Research Square

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Association between inflammatory markers and the risk of severe pain after mixed hemorrhoidectomy: A retrospective cohort study

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Abstract

Background

The severe pain that may occur after hemorrhoidectomy exerts adverse effects on patients' quality of life. This study aimed to explore the association between inflammatory markers and the risk of severe pain after hemorrhoidectomy in patients with mixed hemorrhoids.

Methods

This retrospective cohort study enrolled patients who underwent hemorrhoidectomy and had complete preoperative routine blood test data. Severe pain was defined as the Visual Analog Scale (VAS) score of ≥ 7 within 24 hours after surgery. Inflammatory indicators, including neutrophil-to-lymphocyte ratio (NLR), platelet-to-lymphocyte ratio (PLR), systemic immune-inflammation index (SII), and systemic inflammation response index (SIRI), were calculated. The association between inflammatory indicators (NLR, PLR, SII, SIRI) and severe pain risk was analyzed using logistic regression analysis. The latent class analysis (LCA) was used to cluster the ordered multi-class Short-Form McGill Pain Questionnaire (SF-MPQ) items in order to evaluate different categories of severe pain.

Results

A total of 561 patients with mixed hemorrhoids were enrolled for analysis. Of these patients, 389 (69.34%) experienced severe pain, while 172 (30.66%) patients did not. SIRI ≥ 13.29 (vs. SIRI < 13.29) was associated with a higher risk of severe pain [OR = 1.80 (95%CI: 1.19–2.75)]. No significant relationships were detected between severe pain and NLR ≥ 2.47 (vs. NLR < 2.47), PLR ≥ 8.78 (vs. PLR < 8.78), or SII ≥ 633.88 (vs. SII < 633.88). Through LCA, the pain patterns of patients with severe pain were grouped into three categories: Group 1 (shooting-stabbing-cramping pain and fearful), Group 2 (heavy-sickening discomfort profile), and Group 3 (throbbing-tiring-exhausting profile). Compared with Group 3, SIRI was found to be a risk factor for the occurrence of the Group 1 pain pattern in patients [SIRI (continuous): OR = 1.05 (95%CI: 1.01–1.09); SIRI ≥ 13.29: OR = 1.81 (95%CI: 1.01–3.27)].

Conclusion

Higher SIRI levels were associated with an increased risk of severe pain in patients after mixed hemorrhoidectomy, and the influence of SIRI may vary across different pain patterns.

Introduction

Hemorrhoids are one of the most common anorectal conditions worldwide and are classified into internal, external, and mixed (concurrent internal and external) hemorrhoids based on their location

relative to the dentate line within the anal canal [1]. The global pooled prevalence of hemorrhoids is approximately 25.92% [2], with the highest prevalence observed among adults aged 45–65 years [3]. Common risk factors for hemorrhoids include aging, obesity, abdominal obesity, constipation, diarrhea, cirrhosis, depression, and pregnancy [1, 4]. Initial treatment for hemorrhoids focuses primarily on lifestyle modifications. For internal hemorrhoids in stages I-III, minimally invasive procedures such as hemorrhoid ligation and injection therapy may be used, while hemorrhoidectomy is the recommended surgical procedure for mixed hemorrhoids, particularly in severe cases at stages III-IV [1, 5]. Although hemorrhoidectomy offers significant advantages in terms of symptom relief and recurrence, it is associated with early postoperative pain, leading to a greater need for pain relief and a delayed return to work [1, 6].

Postoperative pain is a significant challenge for patients undergoing hemorrhoidectomy, with approximately 65% of them classifying the pain level as moderate to severe [7]. A follow-up analysis of data from a multicenter randomized controlled trial showed that nearly half of the patients had Numerical Rating Scale (NRS) scores of 6 or higher in the early postoperative period, and more than 25% of patients reported severe pain [8]. Surgical procedure, age, and anesthesia method are known to be important factors affecting postoperative pain [8, 9]. Several studies suggest that perioperative systemic inflammatory responses play an important role in postoperative adverse outcomes, and inflammatory markers such as neutrophil-to-lymphocyte ratio (NLR) and platelet-to-lymphocyte ratio (PLR) have been used to assess postoperative pain [10, 11]. New composite inflammatory markers like systemic inflammation response index (SIRI) and systemic immune-inflammation index (SII) have also been shown to be closely associated with postoperative outcomes in a variety of surgical conditions [12, 13]. The pathological process of hemorrhoids, such as mucosal ulcers, thrombosis formation, and changes in supportive connective tissue, may involve inflammation [14]. However, the relationship between these inflammatory markers and the risk of postoperative pain after hemorrhoidectomy remains unclear. In addition, unidimensional scales such as the Visual Analog Scale (VAS) and NRS are commonly used tools for assessing the intensity of postoperative pain. However, these unidimensional scales cannot capture the complexity of patients' pain experiences. The Simplified McGill Pain Questionnaire (SF-MPQ) is a commonly used multidimensional tool to assess postoperative pain [15]. It includes 11 items assessing pain intensity, 4 items assessing emotional aspects of pain, as well as VAS scores and Present Pain Intensity (PPI) scores, and can help elucidate the characteristics, course, and factors influencing the intensity of pain in patients. Therefore, this study aimed to explore the association between different inflammatory markers and the risk of severe pain after hemorrhoidectomy, and further analyze the influence of inflammatory markers on different pain pattern groups based on SF-MPQ.

Methods

Study design and patients

This retrospective cohort study collected data on patients with mixed hemorrhoids from the First Hospital of Liangshan between January 2025 and December 2025. All patients underwent

hemorrhoidectomy and perianal nerve block therapy. The anesthetic regimen for the procedures consisted of local infiltration anesthesia with lidocaine. This study initially enrolled patients with mixed hemorrhoids who received surgical treatment. Patients were excluded based on the following criteria: (1) patients aged < 18 years; (2) patients who did not complete a postoperative pain assessment; (3) patients with missing preoperative blood tests; (4) patients with other anorectal conditions requiring treatment; and (5) patients undergoing other colorectal surgeries. This research was approved by the Ethics Committee of the First People's Hospital of Liangshan Yi Autonomous Prefecture (No. 2026.18). All the patients signed the informed consent form prior to surgery.

Outcome

Outcome

The occurrence of severe postoperative pain was set as the outcome variable in this study. Early severe pain was defined as the VAS score of ≥ 7 within 24 hours after surgery [16]. For patients experiencing severe pain, the SF-MPQ assessment should be completed further, and 5 mg of dezocine should be administered by intramuscular injection. The SF-MPQ contains 15 items to evaluate the sensory (11 items: throbbing, shooting, stabbing, sharp, cramping, gnawing, hot-burning, aching, heavy, tender, splitting) and affective (4 items: tiring-exhausting, sickening, fearful, punishing-cruel) dimensions of pain [15]. It also incorporates the VAS score and the PPI score. Among the 15 items of the SF-MPQ, each item has 4 options (0 = no pain, 1 = mild, 2 = moderate, and 3 = severe). The VAS score ranges from 0 (no pain) to 10 (worst possible pain), whereas the PPI score is graded from 0 (no pain) to 5 (unbearable pain).

Exposure

In this study, inflammatory indicators served as exposure factors, including NLR, PLR, SII, and SIRI. The calculation formulas for these indicators are as follows: (1) NLR = neutrophil counts / lymphocyte counts; (2) PLR = platelet counts / lymphocyte counts; (3) SII = platelet counts × neutrophil counts / lymphocyte counts; and (4) SIRI = neutrophil counts × monocyte count / lymphocyte counts. The preoperative blood routine test data of the patient were used to calculate these inflammatory indicators. The maximally selected rank statistics [17] were used to determine the optimal cut-off value for classifying these inflammatory indicators: NLR (< 2.47, ≥ 2.47), PLR (< 8.78, ≥ 8.78), SII (< 633.88, ≥ 633.88), and SIRI (< 13.29, ≥ 13.29).

Data collection

Relevant patient data were collected, including age, sex (male, female), ethnic group (The Han people, The Yi people, others), smoking (no, yes), drinking (no, yes), hypertension (no, yes), diabetes (no, yes), heart disease (no, yes), anemia (no, yes), Goligher classification (stage III, stage IV), types of external hemorrhoids (varicose, inflammatory), internal hemorrhoid sclerotherapy injection (no, yes), anal sphincterotomy (no, yes), internal hemorrhoid ligation procedure (no, yes), management of anal papillae

for anal fissures (no, yes), white blood cell (WBC), red blood cell (RBC), hematocrit, mean corpuscular volume (MCV), red cell distribution width-coefficient of variation (RDW-CV), international normalized ratio (INR), fibrinogen, creatinine, total bilirubin, potassium, sodium, chloride, glucose, NLR, PLR, SII, and SIRI.

Statistical analysis

Skewness and kurtosis were employed to assess the normality of continuous data, and Levene's test was adopted for variance homogeneity. Continuous data were expressed as mean ± SD (standard deviation) or median and quartile [M (Q1, Q3)], while categorical data were reported as numbers and percentages [n (%)]. Continuous data were assessed with t-test, t'-test, F-test, Welch's Anova test, Wilcoxon's rank test, or Kruskal-Wallis H test, and categorical data with the chi-square test or Fisher's exact test. For missing values in covariates, those with a missing rate of < 20% were imputed using multiple imputation methods, while those with a missing rate of more than 20% were excluded. The differences before and after imputing missing variables were compared (Supplementary Table 1).

A univariate logistic regression analysis was used to screen for confounders related to severe pain (Supplementary Table 2). Variables with $P < 0.05$ in the univariate analysis were included in the multivariate logistic regression analysis for adjustment. The association between inflammatory indicators (NLR, PLR, SII, SIRI) and severe pain risk was evaluated using logistic regression analysis, and results were shown as odds ratio (OR) and 95% confidence interval (CI). The multivariate logistic regression analysis was adjusted for age, ethnic group, anemia, anal sphincterotomy, internal hemorrhoid ligation procedure, RBC, hematocrit, RDW-CV, INR, and potassium. The variance inflation factor (VIF) was employed to test for multicollinearity among these adjusted variables (Supplementary Table 3). This association was further analyzed in subgroups of age, sex, ethnic group, anemia, Goligher classification, types of external hemorrhoids, and anal sphincterotomy. In addition, among patients with severe postoperative pain, the latent class analysis (LCA) was used to cluster the ordered multi-class SF-MPQ items in order to evaluate different categories of severe pain. The LCA classified pain categories in patients with severe pain based on 15 items from the SF-MPQ and PPI scores. The optimal number of pain categories was determined using the Akaike Information Criterion (AIC), the Bayesian Information Criterion, the Lo-Mendell-Rubin adjusted likelihood ratio test (LMR), classification accuracy (entropy values), and category proportions. The relationship between inflammatory indicators and different pain categories was examined. All analyses were performed using R 4.5.1 software, with significance set at $P < 0.05$.

Results

Characteristics of patients

A total of 593 patients who received mixed hemorrhoidectomy and perianal nerve block therapy were enrolled. Following the exclusion of 32 eligible patients, the final analytical sample comprised 561 patients (Fig. 1). Of the 561 patients, 389 (69.34%) experienced severe postoperative pain, while 172

(30.66%) did not. Table 1 lists the characteristics of these patients. The mean age was 41.83 (± 13.43) years, and 288 (51.34%) patients were male. According to the Goligher classification, 323 (57.58%) patients were at stage III, and 238 (42.42%) at stage IV. The mean values were 2.57 (± 1.39) for NLR, 9.38 (± 4.44) for PLR, 620.21 (± 374.37) for SII, and 13.98 (± 7.97) for SIRI. Among patients with and without severe pain, significant differences were observed in age, ethnic group, anemia, anal sphincterotomy, internal hemorrhoid ligation procedure, RBC, hematocrit, MCV, RDW-CV, INR, fibrinogen, total bilirubin, potassium, PLR, and SIRI.

Association between inflammatory indicators (NLR, PLR, SII, SIRI) and severe pain risk

Table 2 presents the associations of NLR, PLR, SII, and SIRI with severe pain risk among patients with mixed hemorrhoids. No significant association was found between the continuous variables of NLR, PLR, SII, and SIRI and the risk of severe pain ($P > 0.05$). Categorical analysis showed that SIRI ≥ 13.29 (vs. SIRI < 13.29) was associated with a higher risk of severe pain in both univariate [OR = 1.68 (95%CI: 1.16–2.46)] and multivariate [OR = 1.80 (95%CI: 1.19–2.75)] analyses. However, no significant associations were detected between severe pain and NLR ≥ 2.47 (vs. NLR < 2.47, $P = 0.285$), PLR ≥ 8.78 (vs. PLR < 8.78, $P = 0.902$), or SII ≥ 633.88 (vs. SII < 633.88, $P = 0.531$).

The relationship between SIRI and severe pain risk was examined in different subgroups (Fig. 2). SIRI ≥ 13.29 was linked to a higher risk of severe pain in subgroups of age ≥ 40 years [OR = 2.36 (95%CI: 1.34–4.14)], male [OR = 2.12 (95%CI: 1.13–3.98)], The Han people [OR = 1.82 (95%CI: 1.05–3.16)], non-anemia [OR = 1.88 (95%CI: 1.20–2.92)], stage III of Goligher classification [OR = 1.88 (95%CI: 1.07–3.30)], inflammatory external hemorrhoids [OR = 2.22 (95%CI: 1.16–4.26)], non-anal sphincterotomy [OR = 5.48 (95%CI: 1.07–28.04)], and anal sphincterotomy [OR = 1.66 (95%CI: 1.07–2.58)].

Grouping of severe pain patterns based on SF-MPQ items using LCA

The LCA results based on the 15 items of the SF-MPQ and PPI scores indicated that the model parameters for classifying patients with severe pain into 2 to 7 clusters are shown in Supplementary Table 4. Comprehensive evaluation of all LCA indicators demonstrated that the three-class model for stratifying patients with severe pain achieved the optimal fit. Referring to the SF-MPQ item labels, the three clusters were named as: Group 1 (Shooting-stabbing-cramping pain and fearful), Group 2 (Heavy-sickening discomfort profile), and Group 3 (Throbbing-tiring-exhausting profile) (Fig. 3). Patient characteristics based on the distribution of these three groups of severe pain are presented in Supplementary Table 5.

Table 3 presents the correlations between SIRI and different severe pain patterns. When Group 3 (Throbbing-tiring-exhausting profile) was used as the reference group, SIRI was found to be a risk factor

for the occurrence of the Group 1 (Shooting-stabbing-cramping pain and fearful) pain pattern in patients [SIRI (continuous): OR = 1.05 (95%CI: 1.01–1.09); SIRI ≥ 13.29: OR = 1.81 (95%CI: 1.01–3.27)]. However, no association was found between SIRI and the risk of the Group 2 (Heavy-sickening discomfort profile) pain pattern [SIRI (continuous): P = 0.083; SIRI ≥ 13.29: P = 0.157].

Discussion

The current study investigated the association between different inflammatory indicators and severe pain risk in patients with mixed hemorrhoidectomy. High SIRI levels were associated with a higher risk of severe pain, but no significant associations were observed between NLR, PLR, SII, and the risk of severe pain. The severe pain patterns were clustered into three groups using LCA [Group 1 (shooting-stabbing-cramping pain and fearful), Group 2 (heavy-sickening discomfort profile), Group 3 (throbbing-tiring-exhausting profile)]. Compared with Group 3, high SIRI levels were related to the occurrence of the Group 1 pain pattern.

Hemorrhoids are the most prevalent anorectal disorder, affecting approximately one in four individuals worldwide. Hemorrhoids are focal vascular dilations arising from displaced or pathologically enlarged anal cushions [18, 19]. Degradation of anal supportive connective tissue and abnormal blood flow in anal cushions cause prolapse of anal cushions, as well as dilation and deformation of the hemorrhoidal plexus [19]. Surgical excision is an effective treatment for hemorrhoids, but the pain experienced in the early postoperative period affects the quality of life of the patients [20, 21]. Inflammation may be involved in the pathological processes of hemorrhoids, such as mucosal ulcers, ischemia, thrombosis, vasodilation, deformation of the smooth muscle layer, and deformation of the supporting tissues [14]. In the perianal region, tissue damage induces an inflammatory response marked by the infiltration of T lymphocytes, macrophages, neutrophils, monocytes, mast cells, and dendritic cells [22]. The current study analyzed the relationship between inflammatory indicators and severe pain risk. The findings revealed that high SIRI levels were related to a higher risk of severe pain. However, no significant relationships were found between NLR, PLR, SII, and the risk of severe pain. The mixed hemorrhoidectomy involves extensive damage to the anal canal mucosa and subcutaneous tissue. These areas contain a large number of sensory nerve endings and have limited tissue space, which makes them prone to inflammation and congestion. Previous studies have reported an association between the inflammatory markers (NLR and PLR) and the risk of postoperative pain following non-cardiac surgery [10, 11]. A retrospective study investigated the predictive values of NLR, PLR, and SII on thrombotic hemorrhoids, but no significant association was found between these indicators and thrombotic hemorrhoids [23]. Our study elucidates the association between inflammatory markers and the risk of severe postoperative pain in patients with hemorrhoids.

Relative to other inflammatory markers, SIRI combines neutrophils, monocytes, and lymphocytes to comprehensively reflect postoperative innate immune activation, inflammatory overreaction, and immune imbalance, which makes it more sensitive to correlate with severe pain. For the types of severe postoperative pain, we further used LCA to categorize the pain types. The results revealed that elevated

SIRI levels were independently associated with the occurrence of the Group 1 (shooting-stabbing-cramping pain and fearful) pain pattern relative to Group 3 (throbbing-tiring-exhausting profile). Shooting and stabbing pain may be associated with postoperative local tissue damage, the release of inflammatory mediators, and the sensitization of peripheral nerve endings [24, 25]. Elevated SIRI levels indicate a stronger systemic inflammatory response, and local inflammation, edema, and tissue sensitivity may also be more pronounced. In this state, patients are more likely to experience spasm-like or paroxysmal pain. Furthermore, inflammation not only affects peripheral pain perception but may also influence central sensitization and negative emotional responses through neuro-immune pathways [26, 27]. The more sudden, sharp, and unpredictable the pain is, the more likely patients are to experience fear, anxiety, and pain anticipation, thereby further amplifying the pain experience [28, 29]. These may be explanations for the association between elevated SIRI levels and pain patterns in Group 1.

This study supplements evidence regarding the associations between various inflammatory markers and the risk of severe postoperative pain in patients undergoing hemorrhoidectomy. Furthermore, we investigated the multidimensional pain patterns of severe pain following mixed hemorrhoidectomy, which reveals the heterogeneity of pain after mixed hemorrhoidectomy. Nevertheless, several limitations should be acknowledged. First, severe pain was defined as a VAS score ≥ 7. Subjective VAS scores vary widely across individuals and are influenced by psychological status, which may compromise the accuracy of pain assessment. Second, despite the SF-MPQ containing multidimensional items that capture abundant pain-related information, subjective bias cannot be fully excluded from measurements. Third, this study was a single-center retrospective analysis. The association between SIRI and severe pain risk after mixed hemorrhoidectomy requires further validation using external datasets.

Conclusions

Among various inflammatory biomarkers, elevated SIRI levels were associated with an increased risk of severe pain in patients after mixed hemorrhoidectomy. No significant relationships were found between NLR, PLR, SII, and the risk of severe postoperative pain. Further multicenter prospective studies are required to deeply explore the association between SIRI and the risk of severe postoperative pain, as well as to evaluate the prognostic predictive value of SIRI in patients with mixed hemorrhoids.

Declarations

Ethics approval and consent to participate

This research was approved by the Ethics Committee of This research was approved by the Ethics Committee of the First People's Hospital of Liangshan Yi Autonomous Prefecture (No. 2026.18). All the patients signed the informed consent form prior to surgery. This study was conducted in accordance with the Declaration of Helsinki.

Data Availability Statement

The data used in this study are available from the corresponding author upon reasonable request.

Competing interests

No potential conflicts of interest are declared.

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Consent for publication

Not applicable.

Clinical trial number

Not applicable.

Authors' contributions

Yuhang Tai: Conceptualization; Writing-original draft; Methodology; Formal analysis; Writing-review & editing. Yuelong Wang: Investigation; Data curation; Methodology; Formal analysis. Tao Wu: Conceptualization; Methodology; Writing-review & editing.

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Figures

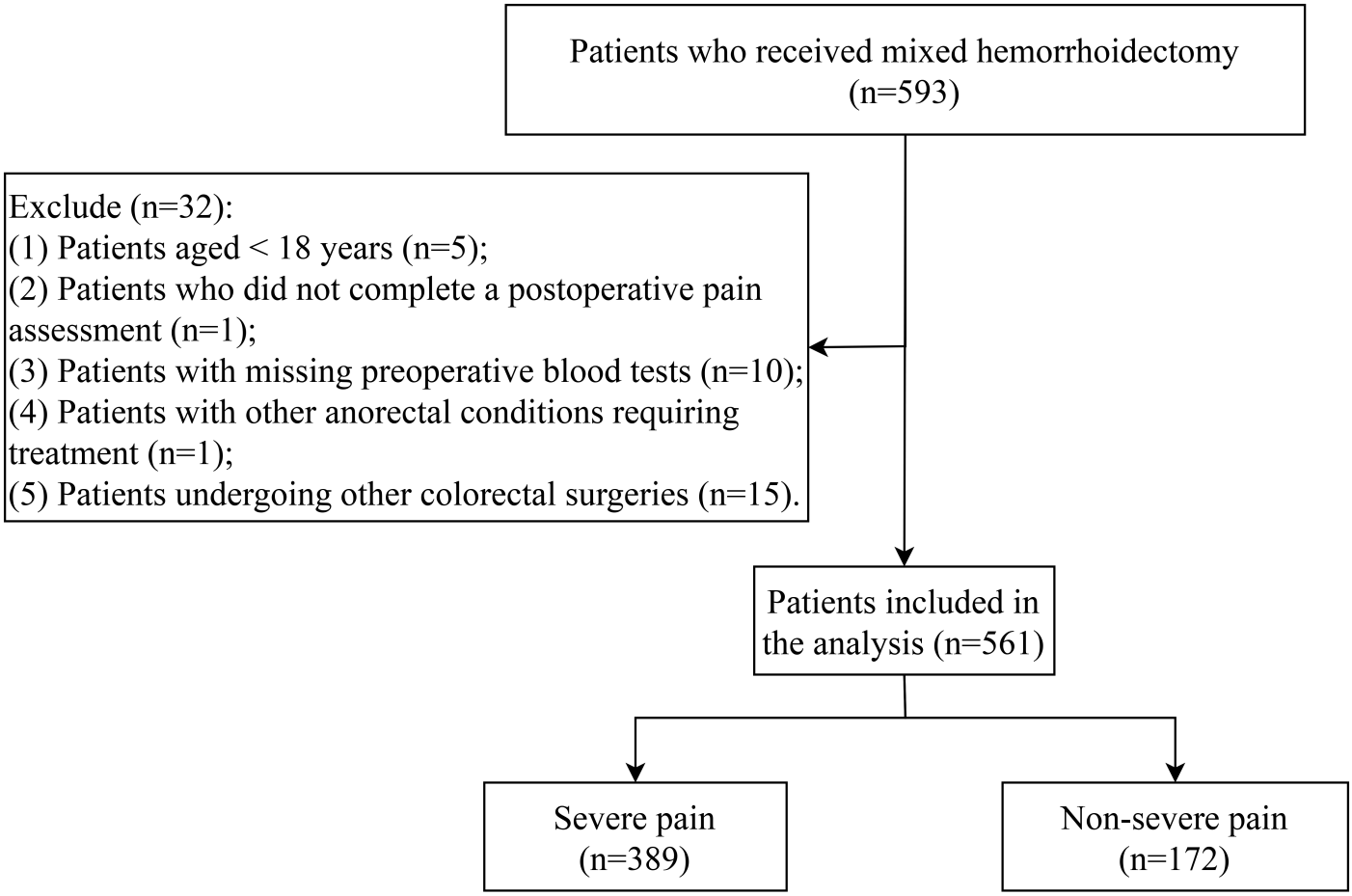


Figure 1

Flowchart of the screening process for the study population.

Subgroups	Outcome/Total	N(%)	OR (95% CI)	*P*	*P* for interaction
Age<40	**213/269**				0.116
SIRI					
<13.29	126/162	162 (60.22)	Ref		
≥13.29	87/107	107 (39.78)	1.22 (0.64−2.33)	0.548	
Age≥40	**176/292**				
SIRI					
<13.29	86/165	165 (56.51)	Ref		
≥13.29	90/127	127 (43.49)	2.36 (1.34−4.14)	0.003	
Sex=Male	**206/288**				0.756
SIRI					
<13.29	102/153	153 (53.12)	Ref		
≥13.29	104/135	135 (46.88)	2.12 (1.13−3.98)	0.020	
Sex=Female	**183/273**				
SIRI					
<13.29	110/174	174 (63.74)	Ref		
≥13.29	73/99	99 (36.26)	1.59 (0.88−2.85)	0.125	
Ethnic group=The Han people	**179/291**				0.779
SIRI					
<13.29	103/178	178 (61.17)	Ref		
≥13.29	76/113	113 (38.83)	1.82 (1.05−3.16)	0.033	
Ethnic group=The Yi people	**204/262**				
SIRI					
<13.29	104/142	142 (54.20)	Ref		
≥13.29	100/120	120 (45.80)	1.92 (0.98−3.79)	0.059	
Anemia=No	**328/486**				0.660
SIRI					
<13.29	191/299	299 (61.52)	Ref		
≥13.29	137/187	187 (38.48)	1.88 (1.20−2.92)	0.005	
Anemia=Yes	**61/75**				
SIRI					
<13.29	21/28	28 (37.33)	Ref		
≥13.29	40/47	47 (62.67)	2.97 (0.40−21.79)	0.285	
Goligher classification=Stage III	**217/323**				0.763
SIRI					
<13.29	116/189	189 (58.51)	Ref		
≥13.29	101/134	134 (41.49)	1.88 (1.07−3.30)	0.029	
Goligher classification=Stage IV	**172/238**				
SIRI					
<13.29	96/138	138 (57.98)	Ref		
≥13.29	76/100	100 (42.02)	1.53 (0.80−2.93)	0.195	
Types of external hemorrhoids=Varicose	**228/314**				0.436
SIRI					
<13.29	119/173	173 (55.10)	Ref		
≥13.29	109/141	141 (44.90)	1.56 (0.88−2.77)	0.126	
Types of external hemorrhoids=Inflammatory	**161/247**				
SIRI					
<13.29	93/154	154 (62.35)	Ref		
≥13.29	68/93	93 (37.65)	2.22 (1.16−4.26)	0.016	
Anal sphincterotomy=No	**29/54**				0.164
SIRI					
<13.29	14/31	31 (57.41)	Ref		
≥13.29	15/23	23 (42.59)	5.48 (1.07−28.04)	0.041	
Anal sphincterotomy=Yes	**360/507**				
SIRI					
<13.29	198/296	296 (58.38)	Ref		
≥13.29	162/211	211 (41.62)	1.66 (1.07−2.58)	0.024	

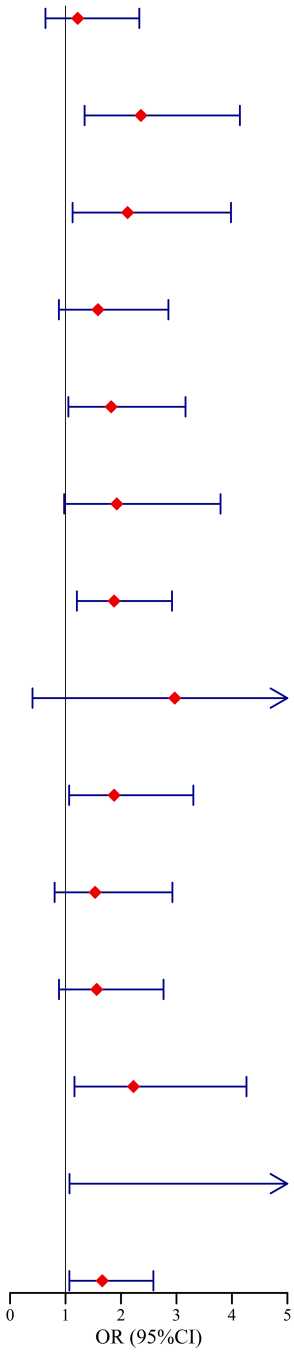


Figure 2

Subgroup analysis of the relationship between SIRI and severe pain risk. SIRI, systemic inflammation response index.

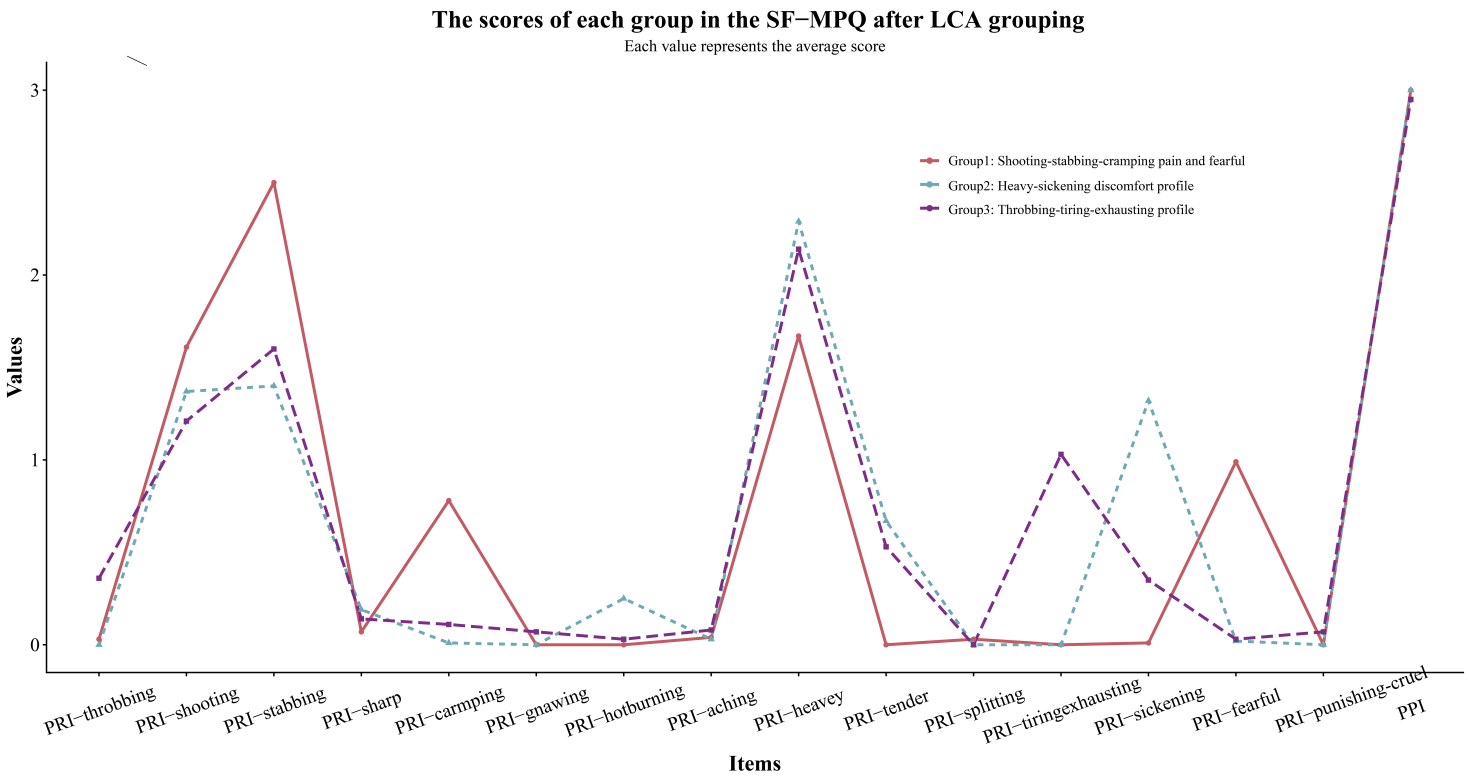


Figure 3

Clustering of severe pain patterns based on SF-MPQ items. SF-MPQ, the Simplified McGill Pain Questionnaire; LCA, the latent class analysis; PRI, pain rating index; PPI, present pain intensity.

Supplementary Files

This is a list of supplementary files associated with this preprint. Click to download.

- Supplementarymaterials.docx