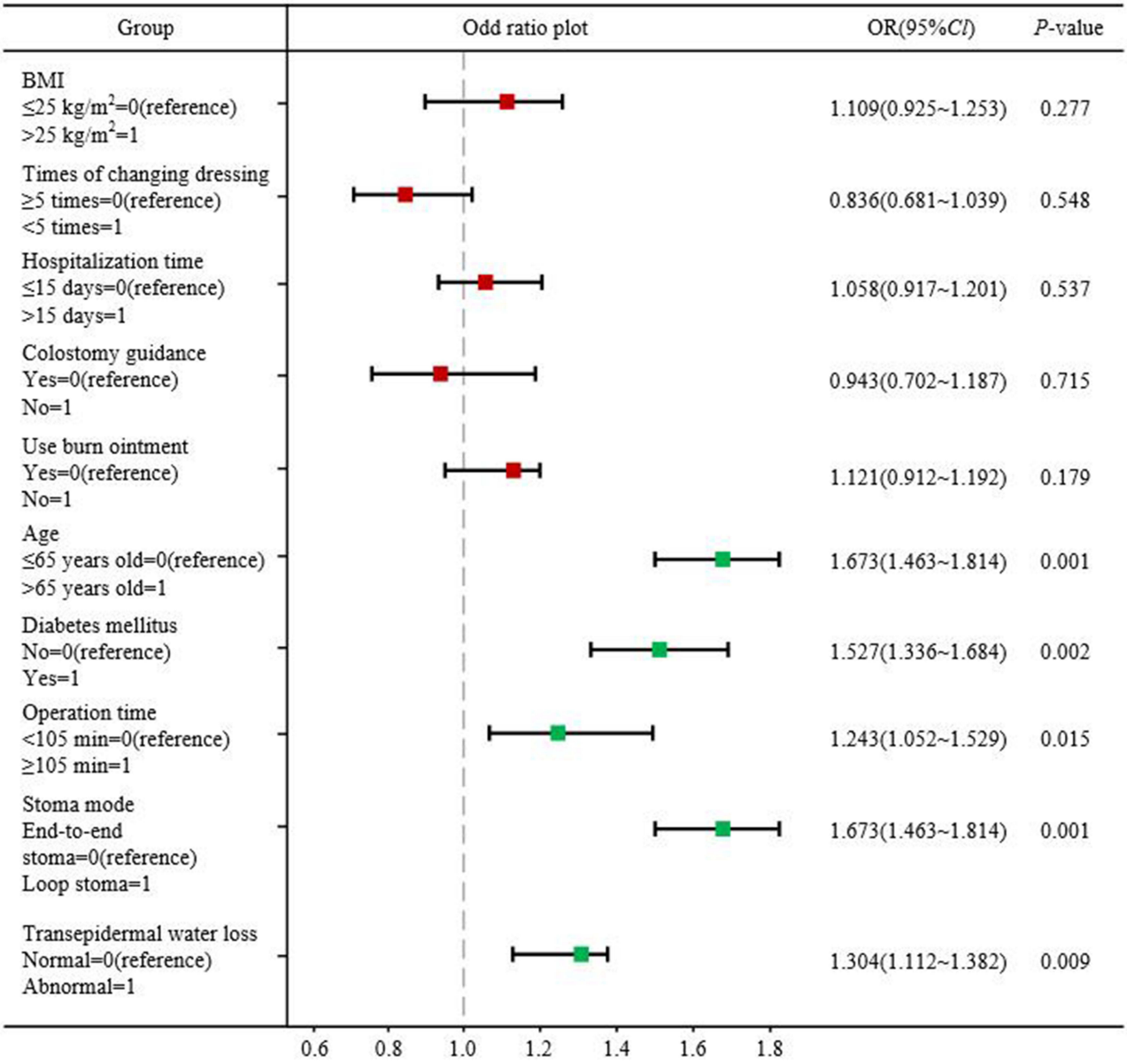

Figure 1 Forest plot of multivariate analysis for postoperative wound infection in patients with rectal cancer undergoing ileostomy.

varied, with age contributing 48.49 points, diabetes 61.87 points, DoO 33.65 points, loop ileostomy 54.44 points and abnormal TEWL 79.90 points. The total score of these five factors reached 277.99 points, corresponding to a predicted wound infection risk of 0.93 and a postoperative wound infection probability of 92.68% (see Figure 2).

Model Evaluation

Internal Validation

The ROC curve was used to assess the discriminatory ability of the nomogram model (Figure 3). The AUC was 0.871 (95% CI: 0.788–0.914, P < 0.001), with a sensitivity of 91.35% and a specificity of 88.79%. The concordance index (C-index) of the model was calculated as 0.871, indicating good discriminatory performance. The calibration curve was used to evaluate the calibration of the model (Figure 4). The predicted probabilities from the nomogram were well aligned with the observed probabilities, and the Hosmer–Lemeshow goodness-of-fit test showed no statistically significant differences (all P > 0.05), demonstrating the high accuracy of the model.

External Validation

External validation of the nomogram model was performed using data from the validation group. The ROC curve was used to assess the discriminatory ability of the nomogram (Figure 5). The AUC for the validation group was 0.872 (95% CI: 0.805–0.933, P < 0.001), with a sensitivity of 90.64% and a specificity of 89.58%. The C-index was calculated as 0.872, demonstrating good discriminatory performance. The calibration curve for the validation group showed that the predicted probabilities from the nomogram were well aligned with the observed probabilities (Figure 6). The Hosmer–Lemeshow goodness-of-fit test also showed no statistically significant differences (P > 0.05), indicating that the model retained high accuracy in external validation.

NLRP3 Gene Single-Nucleotide Polymorphism Analysis and Hardy–Weinberg Equilibrium Test

Sequencing of DNA confirmed that the gene distribution frequencies of the NLRP3 gene rs10754558 conformed to the Hardy–Weinberg equilibrium. The χ^2 values for the infection group and the non-infection group were 0.304 and 0.162, respectively, with no statistically significant differences (P > 0.05). The concordance rates of the three genotypes (ie CC, GG and CG) in the PCR products were all 100% (see Figure 7).

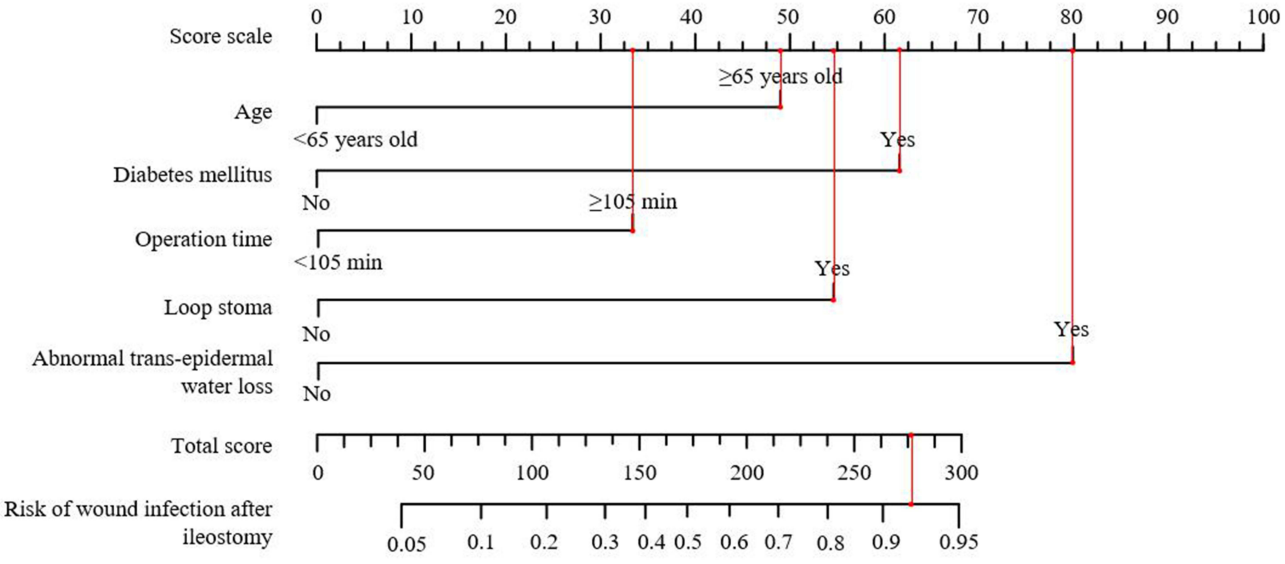

Figure 2 Nomogram risk prediction model for postoperative wound infection in patients with rectal cancer undergoing ileostomy.

https://doi.org/10.2147/IDR.S535810

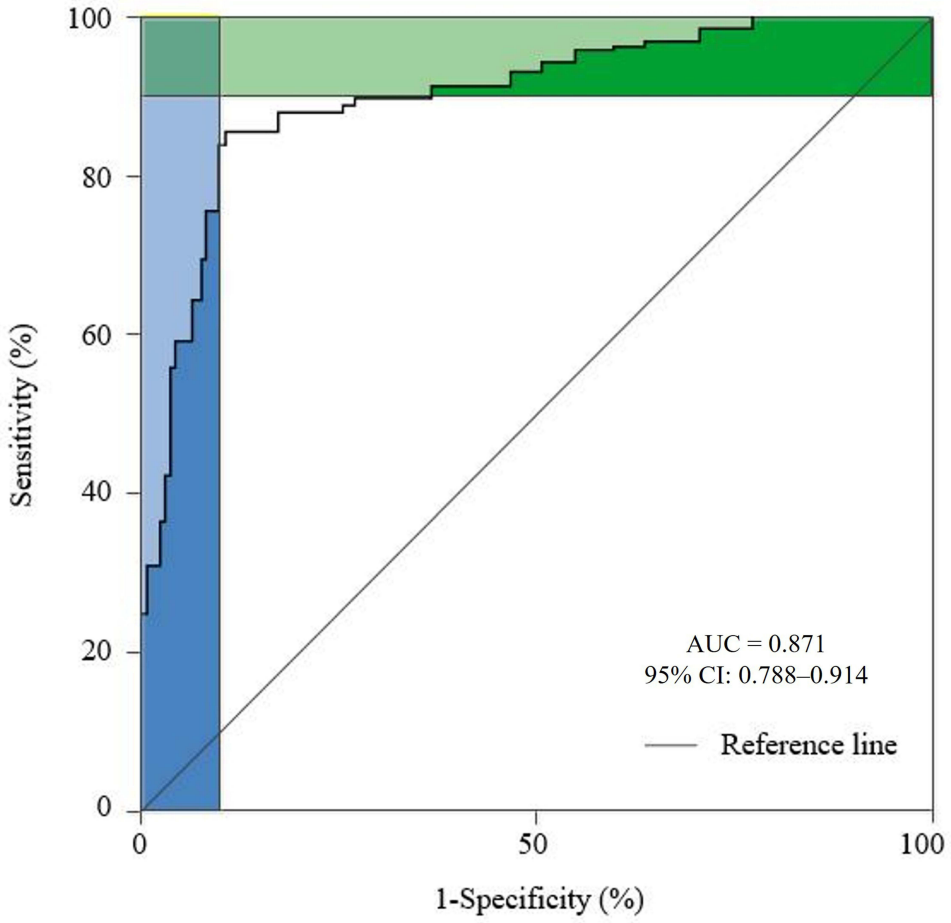

Figure 3 ROC curve of the nomogram risk prediction model in the modeling group.

Comparison of Postoperative Wound Infection Among Patients with Different NLRP3 Genotypes

Among the 260 patients who underwent ileostomy, genotype distribution and within-genotype infection rates were as follows: CC (n = 107) with 32 infections (29.90%), CG (n = 118) with 46 infections (38.98%) and GG (n = 35) with 18 infections (51.43%). The GG genotype exhibited a considerably higher infection rate than CC and CG. At the allele level, the G allele showed a greater frequency in infection cases (82/188, 43.62%) than in non-infection cases (106/188, 56.38%) (see Table 3).

Relationship Between NLRP3 Gene Polymorphism and Risk Factors in the Nomogram Model

Among the 260 patients with rectal cancer, no significant differences were observed in DoO or ostomy type among the three NLRP3 (rs10754558) genotypes (CC, GG and CG) (all $P > 0.05$). This indicates that the NLRP3 (rs10754558) gene polymorphism is not associated with the type of ileostomy or the intraoperative duration. However, NLRP3 (rs10754558) gene polymorphism was closely related to patient age, diabetes comorbidity and postoperative abnormal TEWL. Patients with the GG genotype were older, had a higher proportion of diabetes comorbidity and exhibited more frequent abnormal TEWL, with these differences all demonstrating statistical significance ($P < 0.05$, respectively) (see Table 4).

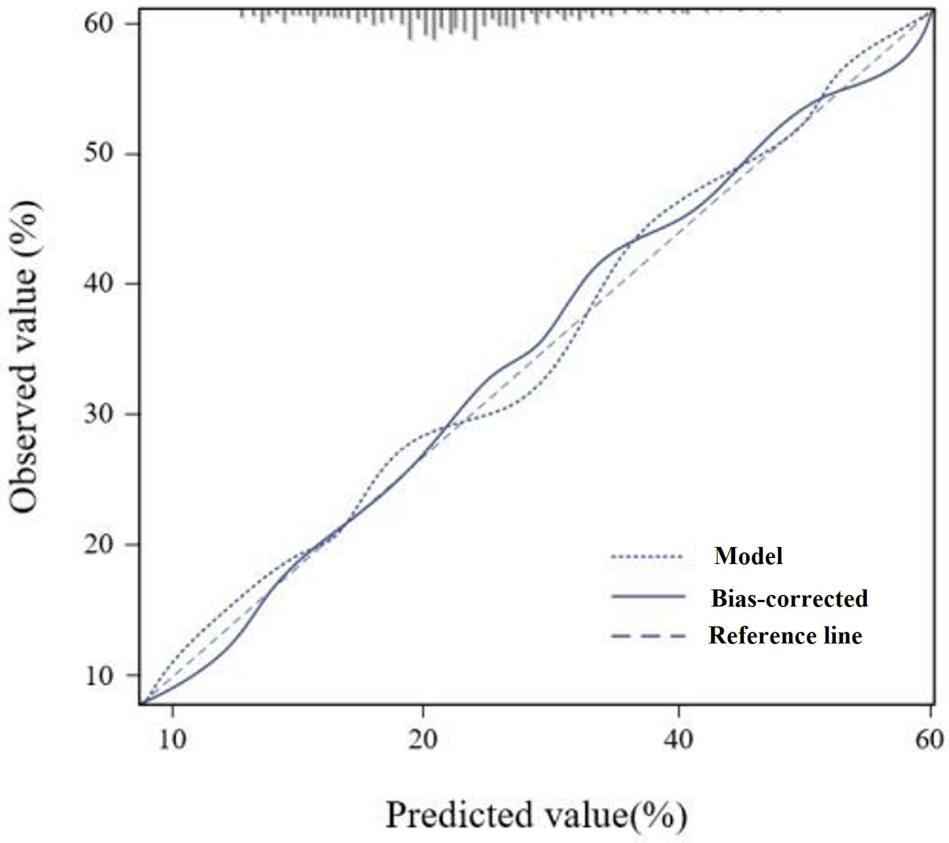

Figure 4 Calibration curve of the nomogram risk prediction model in the modeling group.

Discussion

With the influence of modern dietary habits and the increasing prevalence of obesity, the incidence of rectal cancer among urban populations remains alarmingly high, reaching over 60% in some cases. High-risk factors include rectal polyps, a family history of the disease and insufficient dietary fibre intake. Notably, over 20% of patients with rectal cancer are younger than 40 years old, reflecting a trend towards a younger onset age.[10] Due to the complex pathogenesis of rectal cancer, the primary treatment approach currently involves ileostomy. However, connecting the bowel to the abdominal wall often results in complications such as wound infection, ulceration, stoma stenosis and even necrosis. If not treated promptly, these complications can lead to sepsis, severely affecting patient prognosis and quality of life.[11] Therefore, it is imperative to identify the risk factors for wound infection following ileostomy in patients with rectal cancer, thereby reducing postoperative infection risks and improving patient outcomes.

Studies[12] have shown that although ileostomy is a common surgical procedure for rectal cancer, the risk of postoperative complications remains high, with postoperative wound infection rates ranging from 10% to 47%. In this study, the postoperative infection rate among the 260 patients with rectal cancer in the modelling group was 33.33%, consistent with findings reported in the literature. Recent studies[13] suggest that factors such as uneven skin around the stoma site and the intestinal mucosa of the stoma not being elevated above the skin surface can contribute to post-operative wound infection. Digestive enzymes and gut microbiota present in faeces can cause corrosive erosion if frequently in contact with the peristomal skin. Furthermore, prolonged exposure of the stoma site to a moist environment created by sweat, faeces and secretions promotes bacterial growth, leading to symptoms such as redness, inflammation, pain and ultimately wound infection.[14] Considering differences in age, comorbidities and surgical approaches among patients with rectal cancer, the logistic regression analysis in this study identified advanced age, diabetes, prolonged DoO, loop stoma and abnormal TEWL as independent risk factors for postoperative wound infection. Lu et al[15] also

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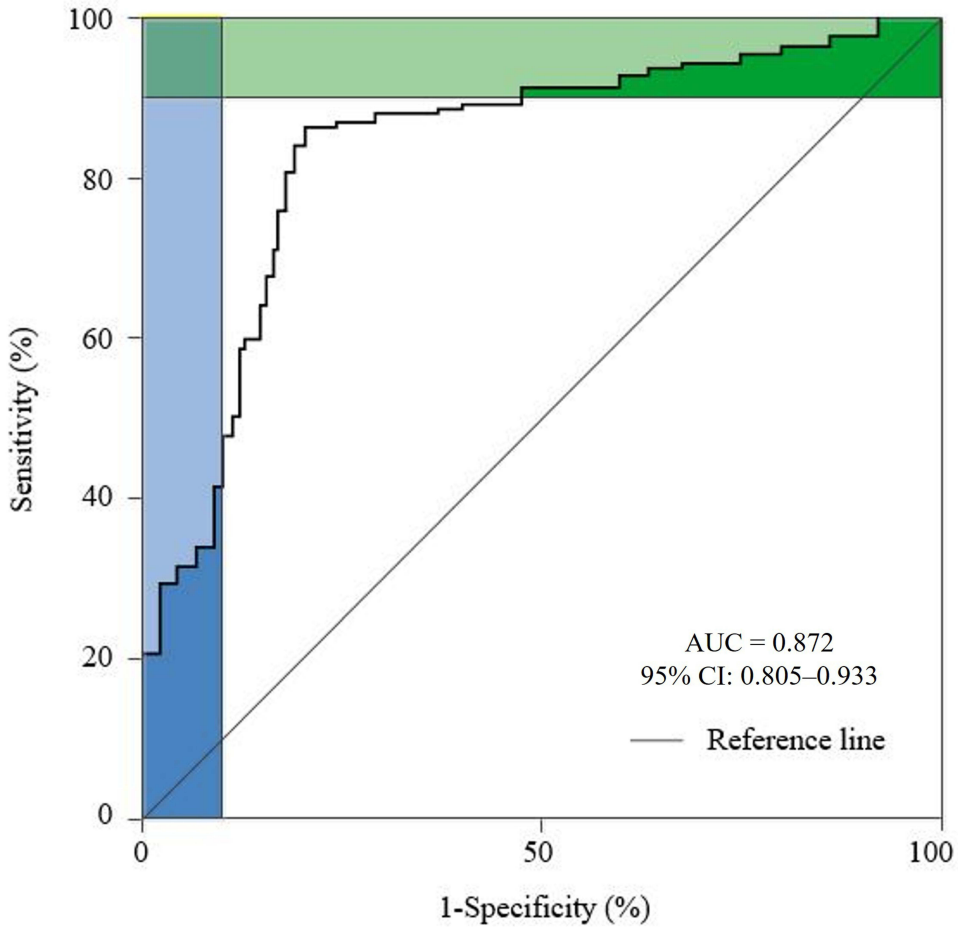

Figure 5 ROC curve of the nomogram risk prediction model in the validation group.

confirmed that variations in ileostomy duration, ostomy type and location are risk factors for peristomal skin damage. In addition, prolonged DoO increases the duration of incision exposure, thereby elevating the risk of infection at the stoma site. As patients age, vascular function naturally declines. Intraoperative trauma can induce stress-related vasoconstriction around the stoma, further impairing vascular function. This disruption in oxygen exchange and material transport weakens wound healing capacity, prolonging recovery and increasing the risk of postoperative infection.[16] In a hyperglycemic environment, bacterial proliferation is facilitated, and diabetic patients are prone to multiple complications. Impaired metabolic function, weakened immunity and reduced tissue repair capacity make postoperative wound healing more challenging, thereby increasing infection risk.[17] Abnormal TEWL reflects severe skin barrier damage. The disruption of skin moisture and oil balance, along with slower keratinocyte turnover, reduces the skin's ability to resist pathogens.[18] Compared with previous studies, this research not only reaffirmed established risk factors such as age and diabetes but also underscored the importance of prolonged DoO, ostomy type and abnormal TEWL as critical risk factors. A nomogram risk prediction model was constructed using these identified risk factors. External validation with data from the validation cohort demonstrated that this model has high predictive accuracy for assessing the risk of wound infection following ileostomy in patients with rectal cancer, indicating substantial clinical value.

This study also explored the relationship between the risk factors in the nomogram model and NLRP3 gene polymorphism. The results showed that among the study participants with the three NLRP3 (rs10754558) genotypes (CC, GG and CG), the infection rate was considerably higher for the GG genotype (51.43%) than for the CC (29.90%) and CG (39.00%) genotypes. Patients carrying the G allele were older, had a higher proportion of diabetes, exhibited more pronounced abnormal TEWL and faced a greater risk of postoperative wound infection. However, NLRP3 (rs10754558) polymorphism was not associated with ostomy type or DoO. Sano M et al[19] found that the rs10754558

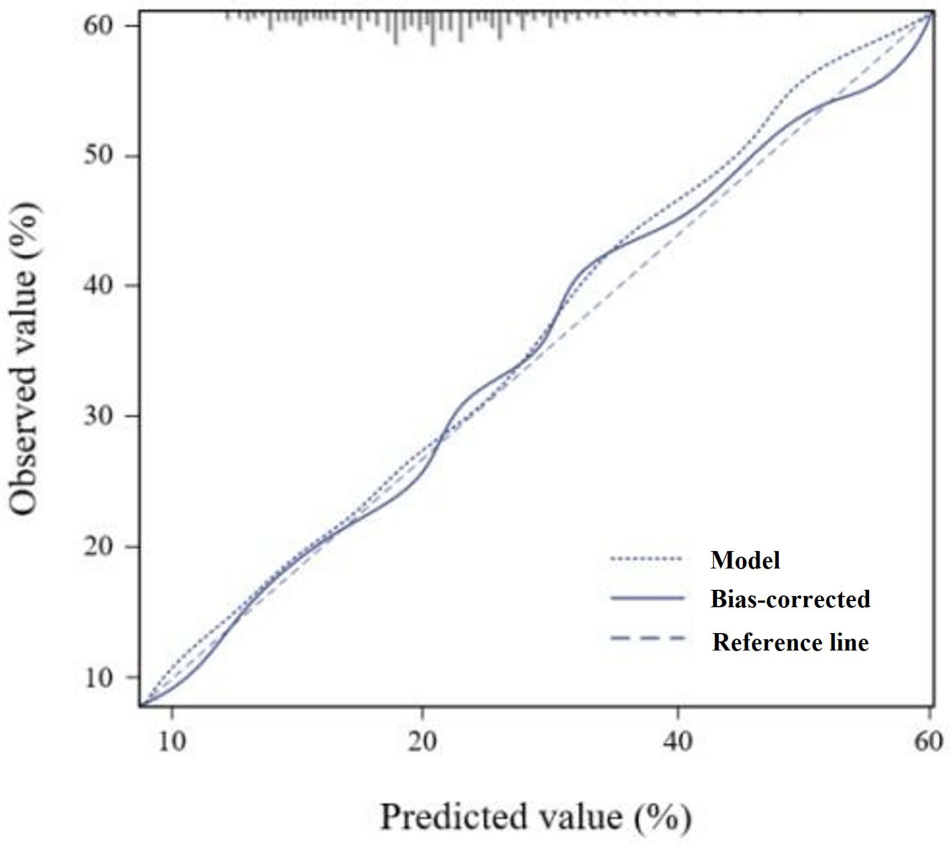

Figure 6 Calibration curve of the nomogram risk prediction model in the validation group.

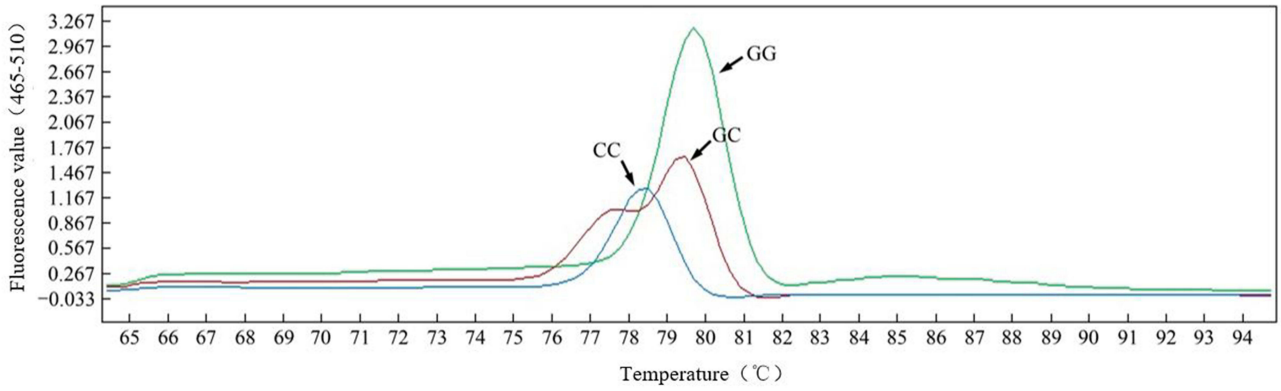

Figure 7 High-resolution melting curves of NLRP3 rs10754558 genotypes.

locus is involved in immune modulation and the inflammatory response of the NLRP3 genome by encoding the expression of inflammasome complexes. The activation and proliferation of immune cells play a crucial role in inflammatory responses. In patients with advanced age and underlying diseases, immune system dysfunction often occurs, leading to severe imbalances in lymphocyte subpopulations. This exacerbates the inflammatory response, further destabilising the genome.[20] We believe that postoperative wound infection arises from inflammation triggered by irritation at the stoma site. Upon activation, NLRP3 regulates the expression of inflammatory factors, suppresses the function of vascular endothelial cells and weakens the body's defences. In patients with rectal cancer, compromised physical function and impaired metabolic activity are typically associated with suboptimal wound healing. The

https://doi.org/10.2147/IDR.S535810

Table 3 Comparison of Gene Distribution Frequencies of the NLRP3 Gene rs10754558 Between the Infection and Non-infection Groups, n(%)

Item	NLRP3 (rs10754558) Genotype			Allele Frequency	
	CC	CG	GG	C	G
Infection Group (*n* = 96)	32 (29.90)	46 (38.98)	18 (51.43)	110 (33.13)	82 (43.62)
Non-infection Group (*n* = 164)	75 (70.10)	72 (61.02)	17 (48.57)	222 (66.87)	106 (56.38)

Notes: n, number of patients; % within each group; rs10754558, NLRP3 gene polymorphism locus.

Table 4 Relationship Between NLRP3 (rs10754558) Gene Polymorphism and Risk Factors for Postoperative Wound Infection, n(%)

Item	CC (n=107)	CG (n=118)	GG (n=35)	*P*	*OR*	95% CI
Age	—	—	—	0.026	3.019	2.561~3.438
≤65 years	65 (60.75)	63 (53.39)	6 (17.14)	—	—	—
>65 years	42 (39.25)	55 (46.61)	29 (82.86)	—	—	—
Diabetes	—	—	—	0.005	3.185	2.622~3.819
Yes	11 (10.28)	33 (27.97)	24 (68.57)	—	—	—
No	96 (89.72)	85 (72.03)	11 (31.43)	—	—	—
DoO	—	—	—	0.289	0.849	0.789~1.369
≤105 min	93 (86.92)	51 (43.22)	8 (22.86)	—	—	—
>105 min	14 (13.08)	67 (56.78)	27 (77.14)	—	—	—
Ostomy type	—	—	—	0.057	0.928	0.835~1.131
End stoma	68 (63.55)	50 (42.37)	14 (40.00)	—	—	—
Loop stoma	39 (36.45)	68 (57.63)	21 (60.00)	—	—	—
TEWL	—	—	—	0.044	2.848	2.484~3.528
Normal	35 (32.71)	29 (24.58)	5 (14.29)	—	—	—
Abnormal	72 (67.29)	89 (75.42)	30 (85.71)	—	—	—

Abbreviations: n, number of patients; OR, odds ratio; 95% CI, 95% confidence interval; rs10754558, NLRP3 polymorphism locus; P, significance level (chi-square or logistic regression).

polymorphism of the NLRP3 inflammasome exacerbates the risk of postoperative wound infection in elderly patients, those with diabetes and individuals with damaged skin barriers. Xu et al[21] confirmed that the G allele of NLRP3 (rs10754558) substantially enhances the stability of NLRP3 genome expression and alters mRNA translation efficiency. Recent work shows that limiting serine and glycine intake both starves tumour cells and reshapes the immune microenvironment. Tong et al.[22] demonstrated that a −SG diet decreases circulating serine/glycine, induces tumour release of CCL5/CXCL11 to recruit and activate $CD8^+$ T cells and, through elevated lactate, drives PD-L1 lactylation and stabilisation, which may blunt T-cell function unless combined with PD-1/PD-L1 blockade. In parallel, Gu et al.[23] Found that tumour-resident microbiota in colorectal liver metastases accelerates lactate production, promotes M2 macrophage polarisation via RIG-I K852 lactylation and suppresses NLRP3 inflammasome signalling, thereby creating an immuno-suppressive niche. Together, these studies highlight how metabolic perturbations – whether dietary or microbiota-driven – can modulate both innate and adaptive immunity, suggesting that combining metabolism-targeted strategies with immunotherapy may improve outcomes in colorectal cancer. In this study, we found a considerable association between the GG genotype of NLRP3 (rs10754558) and an increased risk of postoperative wound infection. Although the NLRP3 rs10754558 GG genotype was not an independent predictor in our clinical risk model (Figure 1), our results demonstrated that the GG genotype co-occurs substantially more often with advanced age (>65 years), diabetes and abnormal TEWL (all $P < 0.05$). Thus, its strong association with key nomogram factors suggests it may contribute indirectly to infection risk by predisposing patients to these clinical conditions. This finding provides a new perspective on the role of genetic factors in postoperative infection and may inform future strategies for individualised medicine.

This study has several limitations. First, the sample size was relatively small, and the data were derived from a single centre, increasing the risk of selection bias. Second, the applicability and validity of the findings have not been investigated in populations outside China, particularly among other ethnic groups. Third, this study lacks data analysis for other loci of the NLRP3 gene, such as rs3806265 and rs4612666. Fourth, because our study is retrospective, uniform data on serum albumin, C-reactive protein and detailed antibiotic regimens were not available for all patients, potentially leading to residual confounding. Finally, although the co-occurrence of the GG genotype with key clinical risk factors (advanced age, diabetes and abnormal TEWL) was observed, the independent predictive value of the NLRP3 genotype remains to be determined. Future multicentre prospective studies with larger sample sizes should collect comprehensive clinical and genetic data, incorporate NLRP3 genotype into multivariate analyses and validate the model in diverse populations. Further exploration is warranted in future studies with larger samples and multicentre data.

Conclusion

In conclusion, advanced age, diabetes, prolonged DoO, loop stoma and abnormal TEWL are independent risk factors for postoperative wound infection. The nomogram risk prediction model developed from these factors demonstrates high clinical value. Its strong discriminatory power and accuracy make it a valuable tool for preoperative assessment, helping physicians develop more targeted preventive measures to reduce postoperative infection rates. The polymorphism of the NLRP3 gene is closely associated with age, diabetes and TEWL. Patients carrying the G allele of NLRP3 (rs10754558) are at higher risk of postoperative infection. The polymorphism of NLRP3 provides a new perspective for prognosis assessment in patients with rectal cancer undergoing ileostomy. The association between NLRP3 polymorphism and infection risk opens possibilities for individualised medicine. In the future, treatment plans can be tailored based on the patient's genetic background to minimise infection risks.

Data Sharing Statement

All data generated or analysed during this study are included in this article. Further enquiries can be directed to the corresponding author.

Ethics Approval and Consent to Participate

This study was conducted in accordance with the Declaration of Helsinki and approved by the ethics committee of The Second Hospital of Hebei Medical University (2024-S00510). Written informed consent was obtained from all participants.

Funding

Hebei Province's 2025 Medical Science Research Project Plan (Project No. 20250410).

Disclosure

All of the authors had no any personal, financial, commercial, or academic conflicts of interest separately.

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